D 2013

U.PORTO
FMUP FACULDADE DE MEDICINA
UNIVERSIDADE DO PORTO

# DIALYSIS ACCESS FOR CHRONIC RENAL REPLACEMENT THERAPY: CLINICAL AND ECONOMIC IMPLICATIONS

**LUÍS COENTRÃO**

TESE DE DOUTORAMENTO APRESENTADA
À FACULDADE DE MEDICINA DA UNIVERSIDADE DO PORTO EM
MEDICINA

U.PORTO
FMUP FACULDADE DE MEDICINA
UNIVERSIDADE DO PORTO

# DIALYSIS ACCESS FOR CHRONIC RENAL REPLACEMENT THERAPY: CLINICAL AND ECONOMIC IMPLICATIONS

**LUÍS COENTRÃO**

2013 | PORTO

**Dissertação de candidatura ao grau de Doutor em Medicina apresentada à Faculdade de Medicina da Universidade do Porto**

Artigo 48, § 3: "A Faculdade não responde pelas doutrinas expendidas na dissertação".

(Regulamento da Faculdade de Medicina da Universidade do Porto, Decreto-Lei nº19337 de 29 de Janeiro de 1931)

**Investigação realizada na Unidade de Investigação e Desenvolvimento de Nefrologia da Faculdade de Medicina da Universidade do Porto** (FCT-725)

**Orientador:** Professor Doutor João Miguel Frazão

**Co-Orientador:** Professor Doutor Manuel Pestana de Vasconcelos

# Corpo Catedrático da Faculdade de Medicina da Universidade do Porto

## Professores Catedráticos Efectivos

- Manuel Alberto Coimbra Sobrinho Simões
- Jorge Manuel Mergulhão Castro Tavares
- Maria Amélia Duarte Ferreira
- José Agostinho Marques Lopes
- Patrício Manuel Vieira Araújo Soares Silva
- Daniel Filipe Lima Moura
- Alberto Manuel Barros da Silva
- José Manuel Lopes Teixeira Amarante
- José Henrique Dias Pinto de Barros
- Maria Fátima Machado Henriques Carneiro
- Isabel Maria Amorim Pereira Ramos
- Deolinda Maria Valente Alves Lima Teixeira
- Maria Dulce Cordeiro Madeira
- Altamiro Manuel Rodrigues Costa Pereira
- Rui Manuel Almeida Mota Cardoso
- António Carlos Freitas Ribeiro Saraiva
- José Carlos Neves da Cunha Areias
- Manuel Jesus Falcão Pestana de Vasconcelos
- João Francisco Montenegro Andrade Lima Bernardes
- Maria Leonor Martins Soares David
- Rui Manuel Lopes Nunes
- José Eduardo Torres Eckenroth Guimarães
- Francisco Fernando Rocha Gonçalves
- José Manuel Pereira Dias de Castro Lopes
- Manuel António Caldeira Pais Clemente
- António Albino Coelho Marques Abrantes Teixeira
- Joaquim Adelino Correia Ferreira Leite Moreira

## Professores Catedráticos Jubilados e Aposentados

- Abel José Sampaio da Costa Tavares
- Abel Vitorino Trigo Cabral
- Alexandre Alberto Guerra Sousa Pinto
- Amândio Gomes Sampaio Tavares
- António Augusto Lopes Vaz
- António Carvalho Almeida Coimbra
- António Fernandes da Fonseca
- António Fernandes Oliveira Barbosa Ribeiro Braga
- António Germano Pina Silva Leal
- António José Pacheco Palha
- António Luís Tomé da Rocha Ribeiro
- António Manuel Sampaio de Araújo Teixeira
- Belmiro dos Santos Patrício
- Cândido Alves Hipólito Reis
- Carlos Rodrigo Magalhães Ramalhão
- Cassiano Pena Abreu e Lima
- Daniel Santos Pinto Serrão
- Eduardo Jorge Cunha Rodrigues Pereira
- Fernando de Carvalho Cerqueira Magro Ferreira
- Fernando Tavarela Veloso
- Francisco de Sousa Lé
- Henrique José Ferreira Gonçalves Lecour de Menezes
- José Augusto Fleming Torrinha
- José Carvalho de Oliveira
- José Fernando Barros Castro Correia
- José Luís Medina Vieira
- José Manuel Costa Mesquita Guimarães
- Levi Eugénio Ribeiro Guerra
- Luís Alberto Martins Gomes de Almeida
- Manuel Augusto Cardoso de Oliveira
- Manuel Machado Rodrigues Gomes
- Manuel Maria Paula Barbosa

- Maria da Conceição Fernandes Marques Magalhães
- Maria Isabel Amorim de Azevedo
- Mário José Cerqueira Gomes Braga
- Serafim Correia Pinto Guimarães
- Valdemar Miguel Botelho dos Santos Cardoso
- Walter Friedrich Alfred Osswald
- Álvaro Jerónimo Leal Machado Aguiar

# Júri

Júri da prova de Doutoramento em Medicina do licenciado Luís Alexandre de Castilho Silva Coentrão, nomeado por despacho vice-reitoral de 5 de março de 2013 com a tese "Dialysis Access for Chronic Renal Replacement Therapy: Clinical and Economic Implications":

## Presidente:

Reitor da Universidade do Porto.

## Vogais:

Doutor Rui Manuel Baptista Alves, professor associado da Faculdade de Medicina da Universidade de Coimbra;

Doutor Edgar Avito Fernandes de Almeida, professor auxiliar convidado da Faculdade de Medicina da Universidade de Lisboa;

Doutor João Miguel Machado Dória Frazão, professor associado da Faculdade de Medicina da Universidade do Porto, orientador da tese;

Doutor João Paulo Ferreira da Silva Oliveira, professor associado convidado da Faculdade de Medicina da Universidade do Porto;

Doutor Daniel Filipe da Lima Moura, professor catedrático da Faculdade de Medicina da Universidade do Porto;

Doutor José Artur Osório de Carvalho Paiva, professor associado convidado da Faculdade de Medicina da Universidade do Porto.

*A memória guarda o passado,*

*O sonho constrói o futuro,*

*… e o agora já passou …*

*Mas a procura dura toda uma vida! …*

MJS

À minha mulher, Inês

Aos meus filhos

# AGRADECIMENTOS

A elaboração desta tese não teria sido possível sem a ajuda e dedicação de muitos que me acompanharam ao longo deste percurso. A todos, a minha sincera gratidão.

Agradeço aos meus orientadores a generosidade, o estímulo e o apoio incondicional.

Ao Professor Doutor João Miguel Frazão, agradeço a confiança, a disponibilidade permanente, a mestria na revisão sistemática e compilação da tese e, sobretudo, a amizade.

Ao Professor Doutor Manuel Pestana, agradeço a coragem, o empenho e a perseverança necessários para a realização desta tese, a partilha de ideais e a presença constante nas vitórias e dissabores alcançados ao longo deste percurso.

Gostaria de agradecer à Dra. Susana Sampaio a amizade sincera, o carinho, o exemplo e profissionalismo inabaláveis.

Gostaria de agradecer ao Professor Doutor Daniel Moura o estímulo, a confiança que sempre depositou no meu trabalho e a amizade de longa data.

Agradeço a todos os colegas e amigos que participaram e colaboraram na elaboração dos trabalhos. Ao Ricardo, pela colheita de dados e pelo companheirismo. À Carla, pela interpretação e análise crítica dos resultados obtidos, pela sua determinação, dedicação e profissionalismo. Ao Bernardo, pelo amigo que é, pelo seu entusiasmo e audácia. Ao Carlos, pelas longas horas passadas no "menos dois" e por todo o apoio na análise económica. À Camila, pela disponibilidade e profissionalismo na elaboração da análise estatística.

Aos enfermeiros que me apoiaram ao longo deste percurso, o meu sincero obrigado. Não posso deixar de manifestar a minha gratidão ao Enf.º Sousa, à Enf.ª Olga e à Enf.ª Silvia, à equipa de enfermagem do sector de diálise peritoneal (Maria João, Dora, Nádia e Elisabete), ao Fausto, Paulo e Aires com quem aprendi a puncionar os primeiros acessos e com os quais partilhei muitos e bons momentos.

À Iva, Isabel e Conceição, administrativas exemplares, agradeço a amizade, o apoio na organização do sector de acessos vasculares e no fornecimento de dados fundamentais para a elaboração desta tese.

Por fim, à Inês, aos pais e sogros, às irmãs e cunhados, a quem tudo devo.

# CONTENTS

# AUTHORS CONTRIBUTIONS

1. **Monitoring dialysis arteriovenous fistulae: it's in our hands**

   Coentrão L, Turmel-Rodrigues L.

   *J Vasc Access* 2013 Apr 18 [Epub ahead of print]. PMID: 23599144.

   LC and LTR wrote this review paper.

2. **Costs and outcomes of endovascular treatment of thrombosed dialysis autogenous fisulae**

   Coentrão L.

   *Nefrologia* (in press)

   LC wrote this review paper.

3. **Effects of starting hemodialysis with an arteriovenous fistula or central venous catheter compared with peritoneal dialysis: a retrospective cohort study.**

   Coentrão L, Santos-Araújo C, Dias C, Neto R, Pestana M

   *BMC Nephrology* 2012 13:88. PMID: 22916962.

   LC designed research; LC, CSA, and RN performed research; LC, CSA, CD and MP analyzed data; LC wrote the paper; CSA and MP revised the manuscript for important intellectual content.

4. **Cost analysis of hemodialysis and peritoneal dialysis accesses in incident dialysis patients**

   Coentrão L, Santos-Araújo C, Ribeiro C, Dias C, Pestana M

   *Perit Dial Int* 2013 Mar 1. [Epub ahead of print]. PMID: 23455977.

   LC designed research; LC, CSA, and CR performed research; LC and CD analyzed data; LC wrote the paper; MP and CSA revised the manuscript for important intellectual content.

5. **Physical examination of dysfunctional arteriovenous fistulae by non-interventionalists: a skill worth teaching**

   Coentrão L, Faria B, Pestana M

   *Nephrol Dial Transplant* 2012;27(5):1993-1996. PMID: 21940486.

LC designed research; LC and BF performed research; LC and BF analyzed data; LC wrote the paper; BF and MP revised the manuscript for important intellectual content.

6. **Percutaneous Treatment of Thrombosed Arteriovenous Fistulas: Clinical and Economic Implications**

   Coentrão L, Bizarro P, Ribeiro C, Neto R, Pestana M

   *Clin J Am Soc Nephrol* 2010;5: 2245-2250. PMID: 20798249

   LC designed research; LC, PB, CR and RN performed research; LC and CR analyzed data; LC wrote the paper; MP revised the manuscript for important intellectual content.

7. **Endovascular treatment of thrombosed dialysis fistulae: a cumulative cost analysis**

   Bizarro P, Coentrão L, Ribeiro C, Neto R, Pestana M.

   *Catheter Cardiovasc Interv* 2011;77:1065-1070. PMID: 21413132.

   LC designed research; LC, PB, CR and RN performed research; LC and CR analyzed data; LC wrote the paper; MP revised the manuscript for important intellectual content.

# PREFACE

Chronic dialysis is an imperfect substitution of renal function. It is expensive and time consuming, indiscriminately removes solutes, fails to substitute for renal hormones, and requires dietary restrictions and drug therapy to maintain the patient in suboptimal health. Furthermore, life-sustaining dialysis requires durable dialysis access to the peritoneal or circulatory systems. The concept of *dialysis access* comprises the vascular access for haemodialysis – the autogenous arteriovenous fistula, the arteriovenous graft and the central venous catheter – and the peritoneal dialysis catheter. Vascular and peritoneal accesses for dialysis, the *condition sine qua none f*or successful dialysis, are not without problems and it have been considered as the *Achilles' heel* of chronic dialysis therapy. Moreover, dialysis access care accounts for a significant proportion of healthcare costs in both incident and prevalent chronic dialysis patients.

This thesis contributes to the field of dialysis access for chronic replacement of renal function by dialysis by examining how vascular and peritoneal accesses and state-of-the-art diagnostic and therapeutic techniques can be used to maximum patient benefit whilst simultaneously optimizing economical resources. In this framework, we thought that an ***Introduction*** would probably be helpful to contextualize the reader in the core knowledge about the dialysis access subject. Chapter 1 is a comprehensive review about the dialysis access issues that concerned physicians since the first dialysis attempts until the present time. Two review articles that we believe summarize the most relevant current knowledge about the monitoring of the arteriovenous fistula and the use of endovascular techniques for the treatment of arteriovenous fistula thrombosis, respectively, constitute Chapters 2 and 3. The original research is thoroughly described in the ***Results*** section, divided into three main chapters – Establishment and maintenance of dialysis access (Chapter 4), Detection of vascular access dysfunction (Chapter 5) and Treatment of vascular access failure (Chapter 6). The discussion and the main conclusions of this thesis are presented in the ***Discussion*** section.

# OBJECTIVES

Vascular and peritoneal accesses for chronic dialysis are recognized to have a significant influence on patient morbidity, mortality and financial resource use. However, comparisons between peritoneal and vascular access use for chronic dialysis are rare in the literature. Evidence from observational studies suggests that the autogenous arteriovenous fistula comes closest to satisfying the criteria of the *ideal haemodialysis access*. Nevertheless, arteriovenous fistula dysfunction is still a common major problem in haemodialysis units. Fistulae stenosis and thrombosis are the most common causes of access dysfunction, and there have been extensive investigations to identify the best methods for detecting accesses at risk. Several studies have reported on the feasibility of the endovascular approach to thrombosed fistulae in recent years. However, as repeated interventions are usually required to achieve long-term access survival, maintenance of a previously thrombosed fistula could be highly expensive. This thesis objective is to contribute to the understanding of both clinical and economic issues concerning the establishment and maintenance of the dialysis access for chronic dialysis patients. The specific objectives of the present thesis are the following:

1. To examine the relationship between mortality and dialysis modality, focusing on the role of vascular and peritoneal access types at the time of dialysis regular program initiation;
2. To compare the resources required to establish and maintain the dialysis access in patients who initiate regular haemodialysis and peritoneal dialysis;
3. To assess the diagnostic accuracy of physical examination in the assessment of dialysis arteriovenous fistula dysfunction;
4. To evaluate the costs and health outcomes of vascular access care in haemodialysis patients with arteriovenous fistula thrombosis;
5. To determine the cumulative costs and outcomes of endovascular treatment of thrombosed arteriovenous fistula.

# PART I
## INTRODUCTION

# Chapter 1

***Dialysis access for chronic kidney disease: a thorn in the side***

## Introduction

*" He is usually subject to constant recurrence of his symptoms; (…) he is suddenly seized with an acute attack of pericarditis, or with a still more acute attack of peritonitis (…) his headaches have been observed to become more frequent; his stomach more deranged; his vision indistinct; his hearing depraved; he is suddenly seized with a convulsive fit, and becomes blind.(…) and before a day or a week has elapsed, worn out by convulsion, or overwhelmed by coma, the painful history of his disease is closed"*

For over a century after this classical description of end-stage renal disease (ESRD) by Richard Bright (1) there was virtually no change in the prognosis of these patients. However, in the past 50 years or so the fate of the patient with irreversible renal failure has changed dramatically. Much of the mental and physical suffering that characterized renal failure has nearly disappeared from our hospital wards. Currently, it is even difficult to expose medical students to the clinical uremic syndrome and to teach them at the bedside the signs and symptoms of ESRD. Today, in many parts of the world, dialysis is readily available for patients with renal failure. The patient no longer asks whether there is a chance for survival or whether treatment by dialysis is possible. Rather, the informed patient asks when dialysis will begin, which is the most suitable dialysis modality for him and, how soon can a transplantation be accomplished.

Dialysis interposes a semi-permeable membrane between a flowing stream of blood and an appropriate rinsing solution. By diffusive and/or convective transport, the composition of body fluids approaches that of the dialysis solution. Simultaneous ultrafiltration decreases body fluid volumes, ordinarily toward normal. Lowering of concentrations of toxic solutes in body fluids by dialysis is ordinarily associated with clinical improvement of the uraemic syndrome, while hypertension and congestive heart failure usually recede as volume excess is corrected. But, because we cannot identify precisely and understand sufficiently the toxicity of the retained solutes, we deplete indiscriminately, removing useful as well as toxic solutes in proportions dictated by membrane permeability and concentration gradients rather than according to the toxic potential. Actually, chronic dialysis is an imperfect substitution of renal function. It is

expensive and time consuming, indiscriminately removes solutes, fails to substitute for renal hormones and metabolic activities, and requires dietary restrictions and drug therapy to maintain the patient in suboptimal health. Last but not the least, both vascular and peritoneal accesses for dialysis, the *condition sine qua none* for successful dialysis therapy, also can offer problems.

## A glimpse at the past

### Angioaccess for Haemodialysis

The credit for the first human haemodialysis (HD) must go to Georg Haas from Gieszen, Germany, who lived from 1886-1971 (2). Assisted by a surgeon colleague, he performed the first human HD in the autumn of 1924 (this dialysis lasted 15 minutes). He first used glass cannulae to obtain arterial blood from the radial artery, which he returned to the cubital vein. Later, he performed a surgical cut-down to place a cannulae into the radial artery and into an adjacent vein. Bleeding occurred from the surgical cannulation wounds and the gums, presumably caused by the anticoagulant. Obviously Hass' dialysis procedures lasted too short for any significant therapeutic effect. In the late 1930's, a young doctor named Willem Johan Kolff, entered the Department of Medicine at the Groningen University Hospital in the north of The Netherlands at the age of 27 (2). Since the begging of his first dialysis experiments, Kolff and his team experienced increasing difficulties with obtaining access to the circulation. First, Kolff used only venipuncture needles to obtain blood from the femoral artery and to reinfuse it by puncturing a vein. Later, he performed surgical cutdown of the radial artery which caused severe bleeding during heparinization. When the $11^{th}$ or $12^{th}$ dialysis failed because no further arteriotomies and venesections were possible, further dialysis had to be abandoned. In 1946, Kolff wrote in his thesis: "(…) in cases of chronic (irreversible) uraemia there is in general no indication for treatment with the artificial kidney (…)".The major obstacle was achieving repeated access to the bloodstream, a problem which had to wait for another 20 years before a new approach was made.

In 1949, Allwall tried to use a rubber tubing and glass cannula device to connect artery and vein, but he failed (3). This idea of Alwall was later taken up by Quinton, Dillard and

Scribner (Seattle, USA) who developed an arteriovenous Teflon shunt (4). Two thin-walled Teflon cannulae with tapered ends were inserted near the wrist in the forearm, one into the radial artery and the other into the adjacent cephalic vein. The external ends were connected by a curved Teflon bypass tube. Later, the Teflon tube was replaced by flexible silicon rubber tubing. The development of a permanent vascular access by the Seattle group was the decisive breakthrough, which made maintenance dialysis possible. It is rightly considered a landmark in the history of dialysis: maintenance HD therapy began on 9 March 1960.

At that time, in 1961, Stanley Shaldon (London, UK) faced the problem of finding a surgeon willing to operate on the radial artery and cephalic vein to introduce cannulae for circulatory access. To become independent, Shaldon introduced hand-made catheters into the femoral artery and vein by the percutaneous Seldinger technique for immediate vascular access (5). After the first use of the subclavian route for HD access by Shaldon in 1961, this technique was adapted by Josef Erben from the former Czechoslovakia, using the infraclavicular route (3). During the following two decades the subclavian approach was the preferred route for temporary vascular access by central venous catheterization. In the late 1980s, Schwab and colleagues introduced the concept of a cuffed catheter for long-term access (6).

The legendary paper “Chronic hemodialysis using venipuncture and a surgically created arteriovenous fistula” was published by Brescia, Cimino, Appell and Hurwich (7). Appell was the surgeon in the team - he had performed a side-to-side-anastomosis between the radial artery and the cephalic vein at the wrist. The first surgically created fistula for the purpose of HD was placed on 19 February 1965. One year after the article of Brescia and Cimino, Sperling (Würzburg, Germany) reported the successful creation of an end-to-end-anastomosis between the radial artery and the cephalic antebrachial vein in the forearm (3). This type of arteriovenous anastomosis gained widespread acceptance during the next decade. In 1968, Lars Röhl from Heidelberg, Germany, published his results in 30 radial-artery-side-to-vein-end anastomoses (3). Today, the artery-side-to-vein-end-anastomosis has become a standard procedure.

The year 1972 saw the introduction of graft materials in dialysis arteriovenous shunts, one biologic and two synthetic (3). The fact that Dacron was not accepted and that polytetrafluoroethylene (PTFE) continues to be the material of choice highlights the fact that in the field of vascular access special criteria must be met by the graft material.

In 1973, Staple (St Louis, USA) described a novel angiographic technique in his paper "Retrograde venography of subcutaneous arteriovenous fistulas created surgically for hemodialysis" (8). This angiographic technique is still used today. The first report on a new angiographic technique, known as digital subtraction angiography, was published in 1979 (9). Later, this technique was adapted to visualize arteriovenous fistulae and prosthetic bridge grafts, using the arterial as well as the venous route. The era of the percutaneous, transluminal angioplasty in vascular accesses started with a publication of David Gordon and Sidney Glanz (New York, USA) in 1982 (10).

## Peritoneal dialysis access

Ganter from Würzburg, Germany, is commonly credited with the first peritoneal dialysis (PD) in humans for the purposes of uraemia treatment (11). His first attempt of sodium chloride infusion into serous cavity was done in Greiswald, Germany, in 1918. He reported on two cases of normal saline infusion into the peritoneal cavity; in both cases he used a needle commonly used at that time for abdominal and pleural punctures. The first case of a patient who survived after peritoneal lavage for the treatment of uraemia in April, 1937, was reported by Wear, Sisk, and Trinkle from Wisconsin, USA (11). A standard gallbladder trochar was introduced in the upper abdomen and another trochar in the lower abdomen. The fluid was introduced into upper cannula and the lower cannula was attached to a bottle on the floor and acted as siphon. The authors used the procedure in five cases, but only one patient survived. The first intermittent peritoneal dialysis in humans was performed by Rhoads from Philadelphia, Pennsylvania in 1936 and 1937 (11). In two patients thought to have acute renal failure, peritoneal lavage was performed. Temporary improvement in the patients was noted; both patients ultimately died.

In these early years of PD the peritoneal cavity access was not specifically designed for the PD, rather the available equipment from general surgery and urology was taken advantage and used for peritoneal access (e.g. trocars, foley catheters). These early devices, used for short-term peritoneal dialysis, were associated with multiple complications, such as pressure on intestines of rigid tubes, constant suction of contaminated air into the peritoneal cavity, leakage of fluid around the access, and difficulties in fixation of the system to the abdominal wall.

After World War II, in the late 1940s, multiple PD solutions compositions and multiple

peritoneal accesses were tried, and first accesses specifically for peritoneal dialysis were designed. Rosenak for the first time developed an access specifically for PD (12). The access consisted of stainless steel flexible coil attached to a rubber drain. However, this device did not gain popularity because its use was associated with major complications (e.g. irritation of the viscera, dialysate leakage, peritoneal contamination).

In the 1950s and particularly 1960s, the development of new accesses with different characteristics resolved most of the problems improving dramatically most complications of PD. In late 1950s Maxwell *et al.* (13) from California, USA, introduced a polyamide catheter with multiple tiny distal perforations. Smooth, plastic materials were much less irritating to the peritoneum and the drainage of fluid from the peritoneal cavity improved, but leakage continued to plague the access. A major step forward in creating a permanent peritoneal access was made in 1964 by Gutch (14) with the use of silicon rubber catheters. He observed much less irritation of the peritoneum with the new material, compared to those with polyvinyl. A major breakthrough came in 1968 when Tenckhoff and Schechter (15) published the results of their studies on a new catheter. The Tenckhoff catheter was composed of an intra-abdominal Dacron cuff, a subcutaneous tunnel and a second external cuff (used to decrease the length of the catheter sinus tract). A shorter subcutaneous tunnel and straight intraperitoneal segment facilitated catheter implantation at the bedside. The original recommendations for the catheter insertion (e.g. arcuate subcutaneous tunnel with downward directions of both intraperitoneal and external exits) are still considered very important elements of catheter implantation. Fewer complications were reported in patients treated by periodic peritoneal dialysis in the supine position. The Tenckhoff catheter has become the gold standard access for peritoneal dialysis.

The introduction of continuous ambulatory peritoneal dialysis in the late 1970s increased catheter related complications due to numerous daily manipulations and higher intra abdominal pressure while the fluid was in the peritoneal cavity. Nevertheless, even today, four decades later, Tenckhoff catheter in its original form is one of the most widely used catheter types.

## Current types of dialysis access

The evolution of chronic dialysis therapy parallels the advances made in vascular and peritoneal accesses, as chronic life-sustaining dialysis requires a durable access to feed the extracorporeal circuit or the peritoneum. At the beginning of the 21st century, the concept of "dialysis access" comprises the vascular access for HD – the autogenous arteriovenous fistula (AVF), the arteriovenous graft (AVG) and the central venous catheter – and the PD catheter. The ideal permanent dialysis access should: (a) provide longevity of use with minimal complication rates from infection and dysfunction and (b) supply sufficient flow rates to deliver the prescribed dialysis dose. Although the current knowledge suggests that some dialysis accesses are superior to others, there's no dialysis access fulfilling these ambitious criteria. Therefore, we might question - which one is best? Perhaps, we should answer, the one that best suits your physiology, lifestyle and life expectancy. Unfortunately, the response is not as simple as it sounds. In the following section, the prevailing HD and PD accesses, as well as its complications, will be briefly described.

### Tunneled haemodialysis catheters

Tunneled HD catheters can provide effective vascular access for months, or years, at a time. Tunneled HD catheters have a subcutaneous Dacron cuff for tissue ingrowth or a plastic grommet to immobilize the catheters below the skin surface. The catheters are made of silicone or other soft polymers and are larger in diameter (14.5 Fr to 16 Fr) than the non-tunneled HD catheters. The design of the catheter tip reflects efforts to prevent catheter thrombosis and recirculation. Although many types of HD catheters are available, trials systematically comparing the various catheters to assess the performance of different materials, catheter shapes, flow rates, and rates of infection or thrombosis are not available. Insertion of a tunneled HD catheter can be performed at the bedside under sterile conditions using the modified Seldinger technique. Dialysis catheters can be placed either by nephrologists, interventional radiologists or surgeons. The right internal jugular vein provides a direct path to the superior vena cava, making it the preferred location for a dialysis catheter. Ultrasound guidance is the standard of care for all HD catheter insertions (16, 17). During insertion of internal jugular and subclavian vein catheters, continuous electrocardiographic monitoring can warn for cardiac dysrrhythmias induced by

wire manipulation or catheter advancement. Fluoroscopy during and after catheter placement allows accurate placement of the catheter tip and ensures that the catheter is not kinked.

Tunneled HD catheters can cause immediate or delayed complications. Immediate complications result from injuries incurred at the time of catheter insertion. Ultrasound guidance appears to minimize the risk of injury during catheter insertion (carotid injury, 10.6% *vs.* 1.1%; hematoma 8.4% *vs.* 0.4%; haemothorax, 1.7% *vs.* 0%, pneumothorax, 2.4% *vs.* 0%) (18). Delayed catheter complications typically occur due to the accumulation of vessel trauma over time. Dysfunctional catheters cannot provide sufficient blood flow for effective dialysis. The minimal blood flow rate of 200 to 300 mL per minute is necessary to sustain conventional HD. Multiple conditions can cause catheter dysfunction, including intraluminal thrombosis, catheter kinking, catheter malposition, and the development of a fibrin sheath around the catheter or its tip. For recently placed catheters, the cause of dysfunction usually involves mechanical obstruction or tip malposition. After 2 weeks, catheter dysfunction is more likely due to progressive occlusion of the catheter tip by thrombus or fibrin. Treatment options for catheter dysfunction caused by fibrin sheaths include catheter exchange, balloon disruption, or sheath stripping. Catheter thrombosis can impair or completely interrupt dialysis. In a nonfunctioning catheter, a 2-mg infusion of tissue plasminogen activator in each lumen can usually reestablish blood flows greater than 200 mL per minute. Failure of tissue plasminogen activator to restore patency warrants treatment with a catheter exchange over a wire or the placement of a new catheter at a different location. Studies comparing these strategies have been scarce and inconclusive. The National Kidney Foundation - Dialysis Outcome Quality Initiative (K/DOQI) guidelines (16) recommend exchange of the catheter and disruption of the fibrin sheath by balloon angioplasty.

Recirculation describes what happens when blood being returned to the patient via the venous lumen of the catheter enters into the arterial “draw” of the catheter and returns back to the dialysis machine. In effect, blood recirculates from the outflow to the inflow part of the catheter, thereby reducing dialysis clearance. Recirculation becomes more pronounced at higher blood flow rates. Functional internal jugular and subclavian venous catheters have low recirculation rates (5%), while femoral catheters have higher rates, especially if the catheter is not long enough to reach the inferior vena cava (19). Inversion of the connecting lines increases recirculation from 3% to 12% (20).

Efforts to prevent catheter thrombosis have focused on the use of locking solutions

instilled into the catheter at the conclusion of HD. The most widely used solution has been unfractionated heparin in concentrations ranging from 500 to 5000 IU/mL. In theory, the volume of locking solution should fill only the catheter itself, thereby preventing catheter thrombosis without causing systemic effects. In practice, the locking solution does not completely remain in the catheter and patients often become systemically anticoagulated. Locking solutions that can act as both an anticoagulant and an antimicrobial have been developed to decreasing the risk of catheter infections and thrombosis compared to heparin locking solution. Solutions consisting of sodium citrate and antiseptic agents have shown promise in decreasing the risk of catheter infections and thrombosis compared to heparin locking solution (21).

Infection ranks second only to cardiovascular disease as the leading cause of death for dialysis patients. (22) The majority of infections derive from vascular access, with catheter use representing the highest overall risk factor. Compared to AVFs, catheters increase the risk of infection by 50%, and this risk more than doubles if catheters are required in the first 6 months of dialysis (16). Catheter-related infections range in severity from localized bacterial colonization to life-threatening systemic sepsis. Exit site infections manifest as erythema, crusting, and exsudate involving the skin around the catheter. They do not cause systemic illness and blood cultures remain negative. Topical antibiotics and local site care can resolve some exit infections in tunneled catheters. Drainage around the catheter from the tunnel should be cultured and treated with antibiotics. Clinical deterioration or failure to respond to these conservative measures requires removal of the catheter. Bloodstream infections represent a potentially lethal complication of dialysis catheters and occur with an incidence of 1.5 to 5.5 episodes per 1000 catheter days (16). Left untreated, catheter-related bacteraemia can lead to endocarditis, osteomyelitis, sepsis, and death. All cases of catheter-related bacteraemia require treatment with antibiotics. However, antibiotics often fail to eradicate catheter-associated infections because of the presence of biofilms on the catheter surface, requiring the removal of the infected catheter with its adherent biofilm in the great majority of cases (21).

Exotic dialysis catheters (e.g. direct catheter placement into the right atrium, transhepatic catheter and translumbar catheter) have been described in the literature (23).

## Arteriovenous dialysis access

There are many arteriovenous access options for HD, and these have been thoroughly described by Spergel *et al.* (24). The most common AVFs and AVGs types are briefly described here.

The radiocephalic AVF is a technically straightforward procedure and preserves other more proximal access options. Radiocephalic AVFs have few complications and may have several locations in the forearm: "snuffbox", wrist and mid-arm. Compared to more proximally based configurations, the radiocephalic AVF has a lower blood flow rate, and maturation can be slower. Several other forearm AVFs types can also be performed (e.g. antecubital vein constructions, basilic vein transposition to radial artery, basilic vein - ulnar artery fistula).

The brachiocephalic AVF is a commonly performed access, which provides higher blood flow and more reliable maturation than a wrist fistula. Because of its more proximal location and greater blood flow, a brachiocephalic AVF also has a higher incidence of edema and ischemic steal syndrome.

The brachiobasilic AVF is a less common performed access, and it can be performed as a 1- or 2-stage procedure (25). The basilic vein's deep location provides protection from trauma related to phlebotomy and intravenous catheters. Often, the basilic vein is the only upper extremity superficial vein that remains patent in patients with previous access procedures. On the down side, brachiobasilic AVFs have a longer recovery time that involves more postoperative edema and pain. They also carry a higher risk of developing ischemic steal syndrome compared to other access types. Transposing the basilic vein to facilitate needle cannulation can be technically challenging especially in cases involving an obese arm.

A variety of materials have been used in the construction of AVGs. Expanded PTFE is the most commonly used material. For the upper extremity the most common diameter is a 6-mm straight PTFE graft. Forearm loop AVGs originate in the antecubital fossa with the brachial artery providing arterial inflow. Venous outflow can employ the cephalic, basilic, median antecubital, or brachial veins. A variety of configurations are possible in the upper arm, depending on the anatomy and prior access procedures. The arterial inflow can be provided by the brachial artery or axillary artery. The venous outflow can use the cephalic, basilic, brachial, or axillary vein. Although upper arm grafts have high blood flow rates, they also have a higher rate of hemodynamic

steal syndrome compared to forearm AVGs. Although prosthetic AVGs offer technically easy cannulation and a shorter lag time from insertion to clinical use, these advantages are offset by a higher rate of thrombosis and infection compared to AVFs (16, 17).

When the upper extremity options have been exhausted, other access locations and configurations are considered. A “necklace” AVG uses the axillary artery for inflow and the contralateral axillary vein or jugular vein for venous outflow. The most common groin access is a prosthetic loop AVG between the distal common femoral artery and the great saphenous or common femoral vein. Groin arteriovenous access sites have a higher incidence of infection and ischemia and should only be used if the upper extremities are not a viable option.

Autogenous fistulae are more likely than AVGs to experience primary failure, defined as a fistula that never provided reliable access for HD. The primary failure rates of radiocephalic, brachiocephalic, and brachiobasilic AVFs are approximately 24 to 35 percent, 9 to 12 percent, and 29 to 36 percent respectively, across a range of studies (16, 26). With respect to AVGs, the K/DOQI guidelines (16) suggest that the primary access failure rates should be no more than the following: 15 percent with forearm straight AVG, 10 percent with forearm loop AVGs and 5 percent with upper arm AVGs. Radiological or surgical intervention to promote maturation may be required to reduce the risk of primary failure. Although AVFs have a high rate of primary failure, their long-term patency is superior to AVGs if they mature. The 5- and 10–year cumulative patencies for radiocephalic AVFs are reported to be 53 and 45 percent, respectively. By comparison, cumulative patency for AVGs at one, two, and four years is approximately 67, 50 and 43 percent, respectively. In general, forearm AVGs have lower cumulative patency than upper arm AVGs (16).

The clinical impact of arteriovenous access complications ranges from mild symptoms causing discomfort and inconvenience to catastrophic conditions that endanger life and limb. Stenosis is the most common complication of both AVFs and AVGs (16). Stenosis may develop in the inflow and/or outflow tract. Inflow stenosis is more frequent in AVFs than in AVGs, whereas outflow stenosis is the most common lesion present in AVGs. The presence of an inflow stenosis precludes the maturation of forearm AVFs, often called “non-maturing fistulae”. Venous obstruction is the most common condition that complicates the placement of an upper extremity arteriovenous access (both AVFs and AVGs). The sheer number of central venous instrumentations performed on dialysis patients directly correlates with the high incidence

of venous stenosis and obstruction. Although subclavian vein catheters pose the highest risk for developing subsequent stenosis, any catheter in any vein can cause venous stenosis or occlusion. Endovascular therapy offers a minimally invasive method of alleviating arterial inflow or venous outflow obstruction. The technical success of endovascular intervention depends on the ability to cross the stenosis or occlusion with a wire followed by balloon angioplasty to dilate the obstructed vessel. Multiple studies confirm that endovascular therapy achieves excellent initial technical success and reasonable mid-term-assisted patency (16, 17). Surgical options are tailored to the location of the lesion and the outflow sources.

Thrombosis represents one of the most dreaded complications. It is the most common cause of arteriovenous access loss and even when successfully treated thrombosis interrupts routine dialysis and necessitates invasive procedures (16). An underlying arterial or venous stenosis precipitates thrombosis in the great majority of cases, highlighting the role of access flow surveillance (16). Other, less common causes of thrombosis include hypotension, external compression and hypercoagulability. Thrombosis mandates urgent treatment. Thrombectomy procedures become more difficult and less durable with time increasing the chance that the patient will need a dialysis catheter. Interventions for thrombosis consist of two components: removal of the thrombus and treatment of the underlying cause of access failure. Various endovascular and open surgical approaches have proven to be safe and effective. Direct comparisons of surgical and percutaneous thrombectomy have been inconclusive (16). Therefore, the choice of intervention depends on the most likely cause of thrombosis, the practitioner's skills and institution policy.

Infection ranks second only to thrombosis as the cause of arteriovenous access failure among dialysis patients (27). Autogenous arteriovenous fistulae have the lowest rate of infections, and therefore, the least amount of accumulated evidence comparing various treatment options (16). The incidence of infection for AVGs ranges from 3% to 19%. The diagnosis of arteriovenous access infection relies on the clinical examination. Explicit signs of infection include purulent drainage. Treatment options include antibiotics and surgical exploration.

Construction of an upper extremity arteriovenous access alters the blood flow patterns to the forearm and hand. Symptomatic arterial steal occurs when blood flow is shunted from the tissue beds distal to the arterial anastomosis and usually occurs in combination with one or more of the following clinical scenarios: arterial inflow stenosis or increased access size leading

to extremely high access flow rates. Failure to recognize and treat arterial steal can lead to limb-threatening ischemia or permanent disability. Fortunately, most patients have sufficiently large inflow arteries to compensate for this physiological steal phenomenon. The ideal intervention for treating arterial steal restores hand perfusion, while preserving the function of the arteriovenous access. The choice of intervention depends on several factors, including the cause of ischemia; the severity of symptoms; the alternatives for dialysis access; and the patient's medical comorbidities. Ischemic monomelic neuropathy - vascular compromise to multiple nerves within the same extremity - is a rare, but potentially devastating complication of arteriovenous access that occurs almost exclusively in elderly, diabetic patients with a history of peripheral neuropathy and/or peripheral vascular disease. Successful treatment requires immediate correction of the ischemic insult to the nerves of the forearm and hand. In most cases, ligation of the fistula represents the most expeditious and accepted intervention.

High-output cardiac failure occurs when symptoms of cardiac failure develop in the presence of an above normal cardiac index. Although it has a simple definition, high-output cardiac failure proves to be difficult to diagnose in dialysis patients because approximately 30% of patients have cardiac failure at the initiation of dialysis. The magnitude of arteriovenous access flow necessary to trigger heart failure varies widely depending on the patient. The only treatment option for high-output cardiac failure and pulmonary hypertension are to reduce or discontinue the flow through the arteriovenous access.

Pseudoaneurysms are associated with a thrombotic, infectious, and haemorrhagic risk to patients receiving HD. Although pseudoaneurysms occur in AVFs, they are more common in AVGs. Pseudoaneurysms generally occur within cannulation areas and result from repeated needle sticks in the same location, so-called "one site-itis". Management involves abandoning the area and adhering to a rotating site or "rope ladder" cannulation strategy. The presence of a scab or extremely thin skin overlying the pseudoaneurysm mandates prompt intervention. Diffuse enlargement of a long-standing AVF represents a true aneurysm involving all layers of the access walls. If the overlying skin is intact and the aneurysm is free of layered thrombus, it will support continued dialysis and does not require intervention. If the aneurysm causes obstructive problems from kinking or compromises the overlying skin, surgical and/or endovascular revision may be required. In many cases, the tortuous, aneurysmal area can be resected and continuity restored by creating an end-to-end anastomosis or interposition bypass between the segments.

## Peritoneal dialysis access

The key to successful chronic PD is a reliable and permanent peritoneal catheter. Peritoneal catheters are composed of silicone or polyurethane. Catheters are defined based on the design of the extraperitoneal (*subcutaneous*) segment and the design of the intraperitoneal segment. The extraperitoneal segment can be precurved (arcuate angle) or straight. The extraperitoneal segment will have either one or two Dacron cuffs. Most catheters placed in the adult population have two cuffs. The proximal (*deep*) cuff is implanted on the pre-peritoneal surface and the distal (*subcutaneous*) cuff lies in the subcutaneous tunnel. The intraperitoneal segment of peritoneal catheters also has multiple designs. The most common peritoneal catheters, the *straight* and the *pigtail*, are both hollow tubes with large end holes. There are a number of variations on the standard single or double Dacron cuff Tenckhoff catheter that are now available which have been developed in an attempt to improve both the infectious complications, such as peritonitis and exit-site infections, and the mechanical complications. These variants include, among others, the Toronto-Western Hospital catheter, the Swan neck catheter, the Moncrief-Popovich catheter and the Swan neck presternal catheter (Missouri) (28).

Double-cuff catheters were initially thought to be associated with a lower incidence of both peritonitis and exit-site infections. However, in a prospective randomized comparison no significant differences between catheters with single or double cuffs could be established with respect to catheter survival, episodes of peritonitis, and exit site infections (29). Similarly, no convincing evidence exists for the superiority of the coiled design of the intraperitoneal portion of the catheter (30). Finally, a downward-directed exit site was thought to result in a reduction in the incidence of exit-site infections and peritonitis, but in a prospective comparison, catheter types employing downward and lateral tunnel-tract and exit-site configurations produced equivalent outcomes for infectious and mechanical complications (31). Whatever the catheter design used, it must allow for the free flow of peritoneal fluid by gravity. Rates of gravity fill and drain must approach up to 3 L in 10 to 15 minutes (300-500 mL per minute) without causing discomfort. International Guidelines suggest that no particular catheter type is proven to be better than another (32).

There are several technique options for the placement of permanent peritoneal catheters. Preferred surgical techniques are placement of catheters via dissection with mini-laparotomy or laparoscopic placement. Nephrologists use a peritoneoscopic placement or a modified

Seldinger technique. International guidelines recommend that: (a) each center should have a dedicated team involved in the implantation and care of peritoneal catheters; (b) local expertise at individual centers should govern the choice of method of peritoneal catheter insertion (32, 33).

Complications associated with peritoneal catheter may occur with different degrees of incidence and may account for approximately 20% of transfers to HD (34). These complications may be divided into mechanical and infectious. The most common mechanical complications are catheter dysfunction by tip migration, obstruction or omental entrapment, dialysate leak, cuff extrusion and hernia formations (34). Intra-abdominal bleeding and visceral perforation are exceedingly rare. Surgery (either open or laparoscopic surgery) is the main treatment. Temporary HD therapy may be required for peritoneal rest. Inflow dysfunction generally occurs due to kink in the subcutaneous tunnel. If an outflow dysfunction is observed in the operating room, the catheter is probably located out of the true pelvis due to insertion in an incorrect location such as the omentum or among viscera, or because of the presence of adhesions. Although laparoscopic insertion is more expensive and laborious, this technique has some advantages to prevent immediate and late causes of poor flow by selective prophylactic omentopexy, selective resection of epiploic appendices and adhesionlysis to eliminate compartmentalization. Cuff extrusion and hernia formation are not directly related to the insertion procedure of the PD catheter. These complications can be prevented if the technique is performed correctly and risk factors are avoided such as placement of a catheter with a straight intercuff segment should never be bent more than to produce a laterally directed exit site. The presence of hernias does not contraindicate catheter insertion or PD treatment, but they must be surgically repaired.

The most common infectious complications related to the peritoneal catheter are peritonitis, exit site and tunnel infections (34). An exit-site infection is defined by the presence of purulent drainage, with or without erythema of the skin at the catheter-epidermal interface. A tunnel infection may present as erythema, edema, or tenderness over the subcutaneous pathway. A tunnel infection usually occurs in the presence of an exit-site infection but rarely occurs alone (35). Oral antibiotic therapy is generally recommended (35). A patient with an exit-site infection that progresses to peritonitis, or who presents with an exit-site infection in conjunction with peritonitis with the same organism will usually require catheter removal (35). Peritonitis is a leading complication of PD and remains a major cause of patients discontinuing PD and switching to HD (35). In addition, severe and prolonged peritonitis can lead to peritoneal

membrane failure and peritonitis is probably the most common cause of technique failure in PD. Patients with peritonitis usually present with cloudy fluid and abdominal pain. Empiric antibiotic therapy for PD-associated peritonitis should be initiated as soon as possible because potentially serious consequences of peritonitis (relapse, catheter removal, permanent transfer to HD, and death) are more likely to occur if treatment is not initiated promptly (35).

## Permanent dialysis access planning

Observational studies suggest a better survival rate in PD than in HD patients during the first few years after starting therapy. However, after 2 or 3 years, outcome on PD becomes equal to HD, or worse, depending upon the study (36-39). Therefore, the European Renal Best Practice Expert Group (40) recommend that "the patient's preference should be taken into account as the primary factor, since patient satisfaction, compliance with therapy and quality of life are better if the patient has been given the opportunity to make his/her own informed choice". In other words, the dialysis modality that best suits our patient needs - the question that bear our minds, nephrologists, in our daily clinical practice – is a question whose answer lays in the willingness of the patient. Consequently, preparation for dialysis access placement begins with patient education. Nephrologists are in privileged position to inform patients about the options for renal replacement therapy and dialysis access placement. In this regard, several studies have shown that morbid-mortality in patients commencing dialysis is higher for those who have not had been supervised by a nephrologist in the months leading up to renal replacement therapy. This observation was made in the United Kingdom in 1984 (41) and has been confirmed by numerous registry and single-center analyses in Europe and North America (42-45). Actually, in most European Countries and also at European Union level, it is compulsory by law to inform patients of all treatment modalities (40).

### Angioaccess for haemodialysis

In an effort to improve vascular access outcomes, the National Kidney Foundation and the European Renal Association - European Dialysis and Transplant Association published the K/DOQI guidelines in 2006 (16) and the European Best Practice Guidelines (EBPG) for vascular

access in 2007 (17), respectively. Although these evidence and opinion-based guidelines have stimulated a large body of epidemiological and clinical studies so far, we must emphasize that some of the recommendations regarding permanent dialysis access planning may be considered as "parachute type" guidelines (e.g. the recommended anatomic order of distal-to-proximal access construction - good surgical practice makes it obvious that when planning permanent access placement, one should always consider the most distal site possible to permit maximum number of future possibilities for access). In contrast, the paucity of randomized clinical trials in the dialysis access field should not lead us, nephrologists, to distrust or nihilism. As an example, the legacy of our predecessors and the evidence from observational studies tell us that AVF placement should be considered first, in comparison with AVG and central venous catheter. Taking this into consideration, the K/DOQI (16) and the EBPG (17) guidelines set an order of preference for placing HD access that reflects several underlying principles of vascular access surgery: (a) always place a primary AVF when possible, and, if not, an AVG; (b) move peripheral to central to preserve as many access sites as possible, preferably in the nondominant extremity, and alternative sites (thigh, chest) used after all upper extremity sites have been exhausted; and (c) catheters should be avoided and only used if no other option is available.

International guidelines (16, 17) recommend that AVF should be placed at least 6 months in advance of the anticipated need for dialysis. Early placement allows adequate time for AVF maturation, evaluation, and even revision if necessary. In contrast, AVGs are ready to use as soon as the postoperative edema resolves and the graft incorporates into the surrounding tissue. Since most prosthetic grafts can be used within 2 to 3 weeks, they require a surgery lead time of only 3 to 6 weeks. Towards achieving these goals, a multidisciplinary team that emphasizes advanced vascular access planning and preparation is strongly recommended. The history and physical examination helps individualize the arteriovenous access treatment plan for each patient. The next step in preparation involves vascular imaging to determine the most appropriate site and type of arteriovenous access. Duplex ultrasound examinations do not require contrast, making them ideal for evaluating patients with residual renal function. Patients with a history of multiple central venous catheters or clinical signs of venous stenosis often require contrast or $CO_2$ venography to determine the patency of the central venous system (16, 17). As function implies that the access not only delivers adequate blood flow for dialysis, but may be cannulated easily, the K/DOQI guidelines (16) stated a simple rule definition for a

functional permanent arteriovenous dialysis access called “Rule of 6s”: (a) an access that has a flow of 600 mL per minute, (b) is less than 0.6 cm below the surface of the skin, and (c) has a minimal diameter of 0.6 cm.

Based on these recommendations, a special project was launched in July 2003 in the United States, called the National Vascular Access Improvement Initiative, which has since become known as the Fistula First Breakthrough Initiative (46). The purpose of the Coalition was to increase the likelihood that every suitable patient would receive the optimal form of vascular access for that patient, and that vascular access complications would be reduced through appropriate access surveillance, monitoring and intervention. The Work Group recognized that in some cases, the “fistula first at all costs” approach may not be the most cost-effective or optimal solution for each individual. In fact, there has probably been no initiative related to dialysis vascular access that has been more misunderstood than the Fistula First. The very meaning of the term is misunderstood; it is taken to mean that every patient who comes to the point in the evolution of their disease that dialysis is indicated should receive an AVF (47). The term should actually be interpreted to mean that when considering the type of vascular access to place in a patient, an AVF should be considered first. In other words, it is only after the possibility of an AVF has first been ruled out that another type of vascular access should be considered. The actual goal is that every patient should receive the most optimal form of vascular access for that patient. A functional fistula is the goal, not the insertion of a fistula with poor chance at maturing.

The idea that a central venous dialysis catheter is mandatory for the ESRD patient needing dialysis, with no arteriovenous access placed in due time, is arguable. There are alternatives to a central venous dialysis catheter. The delusional idea that a peritoneal catheter cannot be used to deliver short-term PD must be overcome. In 2006, the K/DOQI guidelines (16) stated that “A peritoneal dialysis catheter may be used as a bridge for a fistula in “appropriate” patients.” Interestingly, at the International Society of HD Congress, New-Delhi, India in 2011, a series of over 1000 cases in which a Quinton-Scribner shunt had been used to provide immediate dialysis were reported (Dr. Dinesh Khullar). Most of these cases were converted to AVFs at 4-6 weeks, and in many instances, the vein was mature enough to allow for immediate cannulation. The use of an external arteriovenous shunt as a temporary access or as a means for maturing veins for a secondary AVF is a novel idea that is worth considering (47).

## Peritoneal dialysis access

As is the case for patients who choose HD, there are two main ESRD patient groups requiring a PD access for dialysis start: (a) patients with progressive renal failure predicted to need dialysis, in whom the objective is placement of access sufficiently early to enable the patient to train for PD in a timely fashion while residual renal function is sufficient, and to avoid the need for temporary vascular access for HD if there are problems with catheter function; (b) patients with ESRD presenting as uremic emergencies. International Guidelines (32, 33) state that, whenever possible, peritoneal catheter insertion should be performed at least 2 weeks before starting PD. Nevertheless, reliance on small dialysate volumes in the supine position can be used if dialysis is required in the short-term. The advantage of placing peritoneal access in patients who have not had the opportunity to be prepared for renal replacement therapy is that the requirement for prolonged use of central venous access can be reduced (32, 33).

Renal units should have clear protocols for perioperative catheter care (32, 33). Several points should be included in the perioperative catheter care protocol, such as, previous history of abdomino-pelvic surgery, checking for hernias, screening for nasal carriage of *Staphylococcus aureus*, identifying a catheter of a suitable length and marking the exit site with the patient sitting or standing, preparing the bowel with laxatives and ensuring bladder emptying. Administration of prophylactic antibiotics is recommended to reduce the risk of catheter-site infection, peritonitis, and wound sepsis (32, 33). The choice of antibiotic should be based upon local guidelines. Peritoneal access surgery should include facilities for both catheter insertion and catheter removal. International Guidelines (32, 33) suggest that peritoneal catheters should be inserted as day case procedures in selected cases as long as this does not compromise the quality of care. Compared with an upwardly or horizontally-directed PD catheter tunnel, a downwardly-directed tunnel is preferred and recommended by International Guidelines since it may be associated with fewer catheter infections and fewer peritonitis episodes resulting from catheter or tunnel infections (32, 33). Catheters with a permanent bend (eg, Swan Neck catheter) naturally have a downwardly-directed tunnel because of the catheter's configuration. Local expertise at individual centers should govern the choice of method of peritoneal catheter insertion. It is still not known whether any particular peritoneal catheter designs, implantation techniques, or modalities are effective, given the limitations of available trials (48). For more complicated patients, including those with previous significant abdominal surgery, a technique

that involves direct vision is necessary, such as laparoscopic or open insertion (49). Although the effect of a subcutaneous rest period (Moncrief method) on the incidence of peritonitis and exit-site infections is uncertain (50, 51), its use may have advantages for the relationship between the timing of catheter insertion and the start of training.

Peritoneal dialysis is a modality that has been underutilized in many parts of the globe. The idea that: (a) a peritoneal catheter cannot be used to deliver short-term PD; and (b) rapid initiation of PD is unfeasible in unplanned dialysis patients, is a misconception. Studies have shown that PD can be started within the first week or even immediately after peritoneal catheter placement without any major difficulties (52-54).

## Epidemiology of dialysis access

In the early 1960s, when the first chronic dialysis programs were being set up in the United States and elsewhere, it is doubtful that even the most enthusiastic proponents of the new therapy had any notion of the remarkable extent to which it would grow over the ensuing years. Now, nearly five decades after, over one million patients worldwide with ESRD are being kept alive by chronic dialysis. The incidence and prevalence of treated ESRD had for many years been growing inexorably at rates of 4-8% per annum in the developed world (55, 56). It is worth considering why chronic dialysis has grown so dramatically. Clearly, the increasing wealth of nations over the past fifty years, and their consequent ability to pay for such an expensive therapy, is a large factor. Almost as important are the improvements in dialysis technology which have made the therapy simpler to perform, even in older, sicker patients who would not have been treated in the past. These two factors have greatly lowered the threshold for initiation of ESRD patients on chronic dialysis. Another factor, undoubtedly, is the growth that has occurred in the incidence of ESRD. However, some of the growth in rates of treated ESRD may simply represent the therapy being made available to patients who would not have received it in the past.

### Dialysis access use

Dialysis modality and dialysis access use varies widely across countries (27). Reported rates of incident ESRD across the globe show important trends; rates have slowed in some countries,

while rising or remaining stable in others. The United States, Taiwan, Japan, Turkey and Portugal continue to have some of the highest rates, at 369, 361, 288, 252 and 239 per million population in 2010 (27). Taiwan and Japan continued to report the highest rates of prevalent ESRD, at 2,584 and 2,260 per million population, respectively, in 2010. The next highest rate was reported by the United States, at 1,870, followed by Portugal at 1,590 per million population. Haemodialysis continues to be the most common mode of therapy worldwide, evidenced by data showing that, in over 70 percent of reporting countries, at least 80 percent of patients are on this mode of therapy (27).

### *Angioaccess for haemodialysis*

Autogenous fistula use is linked to patient characteristics, with the use of AVF versus an AVG being lower in patients who are elderly, female, have peripheral vascular disease, ischaemic cardiac disease, diabetes mellitus, obesity, are unable to walk or have less education (57). The surgeon's practice pattern also has an impact on the type of vascular access created. In new dialysis patients, early referral to a nephrologist and early patient education strongly predict a successful functioning permanent vascular access at dialysis initiation (57). According to the K/DOQI guidelines in 1997 (58), primary AVFs should be constructed in at least 50% of all new patients. Ultimately, 40% of prevalent patients should be using an AVF and <10% maintained on a catheter as their permanent chronic dialysis access. The 2006 revised K/DOQI guidelines (16) have set a goal ≥65% functional AVF in HD patients and have kept the goal for catheter use to <10%. The Fistula First Initiative set a new prevalence goal of 66% functional AVF in HD patients in 2009 (46).

Haemodialysis patients in Europe were 3-fold more likely to have an AVF in DOPPS I (60). In nearly half of the countries during DOPPS II, 50% of patients initiated dialysis with a catheter (55). This high catheter use was observed despite 60–79% of patients seeing a nephrologist >4 months before starting dialysis and 69–88% seeing a nephrologist >1 month before starting dialysis. For patients seen by a nephrologist <1 month before dialysis start, the catheter use varied from 50% to >90% in all countries. For patients having seen a nephrologist >4 months prior to end-stage renal disease onset, catheter use varied from 10% in Japan to >50% in Canada, the United States and the United Kingdom. As can be seen, despite the different published guidelines, there is still a very high proportion of patients starting HD with a catheter. Late referral to a nephrologic team, which

has been reported in many countries, could be one possible explanation for the high proportion of catheter use. Pre-dialysis care increases the likelihood of a permanent arteriovenous access at dialysis start (58). A recent analysis based upon data from DOPPS I, DOPPS II and DOPPS III (57) showed that the proportion of new patients starting HD with a permanent arteriovenous access was higher when patients were seen for a longer pre-dialysis period by a nephrologist. The mean proportion of catheter use in new patients was 77% and 36% for patients seen by a nephrologist <1 month and >4 months, respectively, before starting HD. The chance for a patient starting HD with a permanent arteriovenous access also decreased with longer delays before being seen by a surgeon and with delays between evaluation and surgery. Countries with a long median time for AVF creation were also the countries most reluctant to cannulate AVF early. In Canada, the United Kingdom and the United States, >90% of the facilities typically first cannulate AVF after 4 weeks, thus making the total time between referral and first AVF cannulation 2–3 months. In these countries, a patient can only start dialysis with a permanent arteriovenous access if seen by a nephrologist >3–4 months prior to dialysis initiation (57).

For prevalent patients, all countries except the United States met the standard of having >40% of patients dialysing via an AVF in DOPPS I and II, while some countries had more than twice this target level (57). Although the United Sates had a high proportion of graft use, it decreased by 29% between DOPPS I and III while AVF use increased to 47%. In Europe, AVF use decreased from 80% to 74% (60). The United States increase in AVF use coincides with a substantial change in vascular access preference within United States dialysis units as indicated by United States dialysis unit medical director responses (61). In April 2012, the incident and prevalent AVF use rate in the United Sates was 18% and 60.6%, respectively (46). The <10% goal of prevalent patients with a catheter was met by five out of seven countries of DOPPS I. In DOPPS II, 6 out of 11 study regions met or nearly met the <10% goal. Japan was the only country in DOPPS III to meet the goal. The increasing use of catheters for HD is a matter of concern all over the world. In Europe, proportion of prevalent patients with permanent catheters has been estimated to be as high as 25% (62). The increase in diabetes from 18% to 33%, and vascular disease from 22% to 34% in HD patients between DOPPS I and III probably led to higher proportions of patients at risk for the failure of AVF creation. Nevertheless, the increase in catheter use was impressive in the non-diabetic, non-elderly dialysis population and affected more females. The risk of having a catheter may reflect practices of resorting to a catheter when repeated permanent access use

has been unsuccessful. Some countries with a significant proportion of patients with catheters have a proportionally low use of AVGs (62).

### *Peritoneal dialysis access*

During the 1980s a rapid growth in the utilization of PD was observed. This rapid growth continued between 1990 and 1995, with annual global growth rates reaching 15% for the period 1991–1994 (63). At the end of 1997 the chronic PD population worldwide was estimated to be one hundred and fifteen thousand, representing 14% of global dialysis population (64). However, since then the growth in use of PD has been slower than the increase in the number of patients undergoing maintenance dialysis worldwide (65). At the end of 2004, one hundred and forty nine thousand patients were undergoing PD, representing 11% of the total dialysis population (i.e., 1,371,000). The reasons for this slow-down in the proportion of PD patients seem multifactorial. As the utilization of PD is declining, particularly among the elderly (66), and the elderly are the largest and fastest growing group of patients with chronic kidney disease, barriers to self-care PD may contribute. Also, the burden of unrealistic high solute clearance targets might have reinforced the notion of PD as an "inadequate" therapy for renal replacement (67). Finally, institutional changes in the delivery of dialysis therapy - e.g., proliferation of HD units and corporatization of dialysis care - are important contributors to this declining trend. The wide variations in the utilization of PD in different countries are striking (68). The proportion of patients on dialysis treated with PD varies from 2 to 4% in countries such as Chile, about 5 to 10% in France, Germany, and the United States, 20 to 30% in the Scandinavian countries, The Netherlands, Australia, and Canada, and >75% in Mexico and Hong Kong (67). In Portugal, in-center HD and peritoneal dialysis were used by 95 and 5 percent of patients, in 2011, respectively (registered by the Portuguese Society of Nephrology).

The disparity in the use of PD in different countries and different parts of the same country has stimulated tremendous interest in elucidating the factors that determine the choice of PD as the modality for renal replacement. A large number of factors impact upon this choice: (a) *Medical factors* - the presence of medical "contraindications" to PD is reported to be more frequent than that for maintenance HD (69); in a recent analysis from the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD) study, previous major abdominal surgery was the most common medical contraindication followed by cystic kidneys, poor lung function, chronic

inflammatory bowel disease, and poor cardiac condition; (b) *Psychosocial factors* - most patients deemed to have a social contraindication to PD were judged by the nephrologist to be incapable of performing the treatment by themselves; however, studies show that up to 70% of adults have neither medical nor social contraindications to either maintenance HD or chronic PD (70, 71); pre-dialysis care is associated with a greater probability of selection of PD (69, 72-74); however, if one accounts for the adequacy of education about dialysis modalities, delayed referral may not be as strong an impediment to the selection of home dialysis modalities; consistent with these observations, adequate pre-dialysis education is associated with a far higher probability of choosing home dialysis (75, 76); physician bias probably also plays an important role in the utilization of PD (77, 78); the nature of patient education is dependent on the physician bias, and in nonurgent situations the decisions of patients depend mostly on the information provided by their doctors; a study from the United States confirms the finding that the majority of patients are not presented with the choice of either chronic PD, home HD, or renal transplantation (70); (c) *Economic factors* –the effect of health care system policy and physician/facility reimbursement on the selection of dialysis modality may vary by the region of the world.

According to Twardowski (11), there are no epidemiologic data on the current use of peritoneal catheters type in the world. The last survey was carried out more than a decade ago, during the XIV$^{th}$ Annual Peritoneal Dialysis Conference in Orlando, Florida, on January 24, 1994 (79). The Tenckhoff catheter was the most popular, followed by Swan-neck catheters. The remaining catheters were used in smaller numbers. A vast majority of nephrologists remained convinced of the superiority of double-cuff catheters over single-cuff ones and the use of the former exceeded 70%.

## Dialysis access-related morbid-mortality

Dialysis access is associated with significant morbidity and mortality and it has been considered by some as the *Achilles' heel* of chronic dialysis.

Haemodialysis with long-term catheters compared with AVFs is associated with: (a) a relative risk of death that is twofold greater; (b) a relative risk of bacteraemia that is at least sevenfold greater; (c) increased rate of hospitalization; (d) a decreased likelihood of adequate dialysis; and (e) an increased number of vascular access procedures (16, 17). Therefore, ideally, all patients

with ESRD who choose HD would have an AVF ready for dialysis and avoid a central venous catheter, as the AVF comes closest to satisfying the criteria of the *ideal haemodialysis access*. The rate of AVF thrombosis is much less than that of AVGs and the number of events are only 14% to 33% of those observed in AVGs (59). Published combined infection rates of arteriovenous accesses infections are calculated to be 1% to 4% for AVFs and 11% to 20% for AVGs during their expected periods of use (79-80). Autogenous arteriovenous fistulae are associated with the lowest risk for bloodstream infection, compared to both AVGs and central venous catheters (0.2/1000 dialysis procedures; relative risk increases 2.5-fold with AVGs, 15.5-fold with tunneled cuffed catheters, and 22.5-fold with uncuffed catheters) (81).

Haemodialysis catheters present a conundrum. On one hand, catheters provide access that is immediately available; on the other hand, complications are high (82). Blood flow frequently is inadequate, thrombolytics frequently are required, and the infection rate is an order of magnitude higher than with AVFs or AVGs. As a result, long-term catheter use, without appropriate adjustments in treatment duration, can compromise dialysis adequacy. Compromise of dialysis adequacy is associated with increased morbidity and mortality (16). The most common complications of HD catheters are thrombosis and infection (83). Even with care, fewer than half the catheters placed as "long-term access" are in use a year after their placement and about a third are removed because they fail to deliver adequate blood flow (84). Although thrombotic occlusions leading to flow delivery problems are more common than infection, catheter-related infection has emerged as the primary barrier to long-term catheter use. Infection is the leading cause of catheter removal and morbidity in dialysis patients. Catheter infection usually requires replacement of the catheter in half the episodes despite antibiotic therapy (85). The most recent USRDS data (27) indicate that the rate of sepsis in HD patients continues high, and hospital admissions for vascular access infection rose steadily until 2005, but since have fallen 24% in 2010. In general, uncuffed catheters have a greater rate of infection, 3.8 to 6.6 episodes/1000 days, compared with tunneled cuffed catheters, with 1.6 to 5.5 episodes/1000 days (16). Catheter infection rates can be decreased to less than 1.5 episodes/1000 days by paying scrupulous attention to the published guidelines (16, 21). Finally, long-term catheter access is associated with a risk for central venous stenosis development, which can preclude the establishment of a permanent vascular access for HD. The K/DOQI guidelines (16) recommend that HD access complications should be as follows: thrombosis (AFV, <0.25 episodes/patient-year at risk; AVG,

< 0.5 episodes/patient-year at risk), infection (AVF, < 1% during the use-life of the access; AVG, <10% during the use-life of the access; tunneled catheter-related infection should be < 10% at 3 months and < 50% at 1 year ) and access patency (AVF, > 3 years; AVG, > 2 years). Patients should be educated on these issues and strongly encouraged to allow creation of an AVF for permanent access whenever possible.

Before the first dissemination of the K/DOQI recommendations on vascular access in 1997, many studies showed that practice patterns were contributing to patient morbidity and mortality. The failure of access was noted to be a major cause of morbidity for patients on HD therapy, with a number of reports indicating that a high percentage of hospitalizations for patients with ESRD were caused by vascular access complications (16). A study using data from the USRDS Morbidity and Mortality Study Wave 1 showed that patients receiving catheters and AVGs had greater mortality risk than patients dialyzed with AVFs (86). A number of subsequent epidemiological studies reaffirmed that greater use of AVF was associated with reduced morbidity and mortality (87-95). As an example, in a study of 616 incident HD patients, 66, 20, and 14 percent of patients were using a catheter, AVG and AVF, respectively (91). At six months, reported rates were 34, 40, and 26 percent. Compared with AVFs, the adjusted relative hazards of death were 1.5 for catheters (95% CI 1.0-2.2) and 1.2 for AVGs (95% CI 0.8-1.8). It has also been shown that incident use of central venous catheters as initial HD access has been associated with increased mortality, even after adjusting for timing of referral (91). Furthermore, conversion from a central venous catheter to an AVF after HD initiation is associated with increased survival (95). In this regard the K/DOQI guidelines (16) recommend that “Although central venous catheters can be used for long-term dialysis, they should be reserved for patients with comorbid conditions limiting life expectancy, those with systolic hypotension in whom attempts to create/maintain an arteriovenous access have met with failure, and those in whom all available sites for AVF or AVG have been exhausted or are not feasible”.

Infectious complications, particularly peritonitis, have long been the proverbial *Achilles heel* of PD and have long accounted for technique failure and catheter loss. Around 18% of the infection-related mortality in PD patients is the result of peritonitis. Although less than 4% of peritonitis episodes result in death, peritonitis is a “contributing factor” in 16% of deaths on PD. In addition, peritonitis remains a major cause of patients discontinuing PD and switching to HD (35). Although PD patients have the highest rate of admission for any infection (at 558 per

1000 patient years in 2010), yet this rate is 16 percent lower than the 663 seen in 1996 (27). The admission rate for peritonitis among these patients has been falling since the mid-1990s and rates of admission for a peritoneal catheter infection have declined 23 percent since 2000 (27). Among HD patients, admissions for vascular access infection rose steadily until 2005, and admissions for bacteraemia/sepsis remain highest for HD patients, at 116 per 1,000 patient years in 2010 (27). Refinements in connectology and use of the twin-bag systems have led to significant declines in the rates of peritonitis from touch contamination and have resulted in a 1-year catheter survival of over 80% (97). The skills of the surgeon or nephrologist involved in the implantation of the catheter and the dedication of the PD team involved in postoperative catheter care now seem to be the most important predictors of catheter survival and complications. With these advances, the peritonitis rates have declined from about 1.4 episodes per patient-year to 0.5 episodes per patient-year in many centers. International guidelines state that center's peritonitis rate should be no more than 1 episode every 18 months (0.67/year at risk) (35).

Comparisons between HD vascular accesses and PD catheter have been scarce in the literature. Aslam *et al.* (98) reported that patients who start dialysis on HD compared with those who start on PD have similar overall rates of infection. However, there were marked differences in both the type of infections and the risks during the first 90 days of dialysis among patients who were on these two modalities. Only HD patients had bacteraemia, and only PD patients had peritonitis. The risk for bacteraemia in HD patients was strikingly increased during the first 90 days of dialysis. The early risk for bacteraemia in HD patients was related to the use of HD catheters as the initial access. Oliver *et al.* (99) have recently demonstrated that patients who choose PD experienced a lower risk of invasive access interventions than patients who choose HD. Peritoneal dialysis patients experienced fewer interventions because PD catheters were more likely to be used, tended to have lower intervention rates during use and had similar patency to AVFs. Previous studies have found that the risk of primary failure of AVF ranges from 41 to 62% compared to 10 to 13% for PD catheters (100, 101). If a patient attempts a dialysis access and it fails then additional procedures are required to establish access. In other words, more interventions must be 'invested' into the HD population than the PD population to establish functional access, because AVF have higher primary failure rates than PD catheters. Finally, Perl *et al.* (102) recently identified the important influence of HD vascular access type on survival comparisons between incident HD and PD patients. Patients starting HD using a central venous

catheter had a higher risk of death in the first year compared with those who started PD, whereas there was no difference in survival between HD-AVF/AVG and PD patients. These relationships persisted over a 5-year follow-up with a small survival benefit in the HD-AVF/AVG group.

## The economics of dialysis

The delivery of a chronic and expensive therapy such as dialysis is a complex process in any society. Delivery models vary significantly from country to country but some broad generalizations can be made (103). Chronic dialysis is so expensive that few individuals anywhere can pay for it out of the pocket. Its delivery on any significant scale is, therefore, possible only in societies with well-developed medical insurance systems. The consequence is that no society has developed a large dialysis delivery system based purely on voluntary private insurance. A case in point is the United States, where dialysis treatment rates have been able to grow because of a landmark act of congress passed in 1972 (104). This act established ESRD as the only medical condition whose treatment was to be funded by Medicare, regardless of the age, income or wealth of the patient concerned. No medical condition, before or since, has been dealt within the United States in this manner. Such an approach was justified at the time by the high cost and particularly stark "life-and-death" nature of the treatment.

The framework of chronic dialysis therapy is composed of several parties, with particular roles and interests, namely, the payer, the facility, the dialysis manufacturing industry and the physician (103). The primary payer for chronic dialysis in most jurisdictions is the government, either directly through a public medical insurance system or indirectly through a government-regulated and sponsored "social" insurance system (105-107). The former is the case in the United States, the United Kingdom, Canada, Scandinavia, Italy, Spain and Portugal; the latter is the case in France, Germany, Belgium, The Netherlands and Japan. In the former the system is funded exclusively or predominantly out of general taxation revenues. In the second group of countries the dedicated insurance payments are made by employees, employers, and sometimes by governments, into compulsory medical insurance funds. These funds are typically also required to support the elderly, the indigent and those who are unable to work. The difference between these two systems in terms of the essential principle under which they operate is not as great as is sometimes implied. In practice, however, these two systems frequently differ in two very

important regards. One is the nature of the split between the payer (or "purchaser") on the one hand, and the facility and the physician on the other. In the public systems, the government that funds dialysis is ultimately the same payer that funds the hospitals that provide the dialysis. There is typically only one such dialysis provider in a given area; consequently, there is little or no competition and no meaningful independent negotiation between purchaser and provider. In contrast, in the second group of countries, the semi-independent social funds that pay for medical treatments such as dialysis for their members will typically have the ability to negotiate a deal with one of a number of separate private dialysis facilities in a given area. Portugal is a mix of the two models. While the government pays for 100% of dialysis, and is funded mainly from general taxation revenues, the Portuguese dialysis delivery system has a very clear purchaser-provider distinction with a multiplicity of facilities that are generally private and quite independent of government.

The economic nature of dialysis facilities is very variable, running the full spectrum from private and independent to government-owned (103, 105-107). In countries with predominantly public health-care systems, dialysis units are principally located in government-owned, "not-for-profit", public hospitals. This model is in place, for example, in Canada, the United Kingdom, Australia and Scandinavia. In contrast are jurisdictions where the bulk of dialysis takes place in privately owned facilities located in either private hospitals or, more often, in free-standing facilities. This model is widely used, for example, in the United States, Japan, France, Germany, Spain, Portugal and Latin America. On the one hand, there are those that are owned by a physician or small group of physicians; on the other hand there are those owned by major national or international dialysis companies. The latter are typically referred to as "dialysis chains". With the expansion of private dialysis, an unsolved controversy has developed over the relative merits of such units, as compared to the public ones (108-111).

Worldwide, there is a trend in recent years for private ownership of dialysis facilities to shift from ownership by physicians and small-scale local operators to ownership by these large dialysis chains (103). The rationale here is that private facilities, especially those belonging to dialysis chains, may be able to provide dialysis more cost-effectively than public ones because of economics of scale, vertical integration, greater expertise, etc. Typically, this involves efforts to estimate the true cost of the various dialysis modalities (103). In Portugal, HD is almost exclusively (~90%) provided by dialysis units run by two "dialysis chains" - Fresenius Medical

Care and Diaverum. Peritoneal dialysis is provided by public hospitals and university centres. In 2008, concerned with budget constraints and the exponential annual rise in dialysis costs, the Portuguese health authorities changed the reimbursement system for both HD and PD treatment to a per capita system that included equipment costs, staff, patient follow-up and checkups, consumable items, reverse-osmosis water, regular laboratory tests, radiology and all medication for the treatment of anaemia, bone mineral disease, nutrition, cardiovascular complications and in-dialysis I.V. antibiotics. The reimbursement/patient/week was set by law with a similar budget for both HD and PD modalities. This package did not include vascular and PD access-related procedures, hospitalizations or patient transportation.

The dialysis industry could once have been easily classified into corporations that manufactured dialysis equipment and supplies and those owned or managed dialysis facilities. However, the past decade has seen consolidation and vertical integration in the dialysis industry, with the result that a number of major international companies now both own facilities and manufacture equipment for use in these facilities. Internationally, the three main players in the dialysis industry are Baxter Healthcare, Fresenius Medical Care and Gambro. All of these were initially involved only in manufacturing dialysis supplies and equipment, but all are now involved to varying degrees in facility ownership and management (103). Baxter Healthcare is a large publicly traded United States corporation with major involvement in production of intravenous solutions and blood products (112). Baxter was founded in 1931 and first produced an artificial kidney machine in 1956. For the past 25 years Baxter has been particularly identified with PD and, in most countries, is the market leader for this modality. Fresenius was initially a German pharmaceutical company that, since the 1960s, has had as its predominant activity the manufacturing of HD machines and dialyzers (113). In 1996 it acquired the largest United States dialysis chain, National Medical Care that had led to the formation of Fresenius Medical Care. Gambro is a Swedish company that has been involved in HD since the mid-1960s (114). In much of Europe and the developing world Gambro has been the dominant force in the provision of HD machines and dialyzers. The renal care history of Diaverum started with the founding of the Gambro Healthcare Division in 1991 (115). Shortly after the divestiture of the Gambro Healthcare Division on July 2007, the name Diaverum was adopted and launched globally while Gambro focused mainly on extracorporeal treatments.

Finally, the physician has a role in dialysis delivery that can, from an economic point of view,

follow one of two broad patterns (103). Most commonly the physician acts as an independent professional and is paid on a "fee-for-service" basis for delivering medical aspects of dialysis care for ESRD patients. Such a system, for example predominates in North America, Japan, Germany and France. In the alternative arrangement the physician is a salaried employee of the payer or of the facility providing the dialysis. This is seen in the United Kingdom, Australia and Scandinavia. The two systems can coexist; thus, in Portugal, nephrologists receive a salary for their general public hospital activities. However, the same individuals may also receive "fee-for-service" income for dialysis provided outside their major public hospital base.

## The costs of dialysis

When estimating dialysis costs, one has to determine whose costs one is looking at. There are several perspectives worth considering – the government, the dialysis facility or provider, the physician and the dialysis manufacturing industry. Each of these perspectives is worth studying in its own right, as they may have different and even conflicting influences on rates of dialysis and on relative use of the different modalities, including renal transplantation. In general, the costs to payers, providers and physicians are most likely to influence practice patterns such as modality distribution (103). A key point to remember is that charges are not equal to actual costs. The former are much easier to calculate but they represent at best an estimate of the true costs to particular payers. To estimate dialysis costs it is essential to indentify the components of the therapy. Generally, costs can be divided into direct medical, direct non-medical and indirect categories (116). Direct costs are the best recognized and include staffing costs, costs of material, radiology, laboratory costs and medications. Direct costs should also include those of hospitalizations and outpatient consultations by other specialties. In contrast, direct non-medical costs are sometimes harder to quantify as they include facilities utilities, building costs and other overheads. Most ESRD cost estimates do not take into account indirect costs, such as loss of productivity, patient's inability to work and the disruption of the work schedule to their family members.

The cost of treating patients with chronic kidney disease who ultimately progress to ESRD begins to increase in the 6 months before dialysis initiation, peaks in the first month of dialysis, and generally reaches a plateau by month 6 of dialysis (116). One reason for this is that mortality

is high during the first 6 months of dialysis, and patient treatment is more expensive in the period immediately prior to a terminal event (117). Also, start-up costs occur with all dialysis modalities and result in higher costs for the first year of dialysis compared to subsequent years. Start-up costs include surgical implantation of an access. A peritoneal catheter must be inserted for PD and a vascular access must be established for HD. Finally, start-up costs for PD include patient training that also contribute to the cost of modality. Haemodialysis cost is driven largely by the fixed costs of facility space and staff. Haemodialysis machines typically cost ~$18,000 to $30,000 each, but the machines have a 5- to 10-year life cycle, and, in a weekly schedule, three to six patients can be treated on one machine. The cost of dialyzers for HD ranges from $1,000 to $5,000 per year (103). Other items that factor into the cost of HD are additional facility costs such as maintenance and utilities, and the costs of transportation to and from the HD facility. In contrast, the economics of PD are driven primarily by variable, or "disposable", costs, such as the costs of solutions and dialysis tubing. A review of the literature determined that the cost of PD materials ranges from $5000 to $25 000 annually (103). Additional costs associated with dialysis are physician fees, medications, laboratory and other diagnostic investigations, hospitalizations and dialysis access care.

It is difficult to estimate the resources committed to chronic dialysis worldwide as costs vary markedly from country to country. The last USRDS report (27) showed that costs for ESRD increased 8.0 percent, to $33 billion, accounting for 6.3 percent of the Medicare budget. Total Medicare expenditures for PD patients rose 7.8 percent in 2010, compared to increases of 5.8 percent for HD; costs reached $23.6 billion for HD and $1.28 for PD. Per person per year Medicare ESRD costs rose just 1.4 and 1.7 percent for HD and PD in 2010, to $87,561 and $66,751, respectively. In 2010, 38 percent of Medicare's ESRD dollars were spent on inpatient services, 34 percent on outpatient care, 21 percent on physician/supplier costs, and 7.2 percent on prescription drugs. In 2008, per person per year total costs were greatest for patients with a catheter or AVG, at $90,110 and $79,337, respectively (118). Costs for patients with an AVF were 28 and 18 percent lower, respectively, at $64,701. Per person per year costs for vascular access events were highest for patients with an AVG or a catheter, reaching $8,683 and $6,402. Costs for patients with an AVF in contrast, were $3,480 - 60 percent lower than those for AVG patients. Costs raised 7 to17 percent for HD patients, but fell nearly 32 percent for those with a PD catheter. In Europe, although dialysis patients make up less than 0.1% of the population, their dialysis

treatment accounts for around one to two percent of total healthcare costs (105). From 1990 to 2020, treatment costs for the global maintenance dialysis population are expected to rise from less than $200 billion to $1.1 trillion (56).

A North American literature review concluded that PD is less expensive than HD and that the difference in cost is dramatic when the PD program is relatively large and well run (103, 119-122). Annual costs for HD patients ranged from ~$48,000 to ~$69,000, while annual costs for PD patients ranged from ~$34,000 to ~$47,000. The cost ratio of HD to PD varied from 1.22 to 1.52 (103). In general, reports from Western Europe are in agreement with the North American findings. In-center HD has, on average, about twice the cost of continuous ambulatory PD (103, 116, 123). The bulk of the cost comparison studies done in Europe have come from France, Italy, Spain, the United Kingdom and Scandinavia (124-133). In France, the estimated annual costs per-patient of in-centre HD, home-HD and PD were €81,449, €49,911 and €49,953, respectively (126). A recent cost-analysis from the United Kingdom showed that the most efficient modalities were automated PD and continuous ambulatory PD, with mean annual costs per-patient of £21,655 and £15,570, respectively. The mean annual costs of in-centre HD (satellite unite) and home-HD were £32,669 and £20,764, respectively (129). Recently, Villa *et al*. (131), based on a review of data sources, estimated that annual dialysis costs per patient in 2010 in Spain were €37,968 for HD and €25,826 for PD. Salonen *et al*. (133) showed that, compared with HD, continuous ambulatory PD may be associated with lower costs, yet the absolute difference was not striking (annual costs were $54,140 in the HD group and $45,262 in the PD group). A systematic literature review found that HD is a more expensive dialysis modality, in comparison with PD, in developed regions of the world. When total direct therapy care expenses of dialysis patients are considered, PD is a lower cost modality than non-home HD. The cost continuum best supported is that expense to payers for dialysis therapy declines in the following order: in-center HD, satellite-HD, and finally, lowest are the home-care modalities, continuous ambulatory PD and home HD (123). Recently, Komenda *et al*. (134), based on a systematic review of available costing literature from the United Kingdom, Canada and Australia, reported that home HD was less expensive than in-center HD. Over time and depending on location, home HD would save payers between $7612 and $12,403 over the first year of in-center HD. Decreased staffing costs coupled with lower facility overhead and medication costs drove this cost differential.

## End-stage renal disease and dialysis modality selection

Economic factors may influence ESRD incidence rates and dialysis modality selection (103, 105, 106, 135-140). End-stage renal disease treatment rates have been a politically controversial issue in recent decades. They are often used as a broad measure of the relative effectiveness of the healthcare systems of different countries. The primary determinant of incidence of treated ESRD is often said to be a nation's wealth. However, other major factor to consider is the dialysis delivery system of the country. The highest recorded incidence rates of treated ESRD at present are seen in the United States, Taiwan, Japan, Turkey and Portugal (27). Canada, Hong Kong, Brazil, Argentina, and many Western Europe countries such as France, Greece, Germany, Italy and Belgium, have incidence rates between 150-200 per million population (27). The next levels of countries are those with acceptance rates in the 80-130 per million population range. These include Finland, Denmark, Norway, Sweden, United Kingdom, Australia and New Zealand, Spain and The Netherlands. It remains controversial as to how much of the discrepancy between these countries represents a truly lower incidence of ESRD as distinct from an unmet need. Perhaps, the key to this controversial issue lies in nation's dialysis delivery systems. As previously stated, health-care systems can be roughly divided into two broad categories or models: those with taxation-based funding and public provision and those with predominantly private insurance-based funding and private provision. However, when applied to dialysis delivery systems, this classification breaks down as no successful system has been based on private insurance alone. Consequently, the specific factor in a dialysis delivery system that has the most influence on incidence rates is not the nature of the medical insurance system per se rather the existence of private providers with a consequent clear purchaser-provider split, whereby the government pays and private enterprise provides (103,105,106). If nations are divided on the basis of these factors there is a relatively clear separation between high and low rate countries (103,105,106). Those with predominantly public provision (e.g., Scandinavia, United Kingdom, Canada, Australia) have the lowest ESRD incident rates. The process through which private provision results in higher treatment rates likely reflects a clearly profit incentive operating in such systems. Nowadays, an additional factor is that some of these chains are also manufacturers of dialysis machines and disposables and so benefit from the guaranteed market they may have for their own products (103).

The widespread variation in HD/PD utilization between countries is well recognized but

must appear strange to those not familiar with the world of ESRD. Within the European Union, countries of similar wealth have very different levels of PD use. Sweden, The Netherlands, and the United Kingdom all have rates of over 25%, while the corresponding figure for France is less than 10% and that for Germany fewer than 5%. In North America, over 20% of Canadian dialysis patients receive PD but the figure for the United States is barely 8%. Similar discrepancies are seen in Asia, where PD use varies from 75% in Hong Kong to less than 5% in similarly affluent Japan; in Latin America, Mexico is at 75% but Chile is under 5% (27). It is no secret that economic rather than medical factors drive these differences (135-140). However, when asked in surveys, physicians respond that financial considerations are not among the primary considerations used in guiding patients to a particular modality (138-140). Reimbursement structure has been called "the ultimate controlling force in the establishment and maintenance of home dialysis" (116). First, it is clear from the above examples that national wealth is not the factor; rather it is the economic structure of the nation's health-care system and, in particular, the nature of the dialysis providers. Countries with predominantly public dialysis providers, such as government-run hospitals, have much higher PD use than those with mainly private providers, such as units owned by physicians or by dialysis chains (103,105,106). The reason that public provider countries such the United Kingdom, Canada, New Zealand, and Hong Kong, use more PD is, of course, that the modality is less expensive and, in these countries, the state is in a position to use its "monopoly" to limit expansion of HD capacity, and so constrain ESRD expenditure.

A matter of greater complexity already raised by Blake (135) is "why, if PD is less expensive, do facilities in private provider countries not follow the same logic and generate greater savings or profit by using more PD?" As the author has pointed out, the underlying principle is that the economic drivers of modality selection in private provider countries are determined much more by the local facility economics than by the global costs that influence governments. First, it can be said that once an HD unit is in place there is a strong economic pressure to maximize its efficiency by operating it at or close to full capacity. Second, the profitability of dialysis depends on reimbursement as well as costs. Peritoneal dialysis may cost less but the payer may reimburse PD at a correspondingly lower level (141). A third factor relates to the size of the unit. Small private providers often do not perceive that they have sufficient potential PD candidates to justify putting in place the infrastructure required to realize the efficiencies and cost savings of PD. Recently, an Editorial comment titled "Why less success of the peritoneal dialysis programmes

in Europe?" by van Biesen *et al.* (142), stressed out that although the success of PD in Hong Kong was very impressive, patient free choice does not really exist in that programme. Consequently, we would not advocate that such a system be copied in Europe, as free patient choice should be the cornerstone of integrated care. A requirement for facilities to make PD available and to show evidence that a reasonable proportion of patients from a given referral base are actually utilizing it would seem a desirable requirement before a license for expansion of HD capacity is granted. Removal of overt economic disincentives by leveling out facility reimbursement and by equalizing physician payments for the two modalities is also an increasingly popular approach. Tying the level of payments for HD to the percentage of patients treated with PD is another possible strategy. Some mix of these approaches is necessary if patients in private provider countries are to have free modality choice and if a more cost-effective approach to treatment of ESRD is to be achieved (143). Among some patients it may be optimal to utilize both HD and PD in a way that provides the advantages of each modality, but without the disadvantages. An optimal strategy, for example, may be an integrated care approach in which incident dialysis patients initially undergo PD, with transfer to HD once complications ensue with PD. This is based in part on the hypothesis that, principally via its ability to preserve residual renal function, PD provides significant benefits as an initial modality (144-147). Other benefits may include preservation of vascular access and perhaps better survival during the first few years of dialysis (144). According to van Biesen *et al.* (143), "We will have to search for an "optimal" modality selection strategy for Europe, and from the above it is clear that political decisions will play a major role in this process".

Economic issues can be quite different in the developing world (103, 105-107, 116, 123). In these settings, the staff costs of HD are relatively less and the price of PD solutions relatively greater. The result is that PD may lose its cost advantage over HD. Mexico is unique in the developing world in that the utilization of PD is approximately 75%. An important reason for the higher utilization of PD in Mexico is that it has been the modality with the best financial support from the social security system and the public health institutions (148). So, paradoxically, in wealthier countries PD is globally less expensive but often underutilized because local facility economics introduce conflicting economic disincentives, and in poorer countries it is often underutilized because it is sometimes globally more expensive. According to Blake, "The economics are truly complex" (135).

# Chapter 2

## *Monitoring dialysis arteriovenous fistulae: it's in our hands*

Coentrão L, Turmel-Rodrigues L.

*J Vasc Access* 2013 Apr 18 [Epub ahead of print]. PMID: 23599144.

J Vasc Access 2013; 00 (00): 000-000
DOI: 10.5301/jva.5000141

REVIEW

# Monitoring dialysis arteriovenous fistulae: it's in our hands

**Luis Coentrão[1], Luc Turmel-Rodrigues[2]**

[1] Nephrology Research and Development Unit, Faculty of Medicine, University of Porto, Sao Joao Hospital Center Porto - Portugal
[2] Department of Cardiovascular Radiology, Clinique St-Gatien, Tours, France

**ABSTRACT**

**Vascular access problems are a daily occurrence in hemodialysis units. Loss of patency of the vascular access limits hemodialysis delivery and may result in underdialysis that leads to increased morbidity and mortality. Despite the known superiority of autogenous fistulae over grafts, autogenous fistulae also suffer from frequent development of stenosis and subsequent thrombosis. International guidelines recommend programmes for detection of stenosis and consequent correction in an attempt to reduce the rate of thrombosis. Physical examination of autogenous fistulae has recently been revisited as an important element in the assessment of stenotic lesions. Prospective observational studies have consistently demonstrated that physical examination performed by trained physicians is an accurate method for the diagnosis of fistula stenosis and, therefore, should be part of all surveillance protocols of the vascular access. However, to optimize hemodialysis access surveillance, hemodialysis practitioners may need to improve their skills in performing physical examination. The purpose of this article is to review the basics and drawbacks of physical examination for dialysis arteriovenous fistulae and to provide the reader with its diagnostic accuracy in the detection of arteriovenous fistula dysfunction, based on current published literature.**

**Key words: Arteriovenous fistulae, Dialysis, Physical examination, Vascular access**

Accepted: January 03, 2013

## INTRODUCTION

Vascular access function and patency are essential for optimal management of hemodialysis (HD) patients. Loss of patency of the vascular access limits HD delivery and may result in underdialysis that leads to increased morbidity and mortality (1-3). In both autogenous arteriovenous fistulae (AVFs) and arteriovenous grafts (AVGs), stenosis and thrombosis are the leading causes of loss of vascular access patency (1-3). Once matured, AVF provides the best access for longevity and lowest association with morbidity and mortality (1-3). Because of that, guidelines from different countries strongly recommend AVF use (1-3). In Europe, Australia and Japan, AVF is the most prevalent vascular access in HD patients (4). As the result of recommendations of the Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines (1), AVF prevalence has increased in the United States in the last decade (5). Despite this known superiority over AVGs, AVFs also suffer from development of stenosis and thrombosis. Although hard evidence is lacking from prospective studies demonstrating higher AVF long-term survival within quality improvement programs based on vascular access monitoring and surveillance (6-10), international guidelines (1-3) recommend programmes for detection of stenosis and correction in an attempt to reduce the rate of thrombosis. Furthermore, there have been no large-scale trials to determine whether correction of only "hemodynamically" significant lesions is superior to correction of all stenoses greater than 50%.

The basic tenet for vascular access monitoring and surveillance is that stenoses develop over variable intervals in the vast majority of vascular accesses and, if detected and corrected, underdialysis can be minimized or avoided and the rate of thrombosis can be reduced (1). The K/DOQI guidelines (1) have settled the following concepts for the detection of vascular access dysfunction: a) *monitoring* refers to the examination and assessment of the vascular access by means of physical examination (…) and; b) *surveillance* refers to the periodic assessment of the vascular access by using tests that may involve special instrumentation (…). It is important to emphasize that *surveillance* and *monitoring* are complementary. Several diagnostic procedures have been recommended for vascular access surveillance, including duplex-ultrasound, blood flow, intra-access static pressure and access

recirculation (1, 2). However, these procedures are time consuming and have a cost. Recently, Bonforte et al (11) analyzed the results of an application of a new zero-cost screening test, called "QB stress test", created to select, together with clinical assessment, the group of low-flow AVFs to refer to more detailed and specific study techniques. The authors demonstrated that this test is simple, low-cost, not operator-dependent and could be a useful tool to identify the group of patients with malfunctioning AVFs, with stenosis located specifically in the inflow tract. Physical examination (PE) of AVFs performed by trained physicians has recently been revisited as an important element in the assessment of stenotic lesions (12-17). In addition, PE is a reliable method to perform several other diagnoses such as, thrombosis, infection, skin necrosis and vascular steal syndrome. It must be performed not only in those patients on hemodialysis but also in those with chronic kidney disease (CKD) stage 4-5 in whom an AVF has been created in preparation for dialysis (18).

The purpose of this article is to review the basics and drawbacks of PE for dialysis AVFs and to provide the reader with its diagnostic accuracy in the detection of AVF dysfunction, based on current published literature.

## BASIC PHYSICS

Normal hemodynamics and the effects of stenosis on hemodynamics of the vascular access have been well reported in the K/DOQI guidelines (1) and concise textbooks (19, 20). Knowledge on the basic physics of the vascular access is a relevant issue for clinicians since the clinical signs suggestive of access dysfunction are the consequence of abnormal hemodynamics of the vascular access.

Flow in the access is directly related to the patient's blood pressure and inversely proportional to the resistance of the access flow circuit. When the blood flows through the access, the energy of the arterial inflow runs into a lower resistance system. The blood pressure drop causes vibration of the tissues, creating a palpable thrill. Flow can be assessed by palpation of the thrill along the entire circuit. Similarly, abnormal increase in pressure can be assessed by noting water-hammer pulsatility (21).

The driving force for access flow is the pressure gradient between the feeding artery and the right atrium (1, 20). The major determinant of access flow is the capacity of the artery and of the arterialized vein to enlarge, which is dependent on their general healthy condition. Therefore, access flow rates of AVGs are limited by the flat size of grafts whereas AVFs may develop much higher flow rates because of the capacity of enlargement of healthy veins. The rate of maturation and the pressure profile also differ in the two access types (1). Grafts attain their maximum flow rate in a period of days to weeks, as opposed to AVFs, which may require weeks to months to mature. The pressure profile in AVGs progressively decreases along the length of the graft whereas, in AVFs, the arterial pressure is dissipated within the first few centimeters of the arterialized vein (except in cases of hyper flow fistulas). Vascular resistance of AVFs is lower than in AVGs, mainly because of the vasoactive properties associated with an intact venous endothelium and in part because of the potential multiple parallel venous pathways returning blood to the central venous system. As a consequence, AVGs work with higher intra-access pressure to maintain flows of 1 L/min or more, compared to AVFs. In other words, patency of AVGs depends on higher flow rates than AVFs (20).

The ideal vascular access flow is the one necessary to provide long-term access patency with no steal syndrome or heart consequence. Therefore, the AVF's flow should be considered in relation to cardiac output, with an assessment of the ratio access flow/cardiac output: a ratio >20% should lead to suspicion of high flow. For AVFs, values of 600 to 800 mL per minute have been proposed as the "ideal" access flow since it is sufficient to provide AVF long-term patency with an access flow/cardiac output ratio <20%. Turbulence associated with high volumes, typically from 500 to 1500 mL per minute, generates the thrill we feel. It is assumed that AVFs flows >2000 mL per minute are susceptible to increased cardiac workload and further development of heart failure (19).

The development of stenoses results in a reduction in access flow rate in both AVGs and AVFs (20). However, the effect on intra-access pressure differs according to access type and site of stenosis. In AVGs, an outflow stenosis will increase the pressure in all locations upstream from the stenosis whereas, in AVFs, the pressure profile will depend on the presence/absence of venous tributaries. Conversely, the presence of an inflow stenosis in AVGs will decrease all pressures downstream of the stenosis whereas, in AVFs, intra-access pressure tends to remain unchanged because of a basically low pressure profile.

In summary, vascular access hemodynamics provide the rationale for observational clinical studies (1, 22-24) showing that: (a) PE findings differ between AVFs and AVGs; (b) AVFs can maintain long-term patency at access flows lower than those in AVGs; (c) access recirculation may develop in half of the AVFs that require intervention because of very low flow, whereas in AVGs it is a very late indicator of access dysfunction.

## PHYSICAL EXAMINATION: BASICS AND DRAWBACKS

### *Basics*

The standards of PE of the dialysis vascular access have been reported in detail by Beathard (25-27). In this article, the basic PE technique for dialysis AVF will be briefly reviewed, while depicting some pitfalls com-

monly presented to HD practitioners in daily clinical practice.

Physical examination of the AVF implies the use of inspection, palpation and auscultation. Thrill and pulse abnormalities felt throughout the entire fistula tract are used as the main PE tools for the diagnosis of AVF dysfunction. In addition, the patient's arm, chest, neck and face should be assessed for the presence of swelling or collateral veins. Patients should be asked about symptoms related to the AVF. Normally, the patient with a functioning AVF should be without complaints (namely pain at rest, paresthesia or weakness). At inspection, no arm or face edema or collateral veins should be observed. The hand should be well perfused. The AVF has a soft appearance and the entire structure is easily compressed. A palpable continuous thrill is felt through the first centimeters of the vein, with higher intensity at the anastomosis. It has been suggested that a palpable thrill at the arterial, middle, and venous segments of the access predicts flows greater than 450 mL per minute and if present in the axilla may correlate with a flow of at least 500 mL per minute (28, 29). A low pitch, continuous bruit is auscultated throughout the venous tract. When the extremity is elevated, the entire arterialized vein will generally collapse (arm elevation test). When the AVF is compressed, the portion of the vein upstream from the occluding finger demonstrates augmentation of pulse (pulse augmentation test). This pulse augmentation is nevertheless weakened when tributaries leave the main vein between the anastomosis and the compressed area. Under normal circumstances, this simple examination should take no more than three minutes.

Fistulae that never develop adequately for use or those that fail within the first three months of use are classified as early failures. The most common cause of early fistula failure is the presence of a juxta-anastomotic venous stenosis. This lesion can be easily diagnosed by palpation of the anastomosis and outflow vein. A water-hammer pulse is felt at the anastomosis and the thrill is present only in systole. As one moves up the vein the pulse goes away and the vein is poorly developed. The stenosis itself can frequently be felt as a tough cord or an abrupt diminution in the size of the vein. However, it may be impossible to differentiate a stenosis of the anastomosis itself from a stenosis of the feeding artery.

Once the AVF is functional, the most common problems are venous stenosis and thrombosis. Other less frequent complications diagnosed by PE are hand ischemia, aneurysm formation, skin alterations and infection. Venous stenosis is such a common event that many HD practitioners do not recognize these changes as being abnormal. Inflow segment is defined as the feeding artery, anastomosis and the juxta-anastomotic area (first few centimeters of the arterialized vein) upstream from the "arterial" needling site. Outflow segment comprises the body of the vein, the axillary, subclavian and central veins. Body of the fistula is considered to be the cannulation segment extending downstream from the anastomotic area. The diagnostic elements of PE used in the assessment of an inflow stenosis, outflow stenosis, coexisting inflow-outflow stenosis and thrombosis are presented in Table I.

Fistula thrombosis is a clinical diagnosis characterized by undetectable flow by physical examination. Fistula infection and thrombosis (phlebitis) sometimes share similar clinical findings (erythema, warmth, swelling and pain) but require distinct therapeutic approaches. The differential diagnosis between these two entities is therefore essential. Physical examination findings of fluctuation and purulent discharge are diagnostic of the very rare true AVF infection. Conversely, the absence of aspiration of blood or the removal of clots after venous cannulation is highly suggestive of AVF thrombosis.

Distal hypoperfusion ischemic syndrome (30) occurs when the arterial supply to the hand has become insufficient because of pre-existing arterial lesions rendered symptomatic by the blood derived from the feeding artery through the fistula or because of excessive fistula blood flow. In most patients the enlargement of the feeding arteries and the development of collaterals after AVF creation are sufficient to maintain sufficient perfusion to the hand. Physical findings are quite variable; in most instances,

**TABLE I -** DIAGNOSTIC ELEMENTS OF THE PHYSICAL EXAMINATION USED IN THE ASSESSMENT OF AUTOGENOUS ARTERIOVENOUS FISTULA DYSFUNCTION

| | **Thrill** | **Pulse** | **Arm elevation test** | **Pulse augmentation test** |
|---|---|---|---|---|
| Inflow stenosis | Weak, systolic | Weak | Excessive collapse | Weak |
| Outflow stenosis | | | | |
| Body of fistula | Systolic | Strong | No partial vein collapse | n.a. |
| Cephalic arch stenosis | Systolic | Very strong | No partial vein collapse | n.a. |
| Central vein stenosis | Systolic or normal | Strong or normal | No or modest partial vein collapse* | n.a. |
| Coexisting inflow-outflow stenoses | Weak, systolic | Normal | No or modest partial vein collapse | Weak |

n.a., not applicable.
*Edema of the arm and shoulder; breast, supraclavicular, neck, and face swelling may be present as well in brachial-cephalic fistulae only.

it is helpful to compare the affected side to the opposite normal side. The affected hand may be pale or cyanotic in appearance; it feels cold and has a diminished ulnar and/or radial pulse. In severe cases, the patient complains of paresthesia, weakness or pain at rest. Evidence of ischemic changes in the skin may be present.

When the patient complains of severe weakness of the hand and rest pain immediately after fistula creation, while the hand appears warm and well perfused, the diagnosis of ischemic monomelic neuropathy should be recognized since urgent fistula ligation is warranted. This is a typical complication of elbow accesses in diabetic patients.

Aneurysm formation may indicate high chronic intra-access pressures that require study and decompression via outflow stenosis angioplasty. More often, they result from slow chronic enlargement secondary to thinning of skin by repeated needling on the same site. Assessing the pulsatility of the access on PE will help sort out the different scenarios.

## *Drawbacks*

### *Vein collaterals*

The presence of cephalic vein side branches are considered by some experts as the second most common cause of early fistula failure (referred to as accessory veins) (26), while others consider them a consequence of the presence of a venous stenosis in the ouflow tract (referred to as vein collaterals) (31). Regardless of the cause, these AVFs behave weirdly in the hands of an inexperience examiner. The vast majority of these AVFs are forearm fistulae. Vein collaterals can be identified easily through PE. Frequently, they are visible, while the main branch (usually the cephalic vein) is not easily recognized. When the extremity is elevated, the entire fistula will partially collapse. During the pulse augmentation test, the thrill does not disappears and the pulse does not increase its intensity (because of the presence of drainage through vein collaterals). In this particular case, the aim of the PE is to: (a) identify the main drainage vein; (b) identify the venous stenosis, to further guide the endovascular approach.

### *High flow fistulae*

High flow fistulae share some of the PE findings of AVFs with outflow stenosis. The pulse is strong and the vein may not collapse during the arm elevation test. The body of the AVF is large and may present aneurismal formations. This is even more evident in high flow AVFs with non-significant outflow stenosis. One way to solve this problem is to assess the AVF thrill in detail: continuous, systolo-diastolic thrill, in high flow AVF *versus* discontinuous, systolic thrill, in AVFs with outflow lesions. The differential diagnosis is relevant since the therapeutic approaches of these AVFs are distinct.

### *Coexistent venous outlet stenoses*

The coexistence of two or more venous stenoses may preclude the development of clinical signs suggestive of the presence of the more central lesion. The most typical situation is the coexistence of stenoses in the body of the fistula and in a central vein – the more peripheral stenosis may prevent downstream flow to the degree that the central venous stenosis symptoms might be masked. The diagnosis of the central vein lesion is most commonly performed during angiography, raising some doubts regarding the best therapeutic approach.

### *Side-to-side upper-arm fistulae*

Physical examination of side-to-side upper-arm fistulae (Gracz fistula) is a clinical challenge because the presence of venous drainage through vein collaterals (e.g. cephalic, basilic and deep veins) may preclude the development of characteristic PE signs of a stenosis. Usually, it is necessary to manually occlude one vein in order to detect the presence of an outflow stenosis on the other.

### *Transposed brachio-basilic fistulae*

Occasionally, in upper-arm AVFs, there is spontaneous or deliberated occlusion of side branches (as with transposition) and, as a consequence, outflow lesions produce a pressure profile and PE findings very similar to that of AVGs. The AVF turns out to be highly pulsatile and exceedingly thrombogenic.

## DIAGNOSTIC ACCURACY OF PHYSICAL EXAMINATION

Citing Beathard (25) in one of his seminal papers "In this search for the "Holy Grail," the oldest and most time-honored investigative tool available to the diagnostician has been largely ignored: the laying on of hands, i.e., physical examination." In the last decade, PE re-emerged as an important element in the assessment of stenotic lesions; its accuracy in the assessment of stenosis within an AVF when compared with the gold standard (angiography or Doppler ultrasound) has been recently assessed (Tab. II) (12-17). However, it is essential to point out that a dysfunctional vascular access is not only defined by the presence of a significant stenosis (reduction greater than 50% of normal vessel diameter) and that it should not be repaired merely because they are present. Stenosis must be accompanied by a hemodynamic or clinical abnormality. International guidelines (1-3) do not recommend the use of angiography for detecting anatomic stenosis alone, without concomitant measurement of access flow, venous pressure, recirculation, or other physiologic parameters. In other words, when PE suggests the presence of a stenosis, there is no indication

for angiography and treatment unless the stenosis has clinical consequences (e.g. underdialysis, recirculation, increased compression times, difficulties in cannulation) or threatens access patency by excessive decrease in flow rate. For example, moderate arm edema and presence of neck collaterals indicate the likely presence of a central vein stenosis but this stenosis should be treated only in cases of major clinical impairment (32).

To the best of our knowledge, Asif et al (12) was one of the first authors to determine the PE accuracy in the assessment of stenosis within an AVF when compared with the gold standard (angiography). A total of 142 consecutive patients who had AVF dysfunction and were referred for angioplasty were included in this analysis. A complete PE was performed by an interventional nephrologist in all of the patients before any angiography was undertaken. The following locations of the stenoses were determined by PE and angiography: outflow tract, inflow segment, coexisting inflow-outflow stenosis, body of fistula and central veins. There was a moderate-to-strong agreement between PE and angiography in the diagnosis of outflow and inflow stenosis. The findings of this study demonstrated that PE can be an important tool in the diagnosis and localization of an AVF stenosis. A similar study was published by Leon et al (13). The aim of this study was to examine the accuracy of PE of AVF stenosis by a renal fellow in training and to compare them with those of an interventional nephrologist. The findings of this study demonstrated that a renal fellow could be trained in PE and accurately detect and localize stenoses in a vast majority of AVFs with comparable results favorably to those obtained by a nephrologist with expertise in PE. More recently, the PE findings obtained by nephrologists without specific training on fistula PE were compared to those from a nephrology resident trained in vascular access PE (17). Angiography was used as the gold standard examination. A total of 177 consecutive patients who had AVF dysfunction and were referred for angioplasty were included in this analysis. The main findings of this study were: PE performed by the trained nephrology resident strongly agreed with angiography in the detection of AVF inflow and outflow stenosis, whereas there was a moderate agreement between the general nephrologists' PE and angiography in the detection of the same lesions. It is important to emphasize that, in both Asif et al (12) and Leon et al (13) studies, the investigators divided the outflow tract into three different segments: body of the fistula, outflow and central vein stenosis, whereas in this study (17) the authors considered the outflow tract as the entire segment from the anastomosis area to the right atrium. This broad classification of the location of the stenoses within the AVF probably accounts for the slightly better results reported herein.

Two further studies assessed the accuracy of PE in the detection of AVF stenosis (14, 16). Campos et al (14) and Tessitore et al (16) included unselected populations of consecutive prevalent patients with AVFs attending a hemodialysis unit. Physical examination was performed by nephrologists with expertise in PE. The gold standard examinations were Doppler Ultrasound (14) and angiography (16), respectively. Both studies concluded that PE was an accurate method for the diagnosis of stenosis and should be part of all surveillance protocols of stenosis detection in AVF.

As important as accuracy of a method is, the goal of any monitoring or surveillance method is to detect

**TABLE II** - DIAGNOSTIC ACCURACY OF PHYSICAL EXAMINATION IN THE DETECTION OF ARTERIOVENOUS FISTULA STENOSIS

| | Design study | N | Gold standard | Location of stenosis | Sensitivity | Specificity | Cohen K |
|---|---|---|---|---|---|---|---|
| Asif et al (12) | Prospective, observational | 142 | Angiography | Inflow | 85% | 71% | 0.55 |
| | | | | Outflow | 92% | 86% | 0.78 |
| | | | | Overall | - | - | - |
| Leon et al (13) | Prospective, observational | 45 | Angiography | Inflow | 100% | 78% | 0.56 |
| | | | | Outflow | 76% | 68% | 0.63 |
| | | | | Overall | - | - | - |
| Campos et al (14) | Prospective, observational | 84 | DDU | Inflow | - | - | - |
| | | | | Outflow | - | - | - |
| | | | | Overall | 96% | 76% | - |
| Tessitore et al (15) | Prospective, observational | 119 | Angiography | Inflow | 70% | 76% | 0.46 |
| | | | | Outflow | 75% | 93% | 0.63 |
| | | | | Overall | - | - | - |
| Coentrao et al (17) | Prospective, observational | 177 | Angiography | Inflow | 98% | 88% | 0.84 |
| | | | | Outflow | 97% | 92% | 0.92 |
| | | | | Overall | - | - | 0.86 |

DDU, Duplex Doppler Ultrasound.

access stenosis in a timely way so that appropriate correction can be undertaken before thrombosis and vascular access loss. Therefore, multidisciplinary vascular access teams are required to improve vascular access outcomes. These include the presence of nephrologists, interventional nephrologists or radiologists, surgeons and dialysis nurses. Similarly, as in advance life support for critically ill patients, the term *Chain of Survival* provides a useful metaphor for the elements of the vascular access teams' concept. The five links in the hemodialysis access *Chain of Survival* would be: (a) permanent vascular access planning; (b) appropriate cannulation of AVFs and AVGs; (c) detection of access dysfunction; (d) treatment of dialysis access dysfunction and; (e) integrated post-intervention dialysis access monitoring and surveillance. It is easily perceptible that monitoring and surveillance methods would play a crucial role in this *Chain of Survival.* However, if we aim to prolong the survival of vascular access, in addition to avoid its failure, measures need to be taken carefully (33). In the last two decades, observational studies and single-center randomized trials suggested that surveillance of AVFs coupled with appropriate treatment, prolonged access survival (6-10). Unfortunately, the same did not happen in the case of AVGs (34-41). Although the results of observational studies would suggest that elective correction of stenoses before thrombosis might increase the long-term survival of the AVG (at the expense of increased procedures), recent randomized trials showed that prophylatic treatment of stenoses, although reducing thrombosis events, did not extend the useful life span of AVG rates.

## CONCLUSIONS

In summary, in the last decade several reports regarding the use of PE in the detection of AVF dysfunction (stenosis and/or thrombosis) observed that PE of AVFs is easily performed, inexpensive and provides a high level of accuracy to the physician who understands its principles. Cumulative evidence has demonstrated that adding surveillance methods to clinical monitoring, coupled with appropriate treatment, reduce thrombosis rates and may prolong AVF survival. However, as previously stated in the K/DOQI guidelines (1) *"(…) the basic skills have been largely abandoned in favor of technology and need to be taught to all individuals who perform hemodialysis procedures".* If our aim is to optimize the hemodialysis access *Chain of Survival*, nephrologists in hemodialysis units may need to improve their skills in performing PE. Theoretical and hands-on training in PE should therefore be provided for nephrologists in-training and for the dialysis staff.

**Financial support:** None.

**Conflict of interest:** None.

Address for correspondence:
Luis Coentrão
Nephrology Research and Development Unit
Faculty of Medicine, University of Porto
Al. Prof. Hernâni Monteiro
4200 - 319 Porto, Portugal
coentrao@med.up.pt

## REFERENCES

1. KDOQI. Clinical practice guidelines and clinical practice recommendations for vascular access. Am J Kidney Dis. 2006;48:S176-S247.
2. Tordoir J, Canaud B, Haage P, et al. EBPG on vascular access. Nephrol Dial Transplant. 2007;22(Suppl 2):ii88-ii117.
3. Ethier JH, Lindsay RM, Barre PE, Kappel JE, Carlisle EJ, Common A; Canadian Society of Nephrology. Clinical practice guidelines for vascular access. Canadian Society pf Nephrology. J Am Soc Nephrol. 1999;10(Suppl 13): S297-S305.
4. Ethier J, Mendelssohn DC, Elder SJ, et al. Vascular access use and outcomes: an international perspective from the Dialysis Outcomes and Practice Patterns Study. Nephrol Dial Transplant. 2008;23(10):3219-3226.
5. Lok CE. Fistula first initiative: advantages and pitfalls. Clin J Am Soc Nephrol. 2007;2(5):1043-1053.
6. Tessitore N, Bedogna V, Poli A, et al. Adding access blood flow surveillance to clinical monitoring reduces thrombosis rates and costs, and improves fistula patency in the short term: a controlled cohort study. Nephrol Dial Transplant. 2008;23(11):3578-3584.
7. McCarley P, Wingard RL, Shyr Y, Pettus W, Hakim RM, Ikizler TA. Vascular access blood flow monitoring reduces access morbidity and costs. Kidney Int. 2001;60(3): 1164-1172.
8. Wijnen E, Planken N, Keuter X, et al. Impact of a quality improvement programme based on vascular access flow monitoring on costs, access occlusion and access failure. Nephrol Dial Transplant. 2006;21(12):3514-3519.
9. Tessitore N, Mansueto G, Bedogna V, et al. A prospective controlled trial on effect of percutaneous transluminal angioplasty on functioning arteriovenous fistulae survival. J Am Soc Nephrol. 2003;14(6):1623-1627.
10. Tessitore N, Lipari G, Poli A, et al. Can blood flow surveillance and pre-emptive repair of subclinical stenosis prolong the useful life of arteriovenous fistulae? A randomized controlled study. Nephrol Dial Transplant. 2004;19(9): 2325-2333.

11. Bonforte G, Pogliani D, Brenna S, et al. Validation of QB stress test as a useful tool in the detection of native arteriovenous fistula stenosis: results after 22 months of follow-up. Nephrol Dial Transplant. 2010;25(6):1943-1949.
12. Asif A, Leon C, Orozco-Vargas LC, et al. Accuracy of physical examination in the detection of arteriovenous fistula stenosis. Clin J Am Soc Nephrol. 2007;2(6):1191-1194.
13. Leon C, Asif A. Physical examination of arteriovenous fistulae by a renal fellow: does it compare favorably to an experienced interventionalist? Semin Dial. 2008;21(6):557-560.
14. Campos RP, Chula DC, Perreto S, Riella MC, do Nascimento MM. Accuracy of physical examination and intra-access pressure in the detection of stenosis in hemodialysis arteriovenous fistula. Semin Dial. 2008;21(3):269-273.
15. Tessitore N, Bedogna V, Lipari G, et al. Bedside screening for fistula stenosis should be tailored to the site of the arteriovenous anastomosis. Clin J Am Soc Nephrol. 2011;6(5):1073-1080.
16. Tessitore N, Bedogna V, Melilli E, et al. In search of an optimal bedside screening program for arteriovenous fistula stenosis. Clin J Am Soc Nephrol. 2011;6(4):819-826.
17. Coentrão L, Faria B, Pestana M. Physical examination of dysfunctional arteriovenous fistulae by non-interventionalists: a skill worth teaching. Nephrol Dial Transplant. 2012;27(5):1993-1996.
18. Besarab A, Asif A, Roy-Chaudhury P, Spergel LM, Ravani P. The native arteriovenous fistula in 2007. Surveillance and monitoring. J Nephrol. 2007;20(6):656-667.
19. Basile C, Lomonte C, Vernaglione L, Casucci F, Antonelli M, Losurdo N. The relationship between the flow of arteriovenous fistula and cardiac output in haemodialysis patients. Nephrol Dial Transplant. 2008;23(1):282-287.
20. Besarab A, Frinak S, Aslam MA. Pressure measurements in the surveillance of vascular accesses. In Gray RJ, Sands JJ, eds. Dialysis Access: A Multidisciplinary Approach. Philadelphia, PA: Lippincott Williams & Wilkins, 2002;137-150.
21. Gelbfish GA. Clinical surveillance and monitoring of arteriovenous access for hemodialysis. Tech Vasc Interv Radiol. 2008;11(3):156-166.
22. Lindsay RM, Blake PG, Malek P, Posen G, Martin B, Bradfield E. Hemodialysis access blood flow rates can be measured by a differential conductivity technique and are predictive of access clotting. Am J Kidney Dis. 1997;30(4):475-482.
23. May RE, Himmelfarb J, Yenicesu M, et al. Predictive measures of vascular access thrombosis - a prospective study. Kidney Int. 1997;52(6):1652-1662.
24. Wang E, Schneditz D, Nepomuceno C, et al. Predictive values of access blood flow in detecting failure of vascular access. ASAIO J. 1998;44:554-557.
25. Beathard GA. Physical examination of the dialysis vascular access. Semin Dial. 1998;11(4):231-236.
26. Beathard GA. An algorithm for the physical examination of early fistula failure. Semin Dial. 2005;18(4):331-335.
27. Beathard GA. Physical examination: the forgotten tool. In Gray RJ, Sands JJ, eds. Dialysis Access: A Multidisciplinary Approach. Philadelphia, PA: Lippincott Williams & Wilkins, 2002;111-118.
28. Trerotola SO, Scheel PJ Jr, Powe NR, et al. Screening for dialysis access graft malfunction: comparison of physical examination with US. J Vasc Interv Radiol. 1996;7(1):15-20.
29. Agarwal R, McDougal G. Buzz in the axilla: a new physical sign in hemodialysis forearm graft evaluation. Am J Kidney Dis. 2001;38(4):853-857.
30. Leon C, Asif A. Arteriovenous access and hand pain: the distal hypoperfusion ischemic syndrome. Clin J Am Soc Nephrol. 2007;2(1):175-183.
31. Turmel-Rodrigues L, Mouton A, Birmelé B, et al. Salvage of immature forearm fistulas for haemodialysis by interventional radiology. Nephrol Dial Transplant. 2001;16(12):2365-2371.
32. Renaud CJ, Francois M, Nony A, Fodil-Cherif M, Turmel-Rodrigues L. Comparative outcomes of treated symptomatic versus non-treated asymptomatic high-grade central vein stenoses in the outflow of predominantly dialysis fistulas. Nephrol Dial Transplant. 2012;27(4):1631-1638.
33. Besarab A, Ravani P, Spergel LM, Roy-Chaudhury P, Asif A. The native arteriovenous fistula in 2007. Research needs. J Nephrol. 2007;20(6):668-673.
34. Schwab SJ, Raymond JR, Saeed M, Newman GE, Dennis PA, Bollinger RR. Prevention of hemodialysis fistula thrombosis. Early detection of venous stenoses. Kidney Int. 1989;36(4):707-711.
35. Besarab A, Sullivan KL, Ross RP, Moritz MJ. Utility of intra-access pressure monitoring in detecting and correcting venous outlet stenoses prior to thrombosis. Kidney Int. 1995;47(5):1364-1373.
36. Sands JJ, Miranda CL. Prolongation of hemodialysis access survival with elective revision. Clin Nephrol. 1995;44(5):329-333.
37. Lumsden AB, MacDonald MJ, Kikeri D, Cotsonis GA, Harker LA, Martin LG. Prophylactic balloon angioplasty fails to prolong the patency of expanded polytetrafluoroethylene arteriovenous grafts: results of a prospective randomized study. J Vasc Surg. 1997;26(3):382-390, discussion 390-392.
38. Ram SJ, Work J, Caldito GC, Eason JM, Pervez A, Paulson WD. A randomized controlled trial of blood flow and stenosis surveillance of hemodialysis grafts. Kidney Int. 2003;64(1):272-280.
39. Moist LM, Churchill DN, House AA, et al. Regular monitoring of access flow compared with monitoring of venous pressure fails to improve graft survival. J Am Soc Nephrol. 2003;14(10):2545-2653.
40. Dember LM, Holmberg EF, Kaufman JS. Randomized controlled trial of prophylactic repair of hemodialysis arteriovenous graft stenosis. Kidney Int. 2004;66(1):390-398.
41. Robbin ML, Oser RF, Lee JY, Heudebert GR, Mennemeyer ST, Allon M. Randomized comparison of ultrasound surveillance and clinical monitoring on arteriovenous graft outcomes. Kidney Int. 2006;69(4):730-735.

# Chapter 3

## *Costs and outcomes of endovascular treatment of thrombosed dialysis autogenous fistulae*

Coentrão L.

*Nefrologia* (in press)

# COSTS AND OUTCOMES OF ENDOVASCULAR TREATMENT OF THROMBOSED DIALYSIS AUTOGENOUS FISTULAE

# COSTOS Y RESULTADOS DEL TRATAMIENTO ENDOVASCULAR DE LAS TROMBOSIS EN LAS FÍSTULAS AUTÓLOGAS PARA HEMODIÁLISIS

**Short title**: Endovascular treatment of thrombosed fistulae

Luis Coentrão[1]

[1] Nephrology Research and Development Unit, Faculty of Medicine, University of Porto, Sao Joao Hospital Centre, Porto, Portugal

**Correspondence:**

Luís Coentrão M.D.

e-mail: coentrao@med.up.pt;

Phone number: +351910538824; Fax number: +351225512228

Nephrology Research and Development Unit, Faculty of Medicine, University of Porto, Al. Prof. Hernâni Monteiro 4200 - 319 Porto, Portugal

The manuscript has been seen and approved by all authors and that it is not under consideration for publication elsewhere in a similar form, in any language

## Abstract

Functional vascular access is a prerequisite for adequate haemodialysis treatment in patients with end-stage renal disease. Autogenous arteriovenous fistulae are considered superior to synthetic grafts and central venous catheters; however, fistulae are not without problems. Fistulae thrombosis has become a clinical challenge in nephrology practice, with relevant clinical implications for dialysis patients. Several studies have reported on the feasibility and relatively high-clinical success rate of the endovascular approach to thrombosed fistulae in recent years. However, as repeated interventions are usually required to achieve long-term access survival, maintenance of a previously thrombosed fistulae could be a highly expensive policy. The goals of this article are to provide the reader an insight into the multiple endovascular approaches for thrombosed arteriovenous fistulae, bearing in mind its clinical effectiveness and financial implications.

**Key words:** dialysis; autogenous arteriovenous fistulae; percutaneous thrombectomy; endovascular treatment; economic analysis; cost analysis.

## Resumen

El acceso vascular funcional es un requisito previo para el tratamiento renal sustitutivo en pacientes con enfermedad renal crónica. Las fístulas autólogas se consideran superiorer a las protésis vasculares y los catéteres venosos centrales, sin embargo, las fístulas no están exentas de problemas. Las trombosis de la fístula autóloga se ha convertido en un reto en la práctica clínica de nefrología, con importantes implicaciones clínicas para pacientes en diálisis. Varios estudios han informado sobre la viabilidad y la tasa relativamente alta del éxito clínico del abordaje endovascular de fístulas trombosadas en los últimos años. Sin embargo, como las repetidas intervenciones suelen ser necesarios para lograr la supervivencia a largo plazo del acceso, el mantenimiento de una fístula anteriormente trombosada podría ser una política muy cara. Los objetivos de este artículo son proporcionar al lector una idea de los múltiples enfoques endovasculares para fístulas autólogas trombosadas, teniendo en cuenta su eficacia clínica y las implicaciones financieras.

**Palabras clave:** diálisis, fístula arteriovenosa autóloga; trombectomía percutánea, tratamiento endovascular, análisis económico, análisis de costo.

## Introduction

The number of patients undergoing dialysis continues to increase as technology and patient survival improve in this patient population. Portugal has a higher incidence and prevalence of end stage-renal disease (ESRD) compared to most of other European countries. In 2011, a prevalence rate of 1662 patients per million of the population was registered by the Portuguese Society of Nephrology (10,409 patients underwent haemodialysis and 704 patients peritoneal dialysis in 2011). We know that vascular accesses for haemodialysis are plagued with multiple problems, the most common being infection and dysfunction. Although thrombosis of the vascular access is a relatively infrequent complication of autogenous arteriovenous fistulae (AVF), as current clinical practice guidelines recommend that at least 65% of ESRD population should have a functional AVF as a permanent dialysis access (1, 2), AVF thrombosis has become a clinical challenge in our nephrology practice, with relevant clinical implications for dialysis patients. The challenge of determining the most effective treatment for thrombosed AVFs is paramount in the minds of the nephrologists. The goal of this article is to provide the reader an insight into the endovascular approaches of thrombosed AVFs, bearing in mind its clinical effectiveness and financial implications.

## Pre-procedural Patient Assessment

Before the thrombectomy procedure it is important to determine whether the patient has a history of significant cardiac or pulmonary disease. Patients who have a history of right-sided heart failure or pulmonary hypertension are not good candidates for an endovascular thrombectomy procedure since fragments of thrombus can escape from the AVF and travel to the lungs as pulmonary emboli during the procedure (3, 4). In these particular clinical scenarios, therapy should be individualized, taking into account the risk-benefit of endovascular thrombectomy.

The patient's vascular access should be examined before draping the extremity. Fistula thrombosis is a clinical diagnosis characterized by the absence of flow in the AVF. Physical examination provides additional information that is of the utmost importance for the

interventionalist since different endovascular approaches are used for AVFs with inflow, outflow, co-existing inflow–outflow problems or AVF thrombosis. Although clinical signs of infection should always be inspected, local inflammation and pain immediately upstream from the stenosis occur frequently in recently thrombosed native fistulae (phlebitis), and the diagnosis of infection is not easy to make.

There are few contra-indications to percutanous declotting. Local infection is the main clinical contraindication. Huge clot burden (>100cc) and large aneurysms with old wall-adherent thrombi are both clinical and technical contraindications because safe removal of thrombi in such conditions is extremely difficult and hazardous to the patient. Immature AVF never previously used for haemodialysis, once considered as a technical contraindication, has recently been revisited by Miller *et al.* (5), reporting a highly success rate of endovascular salvage of immature clotted AVFs.

## Percutanous Thrombectomy Procedure

Throughout the past two decades, there has been a plethora of published reports describing numerous percutaneous techniques for the treatment of thrombosed haemodiaysis grafts and AVFs (6-19). These techniques can be divided into two broad categories; one group uses thrombolytic agents, and the other uses mechanical thrombectomy technique. The category of mechanical thrombectomy techniques includes balloon thrombectomy, mechanical thrombectomy devices and thromboaspiration.

### Basic Technique

Percutaneous declotting of a dialysis AVFs is an outpatient procedure. Patients are monitored by a nurse with pulse oximetry, blood pressure measurement, and electrocardiography. Fentanyl and/or midazolam can be administered intravenously for conscious sedation. Puncture sites are anesthetized with lidocaine. Systemic heparinization with 5000UI of heparin is initiated prior to the procedure. Prophylactic antibiotics are recommended by some authors (13).

Although the technique for declotting a polytetrafluoroethylene graft can be standardized easily, clotted AVFs result in a wide range of difficulties: (a) the thin venous wall is more difficult

to cannulate; (b) the anatomy is irregular, with the presence of collaterals veins; (c) the locations of the stenosis can occur anywhere, and are difficult to traverse; (d) a large volume clots can be encountered; and (e) aneurysms are more frequent than in polytetrafluoroethylene grafts.

The technique for declotting a thrombosed AVFs has been well described by Turmel-Rodrigues *et al.* (13). There are four basic steps to perform during a percutaneous thrombectomy procedure: (a) physical examination is essential to choose the best site for initial catheterization; (b) an initial venogram to evaluate the central and peripheral veins; (c) removal of the thrombus from the vascular access; and (d) treatment of all significant stenoses. An underlying stenosis is unmasked in the great majority of cases. In typical cases, an initial introducer sheath is placed a few centimeters from the anastomosis using an antegrade approach to treat the venous outfow. A catheter is pushed over a wire up to the superior vena cava and then slowly pulled back while contrast medium is injected under fluoroscopy to localize the downstream extension of the thrombosis. The fistula is abandoned at this stage if the venous outflow cannot be traversed or recanalized. A second introducer is placed with a retrograde approach in the direction of the arterial inflow. The fistula is abandoned if it is impossible to traverse the arteriovenous anastomosis with the guidewire. Occasionally, when the stenosis is clinically located a few centimeters from the wrist anastomosis, with no evidence of concomitant outflow stenosis, a single retrograde approach from the vein at the elbow is sufficient to treat the whole fistula. Once access to both the arterial inflow and venous outflow is guaranteed with a guidewire, thombi on the venous side are removed first, before the thrombi on the arterial side. Conventional, high-pressure or cutting balloon angioplasty should be undertaken to remove causative stenotic disease. On completion, both physical examination and fistulogram are performed to visualize the flow from arteriovenous anastomosis to the superior vena cava. Vascular sheaths are removed and haemostasis is achieved by manual compression or using a purse-string suture (20).

Occasionally, an AVF might clot with minimal or no thrombus. At other times, there is moderate-to-severe thrombus burden that accompanies AVF clotting. While percutaneous balloon angioplasty to correct the underlying stenosis might be all that is needed to declot a fistula with no thrombus, endovascular thromboaspiration is required to successfully declot a fistula with moderate thrombus and surgical referral is advisable in the presence of excessive thrombus burden.

### *Thrombolysis*

The introduction of mechanical thrombectomy devices has reduced the popularity of thrombolytic therapy. Urokinase, streptokinase, and tissue plasminogen activator (t-PA) have all been used for infusion thrombolysis (6, 21, 22). To achieve optimum outcome, anterograde vascular access is obtained as close to the arteriovenous anastomosis as possible. Thrombolytic therapy is then administered via a multiple side hole catheter along the length of the fistula for between 3-24 hours, at doses depending on institutional protocol. To improve outcome, adaptations to the technique have been published: pulse spray thrombolysis, in which highly concentrated fibrinolytic therapy is injected as a high-pressure spray directly into thrombus for 15-20 min, thereby reducing procedural time (6). Due to modest success rates, thrombolysis is more frequently used in combination with mechanical thrombectomy to maximize clot clearance and reduce procedural times.

### *Mechanical thrombectomy*

Several methods of mechanical clot dissolution have been published. Balloon thrombectomy was the first published "purely mechanical" percutaneous technique used for declotting thtombosed polytetrafluoroethylene grafts (23). This approach was accomplished using a variety of devices to macerate, dislodge or sweep thrombus from the occluded graft into the central venous circulation. This controversial technique was a milestone in the history of haemodialysis access declotting. From this experience gained in grafts, some teams successfully used this technique of deliberated pulmonary embolizations of clots when the volume of thrombus in the AVF was presumed to be equivalent to the encountered in grafts (22). Trerotola and colleagues stopped using this technique soon after, when they experiences a casualty (8). Other casualties have since been reported in the literature (3).

A wide range of mechanical thrombectomy devices have been used in the treatment of failed AVFs. The Arrow-Trerotola PTD (Arrow International, Reading, PA, USA) is a rotating nitinol basket available in 5 and 7 F configurations. A handheld battery powered motor results in a basket rotation speed of approximately 3,000 rpm, macerating thrombus into particles of 1 to 3 mm diameter (24, 25). Thrombus fragments are then aspirated manually using the introducer sheath side port. Simple rotation of a 5 F mini-pigtail catheter (Cook Europe, Bjaeverskov, Denmark) can be used to remove thrombus from occluded AVFs (26). The Oasis recirculation catheter (Boston Scientific/Medi-Tech, Natick, MA) is available in 6 and 8 F systems and uses a standard

angiographic pump injector (27). The Hydrolyser (Cordis, Miami, FL, USA) is a dual lumen 6 or 7 F catheter with a distal side hole and rounded tip and requires the use of a conventional contrast injector to administer saline retrogradely (9, 28-30). The AngioJet catheter (Possis Medical, Minneapolis, MN, USA) is available in 4 to 6 F systems uses a specialized pump drive system that creates high pressures (14, 31). The Amplatz thrombectomy device (ATD; Microvena, White Bear Lake, MN, USA) consists of a sharp blade that is rotated at 150,000 rpm by a compressed gas driven turbine, within a protective metal capsule. Thrombus is macerated by the rotating blade and dispersed into the bloodstream as microscopic particles (15). Manual catheter-directed thromboaspiration is a popular technique in France and Spain that uses a straight 7 to 9 F end-hole catheter (Guider; Boston Scientific, Natick, MA, USA; or Vista Bright Tip; Cordis, Miami, FL, USA) to remove thrombus by manual suction (13, 32).

### Success

No single percutaneous thrombectomy technique has been proven to be more efficacious than other methods (Table 1). Limited data exist regarding outcome of declotting procedures in AVFs using thrombolysis alone. Zaleski *et al.* (22) treated thrombosed AVFs with urokinase thrombolysis and balloon angioplasty and reported a procedural success rate of 82%. Primary patency rate of 64% was achieved at 12 months. Rocek *et al.* (25) reported a 90% clinical success rate in 10 patients treated using the Arrow-Trerotola PTD. The 6-month primary patency rate was 60%. Shmitz-Rode *et al.* (26) reported 100% clinical success rate in 15 AVFs and 11 grafts using the "rotating mini-pigtail catheter", with a primary patency rate of 47% at 6 months. Sahni *et al.* (27) treated 23 thrombosed accesses (5 AVFs and 17 grafts) using the Oasis catheter with a success rate of 86% and a primary patency rate of 50% at 6 months. Vorwek *et al.* (28) reported a clinical success rate of 85% in 19 clotted AVFs and a primary patency rate of 50% at 12 months using the Hydrolyser catheter. Littler *et al.* (31) published the outcomes of AngioJet thrombectomy in 44 occluded AVFs, with a technical success of 89% and a primary patency rate of 34% at 6 months. Similar results were confirmed by Mossavi *et al.* (14). Recently, Wang *et al.* (33) reported a higher success rate using the Arrow-Trerotola PTD, compared to the AngioJet catheter. However, comparable patency rates were obtained at one year of follow-up. A single study examining the clinical outcome of the ATD in occluded AVFs demonstrated a success rate of 89% and a primary patency of 27% at 12 months (15). Turmel-Rodrigues *et al.* (13) reported the results of manual catheter-directed thromboaspiration technique, with a success rate of 93% for forearm and 76% for upper arm AVFs and a primary patency rate of 49% and 9% in the forearm and upper arm at

12 months, respectively. Similar results were reported by Garcia-Medina *et al.* (32) and Bizarro *et al.* (34).

Intervention studies on thrombosed autogenous fistulae have predominantly appeared after the year 2000. A few have compared endovascular with surgical repair, but none was randomized. The results were comparable with the outcome of endovascular treatment in terms of primary success rate (90% *versus* 89%), but 1-year primary (74% *versus* 40%) and secondary patency rates (87% *versus* 72%) were higher (35). However, most studies on surgical thrombectomy of AVFs concerned forearm accesses with the creation of a new, more proximally located arteriovenous anastomosis (35-37).

### Complications

The most frequent procedure-related complication associated with angioplasty of the dialysis vascular access is some type of venous rupture. This complication has been reported to represent 70–75% of all complications (38). Local complications, such as secondary bleeding and pseudoaneurism from the introducer sheath and vessel injury/disruption do occur in daily clinical practice (39), but probably are underreported in the literature.

There are few significant procedure-related complications. The risk of pulmonary embolism is theoretically greater with autogenous AVFs than with polytetrafluoroethylene grafts (40, 41). However, clinically silent pulmonary embolism probably occurs in many patients treated by these methods (40). Arterial embolization can result from clot fragmentation at the arterial anastomosis by catheter or guidewire manipulation, vigorous injection of contrast material, or balloon angioplasty of residual thrombus. However, the reported frequency of arterial embolization has been low (0-7%) (42). Major hemorrhagic complications requiring additional treatment are reported in 1-7% of cases in these series (42). Some experts advocate the use of prophylactic antibiotics due to the risk of infection (13).

## Costs

Probably, no topic has been so underreported in the nephrology literature as the analysis of costs of endovascular procedures for haemodialysis AVF failure. Vascular access costs may account for approximately 10% of the total cost of health care of haemodialysis patient

population, with patients dialyzed with a catheter incurring the highest costs (43, 44). It is well known for interventionalists that mechanical thrombectomy devices are expensive (e.g. Arrow-Trerotola PTD, $600; Hydrolyzer, $600; Oasis, $600). However, they are not the ones responsible for the high expenditure of endovascular procedures. The amount of resources required for endovascular interventions vary among vascular access centers with different endovascular salvage procedures (Table 2). Therefore, cost analysis must take into account all the devices employed during the procedure (p.e. guidewires, balloon angioplasty, stents) the pharmacy (e.g. antibiotics, heparin, thrombolytics) and radiology costs (e.g. angiography suite, contrast media), professional fees and additional overhead expenses.

Published findings regarding the economic value of vascular access surveillance revealed that adding access blood flow surveillance to clinical monitoring of grafts and AVFs may reduce thrombosis rates and costs (45-47). Bittl *et al.* (48) recently reported an economic analysis of angiography and pre-emptive angioplasty to prevent haemodialysis access thrombosis. They observed that pre-emptive angiographic management of malfunctioning nonthrombosed haemodialysis accesses may represent a less efficient use of healthcare resources than increasing the number of patients with AVFs. To our knowledge, cost-effectiveness analyses of endovascular interventions for thrombosed haemodialysis accesses have been performed mainly in patients with clotted prosthetic grafts (49-51). Sands *et al.* (49) performed a retrospective analysis comparing the clinical success and the costs of pharmacomechanical thrombolysis of occluded grafts with surgical thrombectomy. Hospitalization was required for 85% of the cases of surgical thrombectomy and in 17% of cases of pharmacomechanical thrombolysis. Hospital charges and physician costs were obtained for each procedure. Clinical success was similar between lysis and surgical procedures. Hospital, physician and total charges were significantly lower in the lysis group than in the surgical control (US$6,802 *versus* US$12,740). Vesely *et al.* (50) prospectively randomized 20 patients with clotted grafts either to pulse-spray thrombolysis plus angioplasty, or surgical thrombectomy. Thrombolysis and surgical thrombectomy were performed as outpatient procedures in almost of the cases. The technical costs, professional fees, and all other associated costs were obtained. The authors concluded that endovascular thrombolysis and surgical thrombectomy were comparable in cost (US$6,062 *versus* US$5,580), and the technical success and patency rates were also similar. Dougherty *et al.* (51) performed a similar study among 80 patients with clotted grafts. The mean cost of treatment (including room and supply costs but not professional fees) was significantly higher for the endovascular group than for the surgical group (US$2945 *versus* US$1512). In addition, high rate of technical

failure necessitating surgery was observed in the endovascular group. To our knowledge, only recently the costs of percutaneous thrombectomy of clotted AVF were reported in the literature (34, 48). Bizarro *et al.* (34) reported a cost analysis of the use of manual catheter-directed thromboaspiration for the treatment of thrombosed AVFs. A comprehensive measurement of total vascular access care-related costs was obtained. The authors reported that the cost of maintenance of thrombosed AVFs by endovascular means was high. The mean total expense of the percutaneous thrombectomy procedure was US$1,381 and for percutaneous transluminal angioplasty was US$785. At one year of follow-up, the mean cumulative cost of vascular access care was US$2,504 per patient-year at risk. The mean cost was greatest for patients with brachiocephalic AVFs (US$3,578) than for patients with forearm AVFs (US$1,604). In comparison, in the Bittl *et al.* study (48) procedure costs were approximately two times higher (angioplasty, US$1,939; percutaneous thrombectomy, US$3,361). Possible explanations for the differences observed in these two studies are: (a) in the first study (34), the investigators used manual catheter-directed thromboaspiration technique whereas Bittl *et al.* (48) used the AngioJet catheter for thrombosed AVFs; (b) stents were not used in the first study (34), whereas Bittl *et al.* (48) placed stents for several indications and; (c) physician billing differ among countries (52).

Percutaneous thrombectomy is an efficient policy to treat thrombosed failed AVFs. Yes, but an expensive one. Do we, nephrologists, have other cost-effective approaches to deal with failed AVF? Does surgical thrombectomy may overcome the high financial burden of percutaneous thrombectomy, with similar success rates? Does the abandon of failed AVFs toward the creation of a new permanent accesss still an option? To our knowledge, clear-cut data has not been published answering these questions. Recenlty, Miller *et al.* (5) evaluated the efficacy, functionality, and cost associated with the use of percutaneous techniques for the salvage of thrombosed immature fistulae. All fistulae had thrombosed following access creation and had never been used for haemodialysis. The authors concluded that endovascular techniques yield significant cost savings over access abandonment. Coentrao *et al.* (53) compared two distinct policies for the maintenance of vascular access in prevalent haemodiaysis patients with thrombosed AVFs: percutaneous thrombectomy *versus* central venous catheterization to bridge the interval until a new AVF is suitable for cannulation. The authors observed that AVF salvage by endovascular therapy led to a near two-fold reduction in access-related expenses; the added costs associated with the procedure itself was completely offset by the saving associated with lower surgical visits, access dysfunction, and hospitalizations.

Taking into consideration the published high success rates and the costs of percutaneous

thrombectomy of occluded autogenous fistulae, nephrologists, Medical Societies and National Health Services face a new era of vascular access care. If the final decision is to treat failed AVFs, intensive efforts should be undertaken to universalize these interventions.

## Key concept

Several studies have reported on the feasibility and relatively high-clinical success rate of the endovascular approach to thrombosed autogenous arteriovenous fistulae in recent years. However, maintenance of a previously thrombosed arteriovenous fistulae require repeated interventions and thus could be a highly expensive policy. Further prospective cost-effectiveness analyses comparing different thrombectomy procedures (endovascular *versus* surgery) and distinct approaches for the maintenance of functional autogenous fistulae (pre-emptive angioplasty *versus* percutaneous thrombectomy) need to be carried out.

## Conflict of interest

The author declares that there is no conflict of interest associated with this manuscript.

## References

(1). Tordoir J, Canaud B, Haage P, et al. EBPG on vascular access. Nephrol Dial Transpl 2007;22(Suppl 2):ii88-ii117.

(2). KDOQI: Clinical practice guidelines and clinical practice recommendations for vascular access. Am J Kidney Dis 2006;48: S176-S247.

(3). SwanTL, Smyth SH, Ruffenbach SJ, et al. Pulmonary embolism following hemodialysis

access thrombolysis/thrombectomy. *J Vasc Interv Radiol* 1995;6:683-686.

(4). Trerotola SO, Johnson MS, Schauwecker DS, et al. Pulmonary emboli from pulse-spray and mechanical thrombolysis: evaluation with an animal diaysis-graft model. *Radiology* 1996;200:169-176.

(5). Miller GA, Hwang W, Preddie D, et al. Percutaneous Salvage of Thrombosed Immature Arteriovenous Fistulas. *Semin Dial* 2011;24:107-114.

(6). Valji K, Bookstein JJ, Roberts AC, et al. Pulse-spray pharmacomechanical thrombolysis of thrombosed hemodialysis access grafts: comparison of original and current techniques. *AJR Am J Roentgenol* 1995;165:1495-1500.

(7). Beathard GA, Welch BR, Maidment HJ. Mechanical thrombolysis for the treatment of thrombosed hemodialysis grafts. *Radiology* 1996;200:711-716.

(8). Trerotola SO, Vesely TM, Lung GB, et al. Treatment of thrombosed hemodialysis access grafts: Arrow-Trerotola percutaneous thrombolytic device versus pulse-spray thrombolysis. *Radiology* 1998;206:403-414.

(9). Vorweck D, Shurmann K, Muller-Leisse C, et al. Hemodynamic thrombectomy of haemodialysis grafts and fistulae: results of 51 procedures. *Nephrol Dial Transp* 1996;11:1058-1064.

(10). Uflacker R, Rajagopalan PR, Vujic I, t al. Treatment of thombosed dialysis access grafts: randomized trial of surgical thrombectomy versus mechanical thrombectomy with the amplatz device. *J Vasc Interv Radiol* 1996;7:185-192.

(11). Vesely TM, Williams D, Weiss M, et al. Comparison of the AngioJet rheolytic catheter to surgical thrombectomy for the treatment of thrombosed hemodialysis grafts. *J Vasc Interv Radiol* 1999;10:1195-1205.

(12). Turmel-Rodrigues L, Sapoval M, Pengloan J, et al. Manual thromboaspiration and dilation of thrombosed dialysis access: Mid-term results of a simple concept. *J Vasc Interv Radiol* 1997; 8:813-824.

(13). Turmel-Rodrigues L, Pengloan J, Rodrigue H, et al. Treatment of failed native arteriovenous fistulae for hemodialysis by interventional radiology. *Kidney Int* 2000;57:1124-1140.

(14). Moossavi S, Regan JD, Pierson ED, et al. Nonsurgical salvage of thrombosed arterio-venous fistulae: A case series and review of the literature. *Semin Dial* 2000;20:459-464.

(15). Haage P, Vorwerk D, Wilberger JE, et al. Percutaneous treatment of thrombosed primary arteriovenous hemodialysis access fistulae. *Kidney Int* 2000;57:1169-1175.

(16). Liang HL, Pan HB, Chung HM, et al. Restoration of thrombosed Brescia-Cimino dialysis fistulas by using percutaneous transluminal angioplasty. *Radiology* 2002;223:339-344.

(17). Rajan DK, Clark T, Me S, et al. Procedural success and patency after percutaneous treatment of thrombosed autogenous arteriovenous dialysis fistulas. *J Vasc Interv Radiol* 2002;13:1211-1218.

(18). Shatsky JB, Berns JS, Clark TW, et al. Single-center experience with the Arrow-Trerotola percutaneous thrombectomy device in the management of thrombosed native dialysis fistulas. *J Vasc Interv Radiol* 2005;16:1605–1611.

(19). Jain G, Maya ID, Allon M. Outcomes of percutaneous mechanical thrombectomy of arteriovenous fistulas in hemodialysis patients. *Semin Dial* 2008;21:581-583.

(20). Vorwerk D, Konner K, Schurmaan K, et al. A simple trick to facilitate bleeding control after percutaneous hemodialysis fistula and graft interventions. *Cardiovasc Intervent Radiol* 1997;20:159-160.

(21). Kilmas VA, Denny KM, Paganini EP, et al. Low dose streptokinase therapy for thrombosed arteriovenous fistulas. *Trans Am Soc Artif Intern Organs* 1984;30:511-513.

(22). Zaleski GX, Funaki B, Kenney S, et al. Angioplasty and bolus urokinase infusion for the restoration of function in thrombosed Brescia-Cimino dialysis fistulas. *J Vasc Interv Radiol* 1999;10:129-136.

(23). Trerotola SO, Lund GB, Sheel PJ, et al. Thrombosed dialysis access grafts: percutaneous mechanical declotting without urokinase. *Radiology* 1994;191:721-726.

(24). Trerotola SO, McLennan G, Davidson D, et al. Preclinical in vivo testing of the Arrow-Trerotola percutaneous thrombolytic device for venous thrombosis. *J Vasc Interv Radiol* 2001;12:95-103.

(25). Rocek M, Peregrin JH, Lasovickova J, et al. Mechanical thrombolysis of thrombosed hemodialysis native fistulas with use of the Arrow-Trerotola percutaneous thrombolytic device: our preliminary experience. *J Vasc Interv Radiol* 2000;11:1153-1158.

(26). Schmitz-Rode T, Wildberger JE, Hubner D, et al. Recanalization of thrombosed dialysis access with use of a rotating mini-pigtail catheter: follow-up study. *J Vasc Interv Radiol*

2000;11:721-727.

(27). Sahni V, Kaniyur S, Malhotra A, et al. Mechanical thrombectomy of occluded hemodialysis native fistulas and grafts using a hydrodynamic thrombectomy catheter: preliminary experience. *Cardiovasc Intervent Radiol* 2005;28:714-721.

(28). Vorwerk D, Schurmann K, Muller-Leisse C, et al. Hydrodynamic thrombectomy of haemodialysis grafts and fistulae: results of 51 procedures. *Nephrol Dial Transplant* 1996;11:1058-1064.

(29). Overbosch EH, Pattynama PM, Aarts HJ, et al. Occluded hemodialysis shunts: Dutch multicenter experience with the hydrolyser catheter. *Radiology* 1996;201:485-488.

(30). Rousseau H, Sapoval M, Ballini P, et al. Percutaneous recanalization of acutely thrombosed vessels by hydrodynamic thrombectomy (Hydrolyser). *Eur Radiol* 1997;7:935-941.

(31). Littler P, Cullen N, Gould D, et al. AngioJet thrombectomy for occluded dialysis fistulae: outcome data. *Cardiovasc Intervent Radiol* 2009;32:265-270.

(32). García Medina J, Lacasa Pérez N, Muray Cases L et al. Accesos vasculares para hemodiálisis trombosados: rescate mediante técnicas de radiología vascular intervencionista. *Nefrología* 2009;29**:**249-255.

(33). Yang CC, Yang CW, Wen SC *et al.* Comparisons of clinical outcomes for thrombectomy devices with different mechanisms in hemodialysis arteriovenous fistulas. *Catheter Cardiovasc Interv* 2012 Apr 2012 [Epub ahead of print].

(34). Bizarro P. Coentrao L, Ribeiro C. et al. Endovascular treatment of thrombosed dialysis fistulae: a cumulative cost analysis. *Catheter Cardiovasc Interv.* 2011;77:1065-1070.

(35). Tordoir J, Bode A, Peppelenbosch N, et al. Surgical or endovascular repair of thrombosed dialysis vascular access: Is there any evidence? *J Vasc Surg* 2009;50:953-6.

(36). Ponikvar R. Surgical salvage of thrombosed arteriovenous fistulas and grafts. *Ther Apher Dial* 2005;9:245-249.

(37). Lipari G, Tessitore N, Poli A, et al. Outcomes of surgical revision of stenosed and thrombosed forearm arteriovenous fistulae for haemodialysis. *Nephrol Dial Transplant* 2007; 22:2605-2612.

(38). Beathard GA, Urbanes A, Litchfield A. The classification of procedure related

complications-a fresh approach. *Semin Dial* 2006;19:527–534.

(39). Claude J. Renaud CJ, Lopes K, Bourquelot P, et al. Skin and Venous Rupture at a Hemodialysis Needle Cannulation Site during Angioplasty of a Transposed Forearm Fistula. *J Vasc Interv Radio* 2011;22:1488-1489.

(40). Dolmatch BL, Gray RJ, Horton KM. Will iatrogenic pulmonary embolization be our pulmonary embarrassment? *Radiology* 1994;191:615-617.

(41). Swan TL Smyth SH, Ruffenach SJ, et al. Pulmonary embolism following hemodialysis access thrombolysis/thrombectomy. *J Vasc Interv Radiol* 1995;6:683-686.

(42). Valji K. Transcatheter treatment of thrombosed hemodialysis access grafts. *AJR Am J Roentgenol* 1995;164:823-829.

(43). USRDS: The economic cost of ESRD, vascular access procedures, and medicare spending for alternative modalities of treatment. *Am J Kidney Dis* 1997;30:S160-S177.

(44). Amedia Jr C, W. Kline Bolton WK, Trelles C, et al. Vascular Access for HD: Aligning Payment with Quality. *Semin Dial* 2011;24:37-40.

(45). Tessitore N, Bedogna V, Poli A, et al. Adding access blood flow surveillance to clinical monitoring reduces thrombosis rates and costs, and improves fistula patency in the short term: A controlled cohort study. *Nephrol Dial Transpl* 2008;23:3578-3584.

(46). McCarley P, Wingard RL, Shyr Y et al. Vascular access blood flow monitoring reduces access morbidity and costs. *Kidney Int* 2001;60:1164-1172.

(47). Wijnen E, Planken N, Keuter X et al. Impact of a quality improvement programme based on vascular access flow monitoring on costs, access occlusion and access failure. *Nephrol Dial Transplant* 2006;21:3514-3519.

(48). Bittl JA, Cohen DJ, Seek MM, et al. Economic analysis of angiography and preemptive angioplasty to prevent hemodialysis access thrombosis. *Catheter Cardiovasc Interv* 2010;75:14–21.

(49). Sands JJ, Patel S, Plaviak DJ, et al. Pharmacomechanical thrombolysis with urokinase for treatment of thrombosed hemodialysis access grafts. *ASAIO J* 1994;40:M886-M888.

(50). Vesely TM, Idso MC, Audrain J, et al. Thrombolysis versus surgical thrombectomy for the treatment of dialysis graft thrombosis: Pilot study comparing costs. *J Vasc Interv Radiol* 1996;7:507-512.

(51). Dougherty MJ, Calligaro KD, Schindler N et al. Endovascular versus surgical treatment for thrombosed hemodialysis grafts: A prospective, randomized study. *J Vasc Surg* 1999;30:1016-1023.

(52). World Bank: World Development Indicators 2000. Washington DC: World Bank; 2001.

(53). Coentrão L, Bizarro P, Ribeiro C. et al. Percutaneous treatment of thrombosed arteriovenous fistulas: clinical and economic implications. *Clin J Am Soc Nephrol* 2010;5:2245-2250.

**Table 1.** Results of dialysis autogenous arteriovenous fistula (AVF) declotting procedures

| | Technique | Vascular access | N | Clinical success | 6 month 1º patency | 12 month 1º patency | 12 month 2º patency |
|---|---|---|---|---|---|---|---|
| Zaleski *et al*. (22) | Thrombolysis | AVF | 17 | 82% | 71% | 64% | 100% |
| Liang *et al*. (16) | Thrombolysis | AVF | 42 | 90% | 81% | 70% | 80% |
| Rocek *et al*. (25) | Arrow-Trerotola PTD | AVF | 10 | 90% | 60% | - | - |
| Shatsky *et al*. (18) | Arrow-Trerotola PTD | AVF | 62 | 79% | 38% | 18% | 74% |
| Shmitz-Rode *et al*. (26) | Rotating mini-pigtail catheter | AVF + Graft | 26 | 100% | 47% | - | - |
| Sahni *et al*. (27) | Oasis catheter | AVF + Graft | 22 | 86% | 50% | - | - |
| Vorwek *et al*. (28) | Hidrolyser catheter | AVF | 19 | 85% | 50% | 50% | - |
| Littler *et al*. (31) | AngioJet catheter | AVF | 44 | 89% | 34% | - | - |
| Mossavi *et al*. (14) | AngioJet catheter | AVF | 49 | 96% | 55% | 51% | 73% |
| Haage *et al*. (15) | Amplatz thrombectomy | AVF | 81 | 89% | 52% | 27% | 51% |
| Turmel *et.al* (13) | Manual Thromboaspiration | AVF | 93 | 76% to 93% | 18% to 70% | 8% to 49% | 50% to 81% |
| Garcia-Medina *et al*. (32) | Manual Thromboaspiration | AVF | 45 | 84% | - | 38%-57% | 61%-65% |
| Bizarro *et al*. (34) | Manual Thromboaspiration | AVF | 44 | 93% | 72% | 64% | 78% |

1º patency was considered to begin on the day of declotting and to end on the day of access failure or further reintervention.

2º patency included all further radiological treatments (dilation, new percutaneous declotting) but ended with surgical revision.

**Table 2.** Costs of endovascular procedures for dysfunctional and thrombosed haemodialysis autogenous arteriovenous fistula (AVF) and polytetrafluoroethylene graft (PTFE).

| | Vascular access | Intervention | Technical cost | Professional fee | Total cost |
|---|---|---|---|---|---|
| Sands *et al*. (49) | PTFE | Thrombolysis | US$3,970 | US$2,832 | US$6,802 |
| | | Surgical thrombectomy | US$8,691 | US$4,049 | US$12,740 |
| Vesely *et al*. (50) | PTFE | Thrombolysis | US$2,906 | US$3,156 | US$6,062 |
| | | Surgical thrombectomy | US$2,449 | US$3,131 | US$5,580 |
| Dougherty *et al*. (51) | PTFE | Thrombolysis | - | - | US$2,945 |
| | | Surgical thrombectomy | - | - | US$1,512 |
| Wijnen *et al*. (47) | AVF + PTFE | Angioplasty | - | - | €565 |
| Tessitore *et al*. (45) | AVF | Angioplasty | - | - | €571 |
| Bittl *et al*. (48) | AVF + PTFE | Angioplasty | - | - | US$1,939 |
| | | Thrombolysis | - | - | US$3,336 |
| Bizarro *et al*. (34) | AVF | Angioplasty | US$565 | US$220 | US$785 |
| | | Thrombolysis | US$892 | US$489 | US$1,381 |

# PART II
## RESULTS

# Chapter 4

## *Establishment and maintenance of dialysis access*

### 4.1. Effects of starting hemodialysis with an arteriovenous fistula or central venous catheter compared with peritoneal dialysis: a retrospective cohort study.

Coentrão L, Santos-Araújo C, Dias C, Neto R, Pestana M

*BMC Nephrology* 2012 13:88. PMID: 22916962.

Coentrão *et al. BMC Nephrology* 2012, **13**:88
http://www.biomedcentral.com/1471-2369/13/88

BMC Nephrology

RESEARCH ARTICLE Open Access

# Effects of starting hemodialysis with an arteriovenous fistula or central venous catheter compared with peritoneal dialysis: a retrospective cohort study

Luis Coentrão[1*], Carla Santos-Araújo[1], Claudia Dias[2], Ricardo Neto[1] and Manuel Pestana[1]

**Abstract**

**Background:** Although several studies have demonstrated early survival advantages with peritoneal dialysis (PD) over hemodialysis (HD), the reason for the excess mortality observed among incident HD patients remains to be established, to our knowledge. This study explores the relationship between mortality and dialysis modality, focusing on the role of HD vascular access type at the time of dialysis initiation.

**Methods:** A retrospective cohort study was performed among local adult chronic kidney disease patients who consecutively initiated PD and HD with a tunneled cuffed venous catheter (HD-TCC) or a functional arteriovenous fistula (HD-AVF) in our institution in the year 2008. A total of 152 patients were included in the final analysis (HD-AVF, n = 59; HD-TCC, n = 51; PD, n = 42). All cause and dialysis access-related morbidity/mortality were evaluated at one year. Univariate and multivariate analysis were used to compare the survival of PD patients with those who initiated HD with an AVF or with a TCC.

**Results:** Compared with PD patients, both HD-AVF and HD-TCC patients were more likely to be older ($p<0.001$) and to have a higher frequency of diabetes mellitus ($p = 0.017$) and cardiovascular disease ($p = 0.020$). Overall, HD-TCC patients were more likely to have clinical visits ($p = 0.069$), emergency room visits ($p<0.001$) and hospital admissions ($p<0.001$). At the end of follow-up, HD-TCC patients had a higher rate of dialysis access-related complications (1.53 *vs.* 0.93 *vs.* 0.64, per patient-year; $p<0.001$) and hospitalizations (0.47 *vs.* 0.07 *vs.* 0.14, per patient-year; $p = 0.034$) than HD-AVF and PD patients, respectively. The survival rates at one year were 96.6%, 74.5% and 97.6% for HD-AVF, HD-TCC and PD groups, respectively ($p<0.001$). In multivariate analysis, HD-TCC use at the time of dialysis initiation was the important factor associated with death (HR 16.128, 95%CI [1.431-181.778], $p = 0.024$).

**Conclusion:** Our results suggest that HD vascular access type at the time of renal replacement therapy initiation is an important modifier of the relationship between dialysis modality and survival among incident dialysis patients.

## Background

Early referral of chronic kidney disease (CKD) patients to nephrology centres may enable patients to be adequately informed regarding the different renal replacement treatment (RRT) modalities [hemodialysis (HD), peritoneal dialysis (PD) and kidney transplantation (TX)], leading to better results in terms of morbidity and mortality [1-4]. Large registry-based studies have suggested a survival advantage of PD over HD, particularly during the first 1 to 2 years of treatment [5,6]. Although the ability of PD to provide better preservation of residual renal function was invoked as a possible explanation for the survival advantage of PD over HD during the first years of treatment, case mix differences in patients initiating HD may have confounded the interpretation of the studies that examined the influence of the dialysis modality on patient survival [5-7].

* Correspondence: coentrao@med.up.pt
[1]Nephrology Research and Development Unit, Faculty of Medicine, University of Porto & São João Hospital Centre, Alameda Professor Hernani Monteiro, Porto 4202-451, Portugal
Full list of author information is available at the end of the article

Coentrão et al. BMC Nephrology 2012, 13:88
http://www.biomedcentral.com/1471-2369/13/88



The type of vascular access used in HD patients is recognized to have a significant influence on survival. The use of a tunneled cuffed catheter (TCC) is associated with a substantially greater risk of sepsis, hospitalization and mortality compared to the use of an arteriovenous fistula (AVF) [8-12]. Although technique survival with PD is shorter than that with HD, in part due to access-related infections, the frequency of PD catheter-related complications has decreased in recent years, with a low rate of bacteremia/sepsis [13,14]. However, there are few studies comparing the outcomes of incident PD patients with those of HD patients using different vascular access types at dialysis initiation in the literature, to our knowledge [15,16]. In the study presented here, we hypothesize that vascular access type at the time of dialysis initiation accounts for the higher early mortality rate observed in patients who start HD with a catheter, compared to those who initiate HD with a functioning fistula or PD. To test our hypothesis, we compared all-cause and dialysis access-related morbidity/mortality between PD and HD patients with the latter stratified by HD vascular access type at dialysis initiation.

## Methods

### Study design

We conducted a retrospective observational cohort study among CKD patients (age 18 years and older at the start of RRT) who consecutively initiated HD between January 1 and July 1 2008, or PD between January 1, 2008 and July 1, 2009, in our institution.

The study was approved by the Ethics Committee for Health and the Local Institutional Review Board of São João Hospital Centre, Porto, Portugal.

### Setting

Portugal has a higher incidence of end stage-renal disease, ESRD (i.e. the patients who start any RRT modality for the first time) and prevalence in compared to most of other European countries. In 2009, an incidence rate of 240 and a prevalence of 1507 patients per million of the population were registered in ERA-EDTA [17]. Specifically, 10,152 patients underwent HD and 660 patients PD in 2010 (registered by the Portuguese Society of Nephrology). In Portugal, HD is almost exclusively (~90%) provided by outpatient hemodialysis units run by private providers. Hemodialysis patients undergo 4 hours of dialysis three times weekly, aiming for a spKt/V of 1.4 or greater. Patients undergo treatment using high-flux dialyzers; no hemodialyzer is reused. Peritoneal dialysis is provided by public hospitals and university centres. Patients attending our hospital center undergo either continuous ambulatory peritoneal dialysis (CAPD) or automated cyclic peritoneal dialysis (CCPD). All patients have a 1 to 2 week training period before initiation of therapy at home. Treatment of PD patients is individualized: the total Kt/V (renal and peritoneal clearance) aimed for is 1.8 or more and the majority of patients are treated with dextrose-based solutions with daily exchange with Extraneal (Baxter Healthcare Corp, Deerfield, IL, USA).

### Patients

The patients were recruited from the Department of Nephrology of São João Hospital Centre which is a tertiary-care University Hospital responsible for nephrological medical support to ESRD patients beginning RRT within the northwest region of Portugal. Patients were enrolled if they had a diagnosis of end-stage CKD according to a nephrologist and had received outpatient chronic dialysis treatment. Patients who had previously undergone RRT (HD, PD or TX) and restarted during the study period and patients transferred to another district immediately after starting RRT were excluded. The RRT modality adopted was based on patient choice and his/her medical status. Initial dialysis modality was defined as the modality at the first outpatient dialysis treatment: patients starting PD therapy assigned to the PD group and patients starting HD therapy with a tunnelled cuffed catheter or a functioning fistula to the HD-TCC or HD-AVF groups, respectively. Although changes in vascular access type were recorded during follow-up, patients remained in the same index group. Follow-up started on the day dialysis was first performed as an outpatient and continued for 1 year or until death or switching from the RRT modality. Because of the relatively lower number of patients who initiated PD between January 1, 2008 and July 1, 2008 compared to those who initiated HD, the recruitment period for incident PD patients was extended to July 2009.

A total of 191 CKD patients started RRT during the study period (133 HD, 58 PD). Twenty-three HD patients were excluded from the study due to previous RRT (n = 13) or loss to follow-up because of transfer to another district (n =10). In addition, 16 PD patients were excluded from the study because they had previously undergone RRT (HD, 11 patients; TX, 5 patients). A total of 152 patients were included in the final analysis. Of the 110 incident HD patients, 59 started therapy with a functioning AVF and 51 with a TCC. Three cohorts of incident dialysis patients were then established: HD-AVF (n = 59), HD-CVC (n = 51) and PD (n = 42).

### Data

Clinical data and information regarding access type were collected from our hospital database and from outpatient dialysis unit records, when appropriate. A physician assessed the presence of co-morbid illness by

Coentrão et al. BMC Nephrology 2012, 13:88
http://www.biomedcentral.com/1471-2369/13/88



complete review of each patient's records at the enrolment date. Information was collected for the 19 variables that constitute the Charlson Comorbidity Index [18], which has been validated for use in patients with ESRD. The number of clinical and emergency room visits, hospitalizations and dialysis access complications were determined for all participants from our hospital database and from outpatient dialysis unit records, when appropriate.

Complications of HD and PD accesses were classified as mechanical or infectious events [19,20]. Mechanical complications included AVF stenosis, thrombosis, bleeding and limb ischemia; TCC flow dysfunction, thrombosis, bleeding, cuff extrusion and complications of central venous catheterization; PD catheter flow dysfunction, bleeding, leaks, cuff extrusion, hernias and complications related to Tenckhoff catheter placement. Infectious complications included AVF-related bacteremia, TCC-related bacteremia, PD-related peritonitis and bacteremia.

Dates of renal transplantation, switch from the RRT modality and/or death were known until end off follow-up.

### Outcomes

The primary aim of this analysis was to determine the all-cause mortality of HD-AVF, HD-TCC and PD patients at 1 year from the time of first dialysis.

A secondary aim was to examine the dialysis access-related morbidity/mortality of HD-AVF, HD-TCC and PD patients at 1 year from the time of first dialysis.

### Statistical analysis

Data are given as percentages and means ± SD. Categorical variables were compared using Fisher's exact test. The Kruskal-Wallis test was used to analyze differences between continuous variables. Rates were calculated for each patient by dividing the number of events/procedures by the duration of follow-up in years. Survival on dialysis was calculated by the Kaplan-Meier method. Univariate analysis of survival was performed by the log rank method. Multivariate analysis of survival was performed using a Cox proportional hazards model. Covariates were included if the baseline difference between the three groups was <0.10. All tests were two sided, and differences were considered significant at $P<0.05$. All statistical analyses were performed using the SPSS software, version 19 (SPSS, Inc., Chicago, IL, USA).

## Results

### Baseline characteristics

Table 1 lists the baseline characteristics of the study population. Compared with PD patients, both HD-TCC and HD-AVF patients were more likely to be older ($p<0.001$, Table 1) and to have a higher frequency of diabetes mellitus ($p = 0.017$, Table 1), coronary heart disease ($p = 0.007$, Table 1) and congestive heart failure ($p = 0.023$, Table 1). Both HD-AVF and PD groups initiated dialysis with similar levels of serum hemoglobin and serum albumin. In addition, ~80% of both HD-AVF and PD groups were referred to a nephrologist early. HD-TCC patients were more likely to be referred to a nephrologist late ($p<0.001$, Table 1), and to initiate dialysis with lower hemoglobin ($p<0.001$, Table 1) and serum albumin ($p<0.001$, Table 1). HD-AVF patients were more likely to initiate RRT with higher estimated glomerular filtration rate (eGFR) than either HD-TCC or PD patients ($p<0.001$, Table 1).

### Patient outcomes

Table 2 lists the mean numbers of clinical events of the study population.

HD-TCC patients were more likely to have higher numbers of dialysis access-related complications than HD-AVF and PD patients ($p<0.001$, Table 2). In particular, the PD group had the lowest number of mechanical access-related complications ($p<0.001$, Table 2) and the HD-AVF group the lowest infection rate ($p<0.001$, Table 2). Despite the similar number of infection-free patients in the PD and HD-TCC groups at 1 year of follow-up, both catheter-related bacteremia and hospital admissions were significantly higher in the HD-TCC group ($p = 0.004$ and 0.034, respectively; Table 2).

Overall, HD-TCC patients were more likely to have clinical visits ($p = 0.069$, Table 2), emergency room visits ($p<0.001$, Table 2) and hospital admissions ($p<0.001$, Table 2). The mean numbers of hospital days for HD-AVF, HD-TCC and PD patients were 5.5 ± 13.7, 36.6 ± 40.7 and 5.1 ± 15.1 days, per patient-year at risk, respectively ($p<0.001$).

Sixteen patients died during follow-up (HD-AVF, n = 2; HD-TCC, n = 13; PD, n = 1). The main causes of death for HD-TCC patients were catheter-related bacteremia (n = 7), cardiac disease (n = 4), pneumonia (n = 1) and cancer (n = 1); for HD-AVF patients was cancer (n = 2) and for PD patients was pyonephrosis (n = 1). The survival rates at one year were 86.3% and 97.6% for HD and PD patients, respectively ($p = 0.044$, log rank test). When stratified for HD vascular access type, the survival rates at one year were 96.6%, 74.5% and 97.6% for HD-AVF, HD-TCC and PD groups, respectively (Figure 1; $p<0.001$, log rank test). Older age ($p = 0.002$), diabetes ($p = 0.006$), cardiovascular disease ($p = 0.026$), late referral ($p = 0.001$) hypoalbuminemia ($p = 0.001$) and anemia ($p = 0.002$) were all associated with poorer survival by log rank analysis. The impact of HD vascular access at the time of dialysis initiation on survival was considered in more detail in a

Coentrão et al. BMC Nephrology 2012, 13:88
http://www.biomedcentral.com/1471-2369/13/88



**Table 1 Baseline characteristics of enrolled patients treated with different dialysis modalities and vascular accesses (HD-AVF, hemodialysis with arteriovenous fistula; HD-TCC, hemodialysis with catheter; PD, peritoneal dialysis)**

| Variable | HD-AVF (n = 59) | HD-TCC (n = 51) | PD (n = 42) | P |
|---|---|---|---|---|
| Male sex (%) | 60% | 55% | 52% | 0.856 |
| Mean age (y) | 62.8 ± 14.3 | 66.1 ± 15.4 | 55.1 ± 16.1 | 0.001 |
| *18-44 years* | 5 (9%) | 4 (8%) | 9 (21%) | 0.047 |
| *45-64 years* | 19 (32%) | 12 (24%) | 20 (47%) | 0.015 |
| *65+ years* | 35 (59%) | 35 (69%) | 13 (31%) | 0.001 |
| Etiology of kidney disease (%) | | | | |
| *Diabetes* | 26 (44%) | 22 (42%) | 8 (19%) | 0.017 |
| *Hypertension* | 7 (12%) | 4 (8%) | 2 (5%) | 0.471 |
| *Glomerulonephritis* | 7 (12%) | 3 (6%) | 13 (31%) | 0.003 |
| *Tubulointersticial kidney disease* | 8 (14%) | 10 (20%) | 7 (17%) | 0.702 |
| *Unknown* | 11 (18%) | 12 (24%) | 12 (29%) | 0.510 |
| Mean Charlson Comorbidity Index | 5.1 ± 3.1 | 5.0 ± 2.5 | 4.4 ± 2.2 | 0.574 |
| *Low risk (≤ 3)* | 25 (42%) | 17 (34%) | 15 (36%) | 0.745 |
| *Medium risk (4–5)* | 13 (22%) | 11 (21%) | 14 (33%) | 0.133 |
| *High risk (≥6)* | 21 (36%) | 23 (45%) | 13 (31%) | 0.575 |
| Comorbid conditions (%) | | | | |
| *Coronary heart disease* | 26 (44%) | 17 (33%) | 6 (14%) | 0.007 |
| *Congestive heart failure* | 25 (42%) | 18 (35%) | 7 (17%) | 0.023 |
| *Peripheral vascular disease* | 14 (24%) | 11 (22%) | 9 (19%) | 0.104 |
| *Previous stroke* | 7 (12%) | 8 (16%) | 2 (5%) | 0.095 |
| *Diabetes* | 26 (44%) | 23 (45%) | 8 (19%) | 0.015 |
| *Malignant disease* | 10 (20%) | 10 (23%) | 11 (26%) | 0.432 |
| Late referral (%) | 13 (22%) | 44 (86%) | 9 (21%) | <0.001 |
| Time from referral to dialysis initiation, months (mean ± SD) | 39 ± 35 | 11 ± 30 | 34 ± 28 | <0.001 |
| Hemoglobin (g/L) | 104 (101, 108) | 90 (85, 94) | 105 (108, 115) | <0.001 |
| eGFR (ml/min per 1.73 $m^2$)* | 10.0 (9.2, 10.9) | 7.8 (6.8, 8.9) | 8.3 (7.7, 9.0) | <0.001 |
| Serum creatinine (mg/dL) | 5.7 (5.3, 6.1) | 8.0 (7.0, 9.1) | 6.7 (6.0, 7.4) | <0.001 |
| Serum urea (mg/dL) | 218 (203, 231) | 217 (194, 239) | 197 (184, 210) | 0.214 |
| Serum albumin (g/L) | 37 (35, 38) | 33 (31, 34) | 39 (38, 40) | <0.001 |

* eGFR, estimated glomerular filtration rate.

multivariate model to correct for confounding variables. The results of the Cox model are given in Table 3- HD-TCC use at the time of dialysis initiation was independently associated with death (HR 16.128, 95%CI [1.431-181.778], $p = 0.024$).

At the end of follow-up, 97% (n = 57) and 47% (n = 18) of HD-AVF and HD-TCC patients had a functional fistula as permanent vascular access, respectively. Three patients switched definitely from PD to HD due to PD-related peritonitis (n = 2) and tuberculous peritonitis (n = 1). Only 2 patients received a transplant during the study period.

## Discussion

The study presented here shows that incident HD-TCC patients experienced a significantly higher mortality rate at one year of dialysis, in comparison with HD-AVF and PD patients. Infection was the most common cause of death, whereas the second most common cause was death related to cardiovascular disease. Dialysis access-related complications were responsible for 43% (n = 7) of all deaths, and infection was the single cause responsible for such deaths. Death caused by dialysis access complications occurred only in the HD-TCC group. Importantly, HD-TCC patients had approximately twice as many clinical events related to dialysis access than either HD-AVF or PD patients (mainly access-related bacteremia episodes and hospitalizations). In contrast, most of the vascular and peritoneal dialysis access complications in the HD-AVF and PD groups were not serious clinical events, and no dialysis access-related deaths occurred in either these two groups. Although HD-TCC

Coentrão *et al. BMC Nephrology* 2012, **13**:88
http://www.biomedcentral.com/1471-2369/13/88



**Table 2 Dialysis access-related and overall clinical events of enrolled patients treated with different dialysis modalities and vascular accesses (HD-AVF, hemodialysis with arteriovenous fistula; HD-TCC, hemodialysis with catheter; PD, peritoneal dialysis), per patient-year at risk (mean ± SD)**

| Clinical events | HD-AVF (n = 59) | HD-TCC (n = 51) | PD (n = 42) | P |
|---|---|---|---|---|
| **Dialysis access-related** | | | | |
| Mechanical complications | 0.93 ± 1.40 | 0.82 ± 1.49 | 0.07 ± 0.26 | <0.001 |
| *Fistula related* | 0.73 ± 0.99 | 0.29 ± 0.64 | 0 | <0.001 |
| *Catheter related* | 0.20 ± 0.71 | 0.53 ± 1.12 | 0.07 ± 0.26 | 0.114 |
| Infectious complications | | | | |
| *Patients infection free, at year 1, N (%)* | 59 (100%) | 33 (65%) | 24 (57%) | <0.001 |
| *Peritonitis* | 0 | 0 | 0.57 ± 0.74 | 0.002 |
| *Bacteremia* | 0 | 0.71 ± 1.29 | 0 | 0.004 |
| Total | 0.93 ± 1.40 | 1.53 ± 1.89 | 0.64 ± 0.83 | <0.001 |
| **Overall** | | | | |
| Dialysis access-related complications * | 0.93 ± 1.40 | 1.53 ± 1.89 | 0.64 ± 0.83 | <0.001 |
| Clinical visits | 4.17 ± 4.29 | 6.35 ± 10.25 | 3.38 ± 3.41 | 0.069 |
| Emergency room visits | 1.42 ± 2.38 | 3.06 ± 3.23 | 1.62 ± 1.75 | <0.001 |
| Hospital admissions | 0.66 ± 1.14 | 2.04 ± 1.55 | 0.50 ± 0.74 | <0.001 |
| *Dialysis accesss-related* | 0.07 ± 0.25 | 0.47 ± 1.09 | 0.14 ± 0.42 | 0.034 |
| *Other* | 0.59 ± 1.03 | 1.57 ± 1.05 | 0.36 ± 0.62 | 0.010 |
| Total | 7.18 ± 6.76 | 12.98 ± 12.61 | 6.14 ± 4.12 | <0.001 |

* Includes all dialysis access-related mechanical and infectious complications.

patients had similar baseline characteristics to HD-AVF patients, HD-TCC patients were referred to the nephrologist later, which might explain the delay in AVF creation in this group. In contrast, both incident HD-AVF and PD patients were referred to the nephrologist early and could thus benefit from appropriate vascular and peritoneal access placement in due time. Despite different baseline characteristics, both the HD-AVF and PD groups had similarly high survival rates at year 1. Multivariate analysis showed that HD-TCC use at the time of dialysis initiation was the important factor associated with poor prognosis. Taken together, our results strongly suggest that HD vascular access type at the time of dialysis initiation might explain the differences in outcome observed between the incident HD and PD populations. Our results corroborate the recent findings of Perl *et al.*, [15] in incident adult dialysis patients on the Canadian Organ Replacement Register who found that

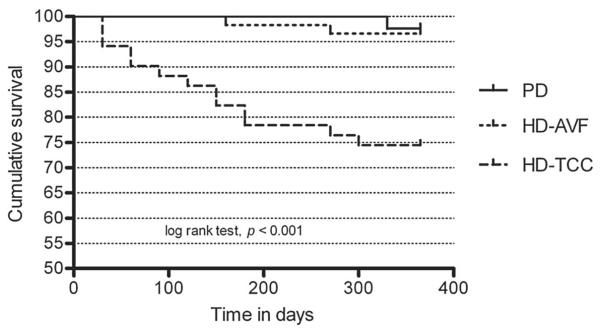


**Figure 1 Kaplan-Meier plots of survival in incident dialysis patients with log rank analysis to assess the significance of dialysis access on survival.** Survival curves for HD-AVF (hemodialysis with arteriovenous fistula, dotted line), HD-TCC (hmodialysis with tunneled cuffed catheter, dashed line), and PD (peritoneal dialysis, solid line) demonstrate higher 1-year mortality in HD-TCC patients.

Coentrão et al. BMC Nephrology 2012, 13:88
http://www.biomedcentral.com/1471-2369/13/88



**Table 3 Results of the Cox multivariate analysis for the relationship between co-morbid factors, dialysis access at dialysis initiation and death in incident dialysis patients (HD-AVF, hemodialysis arteriovenous fistula; HD-TCC, hemodialysis tunneled cuffed catheter; PD, peritoneal dialysis catheter)**

| | Hazard ratio | 95% confidence intervals | *P* |
|---|---|---|---|
| Age (per year) | 1.080 | 0.996-1.171 | 0.062 |
| Diabetes | 0.487 | 0.139-2.288 | 0.318 |
| Coronary heart disease | 1.875 | 0.381-9.227 | 0.439 |
| Congestive heart failure | 0.497 | 0.117-2.158 | 0.497 |
| Peripheral vascular disease | 0.499 | 0.114-2.190 | 0.357 |
| Previous stroke | 0.197 | 0.032-1.225 | 0.081 |
| Late referral | 1.009 | 0.990-1.028 | 0.378 |
| Albumin | 0.917 | 0.814-1.033 | 0.153 |
| Hemoglobin | 0.999 | 0.948-1.054 | 0.975 |
| eGFR* | 1.135 | 0.903-1.426 | 0.279 |
| Dialysis access | | | |
| *PD (reference)* | | | |
| *HD-AVF* | 0.734 | 0.056-9.656 | 0.814 |
| *HD-TCC* | 16.128 | 1.431-181.778 | 0.024 |

* eGFR, estimated glomerular filtration rate.

patients initiating HD with a catheter had a higher risk of death compared to both HD-AVF and PD patients.

Our findings are also in agreement with the recent report of Quinn *et al.*, [21] that showed no difference in survival between PD and HD patients who received > 4 months of predialysis care. Also, Raithatha *et al.* [16] recently showed that the use of HD-catheter is one of the key features of late referral that determines poor prognosis. In the present study, ~80% of both HD-AVF and PD patients were referred to the nephologist early and experienced similarly high survival rates in the first year of dialysis, compared to HD-TCC patients. Our results support the need for early referral of ESRD patients to nephrology centers to provide the opportunity for patient selection of RRT modality and timely creation of the appropriate dialysis access [22].

Most reports that have used USRDS data do not include the critical initial 90-day period on dialysis. This is a time period when a high proportion of HD patients are using catheters as bridging access devices [12]. In the present study, survival rates of HD-TCC, HD-AVF and PD groups at 90 days of follow-up were 88%, 100% and 100%, respectively. Exclusion of this period in the analysis would probably underestimate the morbidity and mortality rates of the HD-TCC group.

One interesting finding of the present study was that bacteremia only occurred in HD-TCC patients, refuting the common misconception that PD is associated with an overall higher rate of severe infection than HD. In addition, PD patients had the lowest number of mechanical access-related complications. Our results support the previous findings of Oliver *et al.* [23,24] and Povlsen *et al.* [2,25,26] by showing that patients who choose PD require fewer access interventions and do not face an increased risk of access-related complications compared to HD patients.

As a retrospective study, this study has the limitations of such an approach. As with all observational studies, there may have been selection bias, in particular influenced by patient treatment preferences and time of referral to the nephrologist. PD patients were younger and had lower comorbid illness, compared to HD patients. The patient population consisted mainly of Caucasian Europeans, which makes it impossible to draw conclusions for other ethnic groups. Peritoneal dialysis patients were treated in a single academic nephrology centre, whereas HD patients were treated in separate peripheral renal centers, although this is a reflection of the local distribution of patients between modalities.

## Conclusion

Our study provides evidence favoring the view that HD vascular access type at renal replacement therapy initiation is an important modifier of the relationship between dialysis modality and survival among incident dialysis patients. Our results emphasize the need for an early referral program for ESRD patients so that those who choose HD have a functioning AVF, and those who choose PD have a Tenckhoff catheter placed in due time. We believe such a policy would decrease the risk of dialysis morbidity/mortality.

#### Competing interests

The authors have no equity interest or financial agreements with any company or commercial entity related to the content of the article and they have not received salary or support from any company related to the article.

#### Authors' contributions

LC: participated in the design of the study, in the acquisition and interpretation of data, performed the statistical analysis and wrote the manuscript. CSA: participated in the acquisition and interpretation of data and revised the manuscript for important intellectual content. CCD: performed the statistical analysis. RN participated in the acquisition of data. MP: participated in the interpretation of data and revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

#### Acknowledgements

The authors thank Professor João Frazão for assistance in manuscript preparation, Ms. Doreen Raine for editing the English and the clinical directors from hemodialysis clinics who kindly agreed to collaborate in this study: A. Baldaia Moreira M.D., A. Caldeira Gomes M.D., A. Castro Henriques M.D., Antunes de Azevedo M.D, Eva Xavier M.D., João C. Fernandes M.D., João M. Frazão M.D., PhD, Jorge P. Baldaia M.D., José M. Madureira M.D., José Pinheiro M.D., Odete Pereira M.D., Sofia Pedroso M.D., Susana Sampaio M.D., Vasco Miranda M.D.

**Author details**
[1]Nephrology Research and Development Unit, Faculty of Medicine, University of Porto & São João Hospital Centre, Alameda Professor Hernani Monteiro, Porto 4202-451, Portugal. [2]Department of Health Information and Decision Sciences, Faculty of Medicine, University of Porto, Alameda Professor Hernani Monteiro, Porto 4202-451, Portugal.

Received: 22 November 2011 Accepted: 20 August 2012
Published: 23 August 2012

**References**

1. Lameire N, Wauters JP, Górriz JL, *et al*: **An update on the referral pattern of patients with end-stage renal disease.** *Kidney Int* 2002, **61:**S27–S34.
2. Górriz J, Sancho A, Pallardó LM, *et al*: **Significado pronóstico de la diálisis programada en pacientes que inician tratamiento substituivo renal. Un estúdio multicéntrico español.** *Nefrologia* 2001, **21:**49–59.
3. Buck J, Baker R, Cannaby AM, *et al*: **Why do patients known to renal services still undergo urgent dialysis initiation? A cross-sectional survey.** *Nephrol Dial Transplant* 2007, **22**(11):3240–3245.
4. Mendelssohn DC, Malmbrg C, Hamandi B: **An integrated review of "unplanned" dialysis initiation: reframing the terminology to "suboptimal" initiation.** *BMC Nephrol* 2009, **10:**22.
5. Weinhandl ED, Foley RN, Gilbertson DT, Arneson TJ, Snyder JJ, Collins AJ: **Propensity-matched mortality comparison of incident hemodialysis and peritoneal dialysis patients.** *J Am Soc Nephrol* 2010, **21:**499–506.
6. Heaf JG, Lokkegaard H, Madsen M: **Initial survival advantage of peritoneal dialysis relative to haemodialysis.** *Nephrol Dial Transplant* 2002, **17:**112–117.
7. Korevaar JC, Feith GW, Dekker FW, van Manen JG, Boeschoten EW, Bossuyt PM, Krediet RT: **Effect of starting with hemodialysis compared with peritoneal dialysis in patients new on dialysis treatment: A randomized controlled trial.** *Kidney Int* 2003, **64:**2222–2228.
8. Manns B, Tonelli M, Yilmaz S, *et al*: **Establishment and maintenance of vascular access in incident hemodialysis patients: a prospective cost analysis.** *J Am Soc Nephrol* 2005, **16:**201–209.
9. Moist LM, Trpeski L, Na Y, Lok CE: **Increased hemodialysis catheter use in Canada and associated mortality risk: Data from the Canadian Organ Replacement Registry 2001–2004.** *Clin J Am Soc Nephrol* 2008, **3:**1726–1732.
10. de Jager DJ, Grootendorst DC, Jager KJ, *et al*: **Cardiovascular and noncardiovascular mortality among patients starting dialysis.** *JAMA* 2009, **302**(16):1782–1789.
11. Astor BC, Eustace JZ, Powe NR, the CHOICE Study, *et al*: **Type of vascular access and survival among incident hemodialysis patients: The Choices for Healthy Outcomes in Caring for ESRD (CHOICE) Study.** *J Am Soc Nephrol* 2005, **16:**1449–1455.
12. Rehman R, Schmidt RJ, Moss AH: **Ethical and Legal Obligation to Avoid Long-Term Tunneled Catheter Access.** *Clin J Am Soc Nephrol* 2009, **4:**456–460.
13. Aslam N, Bernardini J, Fried L, *et al*: **Comparison of infectious complications between incident hemodialysis and peritoneal dialysis patients.** *Clin J Am Soc Nephrol* 2006, **1:**1226–1233.
14. Rodrigues A: **How to persuade peritoneal dialysis-skeptical hemodialysis fans.** *Contrib Nephrol* 2009, **163:**237–242.
15. Perl J, Wald R, McFarlane P, *et al*: **Hemodialysis vascular access modifies the association between dialysis modality and survival.** *J Am Soc Nephrol* 2011, **22:**1113–1121.
16. Raithatha A, McKane W, Kendray D, Evans C: **Catheter access for hemodialysis defines higher mortality in late-presenting dialysis patients.** *Ren Fail* 2010, **32**(10):1183–1188.
17. *ERA-EDTA Registry Annual Report*; 2009. http://www.era-edta-reg.org/ (10 August 2011, date last accessed.
18. Charlson ME, Pompei P, Ales KL: **A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation.** *J Am Soc Nephrol* 1996, **7:**198–207.
19. Allon M, Work J: **Venous catheter access for hemodialysis**. In *Handbook of dialysis*. Edited by Daugirdas J, Blake P, Ing T. Philadelphia, USA: Lippincott Williams & Wilkins; 2007:87–104.
20. Campos RP, Chula DC, Riella MC: **Complications of the peritoneal access and their management.** *Contrib Nephrol* 2009, **163:**183–197.
21. Quinn RR, Hux JE, Oliver MJ, *et al*: **Selection bias explains apparent differential mortality between dialysis modalities.** *J Am Soc Nephrol* 2011, **22:**1534–1542.
22. Covic A, Bammens B, Lobbedez T, *et al*: **Educating end-stage renal disease patients on dialysis modality selection: a clinical advice from the European Renal Best Practice (ERBP) Advisory Board.** *NDT Plus* 2010, **3:**225–233.
23. Oliver MJ, Rothwell DM, Fung K, *et al*: **Late creation of vascular access for hemodialysis and increased risk of sepsis.** *J Am Soc Nephrol* 2004, **15:**1936–1942.
24. Oliver MJ, Verrelli M, Zacharias JM, Blake PG, Garg AX, Johnson JF, Pandeya S, Perl J, Kiss AJ, Quinn RR: **Choosing peritoneal dialysis reduces the risk of invasive access interventions.** *Nephrol Dial Transplant Jun* 2011, **2:** [Epub ahead of print].
25. Povlsen JV, Ivarsen P: **How to start the late referred ESRD patient urgently on chronic APD.** *Nephrol Dial Transplant* 2006, **21**(Suppl 2):ii56–ii59.
26. Povlsen JV: **Unplanned start on assisted peritoneal dialysis.** *Contrib Nephrol* 2009, **163:**261–263.

doi:10.1186/1471-2369-13-88
**Cite this article as:** Coentrão *et al.*: Effects of starting hemodialysis with an arteriovenous fistula or central venous catheter compared with peritoneal dialysis: a retrospective cohort study. *BMC Nephrology* 2012 **13**:88.

# Chapter 4

## *Establishment and maintenance of dialysis access*

### 4.2. Cost analysis of hemodialysis and peritoneal dialysis accesses in incident dialysis patients

Coentrão L, Santos-Araújo C, Ribeiro C, Dias C, Pestana M

*Perit Dial Int* 2013 Mar 1. [Epub ahead of print]. PMID: 23455977.

Peritoneal Dialysis International

*Peritoneal Dialysis International*, inPress
doi: 10.3747/pdi.2011.00309

0896-8608/13 $3.00 + .00


# COST ANALYSIS OF HEMODIALYSIS AND PERITONEAL DIALYSIS ACCESS COSTS IN INCIDENT DIALYSIS PATIENTS

Luis A. Coentrão,[1] Carla S. Araújo,[1] Carlos A. Ribeiro,[2] Claúdia C. Dias,[3] and Manuel J. Pestana[1]

*Nephrology Research and Development Unit[1] and Financial Management Unit,[2] São João Hospital Centre, and Department of Health Information and Decision Sciences,[3] Faculty of Medicine, University of Porto, Portugal*

♦ ***Background:*** **Although several studies have demonstrated the economic advantages of peritoneal dialysis (PD) over hemodialysis (HD), few reports in the literature have compared the costs of HD and PD access. The aim of the present study was to compare the resources required to establish and maintain the dialysis access in patients who initiated HD with a tunneled cuffed catheter (TCC) or an arteriovenous fistula (AVF) and in patients who initiated PD.**

♦ ***Methods:*** **We retrospectively analyzed the 152 chronic kidney disease patients who consecutively initiated dialysis treatment at our institution in 2008 (HD-AVF, *n* = 65; HD-CVC, *n* = 45; PD, *n* = 42). Detailed clinical and demographic information and data on access type were collected for all patients. A comprehensive measure of total dialysis access costs, including surgery, radiology, hospitalization for access complications, physician costs, and transportation costs was obtained at year 1 using an intention-to-treat approach. All resources used were valued using 2010 prices, and costs are reported in 2010 euros.**

♦ ***Results:*** **Compared with the HD-AVF and HD-TCC modalities, PD was associated with a significantly lower risk of access-related interventions (adjusted rate ratios: 1.572 and 1.433 respectively; 95% confidence intervals: 1.253 to 1.891 and 1.069 to 1.797). The mean dialysis access–related costs per patient–year at risk were €1171.6 [median: €608.8; interquartile range (IQR): €563.1 – €936.7] for PD, €1555.2 (median: €783.9; IQR: €371.4 – €1571.7) for HD-AVF, and €4208.2 (median: €1252.4; IQR: €947.9 – €2983.5) for HD-TCC ($p < 0.001$). In multivariate analysis, total dialysis access costs were significantly higher for the HD-TCC modality than for either PD or HD-AVF ($\beta = -0.53$; 95% CI: –1.03 to –0.02; and $\beta = -0.50$; 95% CI: –0.96 to –0.04).**

♦ ***Conclusions:*** **Compared with patients initiating HD, those initiating PD required fewer resources to establish and maintain a dialysis access during the first year of treatment.**

***Perit Dial Int*: inPress** **www.PDIConnect.com**
**doi:10.3747/pdi.2011.00309**

Correspondence to: L. Coentrão, Nephrology Research and Development Unit, São João Hospital Centre, Faculty of Medicine, University of Porto, Porto 4200-319 Portugal.
coentrao@med.up.pt
Received 5 December 2011; accepted 26 July 2012

KEY WORDS: Cost analysis; health economics; hemodialysis; dialysis access; vascular access; peritoneal catheter.

End-stage renal disease (ESRD) patients who choose hemodialysis (HD) require a vascular access, and those who choose peritoneal dialysis (PD) require a peritoneal catheter before initiation of renal replacement therapy (RRT). The type of vascular access used in HD patients is recognized to have a significant influence on patient survival. Compared with use of a native arteriovenous fistula (AVF), use of a tunneled cuffed catheter (TCC) is associated with a substantially greater risk of sepsis, hospitalization, and mortality (1–8). By contrast, PD catheter complications have declined in recent years, with low rates of bacteremia and sepsis (9–22). Recently, Perl *et al.* (9) observed that, compared with patients starting PD or starting HD with a functioning AVF, patients starting HD with a TCC had a higher risk of death during the first year. However, that finding didn't necessarily demonstrate causality between use of a HD catheter and patient death.

Several studies have reported that HD is more expensive than PD, mainly because of costs related to dialysis staff, patient transportation, and overhead (23–30). However, vascular access care accounts for a significant proportion of the health care costs in both incident and prevalent HD patients (31–33). Nonetheless, to our knowledge, few reports have compared the costs of PD and HD access (32). The aim of the present study was to compare the resources required to establish and maintain dialysis access in patients initiating HD with a TCC or with an AVF and in those initiating PD.



PDI in Press. Published on March 1, 2013. doi:10.3747/pdi.2011.00309

## METHODS

### STUDY DESIGN

Our retrospective cost analysis included local chronic kidney disease patients (age 18 years and older at the start of RRT) who consecutively initiated HD between 1 January 2008 and 1 July 2008, or PD between 1 January 2008 and 1 July 2009 at our hospital.

The study was approved by the Ethics Committee for Health and the Local Institutional Review Board of São João Hospital Centre, EPE, Porto, Portugal.

### PATIENT COHORT

The incidence of ESRD—that is, patients who start any RRT modality for the first time—is higher in Portugal than in other European countries (34). An incidence rate of 217 HD patients and 18 PD patients per million population were registered by the Portuguese Society of Nephrology in 2010. Patients were recruited from the nephrology department of São João Hospital Centre, which is a tertiary-care university hospital responsible for nephrologic medical support to ESRD patients starting RRT in the northwest region of Portugal. Patients were enrolled if they had a diagnosis of end-stage chronic kidney disease according to a nephrologist and if they had received outpatient chronic dialysis treatment. Patients who had previously undergone RRT (HD, PD, or transplantation) and those who restarted during the study period or who transferred to another district immediately after RRT start were excluded. The program provided free choice to patients who were eligible for both therapies, but some patients in the HD group had no choice because of contraindications for PD. Treatment modality was assigned at the time of the first attempt at dialysis access placement, on an intention-to-treat basis. Patients were considered PD patients if they had chosen PD and if an attempt was made to place a PD catheter. Otherwise, the patients were considered HD patients. The HD group was subdivided into patients who underwent AVF creation or TCC placement as a first vascular access. Patients were followed for 1 year from the date of dialysis initiation, or until death or switch from their RRT modality. Because of the relatively lower number of patients who initiated PD between 1 January and 1 July 2008, compared with those who initiated HD, the recruitment period for incident PD patients was extended to July 2009.

A total of 191 chronic kidney disease patients started RRT during the study period (133 HD, 58 PD). Among those 191 patients, 23 HD patients were excluded because of previous RRT ($n$ = 13) or loss to follow-up after transfer to another district ($n$ = 10), and 16 PD patients were excluded because of previous RRT (HD, $n$ = 11; transplantation, $n$ = 5). The remaining 152 patients were included in the final analysis. Of the 110 incident HD patients, 65 underwent AVF creation, and 45 underwent TCC placement. Three cohorts of incident dialysis patients were therefore established: HD-AVF ($n$ = 65), HD-TCC ($n$ = 45), and PD ($n$ = 42).

### DATA COLLECTION

Clinical information was collected from hospital and dialysis unit records as appropriate. The presence of comorbidity at the enrolment date was assessed by a physician undertaking a complete review of the patient's records. Information was collected for the 19 variables that constitute the Charlson comorbidity index (35), which has been validated for use in patients with ESRD. Information on all dialysis access surgeries, radiologic imaging studies, and dialysis catheter interventions was collected from our hospital database. Because an access was created before dialysis initiation in some patients, all attempts at dialysis access placement were recorded and included in the final analysis. The clinical records from all hospitalizations for all patients were reviewed by a physician. Information on hospital admissions for which the primary reason for admission was access-related care—as defined by the discharge diagnosis (coded according to the International Classification of Diseases, Ninth Revision)—was captured for all patients.

### PROCEDURES

***Access Surgery:*** Peritoneal dialysis–related procedures (PD catheter insertion, replacement, repositioning, or removal; omentectomy; lysis of adhesions; correction of peritoneal leaks and abdominal hernias) were performed by a dedicated group of general surgeons and nephrologists, in the operating room, under general anesthesia. Fistula-related procedures (fistula creation, revision, and ligation) were performed by vascular surgeons in a specialized room, under local anesthesia. Preoperative ultrasonography screening of vessels and peripheral venograms for access planning were not routinely performed.

***Diagnostic Imaging:*** Diagnostic imaging studies included fistulograms, access-directed thrombolysis, and access-related angioplasties—that is, radiology procedures performed as part of access-related care. These procedures were performed by a dedicated interventional nephrologist in the angiographic suite, under local anesthesia (36).

***TCC-Related Interventions:*** Central venous catheter–related interventions included insertion, exchange, and removal. These procedures were performed by nephrologists at the bedside, under local anesthesia. Catheter dysfunction, defined as the complete inability to withdraw blood or the inability to withdraw blood at a sufficient rate to sustain dialysis (blood flow less than 300 mL/min), was routinely managed by dialysis nurses with local instillation of tissue plasminogen activator.

### COST ANALYSIS

Our study was performed from the public administration perspective, including direct medical and nonmedical costs. Annual dialysis access costs were evaluated using a mixed costing method. All resources used were valued using 2010 prices, and costs are reported in 2010 euros.

The resources required to care for a patient's dialysis access were divided into the categories of access surgery, diagnostic imaging, TCC-related interventions, hospitalization, and patient transportation. Access surgery, diagnostic imaging, and TCC-related intervention costs were obtained using a micro-costing approach:

- The professional fee per intervention was determined from the average fee charged by physicians per year.
- Technical costs per intervention—including supplies, pharmacy and radiology costs, and additional overhead expenses—were obtained for all procedures.

The "total expense" represents the sum of the technical and overhead costs and the professional fees (37). Cost data for dialysis access–related hospitalizations were extracted from the Ministry of Health and Welfare Ordinance Legislation—Diário da República (1st series, No. 147, 31 July 2009, No. 839, and 2nd series, No. 81, 5 April 2000, clause No. 7376/2000). Costs of patient transport for dialysis access care were included in the analysis (€0.47/1 km).

### OUTCOMES

The primary outcome was the costs related to dialysis access at 1 year from the time of first dialysis. The secondary outcome was the dialysis access–related intervention rate per patient–year.

### STATISTICAL ANALYSIS

Data are presented as percentages and means ± standard deviation. Costs are given as means with 95% confidence intervals (CIs). Categorical variables were compared using the Fisher exact test. The Kruskal–Wallis test was used to analyze differences between continuous variables. Rates were calculated for each of the patients by dividing the number of events or procedures by the duration of follow-up in years. Between study groups, the mean intervention rates per patient were compared using Poisson regression. Because costs were not normally distributed, they were log-transformed before statistical testing. Multivariate linear regression was used to assess the impact of various comorbid factors on the dialysis access–related costs. Covariates were included if the baseline difference between the three groups was less than 0.10 in the univariate comparison. To address the impact on costs of variations in duration of follow-up resulting from early death, the year 1 cost of patient care by access type and dialysis modality was calculated by direct extrapolation from the truncated costing period for patients who died during year 1. This approach permitted the cost per patient–year at risk to be reported. All tests were two-sided, and differences were considered significant at $p < 0.05$. All statistical analyses were performed using the SPSS software application (version 19: SPSS, Chicago, IL, USA).

## RESULTS

### BASELINE CHARACTERISTICS

Table 1 shows the baseline characteristics of the study population. Compared with the PD patients, the HD-TCC and HD-AVF patients were more likely to be older and to have a higher frequency of diabetes mellitus, coronary artery disease, congestive heart failure, and cerebrovascular disease. Time from referral to dialysis initiation was significantly lower in the HD-TCC patients than in the HD-AVF and PD patients.

The mean distances between the homes of the HD-AVF, HD-TCC, and PD patients and our hospital center were 42.1 ± 33.9 km, 53.0 ± 33.8 km, and 30.3 ± 23.4 km respectively ($p = 0.004$).

### RESOURCE USE

We were able to assess costs for the full 12-month observation period in 131 of the 152 study patients. For the remaining 21 patients (16 of whom died, 2 of whom received a renal graft, and 3 of whom permanently switched from PD to HD), only the corresponding portion of the 12-month period was costed.

### DESCRIPTION OF PROCEDURES

Table 2 presents the frequencies and types of invasive procedures performed during the interventions. In the

TABLE 1
Baseline Characteristics of Enrolled Patients by Dialysis Modality and Vascular Access Type

| Variable | Hemodialysis With AVF | Hemodialysis With TCC | Peritoneal dialysis | *p* Value |
|---|---|---|---|---|
| Patients (*n*) | 65 | 45 | 42 | |
| Sex (% men) | 60 | 55 | 52 | 0.856 |
| Mean age (years) | 63.1±13.9 | 66.4±15.3 | 55.1±16.1 | 0.001 |
| Age groups [*n* (%)] | | | | |
| 18–44 Years | 5 (8) | 4 (9) | 9 (21) | 0.046 |
| 45–64 Years | 20 (31) | 11 (24) | 20 (47) | 0.019 |
| 65+ Years | 40 (61) | 30 (67) | 13 (31) | 0.001 |
| Cause of kidney disease [*n* (%)] | | | | |
| Diabetes | 29 (45) | 19 (42) | 8 (19) | 0.016 |
| Hypertension | 8 (12) | 3 (7) | 2 (5) | 0.405 |
| Glomerulonephritis | 7 (11) | 3 (7) | 13 (31) | 0.005 |
| Tubulointerstitial nephritis | 9 (14) | 9 (20) | 7 (17) | 0.699 |
| Unknown | 12 (19) | 11 (24) | 12 (29) | 0.445 |
| Mean CCI score | 5.1±3.1 | 5.0±2.5 | 4.4±2.2 | 0.574 |
| CCI risk group [*n* (%)] | | | | |
| Low (≤3) | 25 (39) | 14 (31) | 15 (36) | 0.746 |
| Medium (4–5) | 12 (19) | 12 (27) | 14 (33) | 0.138 |
| High (≥6) | 28 (43) | 19 (42) | 13 (31) | 0.424 |
| Comorbid conditions [*n* (%)] | | | | |
| Coronary artery disease | 28 (43) | 15 (33) | 6 (14) | 0.006 |
| Congestive heart failure | 26 (40) | 17 (38) | 7 (17) | 0.025 |
| Peripheral vascular disease | 16 (25) | 9 (20) | 9 (19) | 0.797 |
| Previous stroke | 9 (14) | 6 (13) | 2 (5) | 0.330 |
| Diabetes | 30 (46) | 19 (42) | 8 (19) | 0.011 |
| Malignancy | 11 (17) | 9 (20) | 11 (26) | 0.591 |
| Late referral [*n* (%)] | 9 (14) | 40 (89) | 9 (21) | <0.001 |
| Mean duration from referral to dialysis initiation (months) | 42±40 | 5±19 | 34±28 | <0.001 |
| Laboratory values [median (range)] | | | | |
| Hemoglobin (g/L) | 104 (101–108) | 88 (83–92) | 105 (108–115) | <0.001 |
| eGFR (mL/min/1.73 $m^2$) | 10.0 (9.2–10.9) | 7.6 (6.6–8.7) | 8.3 (7.7–9.0) | <0.001 |
| Serum creatinine (mg/dL) | 5.8 (5.3–6.1) | 8.3 (7.2–9.4) | 6.7 (6.0–7.4) | <0.001 |
| Serum urea (mg/dL) | 216 (203–229) | 219 (194–244) | 197 (184–210) | 0.171 |
| Serum albumin (g/L) | 37 (35–38) | 32 (31–34) | 39 (38–40) | <0.001 |

AVF = arteriovenous fistula; TCC = tunneled cuffed catheter; CCI = Charlson comorbidity index; eGFR = estimated glomerular filtration rate.

PD group, 76% and 24% of the procedures were related to PD and HD catheters respectively. Eight PD patients used at least 1 HD catheter. The reasons for HD catheter use in the PD group were catheter malfunction ($n = 2$), peritonitis ($n = 2$), catheter "break-in" period ($n = 2$), abdominal leak ($n = 1$), and requirement for continuous renal replacement therapy ($n = 1$). In the HD-AVF group, 75% and 25% of the procedures were related to the AVF and the TCC accesses respectively. Eleven patients required at least 1 TCC insertion during dialysis because of AVF failure. In the HD-TCC group, 30% and 70% of the procedures were related to the AVF and TCC accesses respectively. During dialysis, 34 patients underwent at least 1 AVF creation attempt. The primary failure rates (including failed attempts) were 2% for the PD group (1 of 44), 23% for the HD-AVF group (17 of 75), and 9% for HD-CVC group (6 of 67).

Table 3 lists the mean numbers of interventions in the study population. The mean numbers of access surgeries and diagnostic imaging studies were higher for the HD-AVF group than for the HD-TCC and PD groups ($p = 0.083$ and $p < 0.001$ respectively). In contrast, the

TABLE 2
Invasive Access Interventions by Dialysis Modality and Vascular Access Type

| Intervention | Hemodialysis With AVF (*n*=65) (*n*) | (%)[a] | Hemodialysis With TCC (*n*=45) (*n*) | (%)[a] | Peritoneal dialysis (*n*=42) (*n*) | (%)[a] |
|---|---|---|---|---|---|---|
| Hemodialysis fistula | | | | | | |
| Creation | 75 | 55.1 | 40 | 24.5 | 0 | 0 |
| Surgical revision or ligation | 7 | 5.2 | 3 | 1.8 | 0 | 0 |
| Angioplasty | 15 | 11.0 | 5 | 3.1 | 0 | 0 |
| Thrombectomy | 5 | 3.7 | 1 | 0.6 | 0 | 0 |
| Hemodialysis catheter | | | | | | |
| Insertion | 17 | 12.5 | 67 | 41.1 | 8 | 11.9 |
| Exchange or removal | 11 | 8.1 | 26 | 16.0 | 8 | 11.9 |
| Thrombolysis | 6 | 4.4 | 21 | 12.9 | 0 | 0 |
| Peritoneal dialysis | | | | | | |
| Catheter insertion | 0 | 0 | 0 | 0 | 44 | 65.7 |
| Catheter manipulation | 0 | 0 | 0 | 0 | 1 | 1.5 |
| Catheter removal | 0 | 0 | 0 | 0 | 4 | 6.0 |
| Lysis of adhesions or omentectomy | 0 | 0 | 0 | 0 | 1 | 1.5 |
| Correction of peritoneal leaks | 0 | 0 | 0 | 0 | 1 | 1.5 |
| TOTAL | 136 | 100 | 163 | 100 | 67 | 100 |

[a] Of total interventions.

TABLE 3
Dialysis Access–Related Interventions[a] of Enrolled Patients, by Dialysis Modality and Vascular Access Type, per Patient–Year at Risk

| Intervention | Hemodialysis (HD) With AVF (*n*=65) | Hemodialysis (HD) With TCC (*n*=45) | Peritoneal dialysis (*n*=42) | *p* Value |
|---|---|---|---|---|
| Access surgery | 1.39±0.82 | 0.84±0.75 | 1.21±0.47 | 0.085 |
| HD catheter intervention | 0.58±1.40 | 2.24±1.95 | 0.19±0.39 | <0.001 |
| Diagnostic imaging | 0.34±0.60 | 0.12±0.38 | 0 | <0.001 |
| Hospitalization | 0.07±0.25 | 0.47±1.09 | 0.14±0.35 | 0.025 |
| TOTAL | 2.38±2.06 | 3.67±2.50 | 1.54±0.73 | <0.001 |

[a] Mean ± standard deviation.

mean numbers of TCC-related interventions and hospitalizations were significantly higher for the HD-TCC group than for either the HD-AVF or the PD group ($p < 0.001$ and $p = 0.025$ respectively). The main causes of dialysis access–related hospital admissions were peritonitis ($n = 4$, 67%) for PD patients, access surgery ($n = 3$, 75%) for HD-AVF patients, and catheter-related bacteremia ($n = 13$, 81%) for HD-TCC patients. The mean number of bacteremic episodes for HD-TCC patients was 0.58 ± 1.18 per patient–year at risk.

Overall, rates for dialysis access–related interventions were significantly lower in the PD group than in either the HD-AVF or the HD-TCC group ($p < 0.001$, Table 3). In multivariate analysis, the PD modality was associated with a significantly lower risk of access-related interventions than were the HD-AVF and HD-TCC modalities (adjusted rate ratios: 1.572 and 1.433 respectively; 95% CIs: 1.253 to 1.891 and 1.069 to 1.797). None of the covariates in the models were associated with the risk or rate of intervention.

COST ANALYSIS

Table 4 sets out the itemized dialysis access–related costs.

TABLE 4
Costs of Surgical Procedures for Dialysis Access, Diagnostic Imaging, and Catheter Interventions

| Procedure | Cost in euros (€) Professional fees | Technical fees | Total per intervention |
|---|---|---|---|
| Fistula creation | 177 | 85 | 262 |
| Placement of Tenckhoff catheter | 203 | 323 | 526 |
| Placement of tunneled cuffed catheter | 148 | 234 | 382 |
| Local catheter thrombolysis | 11 | 35 | 46 |
| Percutaneous transluminal angioplasty | 168 | 432 | 600 |
| Manual catheter-directed thrombo-aspiration | 336 | 680 | 1016 |

TABLE 5
Dialysis Access–Related Costs of Enrolled Patients, by Dialysis Modality and Vascular Access Type, per Patient–Year at Risk

| Intervention | Mean cost in euros [€ (95% confidence interval)] Hemodialysis (HD) With AVF (*n*=65) | With TCC (*n*=45) | Peritoneal dialysis (*n*=42) | *p* Value |
|---|---|---|---|---|
| Access surgery | 401.7 (343.8 to 459.6) | 252.9 (190.5 to 315.4) | 540.7 (526.8 to 584.7) | <0.001 |
| HD catheter interventions | 141.2 (57.7 to 234.6) | 718.7 (576.0 to 861.5) | 72.8 (26.9 to 118.8) | <0.001 |
| Diagnostic imaging | 344.7 (187.8 to 501.7) | 151.3 (52.9 to 249.8) | 0 | <0.001 |
| Hospitalization | 469.2 (57.9 to 996.3) | 2746.2 (494.8 to 4997.5) | 516.7 (67.5 to 965.9) | 0.010 |
| Transportation | 193.4 (128.3 to 258.5) | 339.1 (236.0 to 442.2) | 41.4 (28.1 to 54.6) | <0.001 |
| TOTAL | 1555.2 (974.0 to 2136.2) | 4208.2 (2050.7 to 6365.9) | 1171.6 (737.6 to 1526.0) | <0.001 |

The mean cost of access surgery per patient–year was higher for PD patients than for either the HD-AVF or the HD-TCC patients ($p < 0.001$, Table 5). On the other hand, the costs of diagnostic imaging procedures were higher for the HD-AVF patients ($p < 0.001$, Table 5), and the costs of hospitalization related to TCC interventions and of patient transportation were higher for the HD-TCC patients ($p = 0.010$ and $p < 0.001$ respectively; Table 5). Overall, the mean dialysis access–related costs per patient–year at risk were €1171.6 [median: €608.8; interquartile range (IQR): 563.1 – 936.7] for the PD patients, €1555.2 (median: €783.9; IQR: 371.4 – 1571.7) for the HD-AVF patients, and €4208.2 (median: €1252.4; IQR: 947.9 – 2983.5) for the HD-TCC patients ($p < 0.001$, Table 5). In multivariate analysis, total access-related costs were significantly higher for the HD-TCC modality than for either the PD or the HD-AVF modality ($\beta = -0.53$; 95% CI: −1.03 to −0.02; and $\beta = -0.50$; 95% CI: −0.96 to −0.04).

## DISCUSSION

The present study demonstrates that dialysis access–related intervention rates were significantly lower for patients initiating PD than for those initiating HD. Peritoneal dialysis patients had the lowest numbers of access surgeries and catheter-related interventions. In contrast, HD-AVF patients underwent a higher number of access surgeries and diagnostic imaging procedures, and HD-TCC patients underwent a higher number of catheter-related interventions and hospitalizations (mainly because of catheter-related bacteremia). Our

results accord with those of Oliver *et al.* (38) who recently reported that, compared with patients who chose HD, those who chose PD had a lower risk of invasive access interventions. In addition, we further demonstrated that the risks of catheter-related interventions and hospitalizations were significantly lower with the PD modality than with the HD-TCC modality, emphasizing the fact that patients who choose PD do not face an increased risk of catheter-related adverse events (10,39–41).

Our cost analysis showed that the costs related to dialysis access were lower for the PD modality. Even after considering the additional technical and overhead costs associated with PD catheter placement (operating room, general anesthesia, and surgical team) and the costs associated with primary nonfunction of all access types, patients who initiated PD incurred the lowest costs, and those who initiated HD-TCC, the highest costs during the first year of dialysis. In this regard, Lee *et al.* (32) reported that costs related to catheter placement and diagnostic imaging procedures accounted for the higher expenditure observed among prevalent HD patients with permanent catheters than among HD-AVF and PD patients. On the other hand, Manns *et al.* (31) observed that the largest cost component in patients dialyzed exclusively with a HD catheter (rather than an AVF) was hospitalization for access-related complications. In the present study, we observed that, in PD and HD-AVF patients, about 50% of dialysis access costs were related to access surgery, HD catheter interventions, and diagnostic imaging studies; in the HD-TCC group, about 75% of dialysis access costs were related to vascular access–related hospitalizations and patient transportation. In this regard, we observed that HD-TCC patients incurred the highest number of transportation runs (with the highest mean distances) between their homes and our hospital center. Total access-related costs were not statistically significantly different between the PD modality and the HD-AVF modality. Nevertheless, we observed that the costs for invasive interventions related to the dialysis access (mainly diagnostic imaging studies and catheter-related procedures) were higher in the HD-AVF modality. In this regard, Oliver *et al.* (38) also reported that, compared with PD patients, HD-AVF patients incurred a higher risk of invasive interventions.

The cost factor plays a leading role in health care economics. Because it is not easy to extrapolate costs from one country to another, studies that evaluate local realities are needed to guide appropriate economic decisions about the dialytic management of ESRD patients. Within the Portuguese National Health System, RRT is free of charge for the patient. In 2008, concerned with budget constraints and the exponential annual rise in dialysis costs, the Portuguese health authorities changed the reimbursement system for both HD and PD treatment to a per capita system that includes equipment costs, staff, patient follow-up and checkups, consumables, reverse-osmosis water, regular laboratory tests, radiology, and all medications for the treatment of anemia, bone-mineral disease, nutrition, cardiovascular complications, and in-dialysis intravenous antibiotics. The reimbursement per patient–week was set by law at €547.94 [Ministry of Health and Welfare Ordinance Legislation—Diário da República (2nd series, No. 35, 19 February 2008, clause No. 4325/2008)] for the HD and PD modalities alike. This package did not include vascular and PD access–related procedures, hospitalizations, or patient transportation. Our results, based on patients treated with contemporary dialysis modalities in Portugal, suggest that when a health care reimbursement system is the same for HD and PD, as occurs in Portugal, dialysis access–related costs may account for an approximate 4%, 5%, and 15% increase in annual dialysis treatment expenses for the PD, HD-AVF, and HD-TCC modalities respectively. Our findings accord with those of Manns *et al.* (31), who reported that HD vascular access costs may account for approximately 10% of the health care cost for incident HD patients, with patients selected for arteriovenous graft or catheter placement incurring the highest costs.

The present study may have important implications for policymakers. For health care systems that are promoting PD as a strategy to lower consumption of health care resources, our study suggests that the resources required to establish and maintain a dialysis access in the first year of treatment are lower for patients who chose PD.

As with all retrospective studies, selection bias may have occurred, in particular influenced by patient treatment preferences and time of referral to the nephrologist. In addition, the time at risk after the first access attempt was different between study groups. Further, the small sample size, short-term follow-up, and single-center nature of the study may limit its reproducibility. Also, the PD patients were treated at a single academic nephrology center, and the HD patients were treated at separate peripheral renal centers (although this situation reflects the distribution of patients between modalities in our country). The costs of certain health care procedures vary between countries. However, the relative resources required for an intervention and the determinants of the costs of vascular access are likely to be similar between centers. Finally, the extrapolation of data may inflate costs in the groups containing sicker patients.

## CONCLUSIONS

Our study suggests that, compared with patients who initiate HD, those who initiate PD require fewer resources to establish and maintain a dialysis access during the first year of treatment. In addition, our findings emphasize that PD is a cost-effective option for incident dialysis patients.

## ACKNOWLEDGMENTS

The authors thank Professor João Frazão for assistance with manuscript preparation, Ms. Doreen Raine for editing the English, and the clinical directors of the HD clinics who kindly agreed to collaborate in the study: A. Baldaia Moreira MD, A. Caldeira Gomes MD, A. Castro Henriques MD, Antunes de Azevedo MD, Eva Xavier MD, João C. Fernandes MD, João M. Frazão MD PhD, Jorge P. Baldaia MD, José M. Madureira MD, José Pinheiro MD, Odete Pereira MD, Sofia Pedroso MD, Susana Sampaio MD, and Vasco Miranda MD.

## DISCLOSURES

The authors have no equity interest or financial agreements with any company or commercial entity related to the content of the article and they have not received salary or support from any company related to the article.

## REFERENCES

1. Astor BC, Eustace JA, Powe NR, Klag MJ, Fink NE, Coresh J on behalf of the CHOICE Study. Type of vascular access and survival among incident hemodialysis patients: the Choices for Healthy Outcomes in Caring for ESRD (CHOICE) Study. *J Am Soc Nephrol* 2005; 16:1449–55.
2. Rehman R, Schmidt RJ, Moss AH. Ethical and legal obligation to avoid long-term tunneled catheter access. *Clin J Am Soc Nephrol* 2009; 4:456–60.
3. Moist LM, Trpeski L, Na Y, Lok CE. Increased hemodialysis catheter use in Canada and associated mortality risk: data from the Canadian Organ Replacement Registry 2001 – 2004. *Clin J Am Soc Nephrol* 2008; 3:1726–32.
4. Carrero JJ, de Jager DJ, Verduijn M, Ravani P, De Meester J, Heaf JG, *et al.* Cardiovascular and noncardiovascular mortality among men and women starting dialysis. *Clin J Am Soc Nephrol* 2011; 6:1722–30.
5. de Jager DJ, Grootendorst DC, Jager KJ, van Dijk PC, Tomas LM, Ansell D, *et al.* Cardiovascular and noncardiovascular mortality among patients starting dialysis. *JAMA* 2009; 302:1782–9.
6. Lee T, Barker J, Allon M. Tunneled catheters in hemodialysis patients: reasons and subsequent outcomes. *Am J Kidney Dis* 2005; 46:501–8.
7. Allon M, Daugirdas J, Depner TA, Greene T, Ornt D, Schwab SJ. Effect of change in vascular access on patient mortality in hemodialysis patients. *Am J Kidney Dis* 2006; 47:469–77.
8. Lacson E Jr, Wang W, Hakim RM, Teng M, Lazarus JM. Associates of mortality and hospitalization in hemodialysis: potentially actionable laboratory variables and vascular access. *Am J Kidney Dis* 2009; 53:79–90.
9. Perl J, Wald R, McFarlane P, Bargman JM, Vonesh E, Na Y, *et al.* Hemodialysis vascular access modifies the association between dialysis modality and survival. *J Am Soc Nephrol* 2011; 22:1113–21.
10. Aslam N, Bernardini J, Fried L, Burr R, Piraino B. Comparison of infectious complications between incident hemodialysis and peritoneal dialysis patients. *Clin J Am Soc Nephrol* 2006; 1:1226–33.
11. Rodrigues A. How to persuade peritoneal dialysis–skeptical hemodialysis fans. *Contrib Nephrol* 2009; 163:237–42.
12. Dell'Aquila R, Chiaramonte S, Rodighiero MP, Spanó E, Di Loreto P, Kohn CO, *et al.* Rational choice of peritoneal dialysis catheter. *Perit Dial Int* 2007; 27(Suppl 2):S119–25.
13. Gokal R, Alexander S, Ash S, Chen TW, Danielson A, Holmes C, *et al.* Peritoneal catheters and exit-site practices toward optimum peritoneal access: 1998 update. *Perit Dial Int* 1998; 18:11–33.
14. Digenis GE, Abraham G, Savin E, Blake P, Dombros N, Sombolos K, *et al.* Peritonitis-related deaths in continuous ambulatory peritoneal dialysis (CAPD) patients. *Perit Dial Int* 1990; 10:45–7.
15. Wilkie M, Wild J. Peritoneal dialysis access—results from a UK survey. *Perit Dial Int* 2009; 29:355–7.
16. Moossavi S, Raasch E, Russell G, Moossavi S, Mauck V, Beekman D, *et al.* Comparison of dialysis access outcomes in peritoneal dialysis and hemodialysis patients at an academic medical center (Abstract). *Perit Dial Int* 2007; 27(Suppl 3):S24.
17. McDonald SP, Marshall MR, Johnson DW, Polkinghorne KR. Relationship between dialysis modality and mortality. *J Am Soc Nephrol* 2009; 20:155–63.
18. Weinhandl ED, Foley RN, Gilbertson DT, Arneson TJ, Snyder JJ, Collins AJ. Propensity-matched mortality comparison of incident hemodialysis and peritoneal dialysis patients. *J Am Soc Nephrol* 2010; 21:499–506.
19. Heaf JG, Løkkegaard H, Madsen M. Initial survival advantage of peritoneal dialysis relative to haemodialysis. *Nephrol Dial Transplant* 2002; 17:112–17.
20. Korevaar JC, Feith GW, Dekker FW, van Manen JG, Boeschoten EW, Bossuyt PM, *et al.* on behalf of the NECOSAD Study Group. Effect of starting with hemodialysis compared with peritoneal dialysis in patients new on dialysis treatment: a randomized controlled trial. *Kidney Int* 2003; 64:2222–8.
21. Hiramatsu M on behalf of the Japanese Society for Elderly Patients on Peritoneal Dialysis. How to improve survival in geriatric peritoneal dialysis patients. *Perit Dial Int* 2007; 27(Suppl 2):S185–9.
22. Huang CC, Cheng KF, Wu HD. Survival analysis: comparing peritoneal dialysis and hemodialysis in Taiwan. *Perit Dial Int* 2008; 28(Suppl 3):S15–20.

23. Klarenbach S, Manns B. Economic evaluation of dialysis therapies. *Semin Nephrol* 2009; 29:524–32.
24. Salonen T, Reina T, Oksa H, Sintonen H, Pasternack A. Cost analysis of renal replacement therapies in Finland. *Am J Kidney Dis* 2003; 42:1228–38.
25. Baboolal K, McEwan P, Sondhi S, Spiewanowski P, Wechowski J, Wilson K. The cost of renal dialysis in a UK setting—a multicentre study. *Nephrol Dial Transplant* 2008; 23:1982–9.
26. Sennfalt K, Magnusson M, Carlsson P. Comparison of hemodialysis and peritoneal dialysis—a cost–utility analysis. *Perit Dial Int* 2002; 22:39–47.
27. Pacheco A, Saffie A, Torres R, Tortella C, Llanos C, Vargas D, *et al.* Cost/utility study of peritoneal dialysis and hemodialysis in Chile. *Perit Dial Int* 2007; 27:359–63.
28. Villa G, Fernández–Ortiz L, Cuervo J, Rebollo P, Selgas R, González T, *et al.* Cost-effectiveness analysis of the Spanish renal replacement therapy program. *Perit Dial Int* 2012; 32:192–9.
29. Villa G, Rodríguez–Carmona A, Fernández-Ortiz L, Cuervo J, Rebollo P, Otero A, *et al.* Cost analysis of the Spanish renal replacement therapy programme. *Nephrol Dial Transplant* 2011; 26:3709–14.
30. Haller M, Gutjahr G, Kramar R, Harnoncourt F, Oberbauer R. Cost-effectiveness analysis of renal replacement therapy in Austria. *Nephrol Dial Transplant* 2011; 26:2988–95.
31. Manns B, Tonelli M, Yilmaz S, Lee H, Laupland K, Klarenbach S, *et al.* Establishment and maintenance of vascular access in incident hemodialysis patients: a prospective cost analysis. *J Am Soc Nephrol* 2005; 16:201–9.
32. Lee H, Manns B, Taub K, Ghali WA, Dean S, Johnson D, *et al.* Cost analysis of ongoing care of patients with end-stage renal disease: the impact of dialysis modality and dialysis access. *Am J Kidney Dis* 2002; 40:611–22.
33. Allon M, Dinwiddie L, Lacson E Jr, Latos DL, Lok CE, Steinman T, *et al.* Medicare reimbursement policies and hemodialysis vascular access outcomes: a need for change. *J Am Soc Nephrol* 2011; 22:426–30.
34. ERA-EDTA Registry. *ERA-EDTA Registry Annual Report 2009*. Amsterdam, Netherlands: Academic Medical Center, Department of Medical Informatics; 2011. [Available online at: http://www.era-edta-reg.org/files/annualreports/pdf/AnnRep2009.pdf; accessed 19 January 2013]
35. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40:373–83.
36. Coentrão L, Bizarro P, Ribeiro C, Neto R, Pestana M. Percutaneous treatment of thrombosed arteriovenous fistulas: clinical and economic implications. *Clin J Am Soc Nephrol* 2010; 5:2245–50.
37. Bizarro P, Coentrão L, Ribeiro C, Neto R, Pestana M. Endovascular treatment of thrombosed dialysis fistulae: a cumulative cost analysis. *Catheter Cardiovasc Interv* 2011; 77:1065–70.
38. Oliver MJ, Verrelli M, Zacharias JM, Blake PG, Garg AX, Johnson JF, *et al.* Choosing peritoneal dialysis reduces the risk of invasive access interventions. *Nephrol Dial Transplant* 2012; 27:810–16.
39. Povlsen JV, Ivarsen P. How to start the late referred ESRD patient urgently on chronic APD. *Nephrol Dial Transplant* 2006; 21(Suppl 2):ii56–9.
40. Povlsen JV. Unplanned start on assisted peritoneal dialysis. *Contrib Nephrol* 2009; 163:261–3.
41. Povlsen JV, Ivarsen P. Assisted peritoneal dialysis: also for the late referred elderly patient. *Perit Dial Int* 2008; 28:461–7.

# Chapter 5
## *Detection of vascular access dysfunction*

### 5.1. Physical examination of dysfunctional arteriovenous fistulae by non-interventionalists: a skill worth teaching

Coentrão L, Faria B, Pestana M

*Nephrol Dial Transplant* 2012;27(5):1993-1996. PMID: 21940486

Nephrol Dial Transplant (2012) 27: 1993–1996
doi: 10.1093/ndt/gfr532
Advance Access publication 21 September 2011

*Original Articles*

NDT
Nephrology Dialysis Transplantation

# Physical examination of dysfunctional arteriovenous fistulae by non-interventionalists: a skill worth teaching

Luís Coentrão[1], Bernardo Faria[2] and Manuel Pestana[1]

[1]Nephrology Research and Development Unit, Department of Nephrology, Hospital São João, Faculty of Medicine, University of Porto, Portugal and [2]Department of Nephrology, Hospital São Teotónio, Viseu, Portugal

*Correspondence and offprint requests to:* Luís Coentrão; E-mail: coentrao@med.up.pt

**Abstract**

**Background.** Physical examination (PE) of arteriovenous fistulae (AVF) has recently emerged as an important element in the detection of stenotic lesions. This study examines the accuracy of PE in the assessment of AVF dysfunction by non-interventionalists in comparison with angiography.

**Methods.** A total of 177 consecutive patients who had AVF dysfunction and were referred to our centre by general nephrologists for angioplasty between November 2009 and July 2010 were included in this analysis. Eleven referring general nephrologists completed a form reporting the PE findings regarding their patients' AVFs. Before angiography examination was carried out, a trained nephrology resident performed a PE in all the cases. Angiography of the AVFs was then performed by an interventionalist. Cohen's κ value was used as the measurement of the level of agreement beyond chance between the diagnosis made on PE and angiography.

**Results.** There was a moderate agreement beyond chance between the general nephrologists' PE and angiography in the detection of AVF inflow stenosis ($\kappa = 0.49$), outflow stenosis ($\kappa = 0.58$) and thrombosis ($\kappa = 0.52$). On the other hand, PE performed by the trained nephrology resident strongly agreed with angiography in the detection of AVF inflow stenosis ($\kappa = 0.84$), outflow stenosis ($\kappa = 0.92$) and thrombosis ($\kappa = 0.98$). The agreement between PE and angiography in the detection of co-existing AVF inflow–outflow stenosis was poor for the general nephrologists and moderate for the trained nephrology resident ($\kappa = 0.14$ versus $\kappa = 0.55$, respectively).

**Conclusion.** PE may provide an accurate means of diagnosis of AVF dysfunction. Theoretical and hands-on training in PE of dysfunctional AVFs should be provided for nephrologists in-training and for the dialysis staff.

**Keywords:** arteriovenous fistulae; dialysis; physical examination

## Introduction

Arteriovenous fistula (AVF) dysfunction is a common major problem in haemodialysis units. The European Renal Best Practice (ERBP) and Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines [1, 2] have therefore recommended a programme for the detection of stenosis and its subsequent correction in an attempt to reduce the occurrence of thrombosis. AVF stenosis and thrombosis are in fact the most common causes of access dysfunction, and there have been extensive investigations to identify the best methods for detecting accesses at risk [3–9]. Several diagnostic procedures have been recommended for vascular access surveillance, including blood flow, intra-access static pressure and access recirculation [1, 2]. However, these procedures are time consuming and costly. Physical examination (PE) of AVFs performed by trained physicians has recently emerged as an important element in the assessment of stenotic lesions [8, 10–15]. However, there are no studies reporting the accuracy of PE in the diagnosis of AVF dysfunction when performed by dialysis staff to our knowledge. We therefore designed this study to determine the accuracy of PE by general nephrologists in the assessment of AVF dysfunction in comparison with angiography. The study also evaluated the agreement between PE of dysfunctional AVFs performed by a trained nephrology resident and angiography.

### Materials and methods

Hospital São João is a tertiary-care University Hospital that carries out interventional procedures in patients on regular haemodialysis referred from other hospitals and satellite haemodialysis units. The patients treated in these haemodialysis units are monitored for clinical signs of access dysfunction by the nephrologists treating them. Patients are referred for diagnostic angiography and/or angioplasty as appropriate, on the basis of clinical signs of vascular access dysfunction.

We analysed a database of a prospective observational study conducted in a population of 177 haemodialysis patients consecutively referred to our centre by general nephrologists for angioplasty, between November 2009 and July 2010. Eleven referring general nephrologists without specific training on AVF PE and angiography completed a form reporting the PE findings regarding their patients' AVFs. This information was recorded and placed in a sealed envelope. Before the angiography procedure was carried out, a nephrology resident with 6 months training in vascular access PE and angiography performed a PE in all the cases, unaware of the general nephrologists' PE findings. Angiography examination of the AVFs was performed in our hospital centre by an interventionalist, blind to both the general nephrologists' and the nephrology resident's reports. The

study was limited to interventions involving autogenous AVFs. This investigation was reviewed and approved by the Hospital São João Institutional Review Board.

*Procedures*

*Angiography examination.* Angiography was defined as the gold standard examination for diagnosis of AVF dysfunction. Angiography was performed to evaluate the AVF from the feeding artery to the right atrium (Mobile C-arm BV Pulsera; Philips Medical Systems, Eindhoven, The Netherlands). AVF dysfunction was classified into four major disorders: inflow stenosis, outflow stenosis, co-existing inflow–outflow stenosis and AVF thrombosis. The inflow segment was defined as the feeding artery, anastomosis and the juxta-anastomosis area (first few centimetres of the fistula). Outflow was defined as the entire segment from the juxta-anastomosis area to the right atrium. Stenosis was defined as 50% luminal narrowing compared to the normal vascular segment located adjacent to the stenosis according to K/DOQI [2]. Thrombosis of the AVF was ascertained according to the presence of clots in the arterial and/or venous sides of the AVF. Clinical criteria of access dysfunction prompting angiography were applied according to the K/DOQI [2].

*Physical examination.* Pulse abnormalities and thrill were used as the main PE tools for the diagnosis of AVF dysfunction [11, 12]. In addition, inspection of the arm, chest, neck and face, palpation of the entire AVF tract, arm elevation and pulse augmentation tests were considered important to detect the cause of AVF dysfunction. Pulse augmentation consists of the complete occlusion of the access several centimetres beyond the arterial anastomosis and evaluation of the strength of the pulse. The test is considered normal when the portion of fistula upstream from the occluding finger demonstrates augmentation of pulse [12]. The arm elevation test consists of the elevation of the extremity with the fistula and examination of the normal collapse of the access [12]. The test is considered normal when the fistula collapses after arm elevation. The diagnostic elements of the PE are reported in Table 1.

*Statistical analysis*

Diagnostic variables for both the PE and angiography were dichotomous (presence or absence of the lesion). The general nephrologists were considered to be a homogeneous population since none of them had received specific training in AVF PE and angiography. Accuracy, sensitivity, specificity and predictive positive and negative values were measured in relation to angiography as the gold standard method. Cohen's κ value was used as a measurement of the level of agreement beyond chance between the diagnoses made by PE and angiography. κ values range from 0 to 1.0, with zero indicating no agreement beyond chance and 1.0 denoting perfect agreement. κ values between 0 to 0.20 and 0.21 to 0.40 confer a poor and a fair agreement beyond chance, respectively; those between 0.41 to 0.60 and 0.61 to 0.80 a moderate and a substantial agreement; and those exceeding 0.80 a near-perfect agreement [16]. All statistical analyses were performed using SPSS software, version 11 (SPSS, Chicago, IL).

## Results

One hundred (56%) patients were male. The mean age was $64 \pm 13$ years. Eighty-four (48%) AVFs were located in the forearm (82 radio-cephalic AVFs and 2 ulnar-basilic AVFs) and 93 (52%) were located in the upper arm (70 brachio-cephalic AVFs and 23 brachio-basilic AVFs). Inflow and outflow stenoses were the most common types of disorder (37 and 28%, respectively). Co-existing inflow–outflow stenosis and AVF thrombosis were present in 14 and 21% of the patients, respectively. In forearm AVFs, inflow stenosis was the most common type of disorder, whereas outflow stenosis was the most frequent one in upper-arm AVFs (50 and 38%, respectively).

The accuracy of PE by the general nephrologists in the detection of inflow, outflow, co-existing inflow–outflow stenosis and AVF thrombosis was 77, 83, 85 and 81%, respectively (Table 2). The sensitivity and specificity were 57 and 89% for inflow stenosis, 80 and 84% for outflow stenosis, 12 and 97% for co-existing inflow–outflow stenosis and 86 and 79% for AVF thrombosis, respectively (Table 2). There was a moderate agreement beyond chance between PE by general nephrologists and angiography for the assessment of AVF dysfunction ($\kappa = 0.49$, 95% CI 0.40–0.57; Table 3). More specifically, there was a moderate agreement between PE and angiography in the diagnosis of AVF inflow and outflow stenosis and AVF thrombosis ($\kappa = 0.49$, 95% CI 0.34–0.64; $\kappa = 0.58$, 95% CI 0.44–0.73; $\kappa = 0.52$, 95% CI 0.38–0.65, respectively;

**Table 1.** Diagnostic elements of the PE used in the evaluation of AVF dysfunction [7, 8][a]

| Diagnosis | Thrill | Pulse | Arm elevation test | Pulse augmentation test |
|---|---|---|---|---|
| Inflow stenosis | Weak, discontinuous | Weak | Excessive collapse | Failure of the pulse to increase |
| Outflow stenosis | Strong, systolic | Strong | No partial vein collapse | n.a. |
| Co-existing inflow–outflow stenosis | Weak, discontinuous | n.a. | No partial vein collapse | Failure of the pulse to increase |
| Fistula thrombosis[b] | Absent | Strong or absent | n.a. | n.a. |

[a]n.a., not applicable.
[b]Additional physical examination finding was the presence of a palpable clot.

**Table 2.** Diagnostic accuracy of PE in the detection of AVF dysfunction by general nephrologists (GNs) and nephrology resident (NR)[a]

| Diagnosis | | ACC | SEN | SPE | PPV | NPV | PREV |
|---|---|---|---|---|---|---|---|
| Inflow stenosis | GN | 0.77 (0.62–0.89) | 0.57 (0.45–0.68) | 0.89 (0.82–0.94) | 0.76 (0.65–0.84) | 0.78 (0.70–0.85) | 0.37 |
| | NR | 0.92 (0.87–0.96) | 0.98 (0.92–1) | 0.88 (0.81–0.93) | 0.83 (0.80–0.91) | 0.99 (0.95–1) | |
| Outflow stenosis | GN | 0.83 (0.78–0.89) | 0.80 (0.71–0.90) | 0.84 (0.77–0.90) | 0.67 (0.58–0.75) | 0.91 (0.81–0.96) | 0.28 |
| | NR | 0.97 (0.91–0.99) | 0.96 (0.87–0.99) | 0.97 (0.92–0.99) | 0.92 (0.89–0.98) | 0.98 (0.94–1) | |
| Co-existing inflow–outflow stenosis | GN | 0.85 (0.77–0.94) | 0.12 (0.04–0.30) | 0.97 (0.92–0.99) | 0.43 (0.30–0.55) | 0.87 (0.72–0.93) | 0.14 |
| | NR | 0.92 (0.87–0.96) | 0.44 (0.27–0.63) | 0.99 (0.96–1) | 0.92 (0.87–0.96) | 0.92 (0.89–0.98) | |
| Fistula thrombosis | GN | 0.81 (0.71–0.89) | 0.86 (0.72–0.94) | 0.79 (0.72–0.85) | 0.52 (0.44–0.55) | 0.95 (0.89–0.99) | 0.21 |
| | NR | 0.99 (0.98–1) | 0.97 (0.86–1) | 1 (0.97–1) | 1 (0.96–1) | 0.99 (0.97–1) | |

[a]ACC, accuracy; NPV, negative predictive value; PPV, positive predictive value; PREV, prevalence of diagnosis by angiography; SEN, sensitivity; SPE, specificity.

Table 3) and a poor agreement between PE and angiography in the diagnosis of co-existing inflow–outfllow stenosis ($\kappa = 0.14$, 95% CI 0.02–0.26; Table 3). Analysis of the forearm and upper-arm AVF findings revealed a fair-to-moderate agreement between the PE and angiography for the assessment of dysfunctional forearm and upper-arm AVFs, respectively ($\kappa = 0.34$, 95% CI 0.19–0.41 versus $\kappa = 0.60$, 95% CI 0.51–0.71; Table 4).

The accuracy of PE by the trained nephrology resident for the detection of inflow, outflow, co-existing inflow–outflow stenosis and AVF thrombosis was 92, 97, 92 and 99%, respectively (Table 2). The sensitivity and specificity were 98 and 88% for inflow stenosis, 96 and 97% for outflow stenosis, 44 and 99% for co-existing inflow–outflow stenosis and 97 and 100% for AVF thrombosis, respectively (Table 2). There was a near-perfect agreement beyond chance between PE by the trained nephrology resident and angiography for the assessment of AVF dysfunction ($\kappa = 0.86$, 95% CI 0.77–0.95; Table 3). More specifically, there was a near-perfect agreement between the PE and angiography in the diagnosis of inflow and outflow stenosis and AVF thrombosis ($\kappa = 0.84$, 95% CI 0.69–0.98; $\kappa = 0.92$, 95% CI 0.77–1.0; $\kappa = 0.98$, 95% CI 0.84–1.0, respectively; Table 3) and a moderate agreement between PE and angiography in the diagnosis of co-existing inflow–outflow stenosis ($\kappa = 0.55$, 95% CI 0.42–0.69; Table 3). Analysis of the forearm and upper-arm AVFs revealed no significant difference in the level of agreement between PE and angiography ($\kappa = 0.82$, 95% CI 0.70–0.91 versus $\kappa = 0.89$, 95% CI 0.78–0.92, respectively; Table 4).

## Discussion

By comparing PE to the gold standard (angiography), the current study objectively assessed the accuracy of PE when performed by general nephrologists and a trained nephrology resident in the diagnosis of various types of disorder responsible for AVF dysfunction. Our results showed that PE by general nephrologists had a poor-to-moderate accuracy for the assessment of AVF dysfunction. The sensitivity was low for the diagnosis of AVF inflow stenosis, particularly for co-existing inflow–outflow lesions. On the other hand, the sensitivity and specificity of PE performed by general nephrologists were relatively high for the diagnosis of AVF outflow stenosis and AVF thrombosis. These findings are consistent with other recent data suggesting that AVFs with outflow stenosis are easier to assess by PE than AVFs with inflow stenosis [8]. With respect to the accuracy of PE in the hands of a trained nephrology resident, we observed a high level of agreement between PE and angiography for the diagnosis of AVF dysfunction, particularly for inflow and outflow stenosis and AVF thrombosis. Our results agree well with the previous findings by Asif *et al.* [13] confirming that PE performed by trained physicians is an accurate diagnostic tool for the detection of stenosis in a great majority of dysfunctional AVFs.

With respect to the location of the AVFs, general nephrologists did better with upper-am AVFs compared with forearm AVFs, whereas the trained nephrology resident presented a same level of agreement similar results with both upper-arm and forearm AVFs (Table 4). The discrepancy observed among the general nephrologists may be explained by the fact that outflow stenosis was the most common type of disorder in upper-arm AVF, whereas inflow stenosis was the most frequent one in forearm AVFs.

The value of PE in the detection of AVF stenosis has recently been compared with angiography and Doppler ultrasound [8, 13–15]. Asif *et al.* [13] and Campos *et al.* [15] determined the accuracy of PE in the detection of stenosis in AVFs, with excellent results. However, PE was

**Table 3.** κ value for PE in the diagnosis of various types of disorder by general nephrologists and nephrology resident

| Diagnosis | General nephrologists (κ) | Nephrology resident (κ) |
|---|---|---|
| Inflow stenosis | 0.49 [0.34–0.64] ($P < 0.001$) | 0.84 [0.69–0.98] ($P < 0.001$) |
| Outflow stenosis | 0.58 [0.44–0.73] ($P < 0.001$) | 0.92 [0.77–1] ($P < 0.001$) |
| Co-existing inflow–outflow stenosis | 0.14 [0.02–0.26] ($P = 0.021$) | 0.55 [0.42–0.69] ($P < 0.001$) |
| Fistula thrombosis | 0.52 [0.38–0.65] ($P < 0.001$) | 0.98 [0.84–1] ($P < 0.001$) |
| Overall | 0.49 [0.40–0.57] ($P < 0.001$) | 0.86 [0.77–0.95] ($P < 0.001$) |

**Table 4.** κ values for PE of dysfunctional forearm and upper-arm fistulae by general nephrologists and nephrology resident

| Diagnosis | | General nephrologists (κ) | Nephrology resident (κ) |
|---|---|---|---|
| Inflow stenosis | Forearm | 0.31 ($P = 0.003$) | 0.80 ($P < 0.001$) |
| | Upper arm | 0.63 ($P < 0.001$) | 0.87 ($P < 0.001$) |
| Outflow stenosis | Forearm | 0.43 ($P < 0.001$) | 0.91 ($P < 0.001$) |
| | Upper arm | 0.65 ($P < 0.001$) | 0.93 ($P < 0.001$) |
| Co-existing inflow–outflow stenosis | Forearm | 0.15 ($P = 0.12$) | 0.59 ($P < 0.001$) |
| | Upper arm | 0.02 ($P = 0.20$) | 0.50 ($P < 0.001$) |
| Fistula thrombosis | Forearm | 0.43 ($P < 0.001$) | 1.0 ($P < 0.001$) |
| | Upper arm | 0.60 ($P < 0.001$) | 0.97 ($P < 0.001$) |
| Overall | Forearm | 0.34 ($P < 0.001$) | 0.82 ($P < 0.001$) |
| | Upper arm | 0.60 ($P < 0.001$) | 0.89 ($P < 0.001$) |

performed by only one physician with experience in this field. In addition, Campos *et al.* [15] determined the accuracy of PE in the detection of AVF stenosis in comparison with Doppler ultrasound and Asif *et al.* [13] with angiography (albeit in a restricted manner because only still images were evaluated). Leon *et al.* [14] reported a similar accuracy of PE performed by an experienced interventionalist and a trained nephrology fellow (however, the two examiners performed the PE in different populations). Recently, Tessitore *et al.* [8] reported that the level of agreement of PE in the detection of AVF stenosis was fair-to-moderate among nephrologists with different expertise on vascular access monitoring. Our results agree well with the previous findings of Tessitore *et al.* [8] and further suggest that the accuracy of PE in the assessment of AVF dysfunction depends on the specific training of the examiner rather than on the cumulative experience in dialysis clinical practice. In addition, by assessing the accuracy of PE performed by general nephrologists in their own daily clinical practice, our study allows us to examine the quality of AVF monitoring in 'real practice in a real world'.

The fundamental concept of vascular access monitoring and surveillance is that stenosis develops over varying intervals in the great majority of AVFs and, if detected and corrected in time, maturation can be promoted, underdialysis minimized or avoided and thrombosis avoided or reduced [17, 18]. There are several factors that can suggest the presence of AVF dysfunction, such as low access blood flow, elevated intra-access pressure, unexplained decreases in delivered dialysis dose or access recirculation. However, they do not detect the cause of AVF dysfunction. PE provides a means of access evaluation that incurs no extra cost and is readily available. Moreover, PE provides additional information that is of the utmost importance for the interventionalist since different endovascular approaches are used for AVFs with inflow, outflow, co-existing inflow–outflow problems or AVF thrombosis. Detection of AVF dysfunction therefore requires an accurate diagnosis of its cause.

We are aware that our study has its limitations. This is not a randomized clinical study; the order of the assessors was not random and, for logistic (and cost) reasons, one rater always performed later and this may have introduced a bias. The results obtained by the general nephrologists may have been influenced by the fact that the PE was conducted in their own dialysis patients, and different interpretations of the PE findings used for the evaluation of AVF dysfunction may have occurred. Also, the results of this study apply only to a cohort of dysfunctional AVFs and may not apply to unselected AVF populations. In addition, the analysis did not address any variability in the interpretation of the angiography.

## Conclusion

PE of AVFs is non-invasive, incurs no extra cost and may provide an accurate means by which to diagnose AVF dysfunction. However, nephrologists in haemodialysis units may need to improve their skills in performing PE. Theoretical and hands-on training in PE should therefore be provided for nephrologists in-training and for the dialysis staff.

*Acknowledgements.* The authors thank Prof João Frazão for his assistance in manuscript preparation and Ms Doreen Raine for editing this article in English.

*Conflict of interest statement*. None declared.

## References

1. Tordoir J, Canaud B, Haage P *et al.* EBPG on vascular access. *Nephrol Dial Transplant* 2007; 22 (Suppl 2): ii88–ii117
2. Vascular Access 2006 Work Group. NKF-DOQI clinical practice guidelines for vascular access: update 2006. *Am J Kidney Dis* 2006; 48 (Suppl 1): S176–S276
3. Tonelli M, Jindal K, Hirsch D *et al.* Screening for subclinical stenosis in native vessel arteriovenous fistulae. *J Am Soc Nephrol* 2001; 12: 1729–1733
4. Schwab SJ, Oliver MJ, Suhocki P *et al.* Hemodialysis arteriovenous access: detection of stenosis and response to treatment by vascular access blood flow. *Kidney Int* 2001; 59: 358–362
5. McCarley P, Wingard RL, Shyr Y *et al.* Vascular access blood flow monitoring reduces access morbidity and costs. *Kidney Int* 2001; 60: 1164–1172
6. Tessitore N, Bedogna V, Gammaro L *et al.* Diagnostic accuracy of ultrasound dilution access blood flow measurement in detecting stenosis abd predicting thrombosis in native forearm arteriovenous fistulae for hemodialysis. *Am J Kidney Dis* 2003; 42: 331–341
7. Tessitore N, Lipari G, Poli A *et al.* Can blood flow surveillance and pre-emptive repair of subclinical stenosis prolong the useful life of arteriovenous fistulae? A randomized controlled study. *Nephrol Dial Transplant* 2004; 19: 2325–2333
8. Tessitore N, Bedogna V, Melilli E *et al.* In search of an optimal bedside screening program for arteriovenous fistula stenosis. *CJASN* 2011; 6: 819–826
9. Tessitore N, Bedogna V, Lipari G *et al.* Bedside screening for fistula stenosis should be tailored to the site of the arteriovenous anastomosis. *CJASN* 2011; 6: 1073–1080
10. Besarab A, Ravani P, Spergel LM *et al.* The native arteriovenous fistula in 2007. Research nedds. *J Nephrol* 2007; 20: 668–673
11. Beathard GA. Physical examination of the dialysis vascular access. *Semin Dial* 1998; 11: 231–236
12. Beathard GA. An algorithm for the physical examination of early fistula failure. *Semin Dial* 2005; 18: 331–335
13. Asif A, Leon C, Orozco-Vargas LC *et al.* Accuracy of physical examination in the detection of arteriovenous fistula stenosis. *Clin J Am Soc Nephrol* 2007; 2: 1191–1194
14. Leon C, Asif A. Physical examination of arteriovenous fistulae by a renal fellow: does it compare favorably to an experienced interventionalist? *Semin Dial* 2008; 21: 557–560
15. Campos RR, Chula DC, Perreto S *et al.* Accuracy of physical examination and intra-access pressure in the detection of stenosis in hemodialysis arteriovenous fistula. *Semin Dial* 2008; 21: 269–273
16. McGinn T, Wyers PC, Newman T *et al.* Tips for learners of evidence-based medicine: measures of observer variability/kappa statistics. *CMAJ* 2004; 171: 1369–1373
17. Campos R, Riella MC. Challenge for the interventional nephrologist: monitoring the arteriovenous fistula. *Contrib Nephrol* 2008; 161: 12–22
18. Besarab A, Asif A, Roy-Chaudhury P *et al.* The native arteriovenous fistula in 2007. Surveillance and monitoring. *J Nephrol* 2007; 20: 656–667

*Received for publication: 9.6.11; Accepted in revised form: 9.8.11*

# Chapter 6
## *Treatment of vascular access failure*

### 6.1. Percutaneous Treatment of Thrombosed Arteriovenous Fistulas: Clinical and Economic Implications

Coentrão L, Bizarro P, Ribeiro C, Neto R, Pestana M

*Clin J Am Soc Nephrol* 2010;5: 2245-2250. PMID: 20798249

# Percutaneous Treatment of Thrombosed Arteriovenous Fistulas: Clinical and Economic Implications

Luís Coentrão,*† Pedro Bizarro,* Carlos Ribeiro,‡ Ricardo Neto,* and Manuel Pestana*

**Nephrology Research and Development Unit, Hospital S. João, and †Institute of Pharmacology and Therapeutics, Faculty of Medicine, University of Porto, Porto, Portugal; and ‡Financial Management Unit, Hospital S. João, Porto, Portugal*

**Background and objectives: Maintenance of previously thrombosed arteriovenous fistulas (AVFs) as functional vascular accesses can be highly expensive, with relevant financial implications for healthcare systems. The aim of our study was to evaluate the costs and health outcomes of vascular access care in hemodialysis patients with AVF thrombosis.**

**Design, setting, participants, & measurements: A retrospective, controlled cohort study was performed among local hemodialysis patients with completely thrombosed AVFs between August 1, 2007, and July 1, 2008. Detailed clinical and demographic information was collected and a comprehensive measure of total vascular access costs was obtained. Costs are reported in 2009 U.S. dollars.**

**Results: A total of 63 consecutive hemodialysis patients with thrombosed AVFs were identified—a cohort of 37 patients treated with percutaneous thrombectomy and a historic cohort of 25 patients with abandoned thrombosed AVFs. The mean cost of all vascular access care at 6 months was $2479. Salvage of thrombosed AVFs led to a near two-fold reduction in access-related expenses, per patient-month at risk ($375 *versus* $706; $P = 0.048$). The costs for access-related hospitalizations ($393 *versus* $91; $P = 0.050$), management of access dysfunction ($106 *versus* $28; $P = 0.005$), and surgical interventions ($35 *versus* $6; $P = 0.001$) were also significantly lower in the percutaneous treatment group. At 6 months, most of these patients had a functional AVF as permanent vascular access (91% *versus* 33%, $P = 0.0001$).**

**Conclusions: Salvage of thrombosed AVF is a highly efficient procedure; therefore, intensive efforts should be undertaken to universalize these interventions.**

*Clin J Am Soc Nephrol* 5: 2245–2250, 2010. doi: 10.2215/CJN.03070410

Functional vascular access is a prerequisite for adequate hemodialysis treatment in patients with ESRD. Autogenous arteriovenous fistulas (AVFs) are considered superior to synthetic grafts as a hemodialysis vascular access; however, AVFs are not without problems (1). In the last decade, management of thrombosed AVFs has been largely accomplished by surgical or endovascular interventions. Despite the existence of well established endovascular procedures to declot a thrombosed AVF (2–10), attempts to salvage these accesses are not universally used.

Percutaneous treatment of thrombosed AVFs is a relatively highly successful procedure. However, repeated interventions are usually required to achieve long-term access survival (11). Therefore, maintenance of a previously thrombosed AVF could be a highly expensive policy. Published data regarding the economic value of vascular access surveillance and prophylactic angioplasty to prevent AVF thrombosis are controversial (12,13), and information about the cost-effectiveness of AVF salvage procedures has been limited.

In the study presented here, we performed a retrospective analysis among adult maintenance dialysis patients with thrombosed AVFs to estimate the costs and health outcomes of vascular access care during the first 6 months post-thrombosis.

## Patients and Methods

### *Patient Population*

The Hospital S. João, Porto, is a university hospital center that serves a large population on regular hemodialysis (approximately 1600 patients). Until the last few years, hemodialysis patients with thrombosed AVFs were referred for surgical revision of the clotted AVF or to our nephrology department for central venous catheterization pending creation of a new AVF. By 2008, endovascular treatment of thrombosed AVFs became a standard procedure in our unit.

Patients were recruited from the Nephrology Unit, Hospital S. João, Porto. All adult maintenance dialysis patients with completely thrombosed AVFs between August 1, 2007 and July 31, 2008, were included in this study. From August 1 and December 31, 2007, patients were referred for central venous catheterization pending creation of a new AVF. From January 1 to July 31, 2008, patients were referred for consideration of a percutaneous thrombectomy.

Sixty-three adult maintenance dialysis patients fulfilled the study criteria. Thirty-seven patients were treated with percutaneous thrombectomy (group A) and 25 patients underwent central venous catheterization to bridge the interval until a new AVF was suitable for

Received April 7, 2010. Accepted July 14, 2010.

*Published online ahead of print. Publication date available at www.cjasn.org.*

**Correspondence:** Dr. Luís Coentrão, Nephrology Research and Development Unit, Faculty of Medicine, University of Porto, Alameda Prof. Hernâni Monteiro, 4200-319 Porto, Portugal. Phone: +35-191-053-8824; Fax: +35-122-551-2228; E-mail: coentrao@med.up.pt



ISSN: 1555-9041/512–2245

cannulation (group B). In only one patient the interventionalist deemed that endovascular intervention was not advisable because of the presence of long segmental aneurysms with an extremely large clot burden. This patient underwent central venous catheterization. Three patients were lost to follow-up. In the final analysis, group A included 35 patients and group B included 24 patients ($n = 59$).

The study was approved by the Ethics Committee for Health of the Hospital S. João, Porto.

### *Procedures*

In our unit, we used the method of manual catheter-directed thromboaspiration (2). If a hemodynamically significant lesion was encountered, a conventional angioplasty balloon, rated burst pressure of 15 atm (Cordis Corporation, Johnson & Johnson Medical N.V/S.A., Waterloo, Belgium), was inflated at the level of the stenotic site. Patients were referred within 72 hours of thrombosis. The only contraindications for percutaneous declotting were infection and the presence of long segmental aneurysms with extremely large clot burdens. Percutaneous thrombectomy was performed as an outpatient procedure.

Tunneled cuffed catheter (TCC) placement (Retro, Spire Biomedical, Inc., Bedford, MA) was performed with ultrasound guidance, as recommended by Dialysis Outcomes Quality Initiatives (14). Postprocedure chest radiography was performed in all patients.

Clinical success was defined as the resumption of dialysis with a blood flow >300 ml/min at the first dialysis session after the intervention (15). Primary (unassisted) patency of the vascular access was calculated from the date of the index procedure to the first subsequent access intervention. Access primary patency ended when any of the following occurred: (*1*) there was an intervention for the treatment of stenosis or thrombosis anywhere within the AVF; (*2*) there was an intervention for the treatment of intracatheter thrombosis, catheter malposition, or kinking; or (*3*) there was an intervention for the treatment of access-related bacteriaemia requiring catheter removal or AVF closure.

### *Cost Analysis*

Our study took the perspective of the healthcare purchaser including direct vascular access care-related costs. All resource use was valued at prices in 2009. All costs were converted to U.S. dollars using an exchange rate of 1 Euro (€) equal to 1.41 U.S.$.

A direct access care-related cost was estimated for each procedure, including all expenses for creation of a new AVF (unitary cost, $420), placement of TCC (unitary cost, $605), and hospitalization for vascular access-related complications (unitary cost for in-hospital care of vascular access infection, $2075). Costs for correcting the AVF stenosis or thrombosis by endovascular means were assessed to be $1401. The cost per procedure was established from the Ministry of Health and Welfare Ordinance Legislation - Diário da República (1st series, no. 147, July 31, 2009, ordinance no. 839 and 2nd series, no. 81, April 5, 2000, dispatch no. 7376/2000).

Information on all vascular access surgeries was captured from our nephrology unit database, which collects surgical data for all patients who undergo vascular access surgery. Information on hospital admissions for management of vascular access-related problems (*e.g.*, local or metastatic infection, limb ischemia, hemorrhage, or thrombosis), endovascular procedures (*i.e.*, all radiology procedures performed as part of access-related care), and catheter placements/local thrombolytic therapy, was collected from our hospital database. Patient's transport costs required for the vascular access care were also included in the analysis. They principally used a taxi or ambulance for hospital visits ($0.66 for 1 km). In addition, we did not collect information on costs specifically related to outpatient use of intravenous antibiotics for access-related infection.

### *Follow-Up*

Patient follow-up started on the day the vascular access intervention was first performed and continued for 6 months. Clinical and demographic data, as well as data on access type, were collected from hospital and satellite unit records. Demographic information was assessed by means of a questionnaire. The presence of comorbid illness was assessed by a physician as of the enrolment date by complete review of patient's records. Information was collected for the 19 variables that constitute the Charlson comorbidity index (16), which has been validated for use in patients with ESRD. Follow-up was censored for patient death or transplant.

### *Study Endpoints*

The primary endpoint of this analysis was to determine the economic effect of endovascular intervention in hemodialysis patients with thrombosed AVF. Secondary outcomes of the study included all access-related clinical adverse events (*e.g.*, bacteriaemia, access dysfunction, surgical interventions, hospital admissions, and death).

### *Statistical Analyses*

Data are given as percentages and mean ± SD. Normally distributed continuous variables were analyzed using Student's unpaired *t* test and categorical variables using Fisher's exact test. Rates were calculated for each of the patients by dividing the number of events/procedures by the duration of follow-up in months. Vascular access patency was analyzed using the Kaplan–Meier method and differences between groups were evaluated by log-rank tests. All tests were two sided, and differences were considered significant at $P < 0.05$. All statistical analyses were performed using the SPSS software, version 11 (SPSS, Inc., Chicago, IL).

## Results

Approximately two thirds of the patients were male. Diabetes, hypertension, and vascular disease were commonly present in both study groups. There were no relevant differences between the two treatment groups at baseline with respect to demographic characteristics and medical history (Table 1).

Percutaneous thrombectomy was successfully performed in 34 patients, with prompt restoration of a thrill and bruit. No stent was deployed. Angioplasty was not feasible in one patient with an upper-arm AVF because of the inability to pass the guidewire through a tight stenotic lesion. This patient underwent TCC placement. Clinical success was observed in 34 patients (success rate = 97%). Twenty-four patients (69%) presented with a radial-cephalic AVF (an underlying stenosis lesion was present in the draining vein in 11 patients and concurrent stenoses at the arterial anastomosis and in the draining vein in 13 patients). Eleven patients (31%) presented with a brachial-cephalic AVF (an underlying stenosis lesion was present in the draining vein in five patients and in the arterial anastomosis in six patients). One patient with upper-arm AVF developed steal syndrome and myocardial infarction, approximately 2 weeks postprocedure, requiring hospitalization and further access surgery. Six patients experienced AVF thrombosis during follow-up (five patients with an upper-arm AVF and one patient with a forearm AVF): three patients were treated

*Table 1.* Baseline characteristics of patients overall and according to treatment group

| Characteristics | Overall ($n$ = 59) | Group A ($n$ = 35) | Group B ($n$ = 24) | $P$ |
|---|---|---|---|---|
| Age, years | 66 ± 13,4 | 64 ± 14 | 69 ± 11.8 | 0.07 |
| Gender, $n$ (%) male | 39 (66%) | 25 (71%) | 14 (58.3%) | 0.29 |
| Previous fistulas, $n$ (%) | 24 (40.7%) | 13 (37%) | 11 (45.8%) | 0.21 |
| Previous dialysis catheter, $n$ (%) | 34 (57.6%) | 21 (60%) | 13 (54.2%) | 0.29 |
| Time on dialysis, years | 3.3 ± 2.6 | 3.9 ± 2.8 | 2.4 ± 1.8 | 0.02 |
| Charlson comorbidity index | 4.7 ± 2.3 | 4.6 ± 2.3 | 4.8 ± 2.3 | 0.4 |
| Comorbid conditions, $n$ (%) | | | | |
| coronary heart disease | 11 (18.60%) | 7 (20%) | 4 (16.70%) | 0.76 |
| congestive heart failure | 19 (32.20%) | 11 (31.40%) | 8 (33.30%) | 0.86 |
| peripheral vascular disease | 14 (23.70%) | 9 (25.7%) | 5 (20.8%) | 0.65 |
| previous stroke | 11 (18.60%) | 5 (14.3%) | 6 (25%) | 0.31 |
| diabetes | 16 (27.10%) | 12 (34.30%) | 4 (16.70%) | 0.14 |

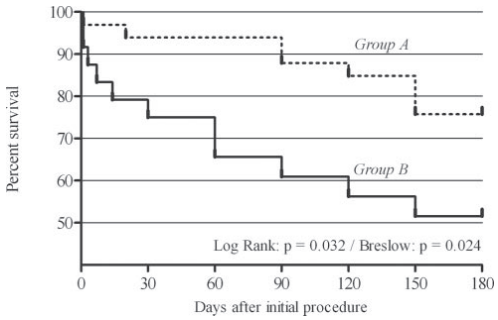


*Figure 1.* Percentage of freedom from subsequent interventions at 6 months. The graph shows the primary patency as of enrollment according to the Kaplan–Meier analysis.

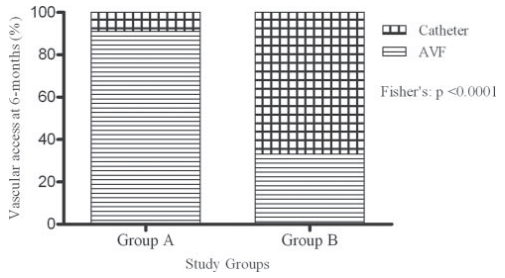


*Figure 2.* Permanent vascular access type at 6 months of follow-up for each study group. At the end of follow-up, a significantly higher number of group A patients had a functioning AVF as a permanent vascular access.

with further percutaneous thrombectomy, two patients were given a TCC placement, and one patient underwent a new AVF creation in the same arm. Two patients died during follow-up because of acute pancreatitis and respiratory infection, respectively. At 6 months, the primary patency rate of the vascular access was 75% (Figure 1). At the end of follow-up, 30 patients (91%) presented a functional AVF as a permanent vascular access (Figure 2).

TCC placement was successfully performed in 24 patients. Nevertheless, clinical success was observed in 22 patients (success rate = 92%). Twenty-two patients (92%) presented with an internal jugular catheter. During follow-up, hospitalization because of catheter-related bacteriaemia ($n$ = 4) or central venous thrombosis ($n$ = 2) was required in six patients. Local catheter thrombolysis (total = 16) was necessary in six patients. Thereafter, four patients underwent catheter removal because of late dysfunction. Nine patients underwent a second TCC placement. At 6 months, the primary patency rate of the vascular access was 51% (Figure 1). Although 22 patients underwent a new AVF creation, only eight patients (33%) were performing dialysis with a functional AVF at the end of follow-up (Figure 2). The mean time for the construction of a new AVF was 33 days (3 to 180 days). Table 2 shows the mean values of secondary outcomes for both study groups.

The cost of vascular access care was substantial, with a mean cost per patient at 6 months of $2479 (median $1455; interquartile range [IQR] $647 to $18,848). The total cost for patient-month at risk was lowest for the endovascular group (mean $374; median $241; IQR $228 to $3146 *versus* mean $706; median $379; IQR $108 to $3018; $P$ = 0.048; Table 3). Furthermore, the mean access-related surgical costs, costs for access-related hospital admissions, and management of access dysfunction were significantly higher for group B patients. The largest expenses for patients treated with central venous catheterization were related with hospitalizations. On the other hand, percutaneous thrombectomy itself was responsible for approximately two thirds of the costs spent with group A patients (Table 3).

*Table 2.* Secondary outcomes at 6 months of follow-up according to study group (median ± SD)

| Outcome | Group A ($n$ = 35) | Group B ($n$ = 24) | $P$ |
|---|---|---|---|
| Access-related surgery | 0.08 ± 0.27 | 0.33 ± 0.47 | 0.01 |
| Access-related hospital admissions | 0.05 ± 0.32 | 0.25 ± 0.43 | 0.047 |
| Management of access dysfunction[a] | 0.16 ± 0.43 | 0.96 ± 1.45 | 0.004 |
| Management of access-related infection | 0 | 0.17 ± 0.47 | 0.036 |
| Patient death, access-related | 0 | 0.08 ± 0.48 | 0.072 |

[a]Includes all radiology procedures performed as part of access-related care, catheter placements, and local thrombolytic therapy.

*Table 3.* Cost analysis in U.S. dollars/patient-month overall and according to treatment group (mean ± SD)

| | Overall ($n$ = 59) | Group A ($n$ = 35) | Group B ($n$ = 24) | $P$ |
|---|---|---|---|---|
| Index procedure | $182 ± 45 | $232 ± 3 | $109 ± 20 | <0.001 |
| Surgical interventions | $18 ± 25 | $6 ± 14 | $35 ± 32 | 0.001 |
| Hospital admissions | $211 ± 428 | $91 ± 327 | $393 ± 50 | 0.050 |
| Management of access dysfunction[a] | $60 ± 75 | $28 ± 54 | $106 ± 88 | 0.005 |
| Patient's transport | $22 ± 22 | $8 ± 3 | $45 ± 29 | 0.002 |
| Total cost | $510 ± 466 | $375 ± 355 | $706 ± 563 | 0.048 |

[a]Includes all radiology procedures performed as part of access-related care, catheter placements, and local thrombolytic therapy.

## Discussion

Vascular access care is responsible for a significant proportion of healthcare costs in prevalent hemodialysis patients (17). Manns *et al.* (18) have shown that the high access-related costs of incident hemodialysis patients with primary AVF failure were partially due to the increased number of diagnostic imaging and radiologic interventions. For healthcare systems with strict economic barriers, this issue may be extremely relevant.

Bittl *et al.* (12) recently published an economic analysis concluding that preemptive angiographic management of AVF dysfunction may represent a less efficient use of healthcare resources than increasing the number of patients with AVF. In the study presented here, we have demonstrated that salvage of clotted AVF by percutaneous thrombectomy rather than waiting for a new mature AVF, was associated with a reduction in access-related costs (Table 2).

Study groups were relatively well matched for baseline parameters and length of follow-up. Despite the relative short time on hemodialysis, near a half of the patients had a previous history of dialysis catheters and vascular access surgeries (Table 1). As such, salvage of the clotted AVF would be of an utmost importance.

Among the previous series (2–10), clinical success and primary patency at 6 months of thrombosed AVFs treated with interventional thrombectomy has ranged between 73% to 96% and 38% to 81%, respectively. For TCC placement, primary patency rates are approximately 60% at 6 months (19). The outcomes of the current series, for endovascular procedure (clinical success 97%, primary patency 75%) and catheter placement (clinical success 92%, primary patency 51%), were at the higher end of these ranges (Figure 1).

In 2006, Allon *et al.* (20) reported that change in vascular access had relevant clinical implications in hemodialysis patients. In the study presented here, 91% of group A patients had a functioning AVF as a permanent vascular access at 6 months. In contrast, we have found only 33% of group B patients with a functional AVF at the end of follow-up. As a consequence, group B patients presented a higher percentage of hospitalizations and comorbidity (Table 2). Local practice patterns may have been responsible for the observed low rate of functioning AVF in group B patients. However, these results are not surprising because even incident hemodialysis patients (without a previous history of failed AVF) with a timely referral to a nephrologist and subsequently to a vascular surgeon still may not have a functioning AVF, as result of a delay in procedure scheduling or failure of the AVF to mature (21).

We found that vascular access care in the first 6 months post-thrombosis was cumbersome, with patients selected for central venous catheterization pending the creation of a new AVF incurring the highest costs. Cost-effectiveness analysis showed that AVF salvage by endovascular therapy led to a near two-fold reduction in access-related expenses per patient-month at risk; the added costs associated with the

procedure itself was completely offset by the saving associated with lower surgical visits, access dysfunction, and hospitalizations (Table 3). In fact, management of access dysfunction and access-related hospitalizations was nearly 4 times higher in group B patients (Table 3), reflecting the lower access survival and the subsequent comorbidity associated with TCC placement. Interestingly, the usual forgotten patient's transport cost required for the establishment and management of the vascular access had a relevant economic effect in group B patients (Table 3). Therefore, the guarantee of a functional AVF with a high primary patency rate is an utmost important issue in hemodialysis patients, with obvious economic benefits.

Although patients were followed-up for only 6 months, we were able to find clinical and economic disparities between the two different approaches. Probably, if a long-term follow-up was performed, differences between cohorts would have been similar because both groups would require more vascular-access interventions to establish or maintain a functional vascular access.

Our study had several limitations. First, as a retrospective study, it shares all of the limitations of that approach. Selection of candidates for AVF salvage therapy and the type of procedure performed may differ among centers and countries, and this may have an effect on the external generalizability of our results. Also, the patient population consisted mainly of Caucasian Europeans, which makes it impossible to draw conclusions for other ethnicities. The cost of certain healthcare procedures has been reported to differ between countries (22). However, the relative amount of resources required for intervention and the determinants of vascular access costs are likely to be similar between centers. We are aware that our study cannot provide a definitive answer regarding the efficiency of percutaneous thrombectomy in AVF thrombosis and that further prospective cost-effectiveness analysis comparing endovascular and surgical procedures needs to be undertaken.

In conclusion, the cost of vascular access care is high among patients with AVF thrombosis and highest for patients selected for central venous catheterization pending the creation of a new AVF. Our study suggests that salvage of thrombosed AVFs by percutaneous thrombectomy is a safe and cost-effective policy; therefore, intensive efforts should be undertaken to universalize these procedures.

## Acknowledgments

We thank the clinical directors from hemodialysis clinics who kindly agreed to collaborate in this study: A. Baldaia Moreira M.D., A. Caldeira Gomes M.D., A. Castro Henriques M.D., Antunes de Azevedo M.D, Eva Xavier M.D., João C. Fernandes M.D., João M. Frazão M.D., Ph.D., Jorge P. Baldaia M.D., José M. Madureira M.D., José Pinheiro M.D., Odete Pereira M.D., Sofia Pedroso M.D., Susana Sampaio M.D., and Vasco Miranda M.D.

## Disclosures

None.

## References

1. Beathard GA: Fistula salvage by endovascular therapy. *Adv Chronic Kidney Dis* 16: 339–351, 2009
2. Turmel-Rodrigues L, Sapoval M, Pengloan J, Billaux L, Testou D, Hauss S, Mouton A, Blanchard D: Manual thromboaspiration and dilation of thrombosed dialysis access: Mid-term results of a simple concept. *J Vasc Interv Radiol* 8: 813–824, 1997
3. Turmel-Rodrigues L, Pengloan J, Rodrigues H, Brillet G, Lataste A, Pierre D, Jourdan JL, Blanchard D: Treatment of failed native arteriovenous fistulae for hemodialysis by interventional radiology. *Kidney Int* 57: 1124–1140, 2000
4. Moossavi S, Regan JD, Pierson ED, Kasey JM, Tuttle AB, Vachharajani TJ, Bettmann MA, Russell GB, Freedman BI: Nonsurgical salvage of thrombosed arterio-venous fistulae: A case series and review of the literature. *Semin Dial* 20: 459–464, 2007
5. Haage P, Vorwerk D, Wilberger JE, Piroth W, Schurmann K, Gunther RW: Percutaneous treatment of thrombosed primary arteriovenous hemodialysis access fistulae. *Kidney Int* 57: 1169–1175, 2000
6. Liang HL, Pan HB, Chung HM, Ger LP, Fang HC, Wu TH, Wu MT, Lai PH, Chen CK, Yang CF: Restoration of thrombosed Brescia-Cimino dialysis fistulas by using percutaneous transluminal angioplasty. *Radiology* 223: 339–344, 2002
7. Rajan DK, Clark T, Simons ME, Kachura JR, Sniderman K: Procedural success and patency after percutaneous treatment of thrombosed autogenous arteriovenous dialysis fistulas. *J Vasc Interv Radiol* 13: 1211–1218, 2002
8. Shatsky JB, Berns JS, Clark TW, Kwak A, Tuite CM, Shlansky-Goldberg RD, Modschein JI, Patel AA, Stavropoulos SW, Soulen MC, Solomon JA, Kobrin S, Chittams JL, Trerotola SO: Single-center experience with the Arrow-Trerotola percutaneous thrombectomy device in the management of thrombosed native dialysis fistulas. *J Vasc Interv Radiol* 16: 1605–1611, 2005
9. Beathard GA, Litchfield T: Physician Operators Forum of RMS Lifeline, Inc: Effectiveness and safety of dialysis vascular access procedures performed by interventional nephrologists. *Kidney Int* 66: 1622–1632, 2004
10. Jain G, Maya ID, Allon M: Outcomes of percutaneous mechanical thrombectomy of arteriovenous fistulas in hemodialysis patients. *Semin Dial* 21: 581–583, 2008
11. Jan H. M. Tordoir JHM, Bode AS, Peppelenbosch N: Surgical or endovascular repair of thrombosed dialysis vascular access: Is there any evidence? *J Vasc Surg* 50: 953–956, 2009
12. Bittl JA, Cohen DJ, Seek MM, Feldman RL: Economic analysis of angiography and preemptive angioplasty to prevent hemodialysis-access thrombosis. *Catheter Cardiovasc Interv* 75: 14–21, 2010
13. Tessitore N, Bedogna V, Poli A, Mantovani W, Lipari G, Baggio E, Mansueto G, Lupo A: Adding access blood flow surveillance to clinical monitoring reduces thrombosis rates and costs, and improves fistula patency in the short term: A controlled cohort study. *Nephrol Dial Transplant* 23: 3578–3584, 2008
14. National Kidney Foundation-Disease Outcomes Quality Initiative: Clinical practice guidelines and clinical practice recommendations for vascular access 2006. *Am J Kidney Dis* 48: S176–S322, 2006

15. Sidawy A, Gray R, Besarab A, Henry M, Ascher E, Silva M Jr: Recommended standards for reports arteriovenous hemodialysis accesses. *J Vasc Surg* 3: 603–610, 2002
16. Charlson ME, Pompei P, Ales KL: A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *J Am Soc Nephrol* 7: 198–207, 1996
17. Lee H, Manns BJ, Taub K, Ghali WA, Dean S, Johnson D, Donaldson C: Cost analysis of ongoing care of patients with end-stage renal disease: The impact of dialysis modality and dialysis access. *Am J Kidney Dis* 40: 611–622, 2002
18. Manns B, Tonelli M, Yilmaz S, Lee H, Laupland K, Klarenbach S: Establishment and maintenance of vascular access in incident hemodialysis patients: A prospective cost analysis. *J Am Soc Nephrol* 16: 201–209, 2005
19. Lee T, Barker J, Allon M: Tunneled catheters in hemodialysis patients: Reasons and subsequent outcomes. *Am J Kidney Dis* 46: 501–508, 2005
20. Allon M, Daugirdas J, Depner T, Greene T, Ornt D, Schwab SJ: Effect of change in vascular access on patient mortality in hemodialysis patients. *Am J Kidney Dis* 47: 469–477, 2006
21. Lok CE: Fistula First Initiative: Advantages and pitfalls. *Clin J Am Soc Nephrol* 2: 1043–1053, 2007
22. World Bank: *World Development Indicators* 2000, Washington DC, World Bank, 2001

# Chapter 6
## *Treatment of vascular access failure*

**6.2. Endovascular treatment of thrombosed dialysis fistulae: a cumulative cost analysis**

Bizarro P, Coentrão L, Ribeiro C, Neto R, Pestana M.

*Catheter Cardiovasc Interv* 2011;77:1065-1070. PMID: 21413132.

**Catheterization and Cardiovascular Interventions 77:1065–1070 (2011)**

# Endovascular Treatment of Thrombosed Dialysis Fistulae: A Cumulative Cost Analysis

**Pedro Bizarro,[1] MD, Luís Coentrão,[1,2*] MD, Carlos Ribeiro,[3] BA, Ricardo Neto,[1] MD, and Manuel Pestana,[1] MD, PhD**

**Objectives: In the present study, we determined the cumulative costs and outcomes of endovascular treatment of thrombosed autogenous arteriovenous fistulae (AVF) at our medical center. Background: Previous studies examining the salvage procedures of thrombosed AVFs have focused exclusively on clinical outcomes, and, in the absence of costing data, current guidelines do not take into consideration economic issues. Methods: A retrospective cohort study was performed among local hemodialysis patients with completely thrombosed AVFs receiving endovascular treatment in our institution between January 1 and December 31, 2008. Forty-four patients were enrolled and followed-up for 1 year. Success and complications were recorded according to consensus definitions, and a comprehensive measurement of total vascular access care-related costs was obtained. Costs are reported in 2010 in U.S. dollars. Results: Clinical success was achieved in 95% of cases. The primary and secondary patency rates were 63 and 78% at 1 year, respectively. Primary patency rate at 12 months was significantly better for radiocephalic AVFs (70% vs. 43%; $P = 0.047$). The mean cumulative cost of all vascular access care during year 1 was $2,504 (median $1,484; range, $1,362–$18,279; Table V) per patient-year at risk. The mean cumulative cost for maintaining radiocephalic and brachiocephalic AVFs was $1,624 (median $1,381; range, $1,130–$3,116) and $3,578 (median $2,092; range, $1,470–$18,279) per patient-year at risk, respectively ($P = 0.022$). Conclusion: The cost of maintenance of a thrombosed AVF by endovascular intervention is high, with patients with clotted radiocephalic fistulae incurring the lowest costs and achieving higher survival times.** © 2011 Wiley-Liss, Inc.

**Key words: autogenous arteriovenous fistulae; percutaneous thrombectomy; economic analysis**

## INTRODUCTION

Thrombosis of the vascular access is a relatively infrequent complication of autogenous arteriovenous fistulae (AVF) [1,2]. However, as current clinical practice guidelines recommend that at least 65% of the end stage renal disease (ESRD) population should have a functional AVF as a permanent dialysis access [1,2], AVF thrombosis has become a clinical challenge in our nephrology practice, with relevant clinical implications for dialysis patients. Several studies have reported on the feasibility and relatively high-clinical success rate of the endovascular approach to thrombosed AVF in recent years [3–12], and salvage procedures have therefore been recommended in the recently published guidelines in order to re-establish the functionality of failed vascular accesses [1,2].

Published findings regarding the economic value of vascular access surveillance revealed that adding access blood flow surveillance to clinical monitoring of AVFs reduces thrombosis rates and costs [13]. Bittl et al. [14] recently reported, in a large observational economic analysis, that preemptive angiographic management of malfunctioning nonthrombosed hemodialysis accesses may represent a less efficient use of healthcare resources than increasing the number of

[1]Nephrology Research and Development Unit, Faculty of Medicine, University of Porto, Hospital S. João, Porto, Portugal
[2]Institute of Pharmacology and Therapeutics, Faculty of Medicine, University of Porto, Portugal
[3]Financial Management Unit, Hospital S. João, Porto, Portugal

Conflict of interest: Nothing to report.

Pedro Bizarro and Luís Coentrão contributed equally to the work.

*Correspondence to: Luís Coentrão, MD, Nephrology Research and Development Unit, Faculty of Medicine, University of Porto, Al. Prof. Hernâni Monteiro, 4200-319 Porto, Portugal.
E-mail: coentrao@med.up.pt

Received 6 October 2010; Revision accepted 22 November 2010

DOI 10.1002/ccd.22913
Published online 16 March 2011 in Wiley Online Library (wileyonlinelibrary.com)

patients with AVFs. Cost-effective analyses of endovascular interventions for thrombosed hemodialysis accesses have been performed only in patients with clotted prosthetic grafts [15–18], and most of these studies have used patient charges rather than actual costs for financial analysis [16–19]. In this regard, reporting standards for percutaneous interventions on dialysis accesses recommend that the cumulative costs per patient should be measured over months or years whenever possible for more insightful comparisons [19].

In the present study, we determined the cumulative costs and outcomes of endovascular treatment of clotted AVFs during the first-year post-thrombosis, at our medical center.

## SUBJECTS AND METHODS

### Patient Population

This investigation was reviewed and approved by the Hospital S. João Institutional Review Board. The Hospital S. João is a tertiary-care University Hospital that carries out interventional procedures for patients from our hospital hemodialysis center and satellite hemodialysis units. The patients in these hemodialysis units were monitored for clinical signs of access dysfunction. On the basis of clinical changes, the patients were referred for diagnostic fistulography and endovascular treatment as appropriate. The exclusion criteria for endovascular treatment were an infected AVF and the presence of old wall-adherent thrombi. Patients with nonthrombosed failing AVFs (low thrill) were excluded from the study. Forty-eight patients with totally occluded AVFs were consecutively referred for the consideration of percutaneous thromboaspiration from January 1 to December 31, 2008. In one patient, the interventionalist deemed that endovascular intervention was not advisable due to the presence of old wall-adherent thrombi. Three patients were excluded from the study due to insufficient data collection. The final analysis included 44 patients.

### Procedures

The method used in our unit was manual catheter-directed thromboaspiration [3]. When a hemodynamically significant lesion was encountered, a conventional angioplasty balloon [(Cordis Corporation, Johnson & Johnson Medical N.V/S.A., Waterloo, Belgium), burst pressure = 15 atm] was inflated at the level of the stenosed site. The intervention was performed as an outpatient procedure. Cases were referred within 96 hr of the detection of the loss of a thrill or bruit in the access. Systematic low-molecular weight heparin was recommended for 2 weeks post-thrombectomy, as previously reported by Turmel-Rodrigues et al. [3,4]. All procedures were performed by the same nephrologist.

Patients with thrombosed AVF for whom the endovascular approach was either unsuccessful or contraindicated underwent tunneled dialysis catheter placement and/or creation of a new AVF, as an outpatient procedure. Tunneled cuffed catheter placement (Retro, Spire Biomedical, Bedford, MA) was performed by a nephrologist and with ultrasound guidance, as recommended by Dialysis Outcomes Quality Initiatives [2]. Postprocedure chest radiography was performed in all patients. Surgical construction of a new AVF was performed by local vascular surgeons as an outpatient procedure.

### Follow-Up

Clinical information was collected retrospectively from both hospital and satellite unit records. Data were assessed by means of a questionnaire. The presence of comorbidity at the enrolment date was assessed by a physician by complete review of patients' records. Information was collected for the 19 variables that constitute the Charlson Comorbidity Index [20], which has been validated for use in patients with ESRD. Follow-up was based on clinical surveillance by the attending nephrologists in the 14 referring hemodialysis centers. Recurrence of abnormalities, such as increased venous pressure, increased time to hemostasis and arm edema, led to further angiography with subsequent intervention. Acute thrombosis was treated percutaneously by aspiration thrombectomy [3]. During follow-up, patients with thrombosed AVF for whom the endovascular approach was either unsuccessful or contraindicated underwent ambulatory dialysis catheter placement and/or creation of a new AVF. Patient follow-up started on the day the vascular access intervention was first performed and continued for 1 year. Follow-up ceased at patient death, renal transplantation, or switching to peritoneal dialysis.

### Definitions

Success, complications, and secondary interventions were recorded according to consensus definitions [19]. Clinical success was defined as the resumption of dialysis with a blood flow $>$ 300 ml/min on the first three dialysis sessions after the intervention. Primary patency was considered to begin on the day of declotting (index procedure) and to end on the day of access failure or further reintervention (either radiological or surgical). Secondary patency included all further radiological treatments (dilation, new percutaneous declotting) but ended with surgical revision.

Catheterization and Cardiovascular Interventions DOI 10.1002/ccd.
Published on behalf of The Society for Cardiovascular Angiography and Interventions (SCAI).

### Cost Analysis

Our study was performed from the perspective of the health care purchaser and included direct vascular access care-related costs. All resource use was valued at prices in 2010. All costs were converted to U.S. dollars using an exchange rate of 1 Euro (€) equal to $1.31US.

The data concerning the hospital costs and professional fees for physicians and nurses were obtained from the Information Management Division. The professional fee per intervention was determined from the average fee charged by Nephrology professionals per year divided by the number of procedures and time spent in the angiography suite. The average technical costs per intervention included the supplies, pharmacy and radiology costs, and additional overhead expenses. The total expense for each procedure represents the sum of the average technical costs and the average professional fees. The cost of hospital admissions for which the primary reason for admission (as defined by the discharge diagnosis [*International Classification of Diseases Ninth Revision codes*]) was related to access care was obtained from the Information Management Division. The vascular access surgical data (outpatient creation of autogenous arteriovenous fistula) in this study are more similar to "charges" than to "costs" in that they were extracted from the Ministry of Health and Welfare Ordinance (unitary cost, $393). Patient's transport costs required for the vascular access care were also included in the analysis. They principally used a taxi or ambulance for hospital visits ($0.66 for 1 km). The cumulative cost represents the sum of all access-related procedures, hospitalizations, and patient's transport required to establish or to maintain a functional vascular access during follow-up. Initial failures and dialysis catheter placements before attempted thrombectomy were included in the analysis.

### Statistical Analysis

Data are given as percentages and mean ± standard deviation. Normally, distributed continuous variables were analyzed using Student's unpaired *t*-test and categorical variables using Fisher's exact test. Rates were calculated for each of the patients by dividing the number of events/procedures by the duration of follow-up. Fistula patency was analyzed using the Kaplan–Meier method, and differences between groups were evaluated by log-rank tests.

## RESULTS

Patient characteristics are summarized in Table I. The average time on dialysis was 3.9 years (range, 0.5–28 years), and mean fistula age was 4.6 years (range, 0.3–28 years). Clotted accesses included 24 (55%) radiocephalic AVFs and 20 (45%) brachiocephalic AVFs (Table I). The mean age was 63.7 ± 8 (SD) years in the radiocephalic fistula group compared to 63.3 ± 4 years in the brachiocephalic fistula group ($P$ = NS), and there were relatively higher number of men in the radiocephalic fistula group (87% in radiocephalic fistula group, 65% in brachiocephalic fistula group, and $P = 0.07$). Twenty-nine percent of patients in the radiocephalic fistula group were diabetic and 25% in the brachiocephalic fistula group ($P$ = NS). Three patients were referred for percutaneous thrombectomy 96 hr after the detection of AVF thrombosis. These patients underwent dialysis catheter placement before the endovascular treatment of the clotted fistula.

**TABLE I. Patient Characteristics at Baseline**

| | |
|---|---|
| Age (years) | 63.6 ± 14.5 |
| Sex, *N* (%) male | 32 (73%) |
| Previous fistulae, *N* (%) | 19 (44%) |
| Previous catheters, *N* (%) | 23 (52%) |
| Mean time on dialysis (years) | 3.9 ± 3.0 |
| Mean fistula age (years) | 4.6 ± 6.1 |
| Fistula location, *N* (%) | |
| Radiocephalic | 24 (55%) |
| Brachiocephalic | 20 (45%) |
| Charlson comorbidity index | 4.7 ± 2.3 |
| Comorbid conditions (%) | |
| CAOD | 19% |
| Congestive heart failure | 32% |
| PAOD | 24% |
| Previous stroke | 18% |
| Diabetes | 27% |
| Hypertension | 71% |
| Cause of ESRD (%) | |
| Unknown | 39% |
| Diabetes | 25% |
| Hypertension | 14% |
| ADPKD | 12% |
| Glomerulonephritis | 10% |

ADPKD, autosomal dominant polycystic kidney disease; ESRD, end-stage renal disease; CAOD, coronary artery occlusive disease; PAOD, peripheral artery occlusive disease.

Manual catheter-directed thromboaspiration was technically successful in 42 patients, with prompt restoration of a thrill and bruit (clinical success rate = 95%). The most frequent lesions are shown in Table II. Stent placements or blood transfusions were not required during the procedure. Angioplasty was not feasible in two patients due to the impossibility of passing the guidewire through a tight stenotic lesion. Both patients underwent tunneled catheter placement. One patient with a brachiocephalic AVF developed steal syndrome and myocardial infarction ~2 weeks postprocedure and required hospitalization and further access surgery. Eleven patients experienced AVF

**TABLE II. Location of Stenosis and Thrombectomy Outcomes**

| | Radiocephalic fistulae | Brachiocephalic fistulae | *P*-value |
|---|---|---|---|
| *N* pts | 24 | 20 | n.a. |
| Location of stenosis | | | |
| Venous outlet | 10 (40%) | 11 (55%) | 0.363 |
| Arterial anastomosis | 16 (65%) | 9 (45%) | 0.142 |
| Central vein | 0 (0%) | 2 (20%) | 0.147 |
| Number of stenotic lesions | | | |
| 1 | 16 (65%) | 10 (50%) | 0.261 |
| ≥2 | 8 (35%) | 12 (60%) | 0.068 |
| "Short-segment thrombus" | 14 (58%) | 5 (25%) | 0.028 |
| Clinical success | 23 (96%) | 19 (95%) | 1 |
| Primary patency rate at year 1[a] | 17 (70%) | 8 (43%) | 0.047 |

[a]Initial failures are included.

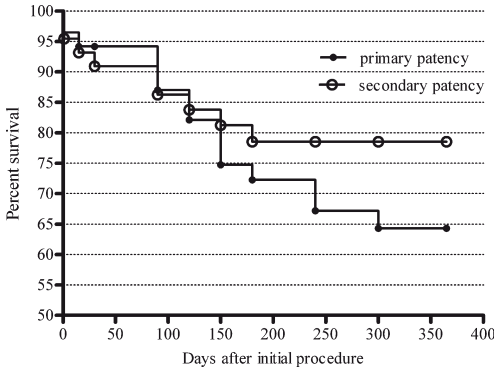


**Fig. 1. Primary and secondary patency rates at 1 year, according to the Kaplan–Meier analysis.**

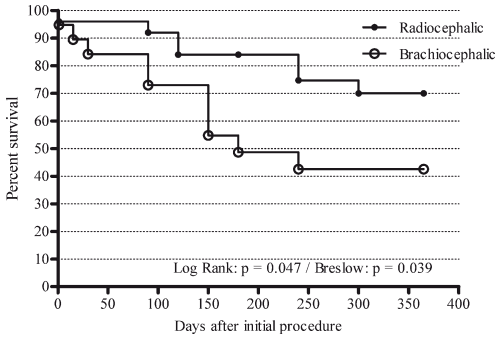


**Fig. 2. Primary patency rates after declotting for radiocephalic and brachiocephalic fistulae, showing better results in radiocephalic fistulae.**

**TABLE III. Mean Expense (in US$) for Each Component of the Procedure**

| | |
|---|---|
| Professional fees | |
| Percutaneous transluminal angioplasty | $220 (range, $110–$450) |
| Manual catheter-directed thromboaspiration | $489 (range, $220–$550) |
| Placement of tunneled cuffed catheter | $194 (range, $150–$400) |
| Technical costs | |
| Percutaneous transluminal angioplasty | $565 (range, $453–$901) |
| Manual catheter-directed thromboaspiration | $892 (range, $596–$1,187) |
| Placement of tunneled cuffed catheter | $307 (range, $261–$554) |

rethrombosis during follow-up (8/3, brachiocephalic/radiocephalic AVF): six patients (4/2, brachiocephalic/radiocephalic AVF) underwent further aspiration thrombectomy; the remaining five patients (4/1, brachiocephalic/radiocephalic AVF) underwent tunneled catheter placement and/or new AVF creation. Three patients developed venous hypertension due to recurrent stenosis, successfully treated with balloon angioplasty. Three patients died during follow-up due to acute pancreatitis, mesenteric infarction, and respiratory infection, respectively. Two patients received a kidney transplant, and one patient switched to peritoneal dialysis. Including the initial failures, the primary and secondary patency rates of all AVF were 63 and 78% at 1 year, respectively (Fig. 1). Primary patency rate at the end of follow-up was significantly better for radiocephalic AVFs (70% vs. 43%; $P = 0.047$; Fig. 2).

The mean expense for each component of the two procedures is presented in Table III. The mean technical cost for the manual catheter-directed thromboaspiration procedure was $892 (range, $596–$1,187). The mean nephrology professional fee was $489 (range, $200–$550). Therefore, mean total expense of the percutaneous thrombectomy procedure was $1381 (range, $1,036–$1,627; Table IV). The mean cumulative cost of vascular access care at year 1 was $2,504 (median $1,484; range, $1,362–$18,279; Table V) per patient-year at risk. The mean cost per patient-year at risk was greatest for patients with brachiocephalic AVFs $3,578 (median $2,092; range, $1,470–$18,279) versus mean $1,604 (median $1,381; range, $1,130–$3,116; $P = 0.022$; Table V).

## DISCUSSION

The present study provides a different perspective on vascular access maintenance and presents the cumulative costs and resources required to treat hemodialysis patients with thrombosed AVF by endovascular means. This study is, to our knowledge, the first study estimating the cumulative cost of percutaneous thrombectomy of autogenous AVF during 1 year of follow-up.

Catheterization and Cardiovascular Interventions DOI 10.1002/ccd.
Published on behalf of The Society for Cardiovascular Angiography and Interventions (SCAI).

**TABLE IV. Costs of Invasive Examinations, Central Venous Catheter Implantation, and Hospitalizations**

| | Average cost per intervention (US$) |
|---|---|
| Percutaneous transluminal angioplasty | $785 (range, $673–$1,121) |
| Manual catheter-directed thromboaspiration | $1381 (range, $1,036–$1,627) |
| Placement of tunneled cuffed catheter | $501 (range, $454–$748) |
| Daily cost of hospitalization in the general ward of the Department of Internal Medicine | $415 |

**TABLE V. Cumulative Cost Analysis in US$/Patient-Year at Risk[a]**

| | Overall ($n = 44$) | Radiocephalic fistulae ($n = 24$) | Brachiocephalic fistulae ($n = 20$) | $P$-value |
|---|---|---|---|---|
| Index procedure (mean ± SD) | $1,381 ± 54 | $1,332 ± 83 | $1,431 ± 94 | N.S. |
| Outpatient access-related surgery (mean ± SD) | $45 ± 150 | $66 ± 185 | $20 ± 86 | N.S. |
| Access-related hospital admissions (mean ± SD) | $702 ± 3,231 | – | $1,545 ± 4,655 | 0.060 |
| Management of access dysfunction[b] (mean ± SD) | $310 ± 535 | $153 ± 381 | $498 ± 624 | 0.017 |
| Patient's transport (mean ± SD) | $66 ± 51 | $53 ± 23 | $84 ± 67 | 0.021 |
| Total cost (mean ± SD) | $2,504 ± 3,219 | $1,604 ± 511 | $3,578 ± 4,518 | 0.022 |

[a]Initial failures are included.
[b]Includes all radiology procedures performed as part of access-related care, dialysis catheter placements, and local catheter thrombolytic therapy.

Among the previous series [3–11], clinical success and primary and secondary patency rates of percutaneous thrombectomy of clotted AVF at 1 year have ranged from 73 to 96%, 18 to 70%, and 27 to 81%, respectively. The outcomes of the current series were at the higher end of these ranges (clinical success, 95%; primary patency rate, 63%; secondary patency rate, 78%; Fig. 1), and the clinical success of percutaneous thromboaspiration was similar in both radiocephalic and brachiocephalic AVFs (Table IV). However, the Kaplan–Meier log-rank analysis showed that manual catheter-directed thromboaspiration of radiocephalic AVFs had better long-term outcome (Fig. 2), as previously reported by Turmel-Rodrigues et al. [4]. This might be explained by the higher percentage of cases with "short-segment thrombus" observed in the radiocephalic fistula group (Table IV). This issue was also addressed by Wu et al. [21] who separated "long segment thrombus" from "short segment thrombus" and showed significant differences in survival, with poorer patency associated with the larger clot burden.

Cost analysis revealed that manual catheter-directed thromboaspiration of totally occluded AVFs is more expensive than percutaneous transluminal angioplasty (Tables III and IV). Although similar results have previously been reported by Bittl et al. [14], procedure costs were approximately two times higher in this study (angioplasty, $1,939 vs. $785; percutaneous thrombectomy, $3,336 vs. $1,381). Professional fees and technical costs might have been responsible for the differences observed between these two cost analyses. First, physician billing has been reported to differ among countries [22], and, second, the amount of resources required for endovascular interventions is likely to vary among vascular access centers with different endovascular salvage procedures. In the present study, a 9-F catheter (Cordis, Miami, FL) and a 50-mL syringe were the mainstay devices for endovascular salvage therapy. Bittl et al. [14] used a rheolytic thrombectomy device (AngioJet, Possis Medical, MN) for thrombosed AVFs. In addition, stents were not used in our patients, whereas Bittl et al. [14] placed stents for several indications.

Although fistula salvage by endovascular means remains a successful approach for the maintenance of a functional vascular access, it is responsible for a significant financial burden on the ongoing care of ESRD patients. The U.S. Renal Data System estimated the cost of vascular access care for prevalent hemodialysis patients as being 8.4% of total Medicare ESRD spending [23]. In our country, the public health care system reimbursement for the ongoing care in outpatient dialysis (equipment costs, staff, consumable items, reverse-osmosis water, regular laboratory and radiology tests, and medications) is $37,335 per patient-year. In the present study, economic analysis revealed that endovascular treatment of thrombosed AVF carries an additional cost of 6.5% on the outpatient dialysis expenses ($2,504 per patient-year at risk, Table V). In addition, we observed that treatment and maintenance of thrombosed radiocephalic AVFs was half as expensive as in brachiocephalic AVFs, representing an additional cost of ~4.3 and 9.6% on the outpatient dialysis expenses, respectively ($1,604 vs. $3,578 per patient-year at risk, respectively; Table V). Access-related hospitalizations, ambulatory management of access dysfunction (including

all radiology procedures performed as part of access-related care, catheter placements/local thrombolytic therapy), and patient's transport were responsible for the higher financial burden observed in the brachiocephalic fistula group (Table V). In fact, few resources were required to maintain the functional patency of a radiocephalic AVF at 1 year, because ~85% of the total expenses were related with the index procedure (Table V). In contrast, ~60% of the expenditure was spent in secondary interventions in patients with brachiocephalic AVFs.

We recognize that this is a retrospective study and thus has all the limitations of such an approach. We are also aware that our study does not provide a definitive answer regarding the efficiency of endovascular treatment of AVF thrombosis and that further prospective cost-effectiveness analyses comparing different thrombectomy procedures (endovascular vs. surgery) and distinct approaches for the maintenance of a functional AVF (pre-emptive angioplasty vs. percutaneous thrombectomy) need to be carried out.

In conclusion, our results indicate that the cumulative cost of maintenance of a thrombosed AVF by endovascular means is high, with patients with clotted radiocephalic AVFs incurring the lowest costs and achieving higher survival times.

## ACKNOWLEDGEMENTS

The authors thank Ms. Doreen Raine for editing the English and the clinical directors from hemodialysis clinics who kindly agreed to collaborate in this study: A. Baldaia Moreira M.D., A. Caldeira Gomes M.D., A. Castro Henriques M.D., Antunes de Azevedo M.D., Eva Xavier M.D., João C. Fernandes M.D., João M. Frazão M.D., PhD, Jorge Baldaia M.D., José Madureira M.D., José Pinheiro M.D., Odete Pereira M.D., Sofia Pedroso M.D., Susana Sampaio M.D., and Vasco Miranda M.D.

## REFERENCES

1. Tordoir J, Canaud B, Haage P, et al. EBPG on vascular access. Nephrol Dial Transpl 2007;22(Suppl 2):ii88–ii117.
2. KDOQI: Clinical practice guidelines and clinical practice recommendations for vascular access. Am J Kidney Dis 2006;48: S176–S247.
3. Turmel-Rodrigues L, Sapoval M, Pengloan J, et al. Manual thromboaspiration and dilation of thrombosed dialysis access: Mid-term results of a simple concept. J Vasc Interv Radiol 1997; 8:813–824.
4. Turmel-Rodrigues L, Pengloan J, Rodrigue H, et al. Treatment of failed native arteriovenous fistulae for hemodialysis by interventional radiology. Kidney Int 2000;57:1124–1140.
5. Moossavi S, Regan JD, Pierson ED, et al. Nonsurgical salvage of thrombosed arterio-venous fistulae: A case series and review of the literature. Semin Dial 2000;20:459–464.
6. Haage P, Vorwerk D, Wilberger JE, et al. Percutaneous treatment of thrombosed primary arteriovenous hemodialysis access fistulae. Kidney Int 2000;57:1169–1175.
7. Liang HL, Pan HB, Chung HM, et al. Restoration of thrombosed Brescia-Cimino dialysis fistulas by using percutaneous transluminal angioplasty. Radiology 2002;223:339–344.
8. Rajan DK, Clark T, Me S, et al. Procedural success and patency after percutaneous treatment of thrombosed autogenous arteriovenous dialysis fistulas. J Vasc Interv Radiol 2002;13: 1211–1218.
9. Shatsky JB, Berns JS, Clark TW, et al. Single-center experience with the Arrow-Trerotola percutaneous thrombectomy device in the management of thrombosed native dialysis fistulas. J Vasc Interv Radiol 2005;16:1605–1611.
10. Beathard GA, Litchfield T. Physician Operators Forum of RMS Lifeline Inc: Effectiveness and safety of dialysis vascular access procedures performed by interventional nephrologists. Kidney Int 2004;66:1622–1632.
11. Jain G, Maya ID, Allon M. Outcomes of percutaneous mechanical thrombectomy of arteriovenous fistulas in hemodialysis patients. Semin Dial 2008;21:581–583.
12. Bittl JA. Percutaneous therapy of dialysis access failure. Catheter Cardiovasc Interv 2002;56:157–161.
13. Tessitore N, Bedogna V, Poli A, et al. Adding access blood flow surveillance to clinical monitoring reduces thrombosis rates and costs, and improves fistula patency in the short term: A controlled cohort study. Nephrol Dial Transpl 2008;23:3578–3584.
14. Bittl JA, Cohen DJ, Seek MM, et al. Economic analysis of angiography and preemptive angioplasty to prevent hemodialysis-access thrombosis. Catheter Cardiovasc Interv 2010;75: 14–21.
15. Vesely TM, Idso MC, Audrain J, et al. Thrombolysis versus surgical thrombectomy for the treatment of dialysis graft thrombosis: Pilot study comparing costs. J Vasc Interv Radiol 1996;7:507–512.
16. Sands JJ, Patel S, Plaviak DJ, et al. Pharmacomechanical thrombolysis with urokinase for treatment of thrombosed hemodialysis access grafts. ASAIO J 1994;40:M886–M888.
17. Schuman E, Quinn S, Standage B, et al. Thrombolysis versus thrombectomy for occluded hemodialysis grafts. Am J Surg 1994;167:473–476.
18. Summers S, Drazan K, Gomes A, et al. Urokinase therapy for thrombosed hemodialysis access grafts. Surg Gynecol Obstet 1993;176:534–538.
19. Gray R, Sacks D, Martin L, et al. Reporting standards for percutaneous interventions in dialysis access. J Vasc Interv Radiol 2003;10:1405–1415.
20. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Am Soc Nephrol 1996;7:198–207.
21. Wu CC, Wen SC, Chen MK, et al. Radial artery approach for endovascular salvage of occluded autogenous radial-cephalic fistulae. Nephrol Dial Transpl 2009;24:2497–2502.
22. World Bank: World Development Indicators 2000. Washington DC: World Bank; 2001.
23. USRDS: The economic cost of ESRD, vascular access procedures, and medicare spending for alternative modalities of treatment. Am J Kidney Dis 1997;30:S160–S17.

# PART III
## DISCUSSION

# Chapter 7
## *General discussion*

# General discussion

## Establishment and maintenance of dialysis access

In the initial two studies, we explored to what extent the vascular access for HD compares (un)favorably to the PD catheter. In the search for an answer to this question, we conducted a retrospective observational cohort study with adult ESRD patients who consecutively initiated HD or PD in our institution. In the first study, we hypothesized that vascular access type at the time of dialysis initiation accounts for the higher early mortality rate observed in patients that start HD with a catheter, compared to those that initiate HD with a functioning AVF, or to those that initiate PD. In the second study, we compared the resources required to establish and maintain the dialysis access in patients who initiated HD with those initiating PD. To test our hypothesis, we compared all-cause and dialysis access-related morbidity and mortality between PD and HD patients, with the latter stratified by HD vascular access type at the time of dialysis initiation. Survival rates, dialysis access-related interventions and costs were determined during the first year after initiation of dialysis.

In the first study, initial dialysis modality was defined as the modality at the first outpatient dialysis treatment. We observed that incident HD-catheter patients experienced a significantly higher mortality rate at one year of dialysis, in comparison with HD-AVF and PD patients. Dialysis access-related complications were responsible for 43% of all deaths and death caused by dialysis access complications occurred only in the HD-catheter group. Importantly, HD-catheter patients had approximately twice as many clinical events related to dialysis access than either HD-AVF or PD patients. In contrast, most of the vascular and peritoneal dialysis access complications in the HD-AVF and PD groups were not serious clinical events, and no dialysis access-related deaths occurred in these two groups. One interesting finding of this study was that bacteraemia only occurred in HD-catheter patients, refuting the common misconception that PD is associated with an overall higher rate of severe infection than HD. In addition, PD patients had the lowest number of mechanical access-related complications. In this study, ~80% of both HD-AVF and PD patients were referred to the nephologist early and could thus benefit from timely information regarding all treatment modalities and appropriate dialysis access placement in due time. Despite different baseline characteristics, both the HD-AVF and PD groups had similar high

survival rates at year 1. By contrast, the HD-catheter patients with similar baseline characteristics compared to HD-AVF patients were referred to the nephrologist later, which might explain the delay in AVF creation in this group. At the end of follow-up, 97% and 47% of HD-AVF and HD-catheter patients had a functional AVF as permanent vascular access, respectively. Multivariate analysis showed that HD-catheter use at the time of dialysis initiation was the important factor associated with poor prognosis. In this study, the critical initial 90-day period on dialysis was included in the follow-up. This is a time period when a high proportion of HD patients are using catheters as bridging access devices and the risk for infection is particularly pronounced (88). Exclusion of this period in the analysis would probably underestimate the morbidity and mortality rates of the HD-catheter group. Taken together, our results corroborate the previous findings of several studies (86-96, 149) reporting that the use of HD catheters is associated with a substantially greater risk of sepsis, hospitalization and mortality compared to the use of an AVF. Moreover, our results also suggest that the outcomes of incident PD patients are as encouraging as of those who initiate HD with an AVF. In addition, our findings suggest that HD vascular access type at the time of dialysis initiation might explain the differences in outcome observed between the incident HD and PD populations. This study supports the need for early referral of ESRD patients to nephrology centers to allow patient selection of renal replacement therapy modality and timely creation of the appropriate dialysis access.

In the second study, treatment modality was assigned at the time of the first dialysis access placement attempt, on an intention-to-treat basis. The study was performed from the Public Administration perspective, including direct medical and non-medical costs. Annual dialysis access costs were evaluated using a mixed costing method. We observed that dialysis access-related intervention rates were significantly lower for patients initiating PD, compared to those who initiated HD, in agreement with previously published literature (99). Haemodialysis patients with an AVF underwent a higher number of access surgeries and diagnostic imaging procedures whereas HD-catheter patients underwent a higher number of catheter-related interventions and hospitalizations. In addition, we further demonstrated that the risk of catheter-related interventions and hospitalizations were significantly lower in PD modality, compared to HD-catheter modality, reinforcing that patients who choose PD do not face an increased risk of catheter-related adverse events (52-54, 98, 99). Cost analysis showed that the costs related to dialysis access were significantly lower in HD-AVF and PD, compared to HD-catheter modality.

In both HD-AVF and PD modalities, approximately half of dialysis access costs were related to access surgery, catheter interventions and diagnostic imaging studies, whereas in the HD-catheter modality over an half of dialysis access costs were related to vascular access-related hospitalizations and patient transportation. In summary, in this study we were able to demonstrate that the resources required for the establishment and maintenance of the dialysis access are significantly higher for those patients who initiate HD with a central venous catheter, compared to those who initiate HD with an AVF or PD. In addition, our results suggest that PD patients incur a lower risk of dialysis access invasive interventions, compared to HD patients.

In the Portuguese National Health System, dialysis is free of charge for the patient. In 2008, concerned with budget constraints and the exponential annual rise in dialysis costs, the Portuguese health authorities changed the reimbursement system for both HD and PD treatment to a per capita system. In order to determine the economic impact of dialysis modality and access type at dialysis initiation, we evaluated the annual health care expenses of ESRD patients initiating HD with a catheter or an AVF and PD, in our institution (150). One year retrospective cost data of the ESRD patients' cohort studied in our previous works were generated and analyzed, using an intention-to-treat approach. Mean annual health care expenses for HD-AVF, HD-catheter and PD patients were €33,621, €42,855 and €32,282 per patient-year at risk, respectively. In multivariate analysis, PD and HD-AVF modalities were associated with approximately €7500 per patient-year cost savings, compared to HD-catheter modality. Our results, based on patients treated with contemporary dialysis modalities in Portugal, suggest that when a health-care reimbursement system is the same for HD and PD, as occurs in Portugal, dialysis access-related costs may account for an approximately 4, 5 and 10% increase in annual dialysis treatment expenses for PD, HD-AVF and HD-catheter patients, respectively.

Several limitations of these studies deserve to be pointed out. As observational studies, bias may occur, in particular influenced by patient treatment preferences and time of referral to the nephrologist. Peritoneal dialysis patients were younger and had lower comorbidities compared to HD patients. In addition, PD dialysis patients were treated in a single academic nephrology centre, whereas HD patients were treated in different peripheral haemodialysis units. The small sample size, the differential time at risk followed from first access attempt, the short-term follow up and the single-center nature of these studies may limit its reproducibility. Finally, annual dialysis access costs were evaluated using a mixed costing method – hospitalization expenses

were more similar to ‘‘charges’’ than to ‘‘costs’’ in that they were extracted from the Ministry of Health and Welfare Ordinance Legislation.

Life-sustaining PD and HD require durable dialysis accesses to the peritoneal and circulatory systems, respectively. While evidence from randomized controlled trials is lacking, there is a broad consensus that dialysis access type not only contributes to patient morbidity but also may contribute independently to patient mortality. The use of central venous catheters and AVGs is associated with a substantially greater risk of sepsis, hospitalization and mortality compared to the use of an AVF (86-96, 149). Despite this broad consensus, incident HD catheter use remains prohibitively high in the United States (approximately 80%) (151) and, according to the DOPPS registries, also in the United Kingdom, Belgium, Sweden and Canada at least 23% of prevalent HD patients used a catheter in 2005-2007. The high prevalent use of catheter in HD patients has even increased in many European countries and Canada. For example, the use of catheters increased 2- to 3-fold in Italy, France, Germany and Spain between the DOPPS I and DOPPS III study intervals. Furthermore, increased dependence upon catheters is not limited to elderly patients with extensive comorbidities. In non-diabetic HD patients 18-70 years old, the use of catheters increased 2-fold in the United States and >3-fold in France, Germany, Italy and Spain from DOPPS I to III (55, 151). Also a concern, AVF use decreased from 80% to 74% in Europe in this analysis (60).

Studies comparing dialysis access-related complications of incident PD patients with those initiating HD using different vascular access types are scarce in the literature (98-102). Evidence suggests that although incident HD and PD patients have similar overall rates of infection, HD patients have a higher risk of bacteraemia and the early risk for bacteraemia in HD patients is related to the use of HD catheters as the initial access (98). The United States Renal Data System Wave 2 Study identified initial dialysis access as the main antecedent of bacteraemia. The risk for bacteraemia for PD catheters was not significantly different from those for AVGs or AVFs but was substantially less than those for permanent or temporary HD catheters (152). A recently published prospective observational study reported that patients who choose PD experienced a lower risk of invasive dialysis access interventions than patients who choose HD (99). Perl *et al.* (102) identified the impact of dialysis access type on incident HD and PD patients survival. Patients starting HD using a central venous catheter had a higher risk of death in the first year compared with those who started PD, whereas there was no difference in survival between HD-

AVF/AVG and PD patients.

With this information one can ask the reason for an increased use of HD catheters, the decrease use of AVFs and the underutilization of PD observed in Europe during the last decades.

Forty years ago, patient selection for dialysis was relatively stringent, and most patients were young, non-diabetic men with minimal comorbidities. Within this selected population, the arteries and veins were generally well preserved allowing construction of AVFs in the wrist. In recent years, as a result of more liberal selection criteria, the chronic dialysis population has become substantially older, more likely to be female and diabetic, and has higher comorbidity, including extensive atherosclerotic vascular disease. Many of these patients appear to have poor vessels for construction of AVFs. Perhaps this is the answer most often heard when nephrologists are asked about the current reality of vascular access epidemiology. However, practice patterns do have a major impact on the prevalence of patients dialyzing with AVFs. First, we must not forget that increased emphasis on dialysis adequacy (Kt/V) has led to the "misfortune" recognition that higher blood flows could improve urea clearance, and thereby permitted delivery of "adequate" dialysis to larger patients without entailing substantial increases in dialysis times. Even more disturbing was the fact that many other patients were submitted to "short-dialysis" as they presented with arteriovenous accesses with high blood flows. These considerations have led to increased utilization of AVGs and decreased use of AVFs, mainly in the United States. Second, and most important, long-term use of an AVF requires overcoming at least four hurdles: (a) first, the surgeon must be able and willing to place an AVF; (b) second, the newly constructed AVF must mature sufficiently to be cannulated with large-bore needles and deliver an acceptable dialysis blood flow; (c) third, the dialysis staff must be proficient in cannulation of AVFs and; (d) fourth, the mature AVF must remain patent. Problems occurring at each of these levels can have a cumulative negative effect on the overall prevalence of patients dialyzing with AVFs. In order to overcome these obstacles, Beathard (153) has suggested the following vascular access policy: (a) maximize the use of the AVF by early referral, early placement, and salvage of poorly developed AVFs; (b) quality assurance program to detect the access at risk by prospective monitoring and surveillance for venous stenosis; (c) implementation of procedures to increase access longevity, such as the prospective treatment of venous stenosis; and (d) system to manage arteriovenous access thrombosis effectively and efficiently. Achieving optimal vascular access outcomes requires agreement on a common set of goals by all individuals involved in the management

of vascular access, including nephrologists, access surgeons, radiologists, dialysis nurses, and the patient. Nephrologists need to deal with the vascular access management problem with the same priority and interest as the other major problems affecting a dialysis population. We need to become experts in vascular access and we need to occupy a pivotal position in directing the decisions that are made and affect dialysis patients welfare.

Another well recognized major contributing factor for the "unexpectedly" increased use of HD catheters and the disuse of AVFs and PD in Europe is the rather frequent late-referred chronic kidney disease patients (154-163). In the DOPPS II, HD catheter use was higher for those patients seen by a nephrologist <1 month before dialysis start, compared to those having seen a nephrologist >4 months prior to dialysis onset (55). It has already been shown that pre-dialysis care increases the likelihood of a permanent arteriovenous access at dialysis start (57, 58). Also, several studies suggested that pre-dialysis care is associated with a greater probability of selection of PD (69, 72-74, 154). A recently published systematic review reported that patients referred earlier to a nephrologist demonstrated significantly reduced short- and long-term mortality and hospitalization, perhaps as a result of better preparation and placement of dialysis access (154). Recently, Quinn *et al.* (164) examined the relative risk of mortality on PD compared with HD in individuals with at least 4 months of pre-dialysis care, all of whom started dialysis electively, as outpatients. The objective was to isolate the association between dialysis modality and patient mortality. The authors were able to conclude that PD and HD associate with similar survival among incident dialysis patients who initiate dialysis electively, and, therefore, selection bias rather than an effect of the treatment itself, likely explains the described change in the relative risk of death over time between HD and PD. Raithatha *et al.* (165) explored the relationship between late presentation, mortality, and the use of catheter access for HD in an attempt to assess the extent to which the increased mortality observed for late-referred patients was operating through the increased use of HD catheter. The authors observed that the use of HD catheter was one of the key features of late-referral that determines poor prognosis. Recently, Mendelssohn *et al.* (155, 156) defined an interesting concept of "suboptimal" dialysis start referring to initiation of dialysis as an inpatient and/or without a permanent access placed (AVF, AVG or PD catheter) and/or with a patient not starting on their chronic modality of choice. In this elegant paper (156), the authors investigated whether a suboptimal initiation of dialysis would be associated with worse health outcomes in the first six months of dialysis. The authors

concluded that suboptimal initiation of dialysis is common in patients referred early or late to the nephrologist and, that the benefits of early referral are lost if dialysis is initiated suboptimally. In other words, of nothing worth being referred early to a nephrologist and subsequently start dialysis as an inpatient or with an HD catheter. An integrated dialysis access management strategy is therefore required for optimizing dialysis access use (166). To adequately inform patients about access options, nephrologists are ethically obligated to systematically explain to patients the harms of HD catheters. If catheters must be used to initiate dialysis, nephrologists should present catheters only as "temporary" measures and "unsafe for long-term use" (167). Interestingly, the K/DOQI guidelines (16) recommend that a "PD catheter may also be used as a bridge for a fistula in "appropriate" patients". The type of dialysis access should therefore be regarded as a key factor to be taken into account in the choice of dialysis modality. Optimal pre-dialysis care is most likely an effective strategy in the long-term management of the patient with chronic kidney disease (168).

Beyond medical and psychosocial factors responsible for the slow-down in the proportion of PD patients in some Western countries, the misconception of PD catheter as an "inadequate" dialysis access for chronic dialysis patients may also play a role. A common perception is that PD is associated with a higher risk for dialysis access-related invasive interventions and infection compared with HD (169, 170). However, as previously discussed, evidence suggests the contrary (98-100, 152). Insufficient level of continuous medical education and fellow training investment is a possible explanation for such fact. In Portugal, the widespread HD catheter placement by nephrologists and renal fellows and the limited timely insertion of a PD catheter may be a strong contributing factor for the underutilization of PD. In this regard, several studies have suggested that PD catheter insertion by nephrologists can have a positive impact on the utilization of PD (171, 172). Moreover, in the unplanned setting, the reports from Povlsen *et al.* (52, 53) and Lobbedez *et al.* (54) showed that the immediate use of a PD catheter right after insertion did not increase the risk of infectious complications nor did affect long-term PD technique or patient survival. These data suggest that PD is a safe and feasible modality for unplanned start on dialysis. Recently, Koch *et al.* (173) compared the outcomes of acute unplanned PD and HD on a prospective observational study. The authors observed that HD patients had a significant higher risk of bacteraemia compared to PD patients and a tendency for higher overall and infectious mortality risk.

Finally, as previously stated, the economic structure of the nation's health-care system may influence dialysis modality selection, and, therefore, dialysis access placement (103, 105, 106, 135-140). What are the financial consequences of inadequate dialysis modality selection and access placement? A key factor influencing the cost of dialysis care is the timing of referral to a nephrologist. When patients are either referred late to a nephrologist's care or have to initiate dialysis urgently without a planned access, they are generally sicker, require longer hospitalization and are nearly always started on HD (116). Early referral and planned start result in cost savings and improved survival (41-45, 174, 175). Patients who are referred earlier to a nephrologist have an extended time prior to starting renal replacement therapy during which access may be planned and placed, and patients may be objectively educated about their treatment choices. Patients who have been exposed to pre-dialysis modality education are more likely to choose PD or to start HD with a functioning AVF (69, 72-76) and therefore contribute to consuming fewer resources to the payer and society (114). This approach has usually been found to result in fewer inpatient hospital days. In fact, hospitalization and dialysis access-related costs contribute substantially to total expenditures for dialysis patients and are considered the major and the most variable costs in caring for dialysis patients. A comprehensive literature review indicates that hospitalization costs, as well as the reasons for hospital admission, are similar for HD and PD patients (176-181). The primary causes of hospital admission in patients receiving HD and PD are infections, cardiovascular disease and dialysis access complications. Up to 30% of hospital admissions in HD patients are related to vascular access complications, and significant outpatient resources, including vascular access monitoring and diagnostic radiology, are used to maintain access patency (22, 182, 183). At present, few studies have reported in detail the cost of dialysis access on the basis of access type (175, 182-184). Lee *et al.* (182) reported in detail the cost of maintaining a functioning dialysis access among prevalent dialysis patients. The cost of access care was highly variable depending on the access type. The annual mean costs per-patient were CAN$2,191, CAN$3,345, CAN$404 and CAN$388 for HD tunneled cuffed catheter, AVG, AVF and PD catheter, respectively. More recently, Manns *et al.* (183) performed a prospective cost analysis among incident HD patients to determine the cost of vascular access care during the first year of dialysis. The mean cost of all vascular access care in year 1 was CAN$6,890. The mean cost of access care per patient-year at risk for maintaining a catheter exclusively, attempting an AVF, or attempting an AVG was $9,180, $7,989 and $11,685 respectively. A similar study was performed by Gruss *et al.* (184). The authors concluded that HD catheter use at any

time was associated with an increased risk of death as well as with a higher net cost. The USRDS estimated the cost of vascular access care for prevalent HD patients as being $6,228 per year at risk (8.4% of total Medicare dialysis spending per patient year), although the type of access used by patients was not known in this study (185). In the study of Lee *et al.* (182), dialysis access-related costs represented approximately 1 to 2% of the total cost of health care for PD catheters and AVFs and 5 to 8% for HD catheters and AVGs. Manns *et al.* (183) reported that vascular access costs represented approximately 10% of the total cost of health care for a similar HD patient population.

In summary, recent evidence suggest that: a) dialysis access strongly contributes to patient morbidity/mortality and annual health care cost and; b) incident PD patients and HD patients with a functioning AV incur the lowest annual morbidity/mortality rates and healthcare costs. Therefore, if our aim is to improve ESRD patients' care while optimizing economic resources, efforts should be made to develop pre-dialysis care in order to provide patients with dialysis modality selection and appropriate dialysis access placement.

## Detection of vascular access dysfunction

Arteriovenous fistulae created with native vessels are currently regarded as the gold standard for HD access because of their lower infection and thrombosis rates compared with other types of HD accesses (16, 17). Autogenous fistulae fail after a median functioning time of 3 to 7 years, whereas AVGs have a shorter lifespan and tend to fail after a median lifetime of only 12 to 18 months. Fewer than half of the HD catheters inserted as "long-term access" are in use a year after their placement (186). Nevertheless, we all recognize that AVFs do have problems. Autogenous fistulae are more likely than AVGs to experience primary failure. Primary failure of an AVF, defined as an access that never provided reliable HD after surgical creation, occurs in up to 50% of cases (26, 187-189). In addition, mature AVFs also suffer from venous and/or arterial stenosis and thrombosis. Professional societies from several countries (16, 17, 190) recommend an organized program to identify failing AVFs and AVGs. Monitoring is carried out with regular physical examination. It also includes review of routine laboratory studies regularly obtained in the dialysis unit, dialysis adequacy and difficulties in cannulation or achieving haemostasis after needle withdrawal, documented recirculation, and other clinical clues. Surveillance refers to the performance of noninvasive testing to gather further information about access structure and

function. Diagnostic testing refers to the performance of procedures, usually invasive, to define access anatomy and haemodynamics. The current gold standard is angiography, but duplex ultrasound can be used for this function as well. Finally, intervention is the performance of a procedure that dilates a stenosis, stents it, bypasses it or resects it. The most common procedure performed for stenosis is percutaneous transluminal angioplasty. If the access is thrombosed, a variety of techniques are available to remove the clot.

Although monitoring dialysis AVFs is widely recognized as standard of care for chronic HD patients, its use is frequently accompanied by misdiagnosis of AVF dysfunction in daily clinical practice. Therefore, within our study titled "Physical examination of dysfunctional arteriovenous fistulae by non-interventionalists: a skill worth teaching" we aimed to determine the accuracy of physical examination in the assessment of AVF dysfunction in the hands of general nephrologists and a trained nephrology resident. We hypothesized that the accuracy of physical examination in the assessment of AVF dysfunction would depend on the specific training of the examiner rather than on the cumulative experience in dialysis clinical practice. We analyzed a database of a prospective observational study conducted in a population of HD patients consecutively referred to our centre by nephrologists for angioplasty. Before the angiography procedure was carried out, a nephrology resident trained in vascular access physical examination and angiography performed a physical examination in all the cases, unaware of the nephrologists' examination findings. Angiography was performed in our hospital centre by an interventionist, blind to both the nephrologists' and the resident's reports. By comparing physical examination to the gold standard, the current study objectively assessed the accuracy of physical examination when performed by nephrologists and a trained resident in the diagnosis of various types of disorders responsible for AVF dysfunction. Our results showed that physical examination by nephrologists had a poor-to-moderate accuracy for the assessment of AVF dysfunction. With respect to the accuracy of physical examination in the hands of a trained resident, we observed a high level of agreement between physical examination and angiography for the diagnosis of the cause of AVF dysfunction. The results of the study presented here suggest that a trained physician is able to detect the cause of the AVF dysfunction by physical examination, corroborating the previous findings of Asif *et al.* (191) and Leon *et al.* (192). In addition, by comparing the outcomes of physical examination performed by general nephrologists with those of a trained physician, our study further suggests that theoretical and hands-on training in physical examination of

AVFs should be provided for nephrologists in-training and for the dialysis staff. It is important to emphasize that our study did not evaluate the screening accuracy of physical examination in the detection of dysfunctional AVFs. The performance of physical examination in diagnosing AVF stenosis was previously evaluated by Campos *et al.* (193) and Tessitore *et al.* (194). In these two studies, the authors included unselected populations of consecutive prevalent patients with AVFs attending a HD unit. Physical examination was performed by nephrologists with expertise in physical examination. The gold standard examinations were duplex ultrasound (193) and angiography (194), respectively. Both studies concluded that physical examination was an accurate method for the diagnosis of stenosis and should be part of all surveillance protocols of stenosis detection in AVF.

According to the K/DOQI (16) the rational for arteriovenous access monitoring/surveillance is expressed in the following statement "The basic tenet for vascular access monitoring and surveillance is that stenosis develop over variable intervals in the great majority of vascular accesses and, if detected and corrected, underdialysis can be minimized or avoided and the rate of thrombosis can be reduced". Published data from AVGs showed an inferior patency of AVGs undergoing thrombectomy as compared with those undergoing elective angioplasty, arguing for a proactive strategy to prevent AVG thrombosis (195-202). Given that underlying stenosis is a major risk factor for AVG thrombosis, timely detection and correction of stenosis would be more beneficial than waiting for an AVG to clot before intervening. Two seminal studies published in the early 90's (203, 204) reported that dynamic and static dialysis venous pressure measurements combined with preemptive angioplasty yielded large reductions in thrombosis rates and replacement of vascular accesses. These considerations have led to the plausible hypothesis that preemptive angioplasty of haemodynamically significant stenosis would reduce the likelihood of AVG thrombosis, and thereby prolong AVG longevity. However, so that K/DOQI's statement be consequent, the program of noninvasive stenosis monitoring/surveillance should fulfill at least four criteria: (a) the epidemiology and natural history of access thrombosis, including development from latent to declared disease should be adequately understood; (b) the monitoring/surveillance test should be highly accurate for the detection of haemodynamically significant stenosis; (c) it should be able to distinguish between stenosed accesses at risk for thrombosis and those that will remain patent without intervention; and (d) preemptive angioplasty should reduce the likelihood of access thrombosis. Unfortunately, at

present, only few of these criteria were accomplished by the international scientific community.

The natural history of the arteriovenous access, as well as, the pathophysiology of venous neointimal hyperplasia and dialysis access stenosis are unclear and under active research (205, 206). A report from Lumsden *et al.* (207) showed that a haemodynamically significant stenosis is nearly always a prerequisite for AVG thrombosis, but its presence does not always predict the thrombotic event. In other words, not every stenosed AVGs will clot. Probably, a similar situation occurs in AVFs. These facts highlight our lack of understanding of the pathophysiology and our inability to appropriately intervene, in order to prevent access thrombosis.

The K/DOQI and EBPG on vascular access recommend that AVGs and AVFs undergo routine surveillance for stenosis with preemptive correction of the lesion (16, 17). However, it is essential to point out that a dysfunctional vascular access is not defined only by the presence of a significant stenosis (reduction greater than 50% of normal vessel diameter) and that it should not be repaired merely because this is present. Stenosis must be accompanied by a haemodynamic or clinical abnormality. International guidelines (16, 17, 190) do not recommend the use of angiography for detecting anatomic stenosis alone, without concomitant measurement of access flow, venous pressure, recirculation, or other physiological parameters. All arteriovenous access surveillance methods are based on the premise that progressive access stenosis will result in a predictable increase in the intra-access pressure and/or a decrease in access blood flow. The three major forms of arteriovenous access surveillance are static dialysis venous pressures, flow monitoring, and duplex ultrasound. Several reports and in-depth reviews have shown that monitoring and/or surveillance of the arteriovenous access (using either of these methods) have a high positive predictive value to detect the presence of AVG stenosis (16, 208-213). Still, how well monitoring or surveillance predict AVF stenosis? Static dialysis venous pressure measurements are much less useful in predicting stenosis in AVFs than in AVGs (16). In contrast, several studies have evaluated the performance of flow monitoring in predicting AVF stenosis, with favorable results (194, 214-218). Practice guidelines recommend performing angiography when access blood flow is <400-500 ml per minute in AVFs (16). Flows of 600-1,000 ml per minute in AVFs may be associated with the presence of stenosis but at these flow levels, intervention might not be necessary as the access can still deliver adequate flow and has a low risk for thrombosis (214, 216, 217).

Although noninvasive surveillance tests are useful in detecting AVF and AVG stenosis, the pertinent question is how well they predict access thrombosis, if preemptive angioplasty is not

performed. The ideal surveillance test would distinguish between accesses with stenosis that predict access thrombosis, and those that do not predict and would remain patent. Such a test would result in preemptive angioplasty in most accesses likely to thrombose, while avoiding unnecessary interventions in accesses that would remain patent. Unfortunately, none of the currently available surveillance methods are reliable in the presence of AVGs (219-223). Although a low access blood flow is associated with an increased risk of thrombosis, this association does not ensure that the test has adequate accuracy in predicting thrombosis. Among AVGs with a baseline access flow of 500 to 700 mL per minute, only 25% to 43% will progress to thrombosis during the subsequent three months of follow-up. Thus, a low access flow was much less predictive of future AVG thrombosis than of AVG stenosis. This means that any surveillance program for AVG stenosis will inevitably result in a substantial number of unnecessary angioplasties on AVGs that would not progress to thrombosis. Similarly, the sensitivity and specificity of flow monitoring for AVG thrombosis was no better when the change in access flow was used, as compared with the absolute access flow. Regarding AVFs, relatively little has been published on this issue (216, 224, 225). Tonneli *et al.* (224) found that flows <500 ml per minute seemed to be the most appropriate threshold for performing angiography. Somewhat different thresholds were found by two Italian groups. Tessitore *et al.* (216) observed that flows <700-1,000 ml per minute and/or a reduction in flow >25% were optimal predictors for stenosis and flows <300 ml per minute predict incipient thrombosis for wrist AVF. Basile *et al.* (225) found that an access flow <700 ml per minute was the best predictor for failure over a period of years, with a sensitivity of 89%, but a specificity of only 69%.

The more clinically relevant question is whether stenosis surveillance and preemptive angioplasty decreases arteriovenous thrombosis or prolongs access longevity. No less important, is the fact that dialysis units that implement a surveillance program usually hire trained technicians to perform the measurements. As a consequence, surveillance adds to the cost of operating a dialysis unit, and it is therefore incumbent to demonstrate that the added cost translates into improved access patency. Numerous publications have reported on the frequency of AVG thrombosis before and after implementing a comprehensive program of clinical monitoring or surveillance for AVG stenosis at a dialysis centre (203, 204, 226, 227). Each of these studies observed a dramatic decrease (~50%) in the frequency of AVG thrombosis during the interventional period as compared with the historical baseline. However, randomized clinical trials (207, 228-231) showed that the frequency of AVG thrombosis was comparable in the

surveillance and control groups. A recent meta-analysis of the randomized studies (232) observed no significant decrease in AVG thrombosis between the surveillance group and the control arm. Similarly, the risk of permanent AVG failure was similar between the two groups. In contrast, to a fair amount of literature available on surveillance for AVG thrombosis and/or failure, relatively little has been published on AVFs. The results of observational studies documenting the frequency of AVF thrombosis during monitoring/surveillance quality improvement programs are mixed. While McCarley *et al.* (233) and Tessitore *et al.* (234) documented a significant decrease in AVF failure and a subsequent increase in access patency (at the expense of an increased number of angioplasty procedures), Wijnen *et al.* (235) and Shahin *et al.* (236) reported that such a programme resulted in a significant increase in the frequency of angioplasty without reducing the thrombosis rate or prolonging AVF survival. Among the few prospective controlled trials performed, Tessitore *et al.* (236) conducted probably the first trial to evaluate the effect of preemptive angioplasty of stenosis with no known access dysfunction on survival of forearm radiocephalic AVFs. The study showed a fourfold increase in median survival and an approximately threefold decrease in risk of failure. Preemptive angioplasty was also associated with a significant decrease risk of hospitalization, central venous catheterization, and thrombectomy. Subsequently, the same group conducted a randomized controlled trial to evaluate the effect of blood flow surveillance and preemptive repair of stenosis on AVF longevity (237). This study also documented a significantly lower rate of AVF thrombosis in the group undergoing flow monitoring and a trend towards the improved AVF survival rate. In contrast, Polkinghorne *et al.* (217) demonstrated that the addition of flow monitoring produced a modest effect on the detection of a significant AVF stenosis, while not decreasing the overall rate of AVF thrombosis.

Finally, when and how often these tests should be done? The K/DOQI (16) recommends that surveillance measurements be taken early in dialysis before ultrafiltration and at least on a monthly basis. However, some authors have argued these recommendations (210, 213). They suggest that measurements should be taken late in a session when haemodynamics most closely approximate the period following a session and, in their opinion, there are insufficient data to make a recommendation with regard to timing of measurements. Furthermore, variation occurs due to cannulation technique and changes in haemodynamic in the dialysis sessions. Therefore, a single measurement of either flows or pressure is not helpful in detecting an evolving stenosis; rather multiple repetitive measurements are required. Also, the relationship

between blood flow and intra-access pressure in a stenotic access depends on the location of the lesions and one single technique may not be able to detect lesions at various locations that can occur in an access. Determination of the rate of progression of the stenotic lesions is crucial for timing of intervention and to prevent unnecessary intervention. Angioplasty of the subclinical stenosis does not improve access outcome and could rather promote stenosis (239). Therefore, sequential measurement of pressure or flow or both is required to identify accesses at risk which will need intervention.

In summary, stenosis surveillance tests for AVGs have several major limitations, including their low positive predictive value for AVG thrombosis, as well as the substantial proportion of AVGs that clot despite a normal surveillance test. The lack of benefit is likely attributable to rapid stenosis recurrence following angioplasty. It is possible that the failure of surveillance to prolong access survival in randomized controlled trials has been caused by false-positive referrals with unnecessary angioplasty procedures. Given the current state of our knowledge, none of the stenosis surveillance tests can be recommended as tools to reduce AVG thrombosis. Cumulative evidence has demonstrated that adding surveillance methods to clinical monitoring, coupled with appropriate treatment, may reduce thrombosis rates and may prolong AVF survival. However, as previously stated in the K/DOQI guidelines (16) "(…) the basic skills have been largely abandoned in favor of technology and need to be taught to all individuals who perform hemodialysis procedures". If our aim is to optimize HD access survival, nephrologists and the dialysis staff may need to improve their monitoring skills.

## Treatment of vascular access failure

Vascular access dysfunction continues to be a major cause of morbidity and mortality (79-89) and is responsible for a significant proportion of healthcare costs in the ESRD patient (175, 182-184). Although AVF thrombosis is well recognized as the most common cause of access failure (16, 17, 190, 240), Basile *et al.* (225) recently reported a very low occurrence rate of vascular access failures/AVF/year and a high actuarial survival of mature radiocephalic wrist AVFs. Nevertheless, as current clinical practice guidelines recommend that at least 65% of ESRD population should have a functional AVF as a permanent dialysis access (46), AVF thrombosis has become a clinical challenge in our nephrology practice, with relevant clinical implications

for dialysis patients. A plenty of research has been published regarding the prevention and treatment of this nosological entity. The monitoring/surveillance quality improvement programs have been previously discussed herein. To the best of our knowledge, the results of pharmacologic therapy and the use of medical devices to improve vascular access patency are mixed and deserve a future enlightenment (241-248). Probably, pharmacologic prevention of arteriovenous access thrombosis should be directed at preventing stenosis (which is caused by neointimal hyperplasia), rather than at the coagulation pathways (205, 206). By contrast, the value of endovascular and surgical salvage procedures for AVGs are relatively well established in the literature (249-264). Both surgical and endovascular salvage procedures can be carried out efficiently, with comparable results (265). Even more recently, intervention studies on thrombosed AVFs have also reported encouraging results (266-282). However, every silver lining has a cloud. First, after thrombosis is established, resolution depends on local expertise. Second, salvage procedures require a long learning curve, hindering their universalization. Third, although interventional thrombectomy and angioplasty of the underlying stenosis have gained wide acceptance, results from larger series of surgical treatment of AVF thromboses are not available. This leads to the astonishing fact that there are no comparable data available to this important field of access care. Finally, a major drawback is the high cost associated with the use of mechanical devices (261, 262). Nonetheless, the K/DOQI and the EBPG (16, 17) recommend either a percutaneous or surgical procedures to treat as early as possible arteriovenous access thrombosis. The EBPG (17) recommend that AVF thrombosis should be treated as early as possible or within 48 hours. The duration, site of AVF thrombosis and the type of access are important determinants of treatment outcome.

In view of the published literature in this field, we carried out a retrospective study aimed to evaluate the costs and health outcomes of vascular access care in HD patients consecutively referred to our institution with AVF thrombosis. In the first study, we compared the results of percutaneous thrombectomy with those of an historical cohort who underwent central venous catheterization pending creation of a new AVF. In the second study, we determined the cumulative costs and outcomes of percutaneous thrombectomy during the first-year post-thrombosis. Both studies were performed from the perspective of the health care purchaser and included direct vascular access care-related costs as well as transportation costs. In the first study, the cost per procedure was established from the Ministry of Health and Welfare Ordinance Legislation and, therefore, are more similar to ‘‘charges’’ than to ‘‘costs’’. In the second study, dialysis access costs

were estimated using a micro-costing approach. The data concerning the hospital costs and professional fees for physicians and nurses were obtained from the Information Management Division of our institution.

Within the first study, we observed that, although the immediate clinical success of both procedures was similarly high (endovascular treatment, 97% versus catheter placement, 95%), the primary patency rates at 6 months of follow-up were quite distinct (endovascular treatment, 75% versus catheter placement, 51%). In addition, we observed that 91% of the patients treated by endovascular means had a functioning AVF as a permanent vascular access at 6 months, whereas only 33% of the historic cohort had functional AVF at the end of follow-up. Local practice patterns may have been responsible for the observed low rate of functioning AVFs in the historic cohort. However, others have reported similar difficulties in the creation of a permanent arteriovenous access among incident HD patients (without a previous history of failed AVFs), with a timely referral to a nephrologist (283). Possibly, the delay in procedure scheduling or failure of the AVF to mature might explain this fact. Cost-effectiveness analysis showed that AVF salvage by endovascular therapy led to a near two-fold reduction in access-related expenses per patient-month at risk; the added costs associated with the procedure itself was completely offset by the saving associated with lower surgical visits, access dysfunction, and hospitalizations. To our knowledge, this was one of the first studies published in the literature corroborating the "parachute type" guidelines stating that "The vascular access should be reopened as soon as possible to resume regular dialysis treatment and avoid resorting to a short-term catheter" (16) and "Timely declotting allows immediate use without the need for a central venous catheter" (17). Supporting this view, Allon *et al.* (284) published an elegant paper regarding the effect of change in vascular access on patient mortality in HD patients. In this study, the authors showed that the relative risks for mortality were 2.38 (95% CI, 1.76 to 3.23) in patients switching from an arteriovenous access to a catheter, and 1.37 (95% CI, 0.81 to 2.32) in patients switching from a catheter to an arteriovenous access.

In the second study, a cohort of HD patients consecutively referred to our institution for percutaneous thromboaspiration of totally occluded AVFs was retrospectively analyzed. The present study provided a different perspective on vascular access maintenance and presented the cumulative costs and resources required to treat HD patients with thrombosed AVFs by endovascular means. To our knowledge, this study was the first estimating the cumulative

cost of percutaneous thrombectomy of autogenous AVFs. Herein, we observed that the clinical success rate, primary and secondary patency rates of all AVFs were high and comparable to the published literature. Cost analysis confirmed that manual catheter-directed thromboaspiration of totally occluded AVFs was more expensive than percutaneous transluminal angioplasty. The mean cumulative cost of vascular access care at year 1 was $2,504 per patient-year at risk. As manual catheter-directed thromboaspiration of radiocephalic AVFs had better long-term outcome than brachiocephalic ones, treatment and maintenance of thrombosed radiocephalic AVFs was half as expensive as in brachiocephalic AVFs. Our results indicate that the cumulative cost of maintenance of a thrombosed AVF by endovascular means is high, with patients with clotted radiocephalic AVFs incurring the lowest costs and achieving higher survival times.

Our studies have several limitations. First, as retrospective studies, they share all of the limitations of that approach. Selection of candidates for AVF salvage therapy and the type of procedure performed may differ among centers and countries, and this may have an effect on the external generalization of our results. The cost of certain healthcare procedures has been reported to differ between countries. We are also aware that our studies do not provide a definitive answer regarding the efficiency of endovascular treatment of AVF thrombosis and that further prospective cost-effectiveness analyses comparing different thrombectomy procedures (endovascular versus surgery) and distinct approaches for the maintenance of a functional AVF (pre-emptive angioplasty versus percutaneous thrombectomy) need to be carried out.

A dysfunctional access is a very real concern to patients, as almost 60% of patients mention access thrombosis as one of the most feared problems associated with haemodialysis, ranking it second only to pain (240). As Beathard has pointed out, “From the perspective of the patient, the focus on whether AVF access patency is maintained longer is inappropriate (…) prevention of thrombosis without prolongation of overall longevity is a worthy outcome” (208). Given the considerable costs and adverse clinical consequences of vascular access dysfunction and the potential costs of implementing an ineffective screening strategy, this issue is important for patients, clinicians, and policy makers. Thus, those in charge of vascular access teams must have the knowledge and skills necessary to salvage an AVF that is failing, has thrombosed or is threatened by any other complications.

# Chapter 8

***Main conclusions***

# Main conclusions

This thesis was carried out to give a contribution on the knowledge necessary for optimization of dialysis access use to maximum patient benefit whilst simultaneously optimizing economical resources.

There is a broad consensus that dialysis access not only contributes to patient morbidity and mortality but also contributes substantially to total expenditures for dialysis patient's care. In Chapter "Establishment and maintenance of dialysis access" we were able to show that the use of HD catheters in incident dialysis patients was associated with a substantially greater risk of sepsis, hospitalization, mortality and annual health care costs in comparison with the use of an AVF or a PD catheter. By contrast, both the AVF and the PD catheter revealed to be adequate permanent dialysis accesses for incident ESRD patients. Furthermore, our results suggest that dialysis access type at the time of dialysis initiation might explain the differences in outcome observed between the incident HD and PD populations. Our findings reinforce the need for early referral of ESRD patients to nephrology centers to provide the opportunity for patient informed self selection of renal replacement therapy modality and timely creation of the appropriate dialysis access.

Professional societies from several countries recommend an organized program to identify the failing arteriovenous access. However, we should keep in mind that vascular access surveillance is intended to supplement clinical monitoring. Surveillance data should always be correlated with clinical findings to determine the need for intervention referral. In the Chapter "Detection of vascular access dysfunction" we could show that physical examination of AVFs is easily performed and provides a high level of accuracy to the physician who understands its principles. Furthermore, we have demonstrated that the accuracy of physical examination in the assessment of AVF dysfunction depends on the specific training of the examiner rather than on the cumulative experience in dialysis clinical practice. Therefore, theoretical and hands-on training in physical examination should be provided to nephrologists and dialysis staff. I believe that regular assessment of physical findings (monitoring) is a crucial part of any surveillance/monitoring program of AVFs and enhances the capacity of an organized surveillance program for timely detection of access dysfunction.

Vascular access dysfunction continues to be a major cause of morbidity and mortality and is responsible for a significant proportion of healthcare costs in the ESRD population. Thrombosis of the access is one of the most feared problems associated with HD. In Chapter "Treatment of vascular access failure" we have demonstrated that the clotted AVF should be reopened as soon as possible to resume regular dialysis treatment with clinical and economic benefits as a consequence of avoiding the use of central venous catheters. Fistulae salvage with an endovascular procedure is costly and responsible for a significant financial burden on the ongoing care of ESRD patients, but it proved to be a successful approach for the maintenance of a functional vascular access. Therefore, major efforts should be undertaken to universalize the availability of endovascular intervention capacity in the nephrology units with the objective of aggressively treat clotted AVFs and improve outcomes.

# PART IV
## ABSTRACT

## ABSTRACT

Chronic life-sustaining peritoneal dialysis and haemodialysis require durable accesses to the peritoneal and circulatory systems, respectively. There is a broad consensus that central venous catheters contributes to patient morbidity and may contribute independently to patient mortality. Nonetheless, we still observe an increased use of central venous catheters as chronic dialysis accesses going along with and an unexpected decrease in the prevalence of arteriovenous fistulae and an underutilization of peritoneal dialysis. Professional societies from several countries recommend an organized preventive program to identify the failing arteriovenous access and the appropriate use of salvage procedures for the thrombosed access. However, in daily clinical practice, misdiagnosis of dysfunctional arteriovenous accesses is frequently observed and the use of corrective procedures to prevent dialysis access failure is infrequent.

With this thesis we expect to contribute and deepen the current knowledge of dialysis access for chronic replacement of renal function looking at the role of diagnostic and therapeutic procedures on dialysis access placement and maintenance, to provide patients the maximum benefit afforded by chronic dialysis while optimizing the economic resources involved in this therapy. First, we investigated whether the vascular access for haemodialysis compares (un) favorably to the peritoneal dialysis catheter in incident dialysis patients. We observed that the use of central venous catheters is associated with a substantially greater risk of sepsis, hospitalization, mortality and annual healthcare costs in comparison with the use of an arteriovenous fistula or a peritoneal catheter. Our results further suggested that dialysis access type at the time of dialysis regular program initiation might explain the differences in outcome observed between the incident haemodialysis and peritoneal dialysis populations.

Regarding the monitorization of the arteriovenous fistula, we analyzed the accuracy of physical examination, performed by a general nephrologist and a nephrology fellow educated on vascular access evaluation, in comparison with angiography. In this study we observed that physical examination is easily performed and provides a high level of accuracy in the assessment of arteriovenous fistula dysfunction. Furthermore, we have also demonstrated that physical examination performance depends on the specific training of the practitioner rather than on the

cumulative experience in dialysis clinical practice.

Finally, we aimed to evaluate the costs and health outcomes of vascular access care in haemodialysis patients with arteriovenous fistula thrombosis. In the first study, we have compared the results of endovascular therapy with those of an historical cohort who underwent central venous catheterization pending creation of a new fistula. In the second study, we have determined the cumulative costs and outcomes of endovascular therapy during the first-year post-thrombosis. In these studies we have demonstrated that, although the cost of endovascular treatment is high, the clotted fistula should be reopened as soon as possible to resume regular dialysis treatment and avoid resorting to a catheter, with clear clinical and economic benefits.

In summary, there is great potential with respect to the optimization of dialysis access placement, management and dialysis modality selection for chronic kidney disease patients. Early referral of chronic kidney disease patients to nephrology centers provides a unique opportunity for patient selection of renal replacement therapy modality and timely creation of the appropriate dialysis access. Vascular access surveillance is intended to supplement clinical monitoring as physical examination is non-invasive, incurs no extra cost and may provide an accurate means of diagnosis of arteriovenous dysfunction. Nephrologists and the dialysis staff may need to improve their vascular access monitoring skills in order to optimize the haemodialysis access survival. Arteriovenous fistula thrombosis is one of the most feared problems associated with haemodialysis. Endovascular salvage procedures have proven to be a successful approach for the treatment of thrombosed vascular accesses. Therefore, intensive efforts should be undertaken to universalize the availability of arteriovenous fistula endovascular interventions, in order to improve vascular access patency.

## RESUMO

O acesso permanente ao peritoneu e ao sistema circulatório é condição necessária para a implementação da diálise peritoneal e de hemodiálise crónica, respectivamente. O acesso de diálise é consensualmente reconhecido como um dos factores responsáveis pela elevada morbi-mortalidade do doente renal crónico. Todavia, o recurso a cateteres venosos centrais como acesso de diálise permanece elevado e tem-se vindo a assistir a um decréscimo inexplicável na utilização de fístulas artériovenosas, ao mesmo tempo que se reconhece que a diálise peritoneal é subutilizada. As sociedades de nefrologia internacionais recomendam a utilização de programas estruturados de monitorização e vigilância do acesso arteriovenoso de diálise e o recurso a técnicas terapêuticas para o tratamento do acesso trombosado. No entanto, o diagnóstico incorrecto de disfunção do acesso arteriovenoso é frequente na prática clínica, bem como a escassez de recursos para o tratamento adequado do acesso em falência.

Com a elaboração desta tese procuramos contribuir e aprofundar o conhecimento actual sobre o acesso de diálise para terapêutica dialítica crónica. Para o efeito, estudamos a utilização de diferentes tipos de acessos de diálise e o recurso a técnicas diagnósticas e terapêuticas que permitam aos doentes usufruir do máximo benefício proporcionado pela diálise crónica, optimizando simultaneamente os recursos económicos implicados nesta terapêutica. Primeiro, realizámos uma análise comparativa entre o acesso de diálise peritoneal e o acesso de hemodiálise em doentes renais crónicos incidentes em diálise. Constatámos que o recurso ao cateter venoso central está associado a um elevado risco de sépsis, hospitalização, mortalidade e custos anuais de saúde, comparativamente ao uso da fístula artériovenosa e do cateter peritoneal. Os resultados obtidos sugerem ainda que o tipo de acesso de diálise utilizado no início da terapêutica dialítica pode contribuir para os resultados díspares observados entre as populações de doentes incidentes em tratamento de hemodiálise e de diálise peritoneal.

Relativamente à monitorização da fístula arteriovenosa para hemodiálise, analisámos o desempenho diagnóstico do exame físico na avaliação da disfunção de fístulas artériovenosas, quando realizado por nefrologistas e um médico interno devidamente treinado, em comparação com a angiografia. Concluímos que o exame físico é um método exequível, proporcionando um elevado rigor diagnóstico na avaliação de fístulas artériovenosas disfuncionantes. Os resultados

obtidos sugerem ainda que o desempenho do exame físico depende fundamentalmente do treino específico adquirido e não da experiência clínica acumulada no tratamento de doentes renais crónicos em diálise.

Por último, tivemos por objetivo estudar as implicações clínicas e económicas do tratamento do acesso vascular em doentes em hemodiálise crónica com fístulas artériovenosas trombosadas. No primeiro trabalho, comparámos os resultados obtidos através da técnica endovascular com os de uma coorte histórica de doentes submetidos a cateterização venosa central e construção subsequente de uma nova fístula artériovenosa. No segundo trabalho, avaliámos o custo anual do tratamento endovascular de fístulas artériovenosas trombosadas. Concluímos que, apesar do elevado custo associado à técnica endovascular, as fístulas trombosadas deverão se repermeabilizadas atempadamente de modo a evitar o recurso ao cateter venoso central, com claros benefícios, clínicos e económicos.

Em resumo, parece-nos existir amplo potencial no que diz respeito à optimização do primeiro acesso de diálise e à opção informada pela modalidade de tratamento de substituição da função renal. A referenciação precoce do doente renal crónico a serviços de nefrologia constitui uma oportunidade única para o pleno esclarecimento do doente renal crónico acerca das diferentes modalidades de tratamento disponíveis e à colocação atempada de um acesso de diálise adequado. A vigilância do acesso vascular visa complementar a monitorização clínica, sendo que o exame físico constitui um método não-invasivo, económico, e rigoroso no diagnóstico de fístulas arteriovenosas disfuncionantes. Todavia, se o nosso objetivo é optimizar a sobrevida do acesso de hemodiálise, os nefrologistas e outros profissionais de saúde envolvidos no tratamento dialítico carecem em aperfeiçoar as suas competências na monitorização do acesso vascular. A trombose da fístula artériovenosa é um dos problemas mais temidos associados à hemodiálise. As terapêuticas de resgate endovascular têm provado ser uma abordagem terapêutica bem sucedida para o acesso vascular trombosado. Cabe-nos a nós, nefrologistas, envidar esforços de modo a proporcionar aos doentes a universalização destas técnicas.

# PART V

## BIBLIOGRAPHY

(1). Bright R. Cases and observations illustrative of renal disease accompanied with the secretion of albuminous urine. *Guys Hosp Rep* 1;338: 1836.

(2). Drukker W. HD: Haemodialysis: A Historical Review. In: Drukker W, Parsons FM, Maher JF (eds). Replacement of Renal function by Dialysis, 3rd edn. Dordrecht, The Netherlands: Kluwer, 1989.

(3). Konner K. History of vascular access for HD. *Nephrol Dial Transplant* 2005;20:2629-2635.

(4). Quinton W, Dillard D, Scribner B. Cannulation of blood vessels for prolonged hemodialysis. *Trans Am Soc Artif Intern* Organs 1960;6:104-113.

(5). Shaldon S, Chiandussi L, Higgs B. HD by percutaneous catheterization of the femoral artery and vein with regional heparinization. *Lancet* 1961;II:857-859.

(6). Schwab S, Buller G, MacCann R, et al. Prospective evaluation of a Dacron cuffed hemodialysis catheter for prolonged use. *Am J Kidney Dis* 1988;11:166-169.

(7). Brescia M, Cimino JE, Appel K, Hurwich B. Chronic hemodialysis using venipuncture and a surgically created arteriovenous fistula. *N Engl J Med* 1966; 275:1089-1092.

(8). Staple T. Retrograde venography of subcutaneous arteriovenous fistulas created surgically for hemodialysis. *Radiology* 1973;106:223-224.

(9). Ergun D, Mistretta C, Kruger R, et al. A hybrid computerized fluoroscopy technique for noninvasive cardiovascular imaging. *Radiology* 1979; 132: 739-742.

(10). Gordon D, Glanz S, Butt K, et al. Treatment of stenotic lesions in dialysis access fistulas and shunts by transluminal angioplasty. *Radiology* 1982;143:53-58.

(11). Twardowski Z. History of peritoneal access development. *Int J Artif Organs* 2006;29:2-40.

(12). Rosenak S, Oppenheimer GD. An improved drain for peritoneal lavage. *Surgery* 1948;23:832-833.

(13). Maxwell M, Rockney R, Kleeman C, et al. Peritoneal dialysis. *JAMA* 1959;170:917-924.

(14). Gutch C. Peritoneal dialysis. *Trans Am Soc Artif Intern Organs* 1964;10;406-407.

(15). Tenckhoff J, Schechter H. A bacteriologically safe peritoneal access device. *Trans Am Soc Artif Organs* 1968; 14:181-187.

(16). NKF-KDOQI. Clinical practice guidelines for vascular access. *Am J Kidney Dis* 2006; 48 (Suppl 1): S248–S272.

(17). Tordoir J, Canaud B, Haage P, et al. EBPG on vascular access. *Nephrol Dial Transpl* 2007;22(Suppl 2):ii88-ii117.

(18). Karakitsos D, Labropoulos N, De Groot E, et al. Real-time ultrasound-guided catheterisation of the internal jugular vein: a prospective comparison with the landmark technique in critical care

patients. *Crit Care* 2006;10:R162.

(19). Little M, Conlon P, Walshe J. Access recirculation in temporary hemodialysis catheters as measured by the saline dilution technique. *Am J Kidney Dis* 2000;36:1135-1139.

(20). Level C, Lasseur C, Chauveau P, et al. Performance of twin central venous catheters: influence of the inversion of inlet and outlet on recirculation. *Blood Purif* 2002;20:182-188.

(21). Vanholder R, Canaud B, Fluck R, et al. Diagnosis, prevention and treatment of HD catheter-related bloodstream infections (CRBSI): a position statement of European Renal Best Practice (ERBP). *NDT Plus* 2010;3:234-246.

(22). Feldman H, Kobrin S, Wasserstein A. Hemodialysis vascular access morbidity. *J Am Soc Nephrol* 1996;7:523-35.

(23). Hyun S, Gunnar B. Exotic Catheter Access, in Gray RJ, Sands JJ (eds): Dialysis Access: A Multidisciplinary Approach. Philadelphia, PA, Lippincott Williams & Wilkins, 2002, pp270-282.

(24). Spergel L, Ravani P, Asif A, et al. Autogenous arteriovenous fistula options. *J Nephrol* 2007; 20: 288-298.

(25). Hossny A. Brachiobasilic arteriovenous fistula: different surgical techniques and their effects on fistula patency and dialysis-related complications. *J Vasc Surg* 2003;37:821-826.

(26). Rooijens P, Tordoir J, Stijnen T, et al. Radiocephalic wrist arteriovenous fistula for hemodialysis: meta-analysis indicates a high primary failure rate. *Eur J Vasc Endovasc Surg* 2004;28:583-589.

(27). USRDS. Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, 2012.

(28). Kraus M. Techniques of Peritoneal Catheter Insertion, in Gray RJ, Sands JJ (eds): Dialysis Access: A Multidisciplinary Approach. Philadelphia, PA, Lippincott Williams & Wilkins, 2002, pp310-321.

(29). Eklund B, Honkanen E, Kyllonen L, et al. Peritoneal dialysis access: prospective randomized comparison of single-cuff and double-cuff straight Tenckhoff catheters. *Nephrol Dial Transplant* 1997;12:2664-2666.

(30). Gokal R, Alexander S, Ash S, et al. Peritoneal catheters and exit-site practices toward optimum peritoneal access: 1998 update. (Official report from the International Society for Peritoneal Dialysis). *Perit Dial Int* 1998; 18: 11–33.

(31). Crabtree J, Burchette R. Prospective comparison of downward and lateral peritoneal dialysis catheter tunnel-tract and exit-site directions. *Perit Dial Int* 2006; 26: 677–683.

(32). Figueiredo A, Goh B, Jenkins S, et al. Clinical practice guidelines for peritoneal access. *Perit Dial Int* 2010; 30:424-429.

(33). Dombros N, Dratwa M, Feriani M, et al. European best practice guidelines for peritoneal dialysis. 3 Peritoneal access. *Nephrol Dial Transplant* 2005; 20(Suppl 9):ix8-12.

(34). Campos R, Chula D, Riella M. Complications of the peritoneal access and their management. *Contrib Nephrol* 2009;163:183-197.

(35). Kam-Tao P, Szeto C, Piraino B, et al. Peritoneal dialysis-related infections: 2010 update. *Perit Dial Int* 2010; 30:393-423.

(36). Bloembergen W, Port F, Mauger E, et al. A compatison of mortality between patients treated with hemodialysis and peritoneal dialysis. *J Am Soc Nephrol* 1995;6:177-183.

(37). Fenton S, Schaubel D, Desmeules M, et al. Hemodialysis versus peritoneal dialysis: a comparison of adjusted mortality rates. *Am J Kidney Dis* 1997;30:334-342.

(38). Collins A, Hao W, Xia H, Ebben J, et al. Mortality risks of peritoneal dialysis and hemodialysis. *Am J Kidney Dis* 1999;34:1065-1074

(39). Heaf J, Lokkegaard H, Madsen M. Initial survival advantage of peritoneal dialysis relative to haemodialysis. *Nephrol dial Transplat* 2002;17:112-117.

(40). Covic A, Bammens B, Lobbedez T, et al. Educating end-stage renal disease patients on dialysis modality selection: a clinical advice from the European Renal Best Practice (ERBP) Advisory Board. *NDT Plus* 2010;3:225-233.

(41). Ratcliffe P, Phillips R, Oliver D. Late referral for maintenance dialysis. *Br Med J (Clin Res Ed)* 1984;288:441–443.

(42). Metcalfe W, Khan I, Prescott G, et al. Can we improve early mortality in patients receiving renal replacement therapy? *Kidney Int*. 2000;57:2539-2545.

(43). Eadington D. Delayed referral for dialysis. *Nephrol Dial Transplant*. 1996;11:2124-2126.

(44). Roderick P, Jones C, Drey N, et al. Late referral for end-stage renal disease: A region-wide survey in the south west of England. *Nephrol Dial Transplant*. 2002;17:1252-1259.

(45). Jungers P, Zingraff J, Albouze G, et al. Late referral to maintenance dialysis: Detrimental consequences. *Nephrol Dial Transplant* 1993;8:1089-1093.

(46). http://www.FistulaFirst.org/.

(47). Beathard G. Vascular Access. *Semin Dial* 2011;24(5):503-507.

(48). Strippoli G, Tong A, Johson D, et al. Catheter-Related Interventions to Prevent Peritonitis in

Peritoneal Dialysis: A Systematic Review of Randomized, Controlled Trials. *J Am Soc Nephrol* 2004;15:2735-2746.

(49). Crabtree J. Fluoroscopic placement of peritoneal dialysis catheters: a harvest of the low hanging fruits. *Perit Dial Int* 2008; 28:134-137.

(50). Danielsson A, Blohme L, Tranaeus A, et a. A prospective randomized study of the effect of a subcutaneously "buried" peritoneal dialysis catheter technique versus standard technique on the incidence of peritonitis and exit-site infection. *Perit Dial Int* 2002; 22:211-19.

(51). Brum S, Rodrigues A, Rocha S, et al. Moncrief-Popovich technique is an advantageous method of peritoneal dialysis catheter implantation. *Nephrol Dial Transplant* 2010;25(9):3070-3075.

(52). Povlsen J, Ivarsen P. How to start the late referred ESRD patient urgently on chronic APD. *Nephrol Dial Transplant* 2006, 21(Suppl 2):ii56-ii59.

(53). Povlsen J. Unplanned start on assisted peritoneal dialysis. *Contrib Nephrol* 2009;163:261-263.

(54). Lobbedez T, Lecouf A, Ficheux M, et al. Is rapid initiation of peritoneal dialysis feasible in unplanned dialysis patients? A single-centre experience. *Nephrol Dial Transplant* 2008;23(10):3290-3294.

(55). Ethier J, Mendelssohn D, Elder S, et al. Vascular access use and outcomes: an international perspective from the dialysis outcomes and practice patterns study. *Nephrol Dial Transplant* 2008;23: 3219-3226.

(56). Lysaght M. Maintenance dialysis population dynamics: current trends and long-term implications. *J Am Soc Nephrol* 2002; 13 (Suppl 1): S37-S40.

(57). Avorn J, Winkelmayer W, Bohn R, et al. Delayed nephrologist referral and inadequate vascular access in patients with advanced chronic kidney failure. *Journal of Clinical Epidemiology* 2002;55:711-716.

(58). Schwab S, Besarab A, Beathard G *et al*. NKF-KDOQI clinical practice guidelines for hemodialysis vascular access. *Am J Kidney Dis* 1997; 30(Suppl 3): S137–S181.

(59). Pisoni R, Young E, Dykstra D et al. Vascular access use in Europe and the United States: results from the DOPPS. *Kidney Int* 2002; 61: 305-316.

(60). Young E, Dykstra D, Goodkin D et al. Hemodialysis vascular access preferences and outcomes in the Dialysis Outcomes and Practice Patterns Study (DOPPS). *Kidney Int* 2002; 61: 2266-2271.

(61). Ravani P, Spergel L, Asif A, et al. Clinical epidemiology of arteriovenous fistula in 2007. *J Nephrol* 2007; 20: 141-149.

(62). Nolph K. Has peritoneal dialysis peaked? The impact of the CANUSA study. The Canadian-USA

Multicenter study. *ASAIO J* 1996;42:136-138.

(63). Annual Baxter World-Wide Survey. Baxter Healthcare Corporation: Deerfield, Illinois, 1998.

(64). Grassmann A, Gioberge S, Moeller S, et al. ESRD patients in 2004: global overview of patient numbers, treatment modalities and associated trends. *Nephrol Dial Transplant* 2005;20:2587-2593.

(65). Oliver M, Quinn R, Richardson E, et al. Home care assistance and the utilization of peritoneal dialysis. *Kidney Int* 2007:71 (7): 673–8.

(66). Blake P. Adequacy of dialysis revisited. *Kidney Int* 2003;63:1587-1599.

(67). Gokal R, Blake P, Passlick-Deetjen J, et al. What is the evidence that peritoneal dialysis is underutilized as an ESRD therapy? *Semin Dial* 2002;15:149-161.

(68). Jager K, Korevaar J, Dekker F, et al. The effect of contraindications and patient preference on dialysis modality selection in ESRD patients in The Netherlands. *Am J Kidney Dis* 2004;43:891-899.

(69). Mehrotra R, Marsh D, Vonesh E, et al. Patient education and access of ESRD patients to renal replacement therapies beyond in-center hemodialysis. *Kidney Int* 2005;1968:378-390.

(70). Little J, Irwin A, Marshall T, et al. Predicting a patient's choice of dialysis modality: experience in a United Kingdom renal department. *Am J Kidney Dis* 2001;37:981-986.

(71). Lameire N, Van Biesen W. The pattern of referral of patients with end-stage renal disease to the nephrologist – a European survey. *Nephrol Dial Transplant* 1999; 14 Suppl 6:16-23.

(72). Diaz-Buxo J. Early referral and selection of peritoneal dialysis as a treatment modality. *Nephrol Dial Transplant* 2000;15:147-149.

(73). Piccoli G, Mezza E, Burdese M, et al. Dialysis choice in the context of an early referral policy: there is room for self care. *J Nephrol* 2005;18:267-275.

(74). Golper T. Patient education: can it maximize the success of therapy? *Nephrol Dial Transplant* 2001;16 Suppl 7:20-24.

(75). Manns B, Taub K, Vanderstraeten C, Jones H, et al. The impact of education on chronic kidney disease patients' plans to initiate dialysis with self-care dialysis: a randomized trial. *Kidney Int* 2005;68:1777-1783.

(76). Nissenson A, Prichard S, Cheng IK, et al. Non-medical factors that impact on ESRD modality selection. *Kidney Int* Suppl 1993;40:S120-S127.

(77). Mignon F, Michel C, Viron B. Why so much disparity of PD in Europe? [editorial]. *Nephrol Dial*

*Transplant* 1998;13:1114-1117.

(78). Twardowski Z, Nolph K, Khanna R, et al. Computer Interactions: Catheters. *Adv Perit Dial* 1994;10:11-18.

(79). Dhingra R, Young E, Hulbert-Shearon T, et al. Type of vascular access and mortality in U.S. hemodialysis patients. *Kidney Int* 2001;60:1443-1451.

(80). Powe N, Jaar B, Furth S, et al. Septicemia in dialysis patients: Incidence, risk factors, and prognosis. *Kidney Int* 1999;55:1081-1090.

(81). Taylor G, Gravel D, Johnston L, et a. Prospective surveillance for primary bloodstream infections occurring in Canadian hemodialysis untis. *Infect Control Hosp Epidemiol* 2002;23:716-720.

(82). Schwab S, Beathard G. The hemodialysis catheter conundrum: Hate living with them, but can't live without them. *Kidney Int* 1999;56:1-17.

(83). Develter W, De Cubber A, Van Biesen W, et al. Survival and complications of indwelling venous catheters for permanent use in hemodialysis patients. *Artif Organs* 2005;29:399-405.

(84). Ponikvar B, Buturovic-Ponikvar J. Temporary hemodialysis catheters as a long-term vascular access in chronic hemodialysis patients. *Ther Apher Dial* 2005;9:250-253.

(85). Marr K, Sexton D, Conlon P, et al. Catheter-related bacteremia and outcome of attempted catheter salvage in patients undergoing hemodialysis. *Ann Intern Med* 1997;127:275-280.

(86). Woods J, Port F. The impact of vascular access for haemodialysis on patient morbidity and mortality. *Nephrol Dial Transplant* 1997;12:657-659.

(87). Pastan S, Soucie J, McClellan WM. Vascular access and increased risk of death among hemodialysis patients. *Kidney Int* 2002;62:620-626.

(88). Xue J, Dahl D, Ebben J, et al. The association of initial hemodialysis access type with mortality outcomes in elderly Medicare ESRD patients. *Am J Kidney Dis* 2003;42:1013-1019.

(89). Polkinghorne K, McDonald S, Atkins R, et al. Vascular access and all-cause mortality: A propensity score analysis. *J Am Soc Nephrol* 2004;15:477-486.

(90). Astor B, Eustace J, Powe N, et al. Timing of nephrologist referral and arteriovenous access use: the CHOICE Study. *Am J Kidney Dis* 2001;38:494-501.

(91). Astor B, Eustace J, Powe N et al. CHOICE Study. Type of vascular access and survival among incident hemodialysis patients: the Choices for Healthy Outcomes in Caring for ESRD (CHOICE) Study. *J Am Soc Nephrol* 2005;16:1449-1455.

(92). Allon M, Daugirdas J, Depner T, et al. Effect of change in vascular access on patient mortality in

hemodialysis patients. *Am J Kidney Dis* 2006;47:469-77.

(93). Moist L, Trpeski L, Na Y, et al. Increased hemodialysis catheter use in Canada and associated mortality risk: data from the Canadian Organ Replacement Registry 2001-2004. *Clin J Am Soc Nephrol* 2008;3:1726-1732.

(94). Pisoni R, Arrington C, Albert J, et al. Facility hemodialysis vascular access use and mortality in countries participating in DOPPS: an instrumental variable analysis. *Am J Kidney Dis* 2009;53:475-491.

(95). de Jager D, Grootendorst D, Jager K, et al. Cardiovascular and noncardiovascular mortality among patients starting dialysis. *JAMA* 2009, 302(16):1782–1789.

(96). Lacson E Jr, Wang W, Lazarus JM, et al. Change in vascular access and mortality in maintenance hemodialysis patients. *Am J Kidney Dis* 2009;54:912-921.

(97). Golper T, Brier M, Bunke M, et al. Risk factors for peritonitis in long-term peritoneal dialysis: the Network 9 peritonitis and catheter survival studies. Academic Subcommittee of the Steering Committee of the Network 9 Peritonitis and Catheter Survival Studies. *Am J Kidney Dis* 1996;28: 428-436.

(98). Aslam N, Bernardini J, Fried L, et al. Comparison of infectious complications between incident hemodialysis and peritoneal dialysis patients. *Clin J Am Soc Nephrol* 2006, 1:1226–1233.

(99). Oliver M, Verrelli M, Zacharias JM, et al. Choosing peritoneal dialysis reduces the risk of invasive access interventions. *Nephrol Dial Transplant* 2012;27:810-816.

(100). Oliver M, Garg A, Blake P et al. Impact of contraindications, barriers to self-care and support on incident peritoneal dialysis utilization. *Nephrol Dial Transplant* 2010;25:2737-2744.

(101). Lok C, Allon M, Moist L et al. Risk equation determining unsuccessful cannulation events and failure to maturation in arteriovenous fistulas (REDUCE FTM I). *J Am Soc Nephrol* 2006;17:3204–3212

(102). Perl J, Wald R, McFarlane P, et al. Hemodialysis vascular access modifies the association between dialysis modality and survival. *J Am Soc Nephrol* 2011;22:1113-1121.

(103). Blake P, Just P. Economics of dialysis. In: Horl WH, Koch KM, Lindsay RM, Ronco C, Winchester JF (eds). Replacement of Renal Function by Dialysis, 5th edn. Dordrecht, The Netherlands: Kluwer, 2004.

(104). Levinsky N, Rettig R. Special Report: the Medicare End-Stage Renal Disease Program. *N Engl J Med* 1991;324:1143-1148.

(105). Lameire N, Joffe P, Wiedemann M. Health care systems and end-stage renal disease (ESRD)

therapies – an international review: access to ESRD treatments. *Nephrol Dial Transplant* 1999;14(suppl.6):3-9.

(106). Horl W, de Alvaro F, Williams P. Health care systems and end-stage renal disease (ESRD) therapies – an international review: access to ESRD treatments. *Nephrol Dial Transplant* 1999;14(Suppl.6):10-15.

(107). De Vecchi A, Dratwa M, Wiedemann M. Healthcare systems and end-stage renal disease (ESRD) therapies – an international review: costs and reimbursement/funding of ESRD therapies. *Nephrol Dial Transplant* 1999; 14(Suppl 6): 31-41.

(108). Garg P, Frick K, Diener-West M, et al. Effects of the ownership of dialysis facilities on patients' survival and referral for transplantation. *N Engl J Med* 1999;341:1653-1660.

(109). Devereaux P, Schunemann H, Ravindran N et al. Comparison of mortality between private for-profit and private not-for-profit hemodialysis centers: a systematic review and meta-analysis. *J Am Med Assoc* 2002;288:2449-2457.

(110). Port F, Wolfe R, Held P. Ownership of dialysis facilities and patients' survival (letter). *N Engl J Med* 2000;342:1053-1054.

(111). Foley R, Fan Q, Liu J. et al. Comparative mortality of hemodialysis patients at for-profit and not-for-profit dialysis facilities in the United States, 1998 to 2003: A retrospective analysis. *BMC Nephrology* 2008, 9:6

(112). www.baxter.com

(113). www.fmc-ag.com

(114). www.gambro.com

(115). www.diaverum.com

(116). Just P, Charro F, Tschosik E et al. Reimbursement and economic factors influencing dialysis modality choice around the world. *Nephrol Dial Transplant* 2008;23:2365-2373.

(117). St Peter W, Khan S, Ebben J *et al*. Chronic kidney disease: the distribution of health care dollars. *Kidney Int Suppl* 2004; 66: 313-321.

(118). USRDS. Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, 2010.

(119). Bruns F, seddon P, Saul M, et al. The cost of caring for end-stage kidney disease patients: an analysis based on hospital financial transaction records. *J Am soc Nephrol* 1998;9:884-890.

(120). McMurray S, Miller J. Impact of capitation on free-standing dialysis facilities: can you survive? *Am J Kidney Dis* 1997;30:542-548.

(121). Prichard S. The costs of dialysis in Canada. *Nephrol Dial Transplant* 1997; 12(Suppl 1): 22-24.

(122). Goeree R, Manalich J, Grootendorst P, et al. Cost analysis of dialysis treatments for end-stage renal disease (ESRD). *Clin Invest Med* 1995;18:455-464.

(123). Just P, Riella M, Tschosik E, et al. Economic evaluations of dialysis treatment modalities. *Health Policy* 2008;86:163-180.

(124). Peeters P, Rublee D, Just P, et al. Analysis and interpretation of cost data in dialysis: review of western European literature. *Health Policy* 2000;54:209-227.

(125). Jacobs C. The costs of dialysis treatments for patients with end-stage renal disease in France. *Nephrol Dial Transplant* 1997;12(Suppl. 1):29-32.

(126). Benain J, Faller B, Briat C, et al. Coût de la prise en charge de la dialyse en France Cost of dialysis in France. *Néphrologie & Thérapeutique* 2007;3:96-106.

(127). Piccoli G. Formica M, Mangeiaortti G et al. The costs of dialysis in Italy. *Nephrol Dial transplant* 1997;12 (Suppl. 1):33-44.

(128). Benaina J, Faller B, Briatc C, et al. Cost of dialysis in France. *Néphrologie & Thérapeutique* 2007;3:96-106.

(129). Baboolal K, McEwan P, Sondhi S, et al. The cost of renal dialysis in a UK setting - a multicentre study. *Nephrol Dial Transplant* 2008;23:1982-1989.

(130). Rodriguez-Carmona A, Perez Fontan M, et al. The economic cost of dialysis: a comparison between peritoneal dialysis and in-center hemodialysis in a Spanish unit. *Advances Peritoneal Dialysis* 1996;12:93-6.

(131). Villa G, Rodrıguez-Carmona A, Fernandez-Ortiz L, et al. Cost analysis of the Spanish renal replacement therapy programme. *Nephrol Dial Transplant* 2011;0:1-6.

(132). Sennfält K, Magnusson M, Carlsson P. Comparison of hemodialysis and peritoneal dialysis – a cost-utility analysis. *Perit Dial Int* 2002;22:39-

(133). Salonen T, Reina T, Oksa H, et al. Cost Analysis of Renal Replacement Therapies in Finland. *Am J Kidney Dis* 2003;42 (6):1228-1238.

(134). Komenda P, Gavaghan M, Garfield S, et al. An economic assessment model for in-center, conventional home, and more frequent home hemodialysis. *Kidney Int* 2012;81:307-313.

(135). Blake P. The complex economics of modality selection. *Perit Dial Int* 2004;24:509-511.

(136). Blake P. Factors affecting international utilization of peritoneal dialysis: implications for increasing utilization in the United States. *Semin Dial* 1999;12:362-369.

(137). Blake P, Finkelstein F. Why is the proportion of patients doing peritoneal dialysis declining in North America? *Perit Dial Int* 2001;21:107-114.

(138). Nissenson A, Prichard S, Cheng I, et al. Non-medical factors that impact on ESRD modality selection. *Kidney Int* 1993;40:S120-127.

(139). Jung B, Blake P, Mehta R, et al. Attitudes of Canadian nephrologists toward dialysis modality selection. *Perit Dial Int* 1999;19:263-268.

(140). Mendhelssohn D, Mullaney S, Jung B, et a. What do American nephrologists think about dialysis modality selection? *Am J Kidney Dis* 2001;37:22-29

(141). Vanholder R, Davenport A, Hannedouche T, et al. Reimbursement of dialysis: a comparison of seven countries. *J Am Soc Nephrol* 2012;23(8):1291-1298.

(142). van Biesen W, Veys N, Lameire N, et al. Why less success of the peritoneal dialysis programmes in Europe? *Nephrol Dial Transplant* 2008;23:1478-1481.

(143). van Biesen W, Lameire N. An evaluation of an integrative care approach to end-stage renal disease patients. *J Am Soc Nephrol* 2000;11:116-125.

(144). Blake P. Integrated end-stage renal disease care: the role of peritoneal dialysis. *Nephrol Dial Transplant* 2001;16 Suppl 5:61.

(145). Mendelssohn D, Pierratos A. Reformulating the integrated care concept for the new millennium. *Perit Dial Int* 2002;22(1):5.

(146). Kawanishi H, Moriishi M. Clinical effects of combined therapy with peritoneal dialysis and hemodialysis. *Perit Dial Int* 2007;27 Suppl 2:S126.

(147). Panagoutsos S, Kantartzi K, Passadakis P et al. Timely transfer of peritoneal dialysis patients to hemodialysis improves survival rates. *Clin Nephrol* 2006;65(1):43.

(148). Correa-Rotter R. The cost barrier to renal replacement therapy and peritoneal dialysis in the developing world. *Perit Dial Int* 2001;21(Suppl 3): S314-S317.

(149). Ocak G, Halbesma N, le Cessie S et al. Haemodialysis catheters increase mortality as compared to arteriovenous accesses especially in elderly patients. *Nephrol Dial Transplant* 2011;26:2611-2617.

(150). Coentrao L, Ribeiro C, Santos-Araújo C, et al. Bundled payment for renal dialysis in a portuguese setting: economic implications. *Nephrol Dial Transplant* 2012;27 (suppl 2):ii252-ii267 [Abstract].

(151). Wish J. Vascular access for dialysis in the United States: progress, hurdles, controversies, and the future. *Semin Dial* 2010;23:614-618.

(152). Ishani A, Collins A, Herzog C et al. Septicemia, access and cardiovascular disease in dialysis patients: The USRDS Wave 2 Study. *Kidney Int* 2005; 68: 311-318.

(153). Beathard G. Integrated vascular access management. *Blood Purif* 2003;21:89-98.

(154). Smart N, Titus T. Outcomes of early versus late nephrology referral in chronic kidney disease: a systematic review. *Am J Med* 2011;124:1073-1080.

(155). Mendelssohn D, Malmberg C, Hamandi B. An integrated review of "unplanned" dialysis initiation: reframing the terminology to "suboptimal" initiation. *BMC Nephrol* 2009;10:22.

(156). Mendelssohn D, Curtis B, Yeates K, et al. Suboptimal initiation of dialysis with and without early referral to a nephrologist. *Nephrol Dial Transplant* 2011;26:2959-2965.

(157). Van Biesen W, Wiedemann M, Lameire N. End-stage renal disease treatment: a European perspective. *J Am Soc Nephrol.* Dec 1998;9 (12Suppl):S55-62.

(158). Arora P, Obrador GT, Ruthazer R, et al. Prevalence, predictors, and consequences of late nephrology referral at a tertiary care center. *J Am Soc Nephrol* 1999;10(6):1281-1286.

(159). Caskey F, Wordsworth S, Ben T, et al. Early referral and planned initiation of dialysis: what impact on quality of life? *Nephrol Dial Transplant* 2003;18(7):1330-1338.

(160). Gallego E, Lopez A, Lorenzo I, et al. Influence of early or late referral to nephrologist over morbidity and mortality in hemodialysis. *Nefrologia* 2003;23(3):234-242.

(161). Lorenzo V, Martn M, Rufino M, et al. Predialysis nephrologic care and a functioning arteriovenous fistula at entry are associated with better survival in incident hemodialysis patients: an observational cohort study. *Am J Kidney Dis* 2004 43(6):999-1007.

(162). Kazmi W, Obrador G, Khan S, et al. Late nephrology referral and mortality among patients with end-stage renal disease: a propensity score analysis. *Nephrol Dial Transplant* 2004;19(7):1808-1814.

(163). Winkelmayer W, Owen W, Jr., Levin R, et al. A propensity analysis of late versus early nephrologist referral and mortality on dialysis. *J Am Soc Nephrol* 2003;14(2):486-492.

(164). Quinn R, Hux J, Oliver M, et al. Selection bias explains apparent differential mortality between dialysis modalities. *J Am Soc Nephrol* 2011;22:1534-1542.

(165). Raithatha A, McKane W, Kendray D, Evans C. Catheter access for hemodialysis defines higher mortality in late-presenting dialysis patients. *Ren Fail* 2010;32(10):1183-1188.

(166). Allon M, Robbin M. Increasing arteriovenous fistulas in hemodialysis patients: problems and

solutions. *Kidney Int* 2002; 62: 1109-1124.

(167). Rehman R, Schmidt R, Moss A. Ethical and legal obligation to avoid long-term tunneled catheter access. *Clin J Am Soc Nephrol* 2009;4:456-460.

(168). Lameire N, Van Biesen W, Vanholder R. Did 20 years of technological innovations in hemodialysis contribute to better patient outcomes? *Clin J Am Soc Nephrol* 2009;4:S30-S40.

(169). Rodrigues A. How to persuade peritoneal dialysis-skeptical hemodialysis fans. *Contrib Nephrol* 2009;163:237-42.

(170). Moossavi S, Raasch E, Russell G, et al. Comparison of dialysis access outcomes in peritoneal dialysis and hemodialysis patients at an academic medical center. *Perit Dial Int* 2007 27:S24.

(171). Asif A, Pflederer T, Vieira C, et al. Does catheter insertion by nephrologists improve peritoneal dialysis utilization? A multicenter analysis. *Semin Dial* 2005;18(2):157-160.

(172). Goh B, Ganeshadeva Y, Chew S, et al. Does peritoneal dialysis catheter insertion by interventional nephrologists enhance peritoneal dialysis penetration? *Semin Dial* 2008;21(6):561-566

(173). Koch M, Kohnle M, Trapp R, et al. Comparable outcome of acute unplanned peritoneal dialysis and haemodialysis. *Nephrol Dial Transplant* 2012;27: 375-380.

(174). McLaughlin K, Manns B, Culleton B et al. An economic evaluation of early versus late referral of patients with progressive renal insufficiency. *Am J Kidney Dis* 2001; 38: 1122-1128.

(175). Ortega T, Ortega F, Diaz-Corte C, et al. The timely construction of arteriovenous fistulae: a key to reducing morbidity and mortality and to improving cost management. *Nephrol Dial Transplant* 2005;20:598-603.

(176). Murphy S, Foley R, Barrett B *et al*. Comparative hospitalization of hemodialysis and peritoneal dialysis patients in Canada. *Kidney Int* 2000; 57: 2557–2563.

(177). Zhang A, Cheng L, Zhu N *et al*. Comparison of quality of life and causes of hospitalization between hemodialysis and peritoneal dialysis patients in China. *Health Qual Life Outcomes* 2007; 5: 49.

(178). Trivedi H, Tan S, Prowant B *et al*. Predictors of hospitalization in patients on peritoneal dialysis: the Missouri experience. *Am J Nephrol* 2007; 27: 483-487.

(179). Lecame M, Lobbedez T, Allard C *et al*. Hospitalization of peritoneal dialysis patients: the impact of peritonitis episodes on the hospitalization rate. *Nephrol Ther* 2006; 2: 82.86.

(180). Metcalfe W, Khan I, Prescott G *et al*. Hospitalization in the first year of renal replacement therapy for end-stage renal disease. *Q J Med* 2003; 96: 899-909.

(181). Fried L, Abidi S, Bernardini J *et al*. Hospitalization in peritoneal dialysis patients. *Am J Kidney Dis*

1999; 33: 927-933.

(182). Lee H, Manns B, Taub K, et al. Cost analysis of ongoing care of patients with end-stage renal disease: The impact of dialysis modality and dialysis access. *Am J Kidney Dis* 2002;40:611–622.

(183). Manns B, Tonelli M, Yilmaz S, et al. Establishment and maintenance of vascular access in incident hemodialysis patients: A prospective cost analysis. *J Am Soc Nephrol* 2005;16:201-209.

(184). Gruss, J. Portolés, A. Tato, et al. Repercusiones clínicas y económicas del uso de catéteres tunelizados de hemodiálisis en un área sanitária. *Nefrología* 2009;29(2):123-129.

(185). USRDS: The economic cost of ESRD, vascular access procedures, and medicare spending for alternative modalities of treatment. *Am J Kidney Dis 1997;*30:S160-S177.

(186). Bittl J. Catheter interventions for hemodialysis fistulas and grafts *J Am Coll Cardiol Intv* 2010;3:1-11.

(187). Dember L, Beck G, Allon M, et al. Effect of clopidogrel on early failure of arteriovenous fistulas for hemodialysis: a randomized controlled trial. *JAMA* 2008;299:2164 –71.

(188). Asif A, Roy-Chaudhury P, Beathard G. Early arteriovenous fistula failure: a logical proposal for when and how to intervene. *Clin J Am Soc Nephrol* 2006;1:332–9.

(189). Patel S, Hughes J, Mills J. Failure of arteriovenous fistula maturation: an unintended consequence of exceeding Dialysis Outcome Quality Initiative guidelines for hemodialysis access. *J Vasc Surg* 2003;38:439–45.

(190). Polkinghorne K. The CARI guidelines. Vascular access surveillance. *Nephrology (Carlton)* 2008; 13(Suppl 2): S1-S11.

(191). Asif A, Leon C, Orozco-Vargas L et al. Accuracy of physical examination in the detection of arteriovenous fistula stenosis. *Clin J Am Soc Nephrol* 2007; 2: 1191-1194.

(192). Leon C, Asif A. Physical examination of arteriovenous fistulae by a renal fellow: does it compare favorably to an experienced interventionalist? *Semin Dial* 2008; 21: 557-560.

(193). Campos R, Chula D, Perreto S et al. Accuracy of physical examination and intra-access pressure in the detection of stenosis in hemodialysis arteriovenous fistula. *Semin Dial* 2008; 21: 269–273.

(194). Tessitore N, Bedogna V, Melilli E, et al. In search of an optimal bedside screening program for arteriovenous fistula stenosis. *Clin J Am Soc Nephrol* 2011; 6: 819-826.

(195). Beathard G. Percutaneous transvenous angioplasty in the treatment of vascular access stenosis. *Kidney Int* 1992; 42:1390-1397.

(196). Beathard G. Mechanical versus pharmacomechanical thrombolysis for the treatment of

thrombosed dialysis access grafts. *Kidney Int* 1994; 45:1401-1406.

(197). Trerotola S, Lund G, Schell P, et al. Thrombosed dialysis access grafts: Percutaneous mechanical declotting without urokinase. *Radiology* 1994; 191:721-726.

(198). Cohen M, Kumpe D, Durham J, Zwerdlinger S. Improved treatment of thrombosed hemodialysis access sites with thrombolysis and angioplasty. *Kidney Int* 1994;46:1375–1380.

(199). Beathard G. Thrombolysis versus surgery for the treatment of thrombosed dialysis access grafts. *J Am Soc Nephrol* 1995; 6:1619–1624.

(200). Beathard G, Welch B, Maidment H. Mechanical thrombolysis for the treatment of thrombosed hemodialysis access grafts. *Radiology* 1996; 200:711–716.

(201). Trerotola S, Vesely T, Lund G, et al. Treatment of thrombosed hemodialysis access grafts: Arrow-Trerotola percutaneous thrombolytic device versus pulse-spray thrombolysis. *Radiology* 1998; 206:403–414.

(202). Turmel-Rodrigues L, Pengloan J, Baudin S, et al. Treatment of stenosis and thrombosis in haemodialysis fistulas and grafts by interventional radiology. *Nephrol Dial Transplant* 2000; 15:2029-2036.

(203). Schwab S, Raymond J, Saeed M, et al. Prevention of hemodialysis fistula thrombosis. Early detection of venous stenoses. *Kidney Int* 1989; 36: 707-711.

(204). Besarab A, Sullivan K, Ross R et al. Utility of intra-access pressure monitoring in detecting and correcting venous outlet stenoses prior to thrombosis. *Kidney Int* 1995; 47: 1364-1373.

(205). Roy-Chaudhury P, Spergel LM, Besarab A, et al. Biology of arteriovenous fistula failure. *J Nephrol* 2007;20(2):150-163.

(206). Lee T, Roy-Chaudhury P. Advances and new frontiers in the pathophysiology of venous neointimal hyperplasia and dialysis access stenosis. *Adv Chronic Kidney Dis* 2009; 16: 329-338.

(207). Lumsden A, MacDonald M, Kikeri D, et al. Prophylactic ballon angioplasty fails to prolong the patency of expanded polytetrafluoroethylene arteriovenous grafts: Results of a prospective randomized study. *J Vasc Surg* 1997; 26:382-392.

(208). Besarab A, Asif A, Roy-Chaudhury P, et al. The native arteriovenous fistula in 2007: Surveillance and monitoring. *J Nephrol* 2007;20:656-667.

(209). Allon M, Robbin M. Hemodialysis vascular access monitoring: Current concepts. *Hemodial Int* 2009; 13:153-162.

(210). Paulson W, Work J. Controversial vascular access surveillance mandate. *Semin Dial* 2010; 23 (1): 92-94.

(211). Work J. Role of Access surveillance and preemptive intervention. *Semin Vasc Surg* 2011;24:137-142.

(212). Kumbar L, Karim J, Besarab A. Surveillance and monitoring of dialysis access. *Int J Nephrol* 2012;2012:649735.

(213). Paulson W, Moist L, Lok C. Vascular access surveillance: an ongoing controversy. *Kidney Int* 2012;81:132-142.

(214). Tonelli M, Hirsch D, Clark T, et al. Access flow monitoring of patients with native vessel arteriovenous fistulae and previous angioplasty. *J Am Soc Nephrol* 2002;13:2969-2973.

(215). Schwarz C, Mitterbauer C, Boczula M, et al. Flow monitoring: Performance characteristics of ultrasound dilution versus color Doppler ultrasound compared with fistulography. *Am J Kidney Dis* 2003; 42:539-545.

(216). Tessitore N, Bedogna V, Gammaro L, et al. Diagnostic accuracy of ultrasound dilution access blood flow measurement in detecting stenosis and predicting thrombosis in native forearm arteriovenous fistulae for hemodialysis. *Am J Kidney Dis* 2003; 42:331-341.

(217). Polkinghorne K, Lau K, Saunder A, et al. Does monthly native arteriovenous fistula blood flow surveillance detect significant stenosis - a randomized controlled trial. *Nephrol Dial Transplant* 2006; 21:2498-2506.

(218). Tessitore N, Bedogna V, Lipari G et al. Bedside screening for fistula stenosis should be tailored to the site of the arteriovenous anastomosis. *Clin J Am Soc Nephrol* 2011; 6: 1073-1080.

(219). Paulson W, Ram S, Birk C et al. Does blood flow accurately predict thrombosis or failure of hemodialysis synthetic grafts? A meta-analysis. *Am J Kidney Dis* 1999; 34: 478-485.

(220). Dember L, Holmberg E, Kaufman J. Value of static venous pressure for predicting arteriovenous graft thrombosis. *Kidney Int* 2002; 61:1899-1904.

(221). McDougal G, Agarwal R. Clinical performance characteristics of hemodialysis graft monitoring. *Kidney Int* 2001; 60: 762-766.

(222). Paulson W, Ram S, Birk C et al. Accuracy of decrease in blood flow in predicting hemodialysis graft thrombosis. *Am J Kidney Dis* 2000; 35:1089-1095.

(223). Ram S, Nassar R, Work J et al. Risk of hemodialysis graft thrombosis: analysis of monthly flow surveillance. *Am J Kidney Dis* 2008; 52: 930–938.

(224). Tonelli M, Jhangri G, Hirsch D, et al. Best threshold for diagnosis of stenosis or thrombosis within six months of access flow measurement in arteriovenous fistulae. *J Am Soc Nephrol* 2003;14(12):3264-3269.

(225). Basile C, Ruggieri G, Vernaglione L, et al. The natural history of autogenous radio-cephalic wrist arteriovenous fistulas of haemodialysis patients: a prospective observational study. *Nephrol Dial Transplant* 2004;19(5):1231-1236.

(226). Safa A, Valji K, Roberts A, et al. Detection and treatment of dysfunctional hemodialysis access grafts: Effect of a surveillance program on graft patency and the incidence of thrombosis. *Radiology* 1996; 199:653-657.

(227). Allon M, Bailey R, Ballard R, et al. A multidisciplinary approach to hemodialysis access: Prospective evaluation. *Kidney Int* 1998; 53:473-479.

(228). Robbin M, Oser R, Lee J, et al. Randomized comparison of ultrasound surveillance and clinical monitoring on arteriovenous graft outcomes. *Kidney Int* 2006; 69:730-735.

(229). Dember L, Holmberg E, Kaufman J. Randomized controlled trial of prophylactic repair of hemodialysis arteriovenous graft stenosis. *Kidney Int* 2004; 66:390-398.

(230). Moist LM, Churchill DN, House AA, et al. Regular monitoring of access flow compared with monitoring of venous pressure fails to improve graft survival. *J Am Soc Nephrol* 2003; 14:2645-2653.

(231). Ram S, Work J, Caldito G, et al- A randomized controlled trial of blood flow and stenosis surveillance of hemodialysis grafts. *Kidney Int* 2003; 64:272-280.

(232). Tonelli M, James M, Wiebe N, et al. Ultrasound monitoring to detect access stenosis in hemodialysis patients: A systematic review. *Am J Kidney Dis* 2008; 51:630-640.

(233). McCarley P, Wingard RL, Shyr Y et al. Vascular access blood flow monitoring reduces access morbidity and costs. *Kidney Int* 2001;60:1164-1172.

(234). Tessitore N, Bedogna V, Poli A, et al. Adding access blood flow surveillance to clinical monitoring reduces thrombosis rates and costs, and improves fistula patency in the short term: A controlled cohort study. *Nephrol Dial Transpl* 2008;23:3578-3584.

(235). Wijnen E, Planken N, Keuter X et al. Impact of a quality improvement programme based on vascular access flow monitoring on costs, access occlusion and access failure. *Nephrol Dial Transplant* 2006;21:3514-3519.

(236). Shahin H, Reddy G, Sharafuddin M, et al. Monthly access flow monitoring with increased prophylactic angioplasty did not improve fistula patency. *Kidney Int* 2005; 68:2352-2361.

(237). Tessitore N, Mansueto G, Bedogna V et al., A prospective controlled trial on effect of percutaneous transluminal angioplasty on functioning arteriovenous fistulae survival. *J Am Soc Nephrol* 2003;14:1623-1627.

(238). Tessitore N, Lipari G, Poli A, et al. Can blood flow surveillance and pre-emptive repair of subclinical stenosis prolong the useful life of arteriovenous fistulae? A randomized controlled study. *Nephrol Dial Transplant* 2004;19:2325-2333.

(239). Chang CJ, Ko PJ, Hsu LA et al. Highly increased cell proliferation activity in the restenotic hemodialysis vascular access after percutaneous transluminal angioplasty: implication in prevention of restenosis. *Am J Kidney Dis* 2004; 43: 74-84.

(240). Bay W, Van Cleef S, Owens M. The hemodialysis access: preferences and concerns of patients, dialysis nurses and technicians, and physicians. *Am J Nephrol* 1998; 18: 379-83.

(241). Schmitz PG, MCClound LK, Reikes ST, et al. Prophylaxis of hemodialysis graft thrombosis with fish oil: double-blind, randomized, prospective trial. J Am Soc Nephrol 2002;13: 184e90.

(242). Dember L, Beck G, Allon M, et al. Effect of clopidogrel on early failure of arteriovenous fistulas for hemodialysis. *JAMA* 2008;299:2164-2171.

(243). Fiskerstrand C, Thompson I, Burnet M, et al. Double blind randomized trial of the effect of ticlodipine in arteriovenous fistulas for hemodialysis. *Artif Organs* 1985;9:61-63.

(244). Kaufman J, O'Connor T, Zhang J, et al. Randomized controlled trial of clopidogrel plus aspirin to prevent hemodialysis access graft thrombosis. *J Am Soc Nephrol* 2003;14:2313-2321.

(245). Crowther M, Clase C, Margetts P, et al. Low-intensity warfarin is ineffective for the prevention of PTFE graft failure in patients on hemodialysis: a randomized controlled trial. *J Am Soc Nephrol* 2002;13:2331-2337.

(246). Dixon B, Beck G, Vazquez M, et al., DAC Study Group. Effect of dipyridamole plus aspirin on hemodialysis graft patency. *N Engl J Med* 2009;360:2191-2201.

(247). Lok C, Moist L, Hemmelgarn B, et al. FISH study group. Effect of fish oil supplementation on graft patency and cardiovascular events among patients with new synthetic arteriovenous hemodialysis grafts: a randomized controlled trial. *JAMA* 2012;307(17): 1809-1816.

(248). Haskal Z., Trerotola S, Dolmatch B, et al. Stent graft versus balloon angioplasty for failing dialysis-access grafts. *N Engl J Med* 2010;362:494-503.

(249). Valji K, Bookstein J, Roberts A, et al. Pulse-spray pharmacomechanical thrombolysis of thrombosed hemodialysis access grafts: comparison of original and current techniques. *AJR Am J Roentgenol* 1995;165:1495-1500.

(250). Beathard G, Welch B, Maidment H. Mechanical thrombolysis for the treatment of thrombosed hemodialysis grafts. *Radiology* 1996;200:711-716.

(251). Trerotola S, Vesely T, Lung G, et al. Treatment of thrombosed hemodialysis access grafts: Arrow-Trerotola percutaneous thrombolytic device versus pulse-spray thrombolysis. *Radiology* 1998;206:403-414.

(252). Trerotola S, Lund G, Sheel P, et al. Thrombosed dialysis access grafts: percutaneous mechanical declotting without urokinase. *Radiology* 1994;191:721-726.

(253). Trerotola S, McLennan G, Davidson D, et al. Preclinical in vivo testing of the Arrow-Trerotola percutaneous thrombolytic device for venous thrombosis. *J Vasc Interv Radiol* 2001;12:95-103.

(254). Schmitz-Rode T, Wildberger JE, Hubner D, et al. Recanalization of thrombosed dialysis access with use of a rotating mini-pigtail catheter: follow-up study. *J Vasc Interv Radiol* 2000;11:721-727.

(255). Overbosch E, Pattynama P, Aarts H, et al. Occluded hemodialysis shunts: Dutch multicenter experience with the hydrolyser catheter. *Radiology* 1996;201:485-488.

(256). Rousseau H, Sapoval M, Ballini P, et al. Percutaneous recanalization of acutely thrombosed vessels by hydrodynamic thrombectomy (Hydrolyser). *Eur Radiol* 1997;7:935-941.

(257). Littler P, Cullen N, Gould D, et al. AngioJet thrombectomy for occluded dialysis fistulae: outcome data. *Cardiovasc Intervent Radiol* 2009;32:265-270.

(258). Schuman E, Quinn S, Standage B, Gross G. Thrombolysis versus thrombectomy for occluded hemodalisis grafts. *Am J Surg* 1994;167: 473-476.

(259). Vesely T, Williams D, Weiss M, et al. Comparison of the AngioJet rheolytic catheter to surgical thrombectomy for the treatment of thrombosed hemodialysis grafts. *J Vasc Interv Radiol* 1999;10:1195-1205.

(260). Uflacker R, Rajagopalan P, Vujic I, t al. Treatment of thombosed dialysis access grafts: randomized trial of surgical thrombectomy versus mechanical thrombectomy with the amplatz device. *J Vasc Interv Radiol* 1996;7:185-192.

(261). Vesely T, Idso M, Audrain J, et al. Thrombolysis versus surgical thrombectomy for the treatment of dialysis graft thrombosis: pilot study comparing costs. *J Vasc Interv Radiol* 1996;7:507-512.

(262). Dougherty M, Calligaro K, Schindler N, et al. Endovascular versus surgical treatment for thrombosed hemodialysis grafts: A prospective, randomized study. *J Vasc Surg* 1999;30:1016-1023.

(263). Marston W, Criado E, Jaques PF, et al. Prospective randomized comparison of surgical versus endovascular management of thrombosed dialysis access grafts. *J Vasc Surg* 1997;26: 373-380.

(264). Uflacker R, Rajagopalan P, Selby JB, et al. Investigators of the Clinical Trial Sponsored by

Microvena Corporation. Thrombosed dialysis access grafts: randomized comparison of the Amplatz Thrombectomy device and surgical thromboembolectomy. *Eur Radiol* 2004;14: 2009-2014.

(265). Tordoir J, Bode A, Peppelenbosch N, et al. Surgical or endovascular repair of thrombosed dialysis vascular access: Is there any evidence? *J Vasc Surg* 2009;50:953-6.

(266). Miller GA, Hwang W, Preddie D, et al. Percutaneous salvage of thrombosed immature arteriovenous fistulas. *Semin Dial* 2011;24:107-114.

(267). Vorweck D, Shurmann K, Muller-Leisse C, et al. Hemodynamic thrombectomy of haemodialysis grafts and fistulae: results of 51 procedures. *Nephrol Dial Transp* 1996;11:1058-1064.

(268). Turmel-Rodrigues L, Sapoval M, Pengloan J, et al. Manual thromboaspiration and dilation of thrombosed dialysis access: Mid-term results of a simple concept. *J Vasc Interv Radiol* 1997; 8:813-824.

(269). Turmel-Rodrigues L, Pengloan J, Rodrigue H, et al. Treatment of failed native arteriovenous fistulae for hemodialysis by interventional radiology. *Kidney Int* 2000;57:1124-1140.

(270). Moossavi S, Regan J, Pierson E, et al. Nonsurgical salvage of thrombosed arterio-venous fistulae: A case series and review of the literature. *Semin Dial* 2000;20:459-464.

(271). Haage P, Vorwerk D, Wilberger J, et al. Percutaneous treatment of thrombosed primary arteriovenous hemodialysis access fistulae. *Kidney Int* 2000;57:1169-1175.

(272). Liang H, Pan H, Chung H, et al. Restoration of thrombosed Brescia-Cimino dialysis fistulas by using percutaneous transluminal angioplasty. *Radiology* 2002;223:339-344.

(273). Rajan D, Clark T, Me S, et al. Procedural success and patency after percutaneous treatment of thrombosed autogenous arteriovenous dialysis fistulas. *J Vasc Interv Radiol* 2002;13:1211-1218.

(274). Shatsky J, Berns J, Clark T, et al. Single-center experience with the Arrow-Trerotola percutaneous thrombectomy device in the management of thrombosed native dialysis fistulas. *J Vasc Interv Radiol* 2005;16:1605–1611.

(275). Jain G, Maya I, Allon M. Outcomes of percutaneous mechanical thrombectomy of arteriovenous fistulas in hemodialysis patients. *Semin Dial* 2008;21:581-583.

(276). Rocek M, Peregrin JH, Lasovickova J, et al. Mechanical thrombolysis of thrombosed hemodialysis native fistulas with use of the Arrow-Trerotola percutaneous thrombolytic device: our preliminary experience. *J Vasc Interv Radiol* 2000;11:1153-1158.

(277). Sahni V, Kaniyur S, Malhotra A, et al. Mechanical thrombectomy of occluded hemodialysis native

fistulas and grafts using a hydrodynamic thrombectomy catheter: preliminary experience. *Cardiovasc Intervent Radiol* 2005;28:714-721.

(278). Vorwerk D, Schurmann K, Muller-Leisse C, et al. Hydrodynamic thrombectomy of haemodialysis grafts and fistulae: results of 51 procedures. *Nephrol Dial Transplant* 1996;11:1058-1064.

(279). García Medina J, Lacasa Pérez N, Muray Cases L et al. Accesos vasculares para hemodiálisis trombosados: rescate mediante técnicas de radiología vascular intervencionista. *Nefrología* 2009;29**:**249-255.

(280). Ponikvar R. Surgical salvage of thrombosed arteriovenous fistulas and grafts. *Ther Apher Dial* 2005;9:245-249.

(281). Georgiadis G, Lazarides M, Lambidis C, et al. Use of short PTFE segments (<6 cm) compares favorably with pure autologous repair in failing or thrombosed native arteriovenous fistulas. *J Vasc Surg* 2005;41:76-81.

(282). Lipari G, Tessitore N, Poli A, et al. Outcomes of surgical revision of stenosed and thrombosed forearm arteriovenous fistulae for haemodialysis. *Nephrol Dial Transplant* 2007; 22:2605-2612.

(283). Lok CE: Fistula First Initiative: advantages and pitfalls. *Clin J Am Soc Nephrol* 2007;2:1043-1053.

(284). Allon M, Daugirdas J, Depner T, et al. Effect of change in vascular access on patient mortality in hemodialysis patients. *Am J Kidney Dis* 2006;47:469-477.

# VI
# PUBLISHED ARTICLES

J Vasc Access 2013; 00 (00): 000-000
DOI: 10.5301/jva.5000141

REVIEW

# Monitoring dialysis arteriovenous fistulae: it's in our hands

**Luis Coentrão[1], Luc Turmel-Rodrigues[2]**

[1] Nephrology Research and Development Unit, Faculty of Medicine, University of Porto, Sao Joao Hospital Center Porto - Portugal
[2] Department of Cardiovascular Radiology, Clinique St-Gatien, Tours, France

**ABSTRACT**

**Vascular access problems are a daily occurrence in hemodialysis units. Loss of patency of the vascular access limits hemodialysis delivery and may result in underdialysis that leads to increased morbidity and mortality. Despite the known superiority of autogenous fistulae over grafts, autogenous fistulae also suffer from frequent development of stenosis and subsequent thrombosis. International guidelines recommend programmes for detection of stenosis and consequent correction in an attempt to reduce the rate of thrombosis. Physical examination of autogenous fistulae has recently been revisited as an important element in the assessment of stenotic lesions. Prospective observational studies have consistently demonstrated that physical examination performed by trained physicians is an accurate method for the diagnosis of fistula stenosis and, therefore, should be part of all surveillance protocols of the vascular access. However, to optimize hemodialysis access surveillance, hemodialysis practitioners may need to improve their skills in performing physical examination. The purpose of this article is to review the basics and drawbacks of physical examination for dialysis arteriovenous fistulae and to provide the reader with its diagnostic accuracy in the detection of arteriovenous fistula dysfunction, based on current published literature.**

**Key words: Arteriovenous fistulae, Dialysis, Physical examination, Vascular access**

Accepted: January 03, 2013

## INTRODUCTION

Vascular access function and patency are essential for optimal management of hemodialysis (HD) patients. Loss of patency of the vascular access limits HD delivery and may result in underdialysis that leads to increased morbidity and mortality (1-3). In both autogenous arteriovenous fistulae (AVFs) and arteriovenous grafts (AVGs), stenosis and thrombosis are the leading causes of loss of vascular access patency (1-3). Once matured, AVF provides the best access for longevity and lowest association with morbidity and mortality (1-3). Because of that, guidelines from different countries strongly recommend AVF use (1-3). In Europe, Australia and Japan, AVF is the most prevalent vascular access in HD patients (4). As the result of recommendations of the Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines (1), AVF prevalence has increased in the United States in the last decade (5). Despite this known superiority over AVGs, AVFs also suffer from development of stenosis and thrombosis. Although hard evidence is lacking from prospective studies demonstrating higher AVF long-term survival within quality improvement programs based on vascular access monitoring and surveillance (6-10), international guidelines (1-3) recommend programmes for detection of stenosis and correction in an attempt to reduce the rate of thrombosis. Furthermore, there have been no large-scale trials to determine whether correction of only "hemodynamically" significant lesions is superior to correction of all stenoses greater than 50%.

The basic tenet for vascular access monitoring and surveillance is that stenoses develop over variable intervals in the vast majority of vascular accesses and, if detected and corrected, underdialysis can be minimized or avoided and the rate of thrombosis can be reduced (1). The K/DOQI guidelines (1) have settled the following concepts for the detection of vascular access dysfunction: a) *monitoring* refers to the examination and assessment of the vascular access by means of physical examination (…) and; b) *surveillance* refers to the periodic assessment of the vascular access by using tests that may involve special instrumentation (…). It is important to emphasize that *surveillance* and *monitoring* are complementary. Several diagnostic procedures have been recommended for vascular access surveillance, including duplex-ultrasound, blood flow, intra-access static pressure and access

recirculation (1, 2). However, these procedures are time consuming and have a cost. Recently, Bonforte et al (11) analyzed the results of an application of a new zero-cost screening test, called "QB stress test", created to select, together with clinical assessment, the group of low-flow AVFs to refer to more detailed and specific study techniques. The authors demonstrated that this test is simple, low-cost, not operator-dependent and could be a useful tool to identify the group of patients with malfunctioning AVFs, with stenosis located specifically in the inflow tract. Physical examination (PE) of AVFs performed by trained physicians has recently been revisited as an important element in the assessment of stenotic lesions (12-17). In addition, PE is a reliable method to perform several other diagnoses such as, thrombosis, infection, skin necrosis and vascular steal syndrome. It must be performed not only in those patients on hemodialysis but also in those with chronic kidney disease (CKD) stage 4-5 in whom an AVF has been created in preparation for dialysis (18).

The purpose of this article is to review the basics and drawbacks of PE for dialysis AVFs and to provide the reader with its diagnostic accuracy in the detection of AVF dysfunction, based on current published literature.

## BASIC PHYSICS

Normal hemodynamics and the effects of stenosis on hemodynamics of the vascular access have been well reported in the K/DOQI guidelines (1) and concise textbooks (19, 20). Knowledge on the basic physics of the vascular access is a relevant issue for clinicians since the clinical signs suggestive of access dysfunction are the consequence of abnormal hemodynamics of the vascular access.

Flow in the access is directly related to the patient's blood pressure and inversely proportional to the resistance of the access flow circuit. When the blood flows through the access, the energy of the arterial inflow runs into a lower resistance system. The blood pressure drop causes vibration of the tissues, creating a palpable thrill. Flow can be assessed by palpation of the thrill along the entire circuit. Similarly, abnormal increase in pressure can be assessed by noting water-hammer pulsatility (21).

The driving force for access flow is the pressure gradient between the feeding artery and the right atrium (1, 20). The major determinant of access flow is the capacity of the artery and of the arterialized vein to enlarge, which is dependent on their general healthy condition. Therefore, access flow rates of AVGs are limited by the flat size of grafts whereas AVFs may develop much higher flow rates because of the capacity of enlargement of healthy veins. The rate of maturation and the pressure profile also differ in the two access types (1). Grafts attain their maximum flow rate in a period of days to weeks, as opposed to AVFs, which may require weeks to months to mature. The pressure profile in AVGs progressively decreases along the length of the graft whereas, in AVFs, the arterial pressure is dissipated within the first few centimeters of the arterialized vein (except in cases of hyper flow fistulas). Vascular resistance of AVFs is lower than in AVGs, mainly because of the vasoactive properties associated with an intact venous endothelium and in part because of the potential multiple parallel venous pathways returning blood to the central venous system. As a consequence, AVGs work with higher intra-access pressure to maintain flows of 1 L/min or more, compared to AVFs. In other words, patency of AVGs depends on higher flow rates than AVFs (20).

The ideal vascular access flow is the one necessary to provide long-term access patency with no steal syndrome or heart consequence. Therefore, the AVF's flow should be considered in relation to cardiac output, with an assessment of the ratio access flow/cardiac output: a ratio >20% should lead to suspicion of high flow. For AVFs, values of 600 to 800 mL per minute have been proposed as the "ideal" access flow since it is sufficient to provide AVF long-term patency with an access flow/cardiac output ratio <20%. Turbulence associated with high volumes, typically from 500 to 1500 mL per minute, generates the thrill we feel. It is assumed that AVFs flows >2000 mL per minute are susceptible to increased cardiac workload and further development of heart failure (19).

The development of stenoses results in a reduction in access flow rate in both AVGs and AVFs (20). However, the effect on intra-access pressure differs according to access type and site of stenosis. In AVGs, an outflow stenosis will increase the pressure in all locations upstream from the stenosis whereas, in AVFs, the pressure profile will depend on the presence/absence of venous tributaries. Conversely, the presence of an inflow stenosis in AVGs will decrease all pressures downstream of the stenosis whereas, in AVFs, intra-access pressure tends to remain unchanged because of a basically low pressure profile.

In summary, vascular access hemodynamics provide the rationale for observational clinical studies (1, 22-24) showing that: (a) PE findings differ between AVFs and AVGs; (b) AVFs can maintain long-term patency at access flows lower than those in AVGs; (c) access recirculation may develop in half of the AVFs that require intervention because of very low flow, whereas in AVGs it is a very late indicator of access dysfunction.

## PHYSICAL EXAMINATION: BASICS AND DRAWBACKS

### *Basics*

The standards of PE of the dialysis vascular access have been reported in detail by Beathard (25-27). In this article, the basic PE technique for dialysis AVF will be briefly reviewed, while depicting some pitfalls com-

monly presented to HD practitioners in daily clinical practice.

Physical examination of the AVF implies the use of inspection, palpation and auscultation. Thrill and pulse abnormalities felt throughout the entire fistula tract are used as the main PE tools for the diagnosis of AVF dysfunction. In addition, the patient's arm, chest, neck and face should be assessed for the presence of swelling or collateral veins. Patients should be asked about symptoms related to the AVF. Normally, the patient with a functioning AVF should be without complaints (namely pain at rest, paresthesia or weakness). At inspection, no arm or face edema or collateral veins should be observed. The hand should be well perfused. The AVF has a soft appearance and the entire structure is easily compressed. A palpable continuous thrill is felt through the first centimeters of the vein, with higher intensity at the anastomosis. It has been suggested that a palpable thrill at the arterial, middle, and venous segments of the access predicts flows greater than 450 mL per minute and if present in the axilla may correlate with a flow of at least 500 mL per minute (28, 29). A low pitch, continuous bruit is auscultated throughout the venous tract. When the extremity is elevated, the entire arterialized vein will generally collapse (arm elevation test). When the AVF is compressed, the portion of the vein upstream from the occluding finger demonstrates augmentation of pulse (pulse augmentation test). This pulse augmentation is nevertheless weakened when tributaries leave the main vein between the anastomosis and the compressed area. Under normal circumstances, this simple examination should take no more than three minutes.

Fistulae that never develop adequately for use or those that fail within the first three months of use are classified as early failures. The most common cause of early fistula failure is the presence of a juxta-anastomotic venous stenosis. This lesion can be easily diagnosed by palpation of the anastomosis and outflow vein. A water-hammer pulse is felt at the anastomosis and the thrill is present only in systole. As one moves up the vein the pulse goes away and the vein is poorly developed. The stenosis itself can frequently be felt as a tough cord or an abrupt diminution in the size of the vein. However, it may be impossible to differentiate a stenosis of the anastomosis itself from a stenosis of the feeding artery.

Once the AVF is functional, the most common problems are venous stenosis and thrombosis. Other less frequent complications diagnosed by PE are hand ischemia, aneurysm formation, skin alterations and infection. Venous stenosis is such a common event that many HD practitioners do not recognize these changes as being abnormal. Inflow segment is defined as the feeding artery, anastomosis and the juxta-anastomotic area (first few centimeters of the arterialized vein) upstream from the "arterial" needling site. Outflow segment comprises the body of the vein, the axillary, subclavian and central veins. Body of the fistula is considered to be the cannulation segment extending downstream from the anastomotic area. The diagnostic elements of PE used in the assessment of an inflow stenosis, outflow stenosis, coexisting inflow-outflow stenosis and thrombosis are presented in Table I.

Fistula thrombosis is a clinical diagnosis characterized by undetectable flow by physical examination. Fistula infection and thrombosis (phlebitis) sometimes share similar clinical findings (erythema, warmth, swelling and pain) but require distinct therapeutic approaches. The differential diagnosis between these two entities is therefore essential. Physical examination findings of fluctuation and purulent discharge are diagnostic of the very rare true AVF infection. Conversely, the absence of aspiration of blood or the removal of clots after venous cannulation is highly suggestive of AVF thrombosis.

Distal hypoperfusion ischemic syndrome (30) occurs when the arterial supply to the hand has become insufficient because of pre-existing arterial lesions rendered symptomatic by the blood derived from the feeding artery through the fistula or because of excessive fistula blood flow. In most patients the enlargement of the feeding arteries and the development of collaterals after AVF creation are sufficient to maintain sufficient perfusion to the hand. Physical findings are quite variable; in most instances,

**TABLE I -** DIAGNOSTIC ELEMENTS OF THE PHYSICAL EXAMINATION USED IN THE ASSESSMENT OF AUTOGENOUS ARTERIOVENOUS FISTULA DYSFUNCTION

| | Thrill | Pulse | Arm elevation test | Pulse augmentation test |
|---|---|---|---|---|
| Inflow stenosis | Weak, systolic | Weak | Excessive collapse | Weak |
| Outflow stenosis | | | | |
| Body of fistula | Systolic | Strong | No partial vein collapse | n.a. |
| Cephalic arch stenosis | Systolic | Very strong | No partial vein collapse | n.a. |
| Central vein stenosis | Systolic or normal | Strong or normal | No or modest partial vein collapse* | n.a. |
| Coexisting inflow-outflow stenoses | Weak, systolic | Normal | No or modest partial vein collapse | Weak |

n.a., not applicable.
*Edema of the arm and shoulder; breast, supraclavicular, neck, and face swelling may be present as well in brachial-cephalic fistulae only.

it is helpful to compare the affected side to the opposite normal side. The affected hand may be pale or cyanotic in appearance; it feels cold and has a diminished ulnar and/or radial pulse. In severe cases, the patient complains of paresthesia, weakness or pain at rest. Evidence of ischemic changes in the skin may be present.

When the patient complains of severe weakness of the hand and rest pain immediately after fistula creation, while the hand appears warm and well perfused, the diagnosis of ischemic monomelic neuropathy should be recognized since urgent fistula ligation is warranted. This is a typical complication of elbow accesses in diabetic patients.

Aneurysm formation may indicate high chronic intra-access pressures that require study and decompression via outflow stenosis angioplasty. More often, they result from slow chronic enlargement secondary to thinning of skin by repeated needling on the same site. Assessing the pulsatility of the access on PE will help sort out the different scenarios.

## *Drawbacks*

### *Vein collaterals*

The presence of cephalic vein side branches are considered by some experts as the second most common cause of early fistula failure (referred to as accessory veins) (26), while others consider them a consequence of the presence of a venous stenosis in the ouflow tract (referred to as vein collaterals) (31). Regardless of the cause, these AVFs behave weirdly in the hands of an inexperience examiner. The vast majority of these AVFs are forearm fistulae. Vein collaterals can be identified easily through PE. Frequently, they are visible, while the main branch (usually the cephalic vein) is not easily recognized. When the extremity is elevated, the entire fistula will partially collapse. During the pulse augmentation test, the thrill does not disappears and the pulse does not increase its intensity (because of the presence of drainage through vein collaterals). In this particular case, the aim of the PE is to: (a) identify the main drainage vein; (b) identify the venous stenosis, to further guide the endovascular approach.

### *High flow fistulae*

High flow fistulae share some of the PE findings of AVFs with outflow stenosis. The pulse is strong and the vein may not collapse during the arm elevation test. The body of the AVF is large and may present aneurismal formations. This is even more evident in high flow AVFs with non-significant outflow stenosis. One way to solve this problem is to assess the AVF thrill in detail: continuous, systolo-diastolic thrill, in high flow AVF *versus* discontinuous, systolic thrill, in AVFs with outflow lesions. The differential diagnosis is relevant since the therapeutic approaches of these AVFs are distinct.

### *Coexistent venous outlet stenoses*

The coexistence of two or more venous stenoses may preclude the development of clinical signs suggestive of the presence of the more central lesion. The most typical situation is the coexistence of stenoses in the body of the fistula and in a central vein – the more peripheral stenosis may prevent downstream flow to the degree that the central venous stenosis symptoms might be masked. The diagnosis of the central vein lesion is most commonly performed during angiography, raising some doubts regarding the best therapeutic approach.

### *Side-to-side upper-arm fistulae*

Physical examination of side-to-side upper-arm fistulae (Gracz fistula) is a clinical challenge because the presence of venous drainage through vein collaterals (e.g. cephalic, basilic and deep veins) may preclude the development of characteristic PE signs of a stenosis. Usually, it is necessary to manually occlude one vein in order to detect the presence of an outflow stenosis on the other.

### *Transposed brachio-basilic fistulae*

Occasionally, in upper-arm AVFs, there is spontaneous or deliberated occlusion of side branches (as with transposition) and, as a consequence, outflow lesions produce a pressure profile and PE findings very similar to that of AVGs. The AVF turns out to be highly pulsatile and exceedingly thrombogenic.

## DIAGNOSTIC ACCURACY OF PHYSICAL EXAMINATION

Citing Beathard (25) in one of his seminal papers "In this search for the "Holy Grail," the oldest and most time-honored investigative tool available to the diagnostician has been largely ignored: the laying on of hands, i.e., physical examination." In the last decade, PE re-emerged as an important element in the assessment of stenotic lesions; its accuracy in the assessment of stenosis within an AVF when compared with the gold standard (angiography or Doppler ultrasound) has been recently assessed (Tab. II) (12-17). However, it is essential to point out that a dysfunctional vascular access is not only defined by the presence of a significant stenosis (reduction greater than 50% of normal vessel diameter) and that it should not be repaired merely because they are present. Stenosis must be accompanied by a hemodynamic or clinical abnormality. International guidelines (1-3) do not recommend the use of angiography for detecting anatomic stenosis alone, without concomitant measurement of access flow, venous pressure, recirculation, or other physiologic parameters. In other words, when PE suggests the presence of a stenosis, there is no indication

for angiography and treatment unless the stenosis has clinical consequences (e.g. underdialysis, recirculation, increased compression times, difficulties in cannulation) or threatens access patency by excessive decrease in flow rate. For example, moderate arm edema and presence of neck collaterals indicate the likely presence of a central vein stenosis but this stenosis should be treated only in cases of major clinical impairment (32).

To the best of our knowledge, Asif et al (12) was one of the first authors to determine the PE accuracy in the assessment of stenosis within an AVF when compared with the gold standard (angiography). A total of 142 consecutive patients who had AVF dysfunction and were referred for angioplasty were included in this analysis. A complete PE was performed by an interventional nephrologist in all of the patients before any angiography was undertaken. The following locations of the stenoses were determined by PE and angiography: outflow tract, inflow segment, coexisting inflow-outflow stenosis, body of fistula and central veins. There was a moderate-to-strong agreement between PE and angiography in the diagnosis of outflow and inflow stenosis. The findings of this study demonstrated that PE can be an important tool in the diagnosis and localization of an AVF stenosis. A similar study was published by Leon et al (13). The aim of this study was to examine the accuracy of PE of AVF stenosis by a renal fellow in training and to compare them with those of an interventional nephrologist. The findings of this study demonstrated that a renal fellow could be trained in PE and accurately detect and localize stenoses in a vast majority of AVFs with comparable results favorably to those obtained by a nephrologist with expertise in PE. More recently, the PE findings obtained by nephrologists without specific training on fistula PE were compared to those from a nephrology resident trained in vascular access PE (17). Angiography was used as the gold standard examination. A total of 177 consecutive patients who had AVF dysfunction and were referred for angioplasty were included in this analysis. The main findings of this study were: PE performed by the trained nephrology resident strongly agreed with angiography in the detection of AVF inflow and outflow stenosis, whereas there was a moderate agreement between the general nephrologists' PE and angiography in the detection of the same lesions. It is important to emphasize that, in both Asif et al (12) and Leon et al (13) studies, the investigators divided the outflow tract into three different segments: body of the fistula, outflow and central vein stenosis, whereas in this study (17) the authors considered the outflow tract as the entire segment from the anastomosis area to the right atrium. This broad classification of the location of the stenoses within the AVF probably accounts for the slightly better results reported herein.

Two further studies assessed the accuracy of PE in the detection of AVF stenosis (14, 16). Campos et al (14) and Tessitore et al (16) included unselected populations of consecutive prevalent patients with AVFs attending a hemodialysis unit. Physical examination was performed by nephrologists with expertise in PE. The gold standard examinations were Doppler Ultrasound (14) and angiography (16), respectively. Both studies concluded that PE was an accurate method for the diagnosis of stenosis and should be part of all surveillance protocols of stenosis detection in AVF.

As important as accuracy of a method is, the goal of any monitoring or surveillance method is to detect

**TABLE II** - DIAGNOSTIC ACCURACY OF PHYSICAL EXAMINATION IN THE DETECTION OF ARTERIOVENOUS FISTULA STENOSIS

| | Design study | N | Gold standard | Location of stenosis | Sensitivity | Specificity | Cohen K |
|---|---|---|---|---|---|---|---|
| Asif et al (12) | Prospective, observational | 142 | Angiography | Inflow | 85% | 71% | 0.55 |
| | | | | Outflow | 92% | 86% | 0.78 |
| | | | | Overall | - | - | - |
| Leon et al (13) | Prospective, observational | 45 | Angiography | Inflow | 100% | 78% | 0.56 |
| | | | | Outflow | 76% | 68% | 0.63 |
| | | | | Overall | - | - | - |
| Campos et al (14) | Prospective, observational | 84 | DDU | Inflow | - | - | - |
| | | | | Outflow | - | - | - |
| | | | | Overall | 96% | 76% | - |
| Tessitore et al (15) | Prospective, observational | 119 | Angiography | Inflow | 70% | 76% | 0.46 |
| | | | | Outflow | 75% | 93% | 0.63 |
| | | | | Overall | - | - | - |
| Coentrao et al (17) | Prospective, observational | 177 | Angiography | Inflow | 98% | 88% | 0.84 |
| | | | | Outflow | 97% | 92% | 0.92 |
| | | | | Overall | - | - | 0.86 |

DDU, Duplex Doppler Ultrasound.

access stenosis in a timely way so that appropriate correction can be undertaken before thrombosis and vascular access loss. Therefore, multidisciplinary vascular access teams are required to improve vascular access outcomes. These include the presence of nephrologists, interventional nephrologists or radiologists, surgeons and dialysis nurses. Similarly, as in advance life support for critically ill patients, the term *Chain of Survival* provides a useful metaphor for the elements of the vascular access teams' concept. The five links in the hemodialysis access *Chain of Survival* would be: (a) permanent vascular access planning; (b) appropriate cannulation of AVFs and AVGs; (c) detection of access dysfunction; (d) treatment of dialysis access dysfunction and; (e) integrated post-intervention dialysis access monitoring and surveillance. It is easily perceptible that monitoring and surveillance methods would play a crucial role in this *Chain of Survival*. However, if we aim to prolong the survival of vascular access, in addition to avoid its failure, measures need to be taken carefully (33). In the last two decades, observational studies and single-center randomized trials suggested that surveillance of AVFs coupled with appropriate treatment, prolonged access survival (6-10). Unfortunately, the same did not happen in the case of AVGs (34-41). Although the results of observational studies would suggest that elective correction of stenoses before thrombosis might increase the long-term survival of the AVG (at the expense of increased procedures), recent randomized trials showed that prophylatic treatment of stenoses, although reducing thrombosis events, did not extend the useful life span of AVG rates.

## CONCLUSIONS

In summary, in the last decade several reports regarding the use of PE in the detection of AVF dysfunction (stenosis and/or thrombosis) observed that PE of AVFs is easily performed, inexpensive and provides a high level of accuracy to the physician who understands its principles. Cumulative evidence has demonstrated that adding surveillance methods to clinical monitoring, coupled with appropriate treatment, reduce thrombosis rates and may prolong AVF survival. However, as previously stated in the K/DOQI guidelines (1) *"(…) the basic skills have been largely abandoned in favor of technology and need to be taught to all individuals who perform hemodialysis procedures"*. If our aim is to optimize the hemodialysis access *Chain of Survival*, nephrologists in hemodialysis units may need to improve their skills in performing PE. Theoretical and hands-on training in PE should therefore be provided for nephrologists in-training and for the dialysis staff.

**Financial support:** None.

**Conflict of interest:** None.

Address for correspondence:
Luis Coentrão
Nephrology Research and Development Unit
Faculty of Medicine, University of Porto
Al. Prof. Hernâni Monteiro
4200 - 319 Porto, Portugal
coentrao@med.up.pt

## REFERENCES

1. KDOQI. Clinical practice guidelines and clinical practice recommendations for vascular access. Am J Kidney Dis. 2006;48:S176-S247.
2. Tordoir J, Canaud B, Haage P, et al. EBPG on vascular access. Nephrol Dial Transplant. 2007;22(Suppl 2):ii88-ii117.
3. Ethier JH, Lindsay RM, Barre PE, Kappel JE, Carlisle EJ, Common A; Canadian Society of Nephrology. Clinical practice guidelines for vascular access. Canadian Society pf Nephrology. J Am Soc Nephrol. 1999;10(Suppl 13): S297-S305.
4. Ethier J, Mendelssohn DC, Elder SJ, et al. Vascular access use and outcomes: an international perspective from the Dialysis Outcomes and Practice Patterns Study. Nephrol Dial Transplant. 2008;23(10):3219-3226.
5. Lok CE. Fistula first initiative: advantages and pitfalls. Clin J Am Soc Nephrol. 2007;2(5):1043-1053.
6. Tessitore N, Bedogna V, Poli A, et al. Adding access blood flow surveillance to clinical monitoring reduces thrombosis rates and costs, and improves fistula patency in the short term: a controlled cohort study. Nephrol Dial Transplant. 2008;23(11):3578-3584.
7. McCarley P, Wingard RL, Shyr Y, Pettus W, Hakim RM, Ikizler TA. Vascular access blood flow monitoring reduces access morbidity and costs. Kidney Int. 2001;60(3): 1164-1172.
8. Wijnen E, Planken N, Keuter X, et al. Impact of a quality improvement programme based on vascular access flow monitoring on costs, access occlusion and access failure. Nephrol Dial Transplant. 2006;21(12):3514-3519.
9. Tessitore N, Mansueto G, Bedogna V, et al. A prospective controlled trial on effect of percutaneous transluminal angioplasty on functioning arteriovenous fistulae survival. J Am Soc Nephrol. 2003;14(6):1623-1627.
10. Tessitore N, Lipari G, Poli A, et al. Can blood flow surveillance and pre-emptive repair of subclinical stenosis prolong the useful life of arteriovenous fistulae? A randomized controlled study. Nephrol Dial Transplant. 2004;19(9): 2325-2333.

11. Bonforte G, Pogliani D, Brenna S, et al. Validation of QB stress test as a useful tool in the detection of native arteriovenous fistula stenosis: results after 22 months of follow-up. Nephrol Dial Transplant. 2010;25(6):1943-1949.
12. Asif A, Leon C, Orozco-Vargas LC, et al. Accuracy of physical examination in the detection of arteriovenous fistula stenosis. Clin J Am Soc Nephrol. 2007;2(6):1191-1194.
13. Leon C, Asif A. Physical examination of arteriovenous fistulae by a renal fellow: does it compare favorably to an experienced interventionalist? Semin Dial. 2008;21(6):557-560.
14. Campos RP, Chula DC, Perreto S, Riella MC, do Nascimento MM. Accuracy of physical examination and intra-access pressure in the detection of stenosis in hemodialysis arteriovenous fistula. Semin Dial. 2008;21(3):269-273.
15. Tessitore N, Bedogna V, Lipari G, et al. Bedside screening for fistula stenosis should be tailored to the site of the arteriovenous anastomosis. Clin J Am Soc Nephrol. 2011;6(5):1073-1080.
16. Tessitore N, Bedogna V, Melilli E, et al. In search of an optimal bedside screening program for arteriovenous fistula stenosis. Clin J Am Soc Nephrol. 2011;6(4):819-826.
17. Coentrão L, Faria B, Pestana M. Physical examination of dysfunctional arteriovenous fistulae by non-interventionalists: a skill worth teaching. Nephrol Dial Transplant. 2012;27(5):1993-1996.
18. Besarab A, Asif A, Roy-Chaudhury P, Spergel LM, Ravani P. The native arteriovenous fistula in 2007. Surveillance and monitoring. J Nephrol. 2007;20(6):656-667.
19. Basile C, Lomonte C, Vernaglione L, Casucci F, Antonelli M, Losurdo N. The relationship between the flow of arteriovenous fistula and cardiac output in haemodialysis patients. Nephrol Dial Transplant. 2008;23(1):282-287.
20. Besarab A, Frinak S, Aslam MA. Pressure measurements in the surveillance of vascular accesses. In Gray RJ, Sands JJ, eds. Dialysis Access: A Multidisciplinary Approach. Philadelphia, PA: Lippincott Williams & Wilkins, 2002;137-150.
21. Gelbfish GA. Clinical surveillance and monitoring of arteriovenous access for hemodialysis. Tech Vasc Interv Radiol. 2008;11(3):156-166.
22. Lindsay RM, Blake PG, Malek P, Posen G, Martin B, Bradfield E. Hemodialysis access blood flow rates can be measured by a differential conductivity technique and are predictive of access clotting. Am J Kidney Dis. 1997;30(4):475-482.
23. May RE, Himmelfarb J, Yenicesu M, et al. Predictive measures of vascular access thrombosis - a prospective study. Kidney Int. 1997;52(6):1652-1662.
24. Wang E, Schneditz D, Nepomuceno C, et al. Predictive values of access blood flow in detecting failure of vascular access. ASAIO J. 1998;44:554-557.
25. Beathard GA. Physical examination of the dialysis vascular access. Semin Dial. 1998;11(4):231-236.
26. Beathard GA. An algorithm for the physical examination of early fistula failure. Semin Dial. 2005;18(4):331-335.
27. Beathard GA. Physical examination: the forgotten tool. In Gray RJ, Sands JJ, eds. Dialysis Access: A Multidisciplinary Approach. Philadelphia, PA: Lippincott Williams & Wilkins, 2002;111-118.
28. Trerotola SO, Scheel PJ Jr, Powe NR, et al. Screening for dialysis access graft malfunction: comparison of physical examination with US. J Vasc Interv Radiol. 1996;7(1):15-20.
29. Agarwal R, McDougal G. Buzz in the axilla: a new physical sign in hemodialysis forearm graft evaluation. Am J Kidney Dis. 2001;38(4):853-857.
30. Leon C, Asif A. Arteriovenous access and hand pain: the distal hypoperfusion ischemic syndrome. Clin J Am Soc Nephrol. 2007;2(1):175-183.
31. Turmel-Rodrigues L, Mouton A, Birmelé B, et al. Salvage of immature forearm fistulas for haemodialysis by interventional radiology. Nephrol Dial Transplant. 2001;16(12):2365-2371.
32. Renaud CJ, Francois M, Nony A, Fodil-Cherif M, Turmel-Rodrigues L. Comparative outcomes of treated symptomatic versus non-treated asymptomatic high-grade central vein stenoses in the outflow of predominantly dialysis fistulas. Nephrol Dial Transplant. 2012;27(4):1631-1638.
33. Besarab A, Ravani P, Spergel LM, Roy-Chaudhury P, Asif A. The native arteriovenous fistula in 2007. Research needs. J Nephrol. 2007;20(6):668-673.
34. Schwab SJ, Raymond JR, Saeed M, Newman GE, Dennis PA, Bollinger RR. Prevention of hemodialysis fistula thrombosis. Early detection of venous stenoses. Kidney Int. 1989;36(4):707-711.
35. Besarab A, Sullivan KL, Ross RP, Moritz MJ. Utility of intra-access pressure monitoring in detecting and correcting venous outlet stenoses prior to thrombosis. Kidney Int. 1995;47(5):1364-1373.
36. Sands JJ, Miranda CL. Prolongation of hemodialysis access survival with elective revision. Clin Nephrol. 1995;44(5):329-333.
37. Lumsden AB, MacDonald MJ, Kikeri D, Cotsonis GA, Harker LA, Martin LG. Prophylactic balloon angioplasty fails to prolong the patency of expanded polytetrafluoroethylene arteriovenous grafts: results of a prospective randomized study. J Vasc Surg. 1997;26(3):382-390, discussion 390-392.
38. Ram SJ, Work J, Caldito GC, Eason JM, Pervez A, Paulson WD. A randomized controlled trial of blood flow and stenosis surveillance of hemodialysis grafts. Kidney Int. 2003;64(1):272-280.
39. Moist LM, Churchill DN, House AA, et al. Regular monitoring of access flow compared with monitoring of venous pressure fails to improve graft survival. J Am Soc Nephrol. 2003;14(10):2545-2653.
40. Dember LM, Holmberg EF, Kaufman JS. Randomized controlled trial of prophylactic repair of hemodialysis arteriovenous graft stenosis. Kidney Int. 2004;66(1):390-398.
41. Robbin ML, Oser RF, Lee JY, Heudebert GR, Mennemeyer ST, Allon M. Randomized comparison of ultrasound surveillance and clinical monitoring on arteriovenous graft outcomes. Kidney Int. 2006;69(4):730-735.


 

Coentrão *et al. BMC Nephrology* 2012, **13**:88
http://www.biomedcentral.com/1471-2369/13/88

BMC Nephrology

RESEARCH ARTICLE Open Access

# Effects of starting hemodialysis with an arteriovenous fistula or central venous catheter compared with peritoneal dialysis: a retrospective cohort study

Luis Coentrão[1*], Carla Santos-Araújo[1], Claudia Dias[2], Ricardo Neto[1] and Manuel Pestana[1]

**Abstract**

**Background:** Although several studies have demonstrated early survival advantages with peritoneal dialysis (PD) over hemodialysis (HD), the reason for the excess mortality observed among incident HD patients remains to be established, to our knowledge. This study explores the relationship between mortality and dialysis modality, focusing on the role of HD vascular access type at the time of dialysis initiation.

**Methods:** A retrospective cohort study was performed among local adult chronic kidney disease patients who consecutively initiated PD and HD with a tunneled cuffed venous catheter (HD-TCC) or a functional arteriovenous fistula (HD-AVF) in our institution in the year 2008. A total of 152 patients were included in the final analysis (HD-AVF, n = 59; HD-TCC, n = 51; PD, n = 42). All cause and dialysis access-related morbidity/mortality were evaluated at one year. Univariate and multivariate analysis were used to compare the survival of PD patients with those who initiated HD with an AVF or with a TCC.

**Results:** Compared with PD patients, both HD-AVF and HD-TCC patients were more likely to be older ($p<0.001$) and to have a higher frequency of diabetes mellitus ($p = 0.017$) and cardiovascular disease ($p = 0.020$). Overall, HD-TCC patients were more likely to have clinical visits ($p = 0.069$), emergency room visits ($p<0.001$) and hospital admissions ($p<0.001$). At the end of follow-up, HD-TCC patients had a higher rate of dialysis access-related complications (1.53 *vs.* 0.93 *vs.* 0.64, per patient-year; $p<0.001$) and hospitalizations (0.47 *vs.* 0.07 *vs.* 0.14, per patient-year; $p = 0.034$) than HD-AVF and PD patients, respectively. The survival rates at one year were 96.6%, 74.5% and 97.6% for HD-AVF, HD-TCC and PD groups, respectively ($p<0.001$). In multivariate analysis, HD-TCC use at the time of dialysis initiation was the important factor associated with death (HR 16.128, 95%CI [1.431-181.778], $p = 0.024$).

**Conclusion:** Our results suggest that HD vascular access type at the time of renal replacement therapy initiation is an important modifier of the relationship between dialysis modality and survival among incident dialysis patients.

## Background

Early referral of chronic kidney disease (CKD) patients to nephrology centres may enable patients to be adequately informed regarding the different renal replacement treatment (RRT) modalities [hemodialysis (HD), peritoneal dialysis (PD) and kidney transplantation (TX)], leading to better results in terms of morbidity and mortality [1-4]. Large registry-based studies have suggested a survival advantage of PD over HD, particularly during the first 1 to 2 years of treatment [5,6]. Although the ability of PD to provide better preservation of residual renal function was invoked as a possible explanation for the survival advantage of PD over HD during the first years of treatment, case mix differences in patients initiating HD may have confounded the interpretation of the studies that examined the influence of the dialysis modality on patient survival [5-7].

* Correspondence: coentrao@med.up.pt
[1]Nephrology Research and Development Unit, Faculty of Medicine, University of Porto & São João Hospital Centre, Alameda Professor Hernani Monteiro, Porto 4202-451, Portugal
Full list of author information is available at the end of the article

The type of vascular access used in HD patients is recognized to have a significant influence on survival. The use of a tunneled cuffed catheter (TCC) is associated with a substantially greater risk of sepsis, hospitalization and mortality compared to the use of an arteriovenous fistula (AVF) [8-12]. Although technique survival with PD is shorter than that with HD, in part due to access-related infections, the frequency of PD catheter-related complications has decreased in recent years, with a low rate of bacteremia/sepsis [13,14]. However, there are few studies comparing the outcomes of incident PD patients with those of HD patients using different vascular access types at dialysis initiation in the literature, to our knowledge [15,16]. In the study presented here, we hypothesize that vascular access type at the time of dialysis initiation accounts for the higher early mortality rate observed in patients who start HD with a catheter, compared to those who initiate HD with a functioning fistula or PD. To test our hypothesis, we compared all-cause and dialysis access-related morbidity/mortality between PD and HD patients with the latter stratified by HD vascular access type at dialysis initiation.

## Methods

### Study design

We conducted a retrospective observational cohort study among CKD patients (age 18 years and older at the start of RRT) who consecutively initiated HD between January 1 and July 1 2008, or PD between January 1, 2008 and July 1, 2009, in our institution.

The study was approved by the Ethics Committee for Health and the Local Institutional Review Board of São João Hospital Centre, Porto, Portugal.

### Setting

Portugal has a higher incidence of end stage-renal disease, ESRD (i.e. the patients who start any RRT modality for the first time) and prevalence in compared to most of other European countries. In 2009, an incidence rate of 240 and a prevalence of 1507 patients per million of the population were registered in ERA-EDTA [17]. Specifically, 10,152 patients underwent HD and 660 patients PD in 2010 (registered by the Portuguese Society of Nephrology). In Portugal, HD is almost exclusively (~90%) provided by outpatient hemodialysis units run by private providers. Hemodialysis patients undergo 4 hours of dialysis three times weekly, aiming for a spKt/V of 1.4 or greater. Patients undergo treatment using high-flux dialyzers; no hemodialyzer is reused. Peritoneal dialysis is provided by public hospitals and university centres. Patients attending our hospital center undergo either continuous ambulatory peritoneal dialysis (CAPD) or automated cyclic peritoneal dialysis (CCPD). All patients have a 1 to 2 week training period before initiation of therapy at home. Treatment of PD patients is individualized: the total Kt/V (renal and peritoneal clearance) aimed for is 1.8 or more and the majority of patients are treated with dextrose-based solutions with daily exchange with Extraneal (Baxter Healthcare Corp, Deerfield, IL, USA).

### Patients

The patients were recruited from the Department of Nephrology of São João Hospital Centre which is a tertiary-care University Hospital responsible for nephrological medical support to ESRD patients beginning RRT within the northwest region of Portugal. Patients were enrolled if they had a diagnosis of end-stage CKD according to a nephrologist and had received outpatient chronic dialysis treatment. Patients who had previously undergone RRT (HD, PD or TX) and restarted during the study period and patients transferred to another district immediately after starting RRT were excluded. The RRT modality adopted was based on patient choice and his/her medical status. Initial dialysis modality was defined as the modality at the first outpatient dialysis treatment: patients starting PD therapy assigned to the PD group and patients starting HD therapy with a tunnelled cuffed catheter or a functioning fistula to the HD-TCC or HD-AVF groups, respectively. Although changes in vascular access type were recorded during follow-up, patients remained in the same index group. Follow-up started on the day dialysis was first performed as an outpatient and continued for 1 year or until death or switching from the RRT modality. Because of the relatively lower number of patients who initiated PD between January 1, 2008 and July 1, 2008 compared to those who initiated HD, the recruitment period for incident PD patients was extended to July 2009.

A total of 191 CKD patients started RRT during the study period (133 HD, 58 PD). Twenty-three HD patients were excluded from the study due to previous RRT (n = 13) or loss to follow-up because of transfer to another district (n =10). In addition, 16 PD patients were excluded from the study because they had previously undergone RRT (HD, 11 patients; TX, 5 patients). A total of 152 patients were included in the final analysis. Of the 110 incident HD patients, 59 started therapy with a functioning AVF and 51 with a TCC. Three cohorts of incident dialysis patients were then established: HD-AVF (n = 59), HD-CVC (n = 51) and PD (n = 42).

### Data

Clinical data and information regarding access type were collected from our hospital database and from outpatient dialysis unit records, when appropriate. A physician assessed the presence of co-morbid illness by

complete review of each patient's records at the enrolment date. Information was collected for the 19 variables that constitute the Charlson Comorbidity Index [18], which has been validated for use in patients with ESRD. The number of clinical and emergency room visits, hospitalizations and dialysis access complications were determined for all participants from our hospital database and from outpatient dialysis unit records, when appropriate.

Complications of HD and PD accesses were classified as mechanical or infectious events [19,20]. Mechanical complications included AVF stenosis, thrombosis, bleeding and limb ischemia; TCC flow dysfunction, thrombosis, bleeding, cuff extrusion and complications of central venous catheterization; PD catheter flow dysfunction, bleeding, leaks, cuff extrusion, hernias and complications related to Tenckhoff catheter placement. Infectious complications included AVF-related bacteremia, TCC-related bacteremia, PD-related peritonitis and bacteremia.

Dates of renal transplantation, switch from the RRT modality and/or death were known until end off follow-up.

### Outcomes

The primary aim of this analysis was to determine the all-cause mortality of HD-AVF, HD-TCC and PD patients at 1 year from the time of first dialysis.

A secondary aim was to examine the dialysis access-related morbidity/mortality of HD-AVF, HD-TCC and PD patients at 1 year from the time of first dialysis.

### Statistical analysis

Data are given as percentages and means ± SD. Categorical variables were compared using Fisher's exact test. The Kruskal-Wallis test was used to analyze differences between continuous variables. Rates were calculated for each patient by dividing the number of events/procedures by the duration of follow-up in years. Survival on dialysis was calculated by the Kaplan-Meier method. Univariate analysis of survival was performed by the log rank method. Multivariate analysis of survival was performed using a Cox proportional hazards model. Covariates were included if the baseline difference between the three groups was <0.10. All tests were two sided, and differences were considered significant at $P<0.05$. All statistical analyses were performed using the SPSS software, version 19 (SPSS, Inc., Chicago, IL, USA).

## Results

### Baseline characteristics

Table 1 lists the baseline characteristics of the study population. Compared with PD patients, both HD-TCC and HD-AVF patients were more likely to be older ($p<0.001$, Table 1) and to have a higher frequency of diabetes mellitus ($p = 0.017$, Table 1), coronary heart disease ($p = 0.007$, Table 1) and congestive heart failure ($p = 0.023$, Table 1). Both HD-AVF and PD groups initiated dialysis with similar levels of serum hemoglobin and serum albumin. In addition, ~80% of both HD-AVF and PD groups were referred to a nephrologist early. HD-TCC patients were more likely to be referred to a nephrologist late ($p<0.001$, Table 1), and to initiate dialysis with lower hemoglobin ($p<0.001$, Table 1) and serum albumin ($p<0.001$, Table 1). HD-AVF patients were more likely to initiate RRT with higher estimated glomerular filtration rate (eGFR) than either HD-TCC or PD patients ($p<0.001$, Table 1).

### Patient outcomes

Table 2 lists the mean numbers of clinical events of the study population.

HD-TCC patients were more likely to have higher numbers of dialysis access-related complications than HD-AVF and PD patients ($p<0.001$, Table 2). In particular, the PD group had the lowest number of mechanical access-related complications ($p<0.001$, Table 2) and the HD-AVF group the lowest infection rate ($p<0.001$, Table 2). Despite the similar number of infection-free patients in the PD and HD-TCC groups at 1 year of follow-up, both catheter-related bacteremia and hospital admissions were significantly higher in the HD-TCC group ($p = 0.004$ and 0.034, respectively; Table 2).

Overall, HD-TCC patients were more likely to have clinical visits ($p = 0.069$, Table 2), emergency room visits ($p<0.001$, Table 2) and hospital admissions ($p<0.001$, Table 2). The mean numbers of hospital days for HD-AVF, HD-TCC and PD patients were 5.5 ± 13.7, 36.6 ± 40.7 and 5.1 ± 15.1 days, per patient-year at risk, respectively ($p<0.001$).

Sixteen patients died during follow-up (HD-AVF, n = 2; HD-TCC, n = 13; PD, n = 1). The main causes of death for HD-TCC patients were catheter-related bacteremia (n = 7), cardiac disease (n = 4), pneumonia (n = 1) and cancer (n = 1); for HD-AVF patients was cancer (n = 2) and for PD patients was pyonephrosis (n = 1). The survival rates at one year were 86.3% and 97.6% for HD and PD patients, respectively ($p = 0.044$, log rank test). When stratified for HD vascular access type, the survival rates at one year were 96.6%, 74.5% and 97.6% for HD-AVF, HD-TCC and PD groups, respectively (Figure 1; $p<0.001$, log rank test). Older age ($p = 0.002$), diabetes ($p = 0.006$), cardiovascular disease ($p = 0.026$), late referral ($p = 0.001$) hypoalbuminemia ($p = 0.001$) and anemia ($p = 0.002$) were all associated with poorer survival by log rank analysis. The impact of HD vascular access at the time of dialysis initiation on survival was considered in more detail in a

**Table 1 Baseline characteristics of enrolled patients treated with different dialysis modalities and vascular accesses (HD-AVF, hemodialysis with arteriovenous fistula; HD-TCC, hemodialysis with catheter; PD, peritoneal dialysis)**

| Variable | HD-AVF (n = 59) | HD-TCC (n = 51) | PD (n = 42) | P |
|---|---|---|---|---|
| Male sex (%) | 60% | 55% | 52% | 0.856 |
| Mean age (y) | 62.8 ± 14.3 | 66.1 ± 15.4 | 55.1 ± 16.1 | 0.001 |
| *18-44 years* | 5 (9%) | 4 (8%) | 9 (21%) | 0.047 |
| *45-64 years* | 19 (32%) | 12 (24%) | 20 (47%) | 0.015 |
| *65+ years* | 35 (59%) | 35 (69%) | 13 (31%) | 0.001 |
| Etiology of kidney disease (%) | | | | |
| *Diabetes* | 26 (44%) | 22 (42%) | 8 (19%) | 0.017 |
| *Hypertension* | 7 (12%) | 4 (8%) | 2 (5%) | 0.471 |
| *Glomerulonephritis* | 7 (12%) | 3 (6%) | 13 (31%) | 0.003 |
| *Tubulointersticial kidney disease* | 8 (14%) | 10 (20%) | 7 (17%) | 0.702 |
| *Unknown* | 11 (18%) | 12 (24%) | 12 (29%) | 0.510 |
| Mean Charlson Comorbidity Index | 5.1 ± 3.1 | 5.0 ± 2.5 | 4.4 ± 2.2 | 0.574 |
| *Low risk (≤ 3)* | 25 (42%) | 17 (34%) | 15 (36%) | 0.745 |
| *Medium risk (4–5)* | 13 (22%) | 11 (21%) | 14 (33%) | 0.133 |
| *High risk (≥6)* | 21 (36%) | 23 (45%) | 13 (31%) | 0.575 |
| Comorbid conditions (%) | | | | |
| *Coronary heart disease* | 26 (44%) | 17 (33%) | 6 (14%) | 0.007 |
| *Congestive heart failure* | 25 (42%) | 18 (35%) | 7 (17%) | 0.023 |
| *Peripheral vascular disease* | 14 (24%) | 11 (22%) | 9 (19%) | 0.104 |
| *Previous stroke* | 7 (12%) | 8 (16%) | 2 (5%) | 0.095 |
| *Diabetes* | 26 (44%) | 23 (45%) | 8 (19%) | 0.015 |
| *Malignant disease* | 10 (20%) | 10 (23%) | 11 (26%) | 0.432 |
| Late referral (%) | 13 (22%) | 44 (86%) | 9 (21%) | <0.001 |
| Time from referral to dialysis initiation, months (mean ± SD) | 39 ± 35 | 11 ± 30 | 34 ± 28 | <0.001 |
| Hemoglobin (g/L) | 104 (101, 108) | 90 (85, 94) | 105 (108, 115) | <0.001 |
| eGFR (ml/min per 1.73 $m^2$)* | 10.0 (9.2, 10.9) | 7.8 (6.8, 8.9) | 8.3 (7.7, 9.0) | <0.001 |
| Serum creatinine (mg/dL) | 5.7 (5.3, 6.1) | 8.0 (7.0, 9.1) | 6.7 (6.0, 7.4) | <0.001 |
| Serum urea (mg/dL) | 218 (203, 231) | 217 (194, 239) | 197 (184, 210) | 0.214 |
| Serum albumin (g/L) | 37 (35, 38) | 33 (31, 34) | 39 (38, 40) | <0.001 |

*** eGFR, estimated glomerular filtration rate.**

multivariate model to correct for confounding variables. The results of the Cox model are given in Table 3- HD-TCC use at the time of dialysis initiation was independently associated with death (HR 16.128, 95%CI [1.431-181.778], $p = 0.024$).

At the end of follow-up, 97% (n = 57) and 47% (n = 18) of HD-AVF and HD-TCC patients had a functional fistula as permanent vascular access, respectively. Three patients switched definitely from PD to HD due to PD-related peritonitis (n = 2) and tuberculous peritonitis (n = 1). Only 2 patients received a transplant during the study period.

## Discussion

The study presented here shows that incident HD-TCC patients experienced a significantly higher mortality rate at one year of dialysis, in comparison with HD-AVF and PD patients. Infection was the most common cause of death, whereas the second most common cause was death related to cardiovascular disease. Dialysis access-related complications were responsible for 43% (n = 7) of all deaths, and infection was the single cause responsible for such deaths. Death caused by dialysis access complications occurred only in the HD-TCC group. Importantly, HD-TCC patients had approximately twice as many clinical events related to dialysis access than either HD-AVF or PD patients (mainly access-related bacteremia episodes and hospitalizations). In contrast, most of the vascular and peritoneal dialysis access complications in the HD-AVF and PD groups were not serious clinical events, and no dialysis access-related deaths occurred in either these two groups. Although HD-TCC

**Table 2 Dialysis access-related and overall clinical events of enrolled patients treated with different dialysis modalities and vascular accesses (HD-AVF, hemodialysis with arteriovenous fistula; HD-TCC, hemodialysis with catheter; PD, peritoneal dialysis), per patient-year at risk (mean ± SD)**

| Clinical events | HD-AVF (n = 59) | HD-TCC (n = 51) | PD (n = 42) | P |
|---|---|---|---|---|
| **Dialysis access-related** | | | | |
| Mechanical complications | 0.93 ± 1.40 | 0.82 ± 1.49 | 0.07 ± 0.26 | <0.001 |
| *Fistula related* | 0.73 ± 0.99 | 0.29 ± 0.64 | 0 | <0.001 |
| *Catheter related* | 0.20 ± 0.71 | 0.53 ± 1.12 | 0.07 ± 0.26 | 0.114 |
| Infectious complications | | | | |
| *Patients infection free, at year 1, N (%)* | 59 (100%) | 33 (65%) | 24 (57%) | <0.001 |
| *Peritonitis* | 0 | 0 | 0.57 ± 0.74 | 0.002 |
| *Bacteremia* | 0 | 0.71 ± 1.29 | 0 | 0.004 |
| Total | 0.93 ± 1.40 | 1.53 ± 1.89 | 0.64 ± 0.83 | <0.001 |
| **Overall** | | | | |
| Dialysis access-related complications * | 0.93 ± 1.40 | 1.53 ± 1.89 | 0.64 ± 0.83 | <0.001 |
| Clinical visits | 4.17 ± 4.29 | 6.35 ± 10.25 | 3.38 ± 3.41 | 0.069 |
| Emergency room visits | 1.42 ± 2.38 | 3.06 ± 3.23 | 1.62 ± 1.75 | <0.001 |
| Hospital admissions | 0.66 ± 1.14 | 2.04 ± 1.55 | 0.50 ± 0.74 | <0.001 |
| *Dialysis accesss-related* | 0.07 ± 0.25 | 0.47 ± 1.09 | 0.14 ± 0.42 | 0.034 |
| *Other* | 0.59 ± 1.03 | 1.57 ± 1.05 | 0.36 ± 0.62 | 0.010 |
| Total | 7.18 ± 6.76 | 12.98 ± 12.61 | 6.14 ± 4.12 | <0.001 |

*** Includes all dialysis access-related mechanical and infectious complications.**

patients had similar baseline characteristics to HD-AVF patients, HD-TCC patients were referred to the nephrologist later, which might explain the delay in AVF creation in this group. In contrast, both incident HD-AVF and PD patients were referred to the nephrologist early and could thus benefit from appropriate vascular and peritoneal access placement in due time. Despite different baseline characteristics, both the HD-AVF and PD groups had similarly high survival rates at year 1. Multivariate analysis showed that HD-TCC use at the time of dialysis initiation was the important factor associated with poor prognosis. Taken together, our results strongly suggest that HD vascular access type at the time of dialysis initiation might explain the differences in outcome observed between the incident HD and PD populations. Our results corroborate the recent findings of Perl *et al.*, [15] in incident adult dialysis patients on the Canadian Organ Replacement Register who found that

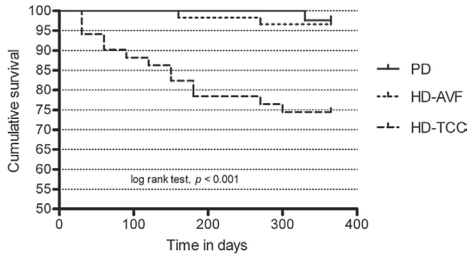


**Figure 1 Kaplan-Meier plots of survival in incident dialysis patients with log rank analysis to assess the significance of dialysis access on survival.** Survival curves for HD-AVF (hemodialysis with arteriovenous fistula, dotted line), HD-TCC (hmodialysis with tunneled cuffed catheter, dashed line), and PD (peritoneal dialysis, solid line) demonstrate higher 1-year mortality in HD-TCC patients.

**Table 3 Results of the Cox multivariate analysis for the relationship between co-morbid factors, dialysis access at dialysis initiation and death in incident dialysis patients (HD-AVF, hemodialysis arteriovenous fistula; HD-TCC, hemodialysis tunneled cuffed catheter; PD, peritoneal dialysis catheter)**

| | Hazard ratio | 95% confidence intervals | *P* |
|---|---|---|---|
| Age (per year) | 1.080 | 0.996-1.171 | 0.062 |
| Diabetes | 0.487 | 0.139-2.288 | 0.318 |
| Coronary heart disease | 1.875 | 0.381-9.227 | 0.439 |
| Congestive heart failure | 0.497 | 0.117-2.158 | 0.497 |
| Peripheral vascular disease | 0.499 | 0.114-2.190 | 0.357 |
| Previous stroke | 0.197 | 0.032-1.225 | 0.081 |
| Late referral | 1.009 | 0.990-1.028 | 0.378 |
| Albumin | 0.917 | 0.814-1.033 | 0.153 |
| Hemoglobin | 0.999 | 0.948-1.054 | 0.975 |
| eGFR* | 1.135 | 0.903-1.426 | 0.279 |
| Dialysis access | | | |
| *PD (reference)* | | | |
| *HD-AVF* | 0.734 | 0.056-9.656 | 0.814 |
| *HD-TCC* | 16.128 | 1.431-181.778 | 0.024 |

* eGFR, estimated glomerular filtration rate.

patients initiating HD with a catheter had a higher risk of death compared to both HD-AVF and PD patients.

Our findings are also in agreement with the recent report of Quinn *et al.*, [21] that showed no difference in survival between PD and HD patients who received > 4 months of predialysis care. Also, Raithatha *et al.* [16] recently showed that the use of HD-catheter is one of the key features of late referral that determines poor prognosis. In the present study, ~80% of both HD-AVF and PD patients were referred to the nephologist early and experienced similarly high survival rates in the first year of dialysis, compared to HD-TCC patients. Our results support the need for early referral of ESRD patients to nephrology centers to provide the opportunity for patient selection of RRT modality and timely creation of the appropriate dialysis access [22].

Most reports that have used USRDS data do not include the critical initial 90-day period on dialysis. This is a time period when a high proportion of HD patients are using catheters as bridging access devices [12]. In the present study, survival rates of HD-TCC, HD-AVF and PD groups at 90 days of follow-up were 88%, 100% and 100%, respectively. Exclusion of this period in the analysis would probably underestimate the morbidity and mortality rates of the HD-TCC group.

One interesting finding of the present study was that bacteremia only occurred in HD-TCC patients, refuting the common misconception that PD is associated with an overall higher rate of severe infection than HD. In addition, PD patients had the lowest number of mechanical access-related complications. Our results support the previous findings of Oliver *et al.* [23,24] and Povlsen *et al.* [2,25,26] by showing that patients who choose PD require fewer access interventions and do not face an increased risk of access-related complications compared to HD patients.

As a retrospective study, this study has the limitations of such an approach. As with all observational studies, there may have been selection bias, in particular influenced by patient treatment preferences and time of referral to the nephrologist. PD patients were younger and had lower comorbid illness, compared to HD patients. The patient population consisted mainly of Caucasian Europeans, which makes it impossible to draw conclusions for other ethnic groups. Peritoneal dialysis patients were treated in a single academic nephrology centre, whereas HD patients were treated in separate peripheral renal centers, although this is a reflection of the local distribution of patients between modalities.

## Conclusion

Our study provides evidence favoring the view that HD vascular access type at renal replacement therapy initiation is an important modifier of the relationship between dialysis modality and survival among incident dialysis patients. Our results emphasize the need for an early referral program for ESRD patients so that those who choose HD have a functioning AVF, and those who choose PD have a Tenckhoff catheter placed in due time. We believe such a policy would decrease the risk of dialysis morbidity/mortality.

#### Competing interests

The authors have no equity interest or financial agreements with any company or commercial entity related to the content of the article and they have not received salary or support from any company related to the article.

#### Authors' contributions

LC: participated in the design of the study, in the acquisition and interpretation of data, performed the statistical analysis and wrote the manuscript. CSA: participated in the acquisition and interpretation of data and revised the manuscript for important intellectual content. CCD: performed the statistical analysis. RN participated in the acquisition of data. MP: participated in the interpretation of data and revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

#### Acknowledgements

The authors thank Professor João Frazão for assistance in manuscript preparation, Ms. Doreen Raine for editing the English and the clinical directors from hemodialysis clinics who kindly agreed to collaborate in this study: A. Baldaia Moreira M.D., A. Caldeira Gomes M.D., A. Castro Henriques M.D., Antunes de Azevedo M.D, Eva Xavier M.D., João C. Fernandes M.D., João M. Frazão M.D., PhD, Jorge P. Baldaia M.D., José M. Madureira M.D., José Pinheiro M.D., Odete Pereira M.D., Sofia Pedroso M.D., Susana Sampaio M.D., Vasco Miranda M.D.

**Author details**
[1]Nephrology Research and Development Unit, Faculty of Medicine, University of Porto & São João Hospital Centre, Alameda Professor Hernani Monteiro, Porto 4202-451, Portugal. [2]Department of Health Information and Decision Sciences, Faculty of Medicine, University of Porto, Alameda Professor Hernani Monteiro, Porto 4202-451, Portugal.

Received: 22 November 2011 Accepted: 20 August 2012
Published: 23 August 2012

**References**

1. Lameire N, Wauters JP, Górriz JL, *et al*: **An update on the referral pattern of patients with end-stage renal disease.** *Kidney Int* 2002, **61**:S27–S34.
2. Górriz J, Sancho A, Pallardó LM, *et al*: **Significado prognóstico de la diálisis programada en pacientes que inician tratamiento substituivo renal. Un estúdio multicéntrico español.** *Nefrologia* 2001, **21**:49–59.
3. Buck J, Baker R, Cannaby AM, *et al*: **Why do patients known to renal services still undergo urgent dialysis initiation? A cross-sectional survey.** *Nephrol Dial Transplant* 2007, **22**(11):3240–3245.
4. Mendelssohn DC, Malmbrg C, Hamandi B: **An integrated review of "unplanned" dialysis initiation: reframing the terminology to "suboptimal" initiation.** *BMC Nephrol* 2009, **10**:22.
5. Weinhandl ED, Foley RN, Gilbertson DT, Arneson TJ, Snyder JJ, Collins AJ: **Propensity-matched mortality comparison of incident hemodialysis and peritoneal dialysis patients.** *J Am Soc Nephrol* 2010, **21**:499–506.
6. Heaf JG, Lokkegaard H, Madsen M: **Initial survival advantage of peritoneal dialysis relative to haemodialysis.** *Nephrol Dial Transplant* 2002, **17**:112–117.
7. Korevaar JC, Feith GW, Dekker FW, van Manen JG, Boeschoten EW, Bossuyt PM, Krediet RT: **Effect of starting with hemodialysis compared with peritoneal dialysis in patients new on dialysis treatment: A randomized controlled trial.** *Kidney Int* 2003, **64**:2222–2228.
8. Manns B, Tonelli M, Yilmaz S, *et al*: **Establishment and maintenance of vascular access in incident hemodialysis patients: a prospective cost analysis.** *J Am Soc Nephrol* 2005, **16**:201–209.
9. Moist LM, Trpeski L, Na Y, Lok CE: **Increased hemodialysis catheter use in Canada and associated mortality risk: Data from the Canadian Organ Replacement Registry 2001–2004.** *Clin J Am Soc Nephrol* 2008, **3**:1726–1732.
10. de Jager DJ, Grootendorst DC, Jager KJ, *et al*: **Cardiovascular and noncardiovascular mortality among patients starting dialysis.** *JAMA* 2009, **302**(16):1782–1789.
11. Astor BC, Eustace JZ, Powe NR, the CHOICE Study, *et al*: **Type of vascular access and survival among incident hemodialysis patients: The Choices for Healthy Outcomes in Caring for ESRD (CHOICE) Study.** *J Am Soc Nephrol* 2005, **16**:1449–1455.
12. Rehman R, Schmidt RJ, Moss AH: **Ethical and Legal Obligation to Avoid Long-Term Tunneled Catheter Access.** *Clin J Am Soc Nephrol* 2009, **4**:456–460.
13. Aslam N, Bernardini J, Fried L, *et al*: **Comparison of infectious complications between incident hemodialysis and peritoneal dialysis patients.** *Clin J Am Soc Nephrol* 2006, **1**:1226–1233.
14. Rodrigues A: **How to persuade peritoneal dialysis-skeptical hemodialysis fans.** *Contrib Nephrol* 2009, **163**:237–242.
15. Perl J, Wald R, McFarlane P, *et al*: **Hemodialysis vascular access modifies the association between dialysis modality and survival.** *J Am Soc Nephrol* 2011, **22**:1113–1121.
16. Raithatha A, McKane W, Kendray D, Evans C: **Catheter access for hemodialysis defines higher mortality in late-presenting dialysis patients.** *Ren Fail* 2010, **32**(10):1183–1188.
17. *ERA-EDTA Registry Annual Report*; 2009. http://www.era-edta-reg.org/ (10 August 2011, date last accessed.
18. Charlson ME, Pompei P, Ales KL: **A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation.** *J Am Soc Nephrol* 1996, **7**:198–207.
19. Allon M, Work J: **Venous catheter access for hemodialysis**. In *Handbook of dialysis*. Edited by Daugirdas J, Blake P, Ing T. Philadelphia, USA: Lippincott Williams & Wilkins; 2007:87–104.
20. Campos RP, Chula DC, Riella MC: **Complications of the peritoneal access and their management.** *Contrib Nephrol* 2009, **163**:183–197.
21. Quinn RR, Hux JE, Oliver MJ, *et al*: **Selection bias explains apparent differential mortality between dialysis modalities.** *J Am Soc Nephrol* 2011, **22**:1534–1542.
22. Covic A, Bammens B, Lobbedez T, *et al*: **Educating end-stage renal disease patients on dialysis modality selection: a clinical advice from the European Renal Best Practice (ERBP) Advisory Board.** *NDT Plus* 2010, **3**:225–233.
23. Oliver MJ, Rothwell DM, Fung K, *et al*: **Late creation of vascular access for hemodialysis and increased risk of sepsis.** *J Am Soc Nephrol* 2004, **15**:1936–1942.
24. Oliver MJ, Verrelli M, Zacharias JM, Blake PG, Garg AX, Johnson JF, Pandeya S, Perl J, Kiss AJ, Quinn RR: **Choosing peritoneal dialysis reduces the risk of invasive access interventions.** *Nephrol Dial Transplant Jun* 2011, **2**: [Epub ahead of print].
25. Povlsen JV, Ivarsen P: **How to start the late referred ESRD patient urgently on chronic APD.** *Nephrol Dial Transplant* 2006, **21**(Suppl 2):ii56–ii59.
26. Povlsen JV: **Unplanned start on assisted peritoneal dialysis.** *Contrib Nephrol* 2009, **163**:261–263.

doi:10.1186/1471-2369-13-88
**Cite this article as:** Coentrão *et al.*: **Effects of starting hemodialysis with an arteriovenous fistula or central venous catheter compared with peritoneal dialysis: a retrospective cohort study.** *BMC Nephrology* 2012 **13**:88.

*Peritoneal Dialysis International*, inPress
doi: 10.3747/pdi.2011.00309

0896-8608/13 $3.00 + .00


# COST ANALYSIS OF HEMODIALYSIS AND PERITONEAL DIALYSIS ACCESS COSTS IN INCIDENT DIALYSIS PATIENTS

Luis A. Coentrão,[1] Carla S. Araújo,[1] Carlos A. Ribeiro,[2] Claúdia C. Dias,[3] and Manuel J. Pestana[1]

*Nephrology Research and Development Unit[1] and Financial Management Unit,[2] São João Hospital Centre, and Department of Health Information and Decision Sciences,[3] Faculty of Medicine, University of Porto, Portugal*

♦ ***Background:*** **Although several studies have demonstrated the economic advantages of peritoneal dialysis (PD) over hemodialysis (HD), few reports in the literature have compared the costs of HD and PD access. The aim of the present study was to compare the resources required to establish and maintain the dialysis access in patients who initiated HD with a tunneled cuffed catheter (TCC) or an arteriovenous fistula (AVF) and in patients who initiated PD.**

♦ ***Methods:*** **We retrospectively analyzed the 152 chronic kidney disease patients who consecutively initiated dialysis treatment at our institution in 2008 (HD-AVF, *n* = 65; HD-CVC, *n* = 45; PD, *n* = 42). Detailed clinical and demographic information and data on access type were collected for all patients. A comprehensive measure of total dialysis access costs, including surgery, radiology, hospitalization for access complications, physician costs, and transportation costs was obtained at year 1 using an intention-to-treat approach. All resources used were valued using 2010 prices, and costs are reported in 2010 euros.**

♦ ***Results:*** **Compared with the HD-AVF and HD-TCC modalities, PD was associated with a significantly lower risk of access-related interventions (adjusted rate ratios: 1.572 and 1.433 respectively; 95% confidence intervals: 1.253 to 1.891 and 1.069 to 1.797). The mean dialysis access–related costs per patient–year at risk were €1171.6 [median: €608.8; interquartile range (IQR): €563.1 – €936.7] for PD, €1555.2 (median: €783.9; IQR: €371.4 – €1571.7) for HD-AVF, and €4208.2 (median: €1252.4; IQR: €947.9 – €2983.5) for HD-TCC ($p < 0.001$). In multivariate analysis, total dialysis access costs were significantly higher for the HD-TCC modality than for either PD or HD-AVF ($\beta = -0.53$; 95% CI: −1.03 to −0.02; and $\beta = -0.50$; 95% CI: −0.96 to −0.04).**

♦ ***Conclusions:*** **Compared with patients initiating HD, those initiating PD required fewer resources to establish and maintain a dialysis access during the first year of treatment.**

*Perit Dial Int*: inPress www.PDIConnect.com
doi:10.3747/pdi.2011.00309

KEY WORDS: Cost analysis; health economics; hemodialysis; dialysis access; vascular access; peritoneal catheter.

End-stage renal disease (ESRD) patients who choose hemodialysis (HD) require a vascular access, and those who choose peritoneal dialysis (PD) require a peritoneal catheter before initiation of renal replacement therapy (RRT). The type of vascular access used in HD patients is recognized to have a significant influence on patient survival. Compared with use of a native arteriovenous fistula (AVF), use of a tunneled cuffed catheter (TCC) is associated with a substantially greater risk of sepsis, hospitalization, and mortality (1–8). By contrast, PD catheter complications have declined in recent years, with low rates of bacteremia and sepsis (9–22). Recently, Perl *et al.* (9) observed that, compared with patients starting PD or starting HD with a functioning AVF, patients starting HD with a TCC had a higher risk of death during the first year. However, that finding didn't necessarily demonstrate causality between use of a HD catheter and patient death.

Several studies have reported that HD is more expensive than PD, mainly because of costs related to dialysis staff, patient transportation, and overhead (23–30). However, vascular access care accounts for a significant proportion of the health care costs in both incident and prevalent HD patients (31–33). Nonetheless, to our knowledge, few reports have compared the costs of PD and HD access (32). The aim of the present study was to compare the resources required to establish and maintain dialysis access in patients initiating HD with a TCC or with an AVF and in those initiating PD.

Correspondence to: L. Coentrão, Nephrology Research and Development Unit, São João Hospital Centre, Faculty of Medicine, University of Porto, Porto 4200-319 Portugal.
coentrao@med.up.pt
Received 5 December 2011; accepted 26 July 2012



PDI in Press. Published on March 1, 2013. doi:10.3747/pdi.2011.00309

## METHODS

### STUDY DESIGN

Our retrospective cost analysis included local chronic kidney disease patients (age 18 years and older at the start of RRT) who consecutively initiated HD between 1 January 2008 and 1 July 2008, or PD between 1 January 2008 and 1 July 2009 at our hospital.

The study was approved by the Ethics Committee for Health and the Local Institutional Review Board of São João Hospital Centre, EPE, Porto, Portugal.

### PATIENT COHORT

The incidence of ESRD—that is, patients who start any RRT modality for the first time—is higher in Portugal than in other European countries (34). An incidence rate of 217 HD patients and 18 PD patients per million population were registered by the Portuguese Society of Nephrology in 2010. Patients were recruited from the nephrology department of São João Hospital Centre, which is a tertiary-care university hospital responsible for nephrologic medical support to ESRD patients starting RRT in the northwest region of Portugal. Patients were enrolled if they had a diagnosis of end-stage chronic kidney disease according to a nephrologist and if they had received outpatient chronic dialysis treatment. Patients who had previously undergone RRT (HD, PD, or transplantation) and those who restarted during the study period or who transferred to another district immediately after RRT start were excluded. The program provided free choice to patients who were eligible for both therapies, but some patients in the HD group had no choice because of contraindications for PD. Treatment modality was assigned at the time of the first attempt at dialysis access placement, on an intention-to-treat basis. Patients were considered PD patients if they had chosen PD and if an attempt was made to place a PD catheter. Otherwise, the patients were considered HD patients. The HD group was subdivided into patients who underwent AVF creation or TCC placement as a first vascular access. Patients were followed for 1 year from the date of dialysis initiation, or until death or switch from their RRT modality. Because of the relatively lower number of patients who initiated PD between 1 January and 1 July 2008, compared with those who initiated HD, the recruitment period for incident PD patients was extended to July 2009.

A total of 191 chronic kidney disease patients started RRT during the study period (133 HD, 58 PD). Among those 191 patients, 23 HD patients were excluded because of previous RRT ($n$ = 13) or loss to follow-up after transfer to another district ($n$ = 10), and 16 PD patients were excluded because of previous RRT (HD, $n$ = 11; transplantation, $n$ = 5). The remaining 152 patients were included in the final analysis. Of the 110 incident HD patients, 65 underwent AVF creation, and 45 underwent TCC placement. Three cohorts of incident dialysis patients were therefore established: HD-AVF ($n$ = 65), HD-TCC ($n$ = 45), and PD ($n$ = 42).

### DATA COLLECTION

Clinical information was collected from hospital and dialysis unit records as appropriate. The presence of comorbidity at the enrolment date was assessed by a physician undertaking a complete review of the patient's records. Information was collected for the 19 variables that constitute the Charlson comorbidity index (35), which has been validated for use in patients with ESRD. Information on all dialysis access surgeries, radiologic imaging studies, and dialysis catheter interventions was collected from our hospital database. Because an access was created before dialysis initiation in some patients, all attempts at dialysis access placement were recorded and included in the final analysis. The clinical records from all hospitalizations for all patients were reviewed by a physician. Information on hospital admissions for which the primary reason for admission was access-related care—as defined by the discharge diagnosis (coded according to the International Classification of Diseases, Ninth Revision)—was captured for all patients.

### PROCEDURES

***Access Surgery:*** Peritoneal dialysis–related procedures (PD catheter insertion, replacement, repositioning, or removal; omentectomy; lysis of adhesions; correction of peritoneal leaks and abdominal hernias) were performed by a dedicated group of general surgeons and nephrologists, in the operating room, under general anesthesia. Fistula-related procedures (fistula creation, revision, and ligation) were performed by vascular surgeons in a specialized room, under local anesthesia. Preoperative ultrasonography screening of vessels and peripheral venograms for access planning were not routinely performed.

***Diagnostic Imaging:*** Diagnostic imaging studies included fistulograms, access-directed thrombolysis, and access-related angioplasties—that is, radiology procedures performed as part of access-related care. These procedures were performed by a dedicated interventional nephrologist in the angiographic suite, under local anesthesia (36).

***TCC-Related Interventions:*** Central venous catheter–related interventions included insertion, exchange, and removal. These procedures were performed by nephrologists at the bedside, under local anesthesia. Catheter dysfunction, defined as the complete inability to withdraw blood or the inability to withdraw blood at a sufficient rate to sustain dialysis (blood flow less than 300 mL/min), was routinely managed by dialysis nurses with local instillation of tissue plasminogen activator.

### COST ANALYSIS

Our study was performed from the public administration perspective, including direct medical and nonmedical costs. Annual dialysis access costs were evaluated using a mixed costing method. All resources used were valued using 2010 prices, and costs are reported in 2010 euros.

The resources required to care for a patient's dialysis access were divided into the categories of access surgery, diagnostic imaging, TCC-related interventions, hospitalization, and patient transportation. Access surgery, diagnostic imaging, and TCC-related intervention costs were obtained using a micro-costing approach:

- The professional fee per intervention was determined from the average fee charged by physicians per year.
- Technical costs per intervention—including supplies, pharmacy and radiology costs, and additional overhead expenses—were obtained for all procedures.

The "total expense" represents the sum of the technical and overhead costs and the professional fees (37). Cost data for dialysis access–related hospitalizations were extracted from the Ministry of Health and Welfare Ordinance Legislation—Diário da República (1st series, No. 147, 31 July 2009, No. 839, and 2nd series, No. 81, 5 April 2000, clause No. 7376/2000). Costs of patient transport for dialysis access care were included in the analysis (€0.47/1 km).

### OUTCOMES

The primary outcome was the costs related to dialysis access at 1 year from the time of first dialysis. The secondary outcome was the dialysis access–related intervention rate per patient–year.

### STATISTICAL ANALYSIS

Data are presented as percentages and means ± standard deviation. Costs are given as means with 95% confidence intervals (CIs). Categorical variables were compared using the Fisher exact test. The Kruskal–Wallis test was used to analyze differences between continuous variables. Rates were calculated for each of the patients by dividing the number of events or procedures by the duration of follow-up in years. Between study groups, the mean intervention rates per patient were compared using Poisson regression. Because costs were not normally distributed, they were log-transformed before statistical testing. Multivariate linear regression was used to assess the impact of various comorbid factors on the dialysis access–related costs. Covariates were included if the baseline difference between the three groups was less than 0.10 in the univariate comparison. To address the impact on costs of variations in duration of follow-up resulting from early death, the year 1 cost of patient care by access type and dialysis modality was calculated by direct extrapolation from the truncated costing period for patients who died during year 1. This approach permitted the cost per patient–year at risk to be reported. All tests were two-sided, and differences were considered significant at $p < 0.05$. All statistical analyses were performed using the SPSS software application (version 19: SPSS, Chicago, IL, USA).

## RESULTS

### BASELINE CHARACTERISTICS

Table 1 shows the baseline characteristics of the study population. Compared with the PD patients, the HD-TCC and HD-AVF patients were more likely to be older and to have a higher frequency of diabetes mellitus, coronary artery disease, congestive heart failure, and cerebrovascular disease. Time from referral to dialysis initiation was significantly lower in the HD-TCC patients than in the HD-AVF and PD patients.

The mean distances between the homes of the HD-AVF, HD-TCC, and PD patients and our hospital center were 42.1 ± 33.9 km, 53.0 ± 33.8 km, and 30.3 ± 23.4 km respectively ($p = 0.004$).

### RESOURCE USE

We were able to assess costs for the full 12-month observation period in 131 of the 152 study patients. For the remaining 21 patients (16 of whom died, 2 of whom received a renal graft, and 3 of whom permanently switched from PD to HD), only the corresponding portion of the 12-month period was costed.

### DESCRIPTION OF PROCEDURES

Table 2 presents the frequencies and types of invasive procedures performed during the interventions. In the

TABLE 1
Baseline Characteristics of Enrolled Patients by Dialysis Modality and Vascular Access Type

| Variable | Hemodialysis With AVF | Hemodialysis With TCC | Peritoneal dialysis | *p* Value |
|---|---|---|---|---|
| Patients (*n*) | 65 | 45 | 42 | |
| Sex (% men) | 60 | 55 | 52 | 0.856 |
| Mean age (years) | 63.1±13.9 | 66.4±15.3 | 55.1±16.1 | 0.001 |
| Age groups [*n* (%)] | | | | |
| 18–44 Years | 5 (8) | 4 (9) | 9 (21) | 0.046 |
| 45–64 Years | 20 (31) | 11 (24) | 20 (47) | 0.019 |
| 65+ Years | 40 (61) | 30 (67) | 13 (31) | 0.001 |
| Cause of kidney disease [*n* (%)] | | | | |
| Diabetes | 29 (45) | 19 (42) | 8 (19) | 0.016 |
| Hypertension | 8 (12) | 3 (7) | 2 (5) | 0.405 |
| Glomerulonephritis | 7 (11) | 3 (7) | 13 (31) | 0.005 |
| Tubulointerstitial nephritis | 9 (14) | 9 (20) | 7 (17) | 0.699 |
| Unknown | 12 (19) | 11 (24) | 12 (29) | 0.445 |
| Mean CCI score | 5.1±3.1 | 5.0±2.5 | 4.4±2.2 | 0.574 |
| CCI risk group [*n* (%)] | | | | |
| Low (≤3) | 25 (39) | 14 (31) | 15 (36) | 0.746 |
| Medium (4–5) | 12 (19) | 12 (27) | 14 (33) | 0.138 |
| High (≥6) | 28 (43) | 19 (42) | 13 (31) | 0.424 |
| Comorbid conditions [*n* (%)] | | | | |
| Coronary artery disease | 28 (43) | 15 (33) | 6 (14) | 0.006 |
| Congestive heart failure | 26 (40) | 17 (38) | 7 (17) | 0.025 |
| Peripheral vascular disease | 16 (25) | 9 (20) | 9 (19) | 0.797 |
| Previous stroke | 9 (14) | 6 (13) | 2 (5) | 0.330 |
| Diabetes | 30 (46) | 19 (42) | 8 (19) | 0.011 |
| Malignancy | 11 (17) | 9 (20) | 11 (26) | 0.591 |
| Late referral [*n* (%)] | 9 (14) | 40 (89) | 9 (21) | <0.001 |
| Mean duration from referral to dialysis initiation (months) | 42±40 | 5±19 | 34±28 | <0.001 |
| Laboratory values [median (range)] | | | | |
| Hemoglobin (g/L) | 104 (101–108) | 88 (83–92) | 105 (108–115) | <0.001 |
| eGFR (mL/min/1.73 m$^2$) | 10.0 (9.2–10.9) | 7.6 (6.6–8.7) | 8.3 (7.7–9.0) | <0.001 |
| Serum creatinine (mg/dL) | 5.8 (5.3–6.1) | 8.3 (7.2–9.4) | 6.7 (6.0–7.4) | <0.001 |
| Serum urea (mg/dL) | 216 (203–229) | 219 (194–244) | 197 (184–210) | 0.171 |
| Serum albumin (g/L) | 37 (35–38) | 32 (31–34) | 39 (38–40) | <0.001 |

AVF = arteriovenous fistula; TCC = tunneled cuffed catheter; CCI = Charlson comorbidity index; eGFR = estimated glomerular filtration rate.

PD group, 76% and 24% of the procedures were related to PD and HD catheters respectively. Eight PD patients used at least 1 HD catheter. The reasons for HD catheter use in the PD group were catheter malfunction (*n* = 2), peritonitis (*n* = 2), catheter "break-in" period (*n* = 2), abdominal leak (*n* = 1), and requirement for continuous renal replacement therapy (*n* = 1). In the HD-AVF group, 75% and 25% of the procedures were related to the AVF and the TCC accesses respectively. Eleven patients required at least 1 TCC insertion during dialysis because of AVF failure. In the HD-TCC group, 30% and 70% of the procedures were related to the AVF and TCC accesses respectively. During dialysis, 34 patients underwent at least 1 AVF creation attempt. The primary failure rates (including failed attempts) were 2% for the PD group (1 of 44), 23% for the HD-AVF group (17 of 75), and 9% for HD-CVC group (6 of 67).

Table 3 lists the mean numbers of interventions in the study population. The mean numbers of access surgeries and diagnostic imaging studies were higher for the HD-AVF group than for the HD-TCC and PD groups ($p$ =0.083 and $p < 0.001$ respectively). In contrast, the

TABLE 2
Invasive Access Interventions by Dialysis Modality and Vascular Access Type

| Intervention | Hemodialysis With AVF (*n*=65) (*n*) | (%)[a] | Hemodialysis With TCC (*n*=45) (*n*) | (%)[a] | Peritoneal dialysis (*n*=42) (*n*) | (%)[a] |
|---|---|---|---|---|---|---|
| Hemodialysis fistula | | | | | | |
| Creation | 75 | 55.1 | 40 | 24.5 | 0 | 0 |
| Surgical revision or ligation | 7 | 5.2 | 3 | 1.8 | 0 | 0 |
| Angioplasty | 15 | 11.0 | 5 | 3.1 | 0 | 0 |
| Thrombectomy | 5 | 3.7 | 1 | 0.6 | 0 | 0 |
| Hemodialysis catheter | | | | | | |
| Insertion | 17 | 12.5 | 67 | 41.1 | 8 | 11.9 |
| Exchange or removal | 11 | 8.1 | 26 | 16.0 | 8 | 11.9 |
| Thrombolysis | 6 | 4.4 | 21 | 12.9 | 0 | 0 |
| Peritoneal dialysis | | | | | | |
| Catheter insertion | 0 | 0 | 0 | 0 | 44 | 65.7 |
| Catheter manipulation | 0 | 0 | 0 | 0 | 1 | 1.5 |
| Catheter removal | 0 | 0 | 0 | 0 | 4 | 6.0 |
| Lysis of adhesions or omentectomy | 0 | 0 | 0 | 0 | 1 | 1.5 |
| Correction of peritoneal leaks | 0 | 0 | 0 | 0 | 1 | 1.5 |
| TOTAL | 136 | 100 | 163 | 100 | 67 | 100 |

[a] Of total interventions.

TABLE 3
Dialysis Access–Related Interventions[a] of Enrolled Patients, by Dialysis Modality and Vascular Access Type, per Patient–Year at Risk

| Intervention | Hemodialysis (HD) With AVF (*n*=65) | Hemodialysis (HD) With TCC (*n*=45) | Peritoneal dialysis (*n*=42) | *p* Value |
|---|---|---|---|---|
| Access surgery | 1.39±0.82 | 0.84±0.75 | 1.21±0.47 | 0.085 |
| HD catheter intervention | 0.58±1.40 | 2.24±1.95 | 0.19±0.39 | <0.001 |
| Diagnostic imaging | 0.34±0.60 | 0.12±0.38 | 0 | <0.001 |
| Hospitalization | 0.07±0.25 | 0.47±1.09 | 0.14±0.35 | 0.025 |
| TOTAL | 2.38±2.06 | 3.67±2.50 | 1.54±0.73 | <0.001 |

[a] Mean ± standard deviation.

mean numbers of TCC-related interventions and hospitalizations were significantly higher for the HD-TCC group than for either the HD-AVF or the PD group ($p < 0.001$ and $p = 0.025$ respectively). The main causes of dialysis access–related hospital admissions were peritonitis ($n$ = 4, 67%) for PD patients, access surgery ($n$ = 3, 75%) for HD-AVF patients, and catheter-related bacteremia ($n$ = 13, 81%) for HD-TCC patients. The mean number of bacteremic episodes for HD-TCC patients was 0.58 ± 1.18 per patient–year at risk.

Overall, rates for dialysis access–related interventions were significantly lower in the PD group than in either the HD-AVF or the HD-TCC group ($p < 0.001$, Table 3). In multivariate analysis, the PD modality was associated with a significantly lower risk of access-related interventions than were the HD-AVF and HD-TCC modalities (adjusted rate ratios: 1.572 and 1.433 respectively; 95% CIs: 1.253 to 1.891 and 1.069 to 1.797). None of the covariates in the models were associated with the risk or rate of intervention.

## COST ANALYSIS

Table 4 sets out the itemized dialysis access–related costs.

TABLE 4
Costs of Surgical Procedures for Dialysis Access, Diagnostic Imaging, and Catheter Interventions

| Procedure | Cost in euros (€) Professional fees | Technical fees | Total per intervention |
|---|---|---|---|
| Fistula creation | 177 | 85 | 262 |
| Placement of Tenckhoff catheter | 203 | 323 | 526 |
| Placement of tunneled cuffed catheter | 148 | 234 | 382 |
| Local catheter thrombolysis | 11 | 35 | 46 |
| Percutaneous transluminal angioplasty | 168 | 432 | 600 |
| Manual catheter-directed thrombo-aspiration | 336 | 680 | 1016 |

TABLE 5
Dialysis Access–Related Costs of Enrolled Patients, by Dialysis Modality and Vascular Access Type, per Patient–Year at Risk

| Intervention | Mean cost in euros [€ (95% confidence interval)] Hemodialysis (HD) With AVF (*n*=65) | With TCC (*n*=45) | Peritoneal dialysis (*n*=42) | *p* Value |
|---|---|---|---|---|
| Access surgery | 401.7 (343.8 to 459.6) | 252.9 (190.5 to 315.4) | 540.7 (526.8 to 584.7) | <0.001 |
| HD catheter interventions | 141.2 (57.7 to 234.6) | 718.7 (576.0 to 861.5) | 72.8 (26.9 to 118.8) | <0.001 |
| Diagnostic imaging | 344.7 (187.8 to 501.7) | 151.3 (52.9 to 249.8) | 0 | <0.001 |
| Hospitalization | 469.2 (57.9 to 996.3) | 2746.2 (494.8 to 4997.5) | 516.7 (67.5 to 965.9) | 0.010 |
| Transportation | 193.4 (128.3 to 258.5) | 339.1 (236.0 to 442.2) | 41.4 (28.1 to 54.6) | <0.001 |
| TOTAL | 1555.2 (974.0 to 2136.2) | 4208.2 (2050.7 to 6365.9) | 1171.6 (737.6 to 1526.0) | <0.001 |

The mean cost of access surgery per patient–year was higher for PD patients than for either the HD-AVF or the HD-TCC patients ($p < 0.001$, Table 5). On the other hand, the costs of diagnostic imaging procedures were higher for the HD-AVF patients ($p < 0.001$, Table 5), and the costs of hospitalization related to TCC interventions and of patient transportation were higher for the HD-TCC patients ($p = 0.010$ and $p < 0.001$ respectively; Table 5). Overall, the mean dialysis access–related costs per patient–year at risk were €1171.6 [median: €608.8; interquartile range (IQR): 563.1 – 936.7] for the PD patients, €1555.2 (median: €783.9; IQR: 371.4 – 1571.7) for the HD-AVF patients, and €4208.2 (median: €1252.4; IQR: 947.9 – 2983.5) for the HD-TCC patients ($p < 0.001$, Table 5). In multivariate analysis, total access-related costs were significantly higher for the HD-TCC modality than for either the PD or the HD-AVF modality (β = –0.53; 95% CI: –1.03 to –0.02; and β = –0.50; 95% CI: –0.96 to –0.04).

## DISCUSSION

The present study demonstrates that dialysis access–related intervention rates were significantly lower for patients initiating PD than for those initiating HD. Peritoneal dialysis patients had the lowest numbers of access surgeries and catheter-related interventions. In contrast, HD-AVF patients underwent a higher number of access surgeries and diagnostic imaging procedures, and HD-TCC patients underwent a higher number of catheter-related interventions and hospitalizations (mainly because of catheter-related bacteremia). Our

results accord with those of Oliver *et al.* (38) who recently reported that, compared with patients who chose HD, those who chose PD had a lower risk of invasive access interventions. In addition, we further demonstrated that the risks of catheter-related interventions and hospitalizations were significantly lower with the PD modality than with the HD-TCC modality, emphasizing the fact that patients who choose PD do not face an increased risk of catheter-related adverse events (10,39–41).

Our cost analysis showed that the costs related to dialysis access were lower for the PD modality. Even after considering the additional technical and overhead costs associated with PD catheter placement (operating room, general anesthesia, and surgical team) and the costs associated with primary nonfunction of all access types, patients who initiated PD incurred the lowest costs, and those who initiated HD-TCC, the highest costs during the first year of dialysis. In this regard, Lee *et al.* (32) reported that costs related to catheter placement and diagnostic imaging procedures accounted for the higher expenditure observed among prevalent HD patients with permanent catheters than among HD-AVF and PD patients. On the other hand, Manns *et al.* (31) observed that the largest cost component in patients dialyzed exclusively with a HD catheter (rather than an AVF) was hospitalization for access-related complications. In the present study, we observed that, in PD and HD-AVF patients, about 50% of dialysis access costs were related to access surgery, HD catheter interventions, and diagnostic imaging studies; in the HD-TCC group, about 75% of dialysis access costs were related to vascular access–related hospitalizations and patient transportation. In this regard, we observed that HD-TCC patients incurred the highest number of transportation runs (with the highest mean distances) between their homes and our hospital center. Total access-related costs were not statistically significantly different between the PD modality and the HD-AVF modality. Nevertheless, we observed that the costs for invasive interventions related to the dialysis access (mainly diagnostic imaging studies and catheter-related procedures) were higher in the HD-AVF modality. In this regard, Oliver *et al.* (38) also reported that, compared with PD patients, HD-AVF patients incurred a higher risk of invasive interventions.

The cost factor plays a leading role in health care economics. Because it is not easy to extrapolate costs from one country to another, studies that evaluate local realities are needed to guide appropriate economic decisions about the dialytic management of ESRD patients. Within the Portuguese National Health System, RRT is free of charge for the patient. In 2008, concerned with budget constraints and the exponential annual rise in dialysis costs, the Portuguese health authorities changed the reimbursement system for both HD and PD treatment to a per capita system that includes equipment costs, staff, patient follow-up and checkups, consumables, reverse-osmosis water, regular laboratory tests, radiology, and all medications for the treatment of anemia, bone-mineral disease, nutrition, cardiovascular complications, and in-dialysis intravenous antibiotics. The reimbursement per patient–week was set by law at €547.94 [Ministry of Health and Welfare Ordinance Legislation—Diário da República (2nd series, No. 35, 19 February 2008, clause No. 4325/2008)] for the HD and PD modalities alike. This package did not include vascular and PD access–related procedures, hospitalizations, or patient transportation. Our results, based on patients treated with contemporary dialysis modalities in Portugal, suggest that when a health care reimbursement system is the same for HD and PD, as occurs in Portugal, dialysis access–related costs may account for an approximate 4%, 5%, and 15% increase in annual dialysis treatment expenses for the PD, HD-AVF, and HD-TCC modalities respectively. Our findings accord with those of Manns *et al.* (31), who reported that HD vascular access costs may account for approximately 10% of the health care cost for incident HD patients, with patients selected for arteriovenous graft or catheter placement incurring the highest costs.

The present study may have important implications for policymakers. For health care systems that are promoting PD as a strategy to lower consumption of health care resources, our study suggests that the resources required to establish and maintain a dialysis access in the first year of treatment are lower for patients who chose PD.

As with all retrospective studies, selection bias may have occurred, in particular influenced by patient treatment preferences and time of referral to the nephrologist. In addition, the time at risk after the first access attempt was different between study groups. Further, the small sample size, short-term follow-up, and single-center nature of the study may limit its reproducibility. Also, the PD patients were treated at a single academic nephrology center, and the HD patients were treated at separate peripheral renal centers (although this situation reflects the distribution of patients between modalities in our country). The costs of certain health care procedures vary between countries. However, the relative resources required for an intervention and the determinants of the costs of vascular access are likely to be similar between centers. Finally, the extrapolation of data may inflate costs in the groups containing sicker patients.

## CONCLUSIONS

Our study suggests that, compared with patients who initiate HD, those who initiate PD require fewer resources to establish and maintain a dialysis access during the first year of treatment. In addition, our findings emphasize that PD is a cost-effective option for incident dialysis patients.

## ACKNOWLEDGMENTS

The authors thank Professor João Frazão for assistance with manuscript preparation, Ms. Doreen Raine for editing the English, and the clinical directors of the HD clinics who kindly agreed to collaborate in the study: A. Baldaia Moreira MD, A. Caldeira Gomes MD, A. Castro Henriques MD, Antunes de Azevedo MD, Eva Xavier MD, João C. Fernandes MD, João M. Frazão MD PhD, Jorge P. Baldaia MD, José M. Madureira MD, José Pinheiro MD, Odete Pereira MD, Sofia Pedroso MD, Susana Sampaio MD, and Vasco Miranda MD.

## DISCLOSURES

The authors have no equity interest or financial agreements with any company or commercial entity related to the content of the article and they have not received salary or support from any company related to the article.

## REFERENCES

1. Astor BC, Eustace JA, Powe NR, Klag MJ, Fink NE, Coresh J on behalf of the CHOICE Study. Type of vascular access and survival among incident hemodialysis patients: the Choices for Healthy Outcomes in Caring for ESRD (CHOICE) Study. *J Am Soc Nephrol* 2005; 16:1449–55.
2. Rehman R, Schmidt RJ, Moss AH. Ethical and legal obligation to avoid long-term tunneled catheter access. *Clin J Am Soc Nephrol* 2009; 4:456–60.
3. Moist LM, Trpeski L, Na Y, Lok CE. Increased hemodialysis catheter use in Canada and associated mortality risk: data from the Canadian Organ Replacement Registry 2001 – 2004. *Clin J Am Soc Nephrol* 2008; 3:1726–32.
4. Carrero JJ, de Jager DJ, Verduijn M, Ravani P, De Meester J, Heaf JG, *et al.* Cardiovascular and noncardiovascular mortality among men and women starting dialysis. *Clin J Am Soc Nephrol* 2011; 6:1722–30.
5. de Jager DJ, Grootendorst DC, Jager KJ, van Dijk PC, Tomas LM, Ansell D, *et al.* Cardiovascular and noncardiovascular mortality among patients starting dialysis. *JAMA* 2009; 302:1782–9.
6. Lee T, Barker J, Allon M. Tunneled catheters in hemodialysis patients: reasons and subsequent outcomes. *Am J Kidney Dis* 2005; 46:501–8.
7. Allon M, Daugirdas J, Depner TA, Greene T, Ornt D, Schwab SJ. Effect of change in vascular access on patient mortality in hemodialysis patients. *Am J Kidney Dis* 2006; 47:469–77.
8. Lacson E Jr, Wang W, Hakim RM, Teng M, Lazarus JM. Associates of mortality and hospitalization in hemodialysis: potentially actionable laboratory variables and vascular access. *Am J Kidney Dis* 2009; 53:79–90.
9. Perl J, Wald R, McFarlane P, Bargman JM, Vonesh E, Na Y, *et al.* Hemodialysis vascular access modifies the association between dialysis modality and survival. *J Am Soc Nephrol* 2011; 22:1113–21.
10. Aslam N, Bernardini J, Fried L, Burr R, Piraino B. Comparison of infectious complications between incident hemodialysis and peritoneal dialysis patients. *Clin J Am Soc Nephrol* 2006; 1:1226–33.
11. Rodrigues A. How to persuade peritoneal dialysis–skeptical hemodialysis fans. *Contrib Nephrol* 2009; 163:237–42.
12. Dell'Aquila R, Chiaramonte S, Rodighiero MP, Spanó E, Di Loreto P, Kohn CO, *et al.* Rational choice of peritoneal dialysis catheter. *Perit Dial Int* 2007; 27(Suppl 2):S119–25.
13. Gokal R, Alexander S, Ash S, Chen TW, Danielson A, Holmes C, *et al.* Peritoneal catheters and exit-site practices toward optimum peritoneal access: 1998 update. *Perit Dial Int* 1998; 18:11–33.
14. Digenis GE, Abraham G, Savin E, Blake P, Dombros N, Sombolos K, *et al.* Peritonitis-related deaths in continuous ambulatory peritoneal dialysis (CAPD) patients. *Perit Dial Int* 1990; 10:45–7.
15. Wilkie M, Wild J. Peritoneal dialysis access—results from a UK survey. *Perit Dial Int* 2009; 29:355–7.
16. Moossavi S, Raasch E, Russell G, Moossavi S, Mauck V, Beekman D, *et al.* Comparison of dialysis access outcomes in peritoneal dialysis and hemodialysis patients at an academic medical center (Abstract). *Perit Dial Int* 2007; 27(Suppl 3):S24.
17. McDonald SP, Marshall MR, Johnson DW, Polkinghorne KR. Relationship between dialysis modality and mortality. *J Am Soc Nephrol* 2009; 20:155–63.
18. Weinhandl ED, Foley RN, Gilbertson DT, Arneson TJ, Snyder JJ, Collins AJ. Propensity-matched mortality comparison of incident hemodialysis and peritoneal dialysis patients. *J Am Soc Nephrol* 2010; 21:499–506.
19. Heaf JG, Løkkegaard H, Madsen M. Initial survival advantage of peritoneal dialysis relative to haemodialysis. *Nephrol Dial Transplant* 2002; 17:112–17.
20. Korevaar JC, Feith GW, Dekker FW, van Manen JG, Boeschoten EW, Bossuyt PM, *et al.* on behalf of the NECOSAD Study Group. Effect of starting with hemodialysis compared with peritoneal dialysis in patients new on dialysis treatment: a randomized controlled trial. *Kidney Int* 2003; 64:2222–8.
21. Hiramatsu M on behalf of the Japanese Society for Elderly Patients on Peritoneal Dialysis. How to improve survival in geriatric peritoneal dialysis patients. *Perit Dial Int* 2007; 27(Suppl 2):S185–9.
22. Huang CC, Cheng KF, Wu HD. Survival analysis: comparing peritoneal dialysis and hemodialysis in Taiwan. *Perit Dial Int* 2008; 28(Suppl 3):S15–20.

23. Klarenbach S, Manns B. Economic evaluation of dialysis therapies. *Semin Nephrol* 2009; 29:524–32.
24. Salonen T, Reina T, Oksa H, Sintonen H, Pasternack A. Cost analysis of renal replacement therapies in Finland. *Am J Kidney Dis* 2003; 42:1228–38.
25. Baboolal K, McEwan P, Sondhi S, Spiewanowski P, Wechowski J, Wilson K. The cost of renal dialysis in a UK setting—a multicentre study. *Nephrol Dial Transplant* 2008; 23:1982–9.
26. Sennfalt K, Magnusson M, Carlsson P. Comparison of hemodialysis and peritoneal dialysis—a cost–utility analysis. *Perit Dial Int* 2002; 22:39–47.
27. Pacheco A, Saffie A, Torres R, Tortella C, Llanos C, Vargas D, *et al.* Cost/utility study of peritoneal dialysis and hemodialysis in Chile. *Perit Dial Int* 2007; 27:359–63.
28. Villa G, Fernández–Ortiz L, Cuervo J, Rebollo P, Selgas R, González T, *et al.* Cost-effectiveness analysis of the Spanish renal replacement therapy program. *Perit Dial Int* 2012; 32:192–9.
29. Villa G, Rodríguez–Carmona A, Fernández-Ortiz L, Cuervo J, Rebollo P, Otero A, *et al.* Cost analysis of the Spanish renal replacement therapy programme. *Nephrol Dial Transplant* 2011; 26:3709–14.
30. Haller M, Gutjahr G, Kramar R, Harnoncourt F, Oberbauer R. Cost-effectiveness analysis of renal replacement therapy in Austria. *Nephrol Dial Transplant* 2011; 26:2988–95.
31. Manns B, Tonelli M, Yilmaz S, Lee H, Laupland K, Klarenbach S, *et al.* Establishment and maintenance of vascular access in incident hemodialysis patients: a prospective cost analysis. *J Am Soc Nephrol* 2005; 16:201–9.
32. Lee H, Manns B, Taub K, Ghali WA, Dean S, Johnson D, *et al.* Cost analysis of ongoing care of patients with end-stage renal disease: the impact of dialysis modality and dialysis access. *Am J Kidney Dis* 2002; 40:611–22.
33. Allon M, Dinwiddie L, Lacson E Jr, Latos DL, Lok CE, Steinman T, *et al.* Medicare reimbursement policies and hemodialysis vascular access outcomes: a need for change. *J Am Soc Nephrol* 2011; 22:426–30.
34. ERA-EDTA Registry. *ERA-EDTA Registry Annual Report 2009*. Amsterdam, Netherlands: Academic Medical Center, Department of Medical Informatics; 2011. [Available online at: http://www.era-edta-reg.org/files/annualreports/pdf/AnnRep2009.pdf; accessed 19 January 2013]
35. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40:373–83.
36. Coentrão L, Bizarro P, Ribeiro C, Neto R, Pestana M. Percutaneous treatment of thrombosed arteriovenous fistulas: clinical and economic implications. *Clin J Am Soc Nephrol* 2010; 5:2245–50.
37. Bizarro P, Coentrão L, Ribeiro C, Neto R, Pestana M. Endovascular treatment of thrombosed dialysis fistulae: a cumulative cost analysis. *Catheter Cardiovasc Interv* 2011; 77:1065–70.
38. Oliver MJ, Verrelli M, Zacharias JM, Blake PG, Garg AX, Johnson JF, *et al.* Choosing peritoneal dialysis reduces the risk of invasive access interventions. *Nephrol Dial Transplant* 2012; 27:810–16.
39. Povlsen JV, Ivarsen P. How to start the late referred ESRD patient urgently on chronic APD. *Nephrol Dial Transplant* 2006; 21(Suppl 2):ii56–9.
40. Povlsen JV. Unplanned start on assisted peritoneal dialysis. *Contrib Nephrol* 2009; 163:261–3.
41. Povlsen JV, Ivarsen P. Assisted peritoneal dialysis: also for the late referred elderly patient. *Perit Dial Int* 2008; 28:461–7.

Nephrol Dial Transplant (2012) 27: 1993–1996
doi: 10.1093/ndt/gfr532
Advance Access publication 21 September 2011

*Original Articles*

NDT
Nephrology Dialysis Transplantation

# Physical examination of dysfunctional arteriovenous fistulae by non-interventionalists: a skill worth teaching

Luís Coentrão[1], Bernardo Faria[2] and Manuel Pestana[1]

[1]Nephrology Research and Development Unit, Department of Nephrology, Hospital São João, Faculty of Medicine, University of Porto, Portugal and [2]Department of Nephrology, Hospital São Teotónio, Viseu, Portugal

*Correspondence and offprint requests to:* Luís Coentrão; E-mail: coentrao@med.up.pt

**Abstract**

**Background.** Physical examination (PE) of arteriovenous fistulae (AVF) has recently emerged as an important element in the detection of stenotic lesions. This study examines the accuracy of PE in the assessment of AVF dysfunction by non-interventionalists in comparison with angiography.

**Methods.** A total of 177 consecutive patients who had AVF dysfunction and were referred to our centre by general nephrologists for angioplasty between November 2009 and July 2010 were included in this analysis. Eleven referring general nephrologists completed a form reporting the PE findings regarding their patients' AVFs. Before angiography examination was carried out, a trained nephrology resident performed a PE in all the cases. Angiography of the AVFs was then performed by an interventionalist. Cohen's κ value was used as the measurement of the level of agreement beyond chance between the diagnosis made on PE and angiography.

**Results.** There was a moderate agreement beyond chance between the general nephrologists' PE and angiography in the detection of AVF inflow stenosis ($\kappa = 0.49$), outflow stenosis ($\kappa = 0.58$) and thrombosis ($\kappa = 0.52$). On the other hand, PE performed by the trained nephrology resident strongly agreed with angiography in the detection of AVF inflow stenosis ($\kappa = 0.84$), outflow stenosis ($\kappa = 0.92$) and thrombosis ($\kappa = 0.98$). The agreement between PE and angiography in the detection of co-existing AVF inflow–outflow stenosis was poor for the general nephrologists and moderate for the trained nephrology resident ($\kappa = 0.14$ versus $\kappa = 0.55$, respectively).

**Conclusion.** PE may provide an accurate means of diagnosis of AVF dysfunction. Theoretical and hands-on training in PE of dysfunctional AVFs should be provided for nephrologists in-training and for the dialysis staff.

**Keywords:** arteriovenous fistulae; dialysis; physical examination

## Introduction

Arteriovenous fistula (AVF) dysfunction is a common major problem in haemodialysis units. The European Renal Best Practice (ERBP) and Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines [1, 2] have therefore recommended a programme for the detection of stenosis and its subsequent correction in an attempt to reduce the occurrence of thrombosis. AVF stenosis and thrombosis are in fact the most common causes of access dysfunction, and there have been extensive investigations to identify the best methods for detecting accesses at risk [3–9]. Several diagnostic procedures have been recommended for vascular access surveillance, including blood flow, intra-access static pressure and access recirculation [1, 2]. However, these procedures are time consuming and costly. Physical examination (PE) of AVFs performed by trained physicians has recently emerged as an important element in the assessment of stenotic lesions [8, 10–15]. However, there are no studies reporting the accuracy of PE in the diagnosis of AVF dysfunction when performed by dialysis staff to our knowledge. We therefore designed this study to determine the accuracy of PE by general nephrologists in the assessment of AVF dysfunction in comparison with angiography. The study also evaluated the agreement between PE of dysfunctional AVFs performed by a trained nephrology resident and angiography.

### Materials and methods

Hospital São João is a tertiary-care University Hospital that carries out interventional procedures in patients on regular haemodialysis referred from other hospitals and satellite haemodialysis units. The patients treated in these haemodialysis units are monitored for clinical signs of access dysfunction by the nephrologists treating them. Patients are referred for diagnostic angiography and/or angioplasty as appropriate, on the basis of clinical signs of vascular access dysfunction.

We analysed a database of a prospective observational study conducted in a population of 177 haemodialysis patients consecutively referred to our centre by general nephrologists for angioplasty, between November 2009 and July 2010. Eleven referring general nephrologists without specific training on AVF PE and angiography completed a form reporting the PE findings regarding their patients' AVFs. This information was recorded and placed in a sealed envelope. Before the angiography procedure was carried out, a nephrology resident with 6 months training in vascular access PE and angiography performed a PE in all the cases, unaware of the general nephrologists' PE findings. Angiography examination of the AVFs was performed in our hospital centre by an interventionalist, blind to both the general nephrologists' and the nephrology resident's reports. The

study was limited to interventions involving autogenous AVFs. This investigation was reviewed and approved by the Hospital São João Institutional Review Board.

*Procedures*

*Angiography examination.* Angiography was defined as the gold standard examination for diagnosis of AVF dysfunction. Angiography was performed to evaluate the AVF from the feeding artery to the right atrium (Mobile C-arm BV Pulsera; Philips Medical Systems, Eindhoven, The Netherlands). AVF dysfunction was classified into four major disorders: inflow stenosis, outflow stenosis, co-existing inflow–outflow stenosis and AVF thrombosis. The inflow segment was defined as the feeding artery, anastomosis and the juxta-anastomosis area (first few centimetres of the fistula). Outflow was defined as the entire segment from the juxta-anastomosis area to the right atrium. Stenosis was defined as 50% luminal narrowing compared to the normal vascular segment located adjacent to the stenosis according to K/DOQI [2]. Thrombosis of the AVF was ascertained according to the presence of clots in the arterial and/or venous sides of the AVF. Clinical criteria of access dysfunction prompting angiography were applied according to the K/DOQI [2].

*Physical examination.* Pulse abnormalities and thrill were used as the main PE tools for the diagnosis of AVF dysfunction [11, 12]. In addition, inspection of the arm, chest, neck and face, palpation of the entire AVF tract, arm elevation and pulse augmentation tests were considered important to detect the cause of AVF dysfunction. Pulse augmentation consists of the complete occlusion of the access several centimetres beyond the arterial anastomosis and evaluation of the strength of the pulse. The test is considered normal when the portion of fistula upstream from the occluding finger demonstrates augmentation of pulse [12]. The arm elevation test consists of the elevation of the extremity with the fistula and examination of the normal collapse of the access [12]. The test is considered normal when the fistula collapses after arm elevation. The diagnostic elements of the PE are reported in Table 1.

*Statistical analysis*

Diagnostic variables for both the PE and angiography were dichotomous (presence or absence of the lesion). The general nephrologists were considered to be a homogeneous population since none of them had received specific training in AVF PE and angiography. Accuracy, sensitivity, specificity and predictive positive and negative values were measured in relation to angiography as the gold standard method. Cohen's κ value was used as a measurement of the level of agreement beyond chance between the diagnoses made by PE and angiography. κ values range from 0 to 1.0, with zero indicating no agreement beyond chance and 1.0 denoting perfect agreement. κ values between 0 to 0.20 and 0.21 to 0.40 confer a poor and a fair agreement beyond chance, respectively; those between 0.41 to 0.60 and 0.61 to 0.80 a moderate and a substantial agreement; and those exceeding 0.80 a near-perfect agreement [16]. All statistical analyses were performed using SPSS software, version 11 (SPSS, Chicago, IL).

## Results

One hundred (56%) patients were male. The mean age was 64 ± 13 years. Eighty-four (48%) AVFs were located in the forearm (82 radio-cephalic AVFs and 2 ulnar-basilic AVFs) and 93 (52%) were located in the upper arm (70 brachio-cephalic AVFs and 23 brachio-basilic AVFs). Inflow and outflow stenoses were the most common types of disorder (37 and 28%, respectively). Co-existing inflow–outflow stenosis and AVF thrombosis were present in 14 and 21% of the patients, respectively. In forearm AVFs, inflow stenosis was the most common type of disorder, whereas outflow stenosis was the most frequent one in upper-arm AVFs (50 and 38%, respectively).

The accuracy of PE by the general nephrologists in the detection of inflow, outflow, co-existing inflow–outflow stenosis and AVF thrombosis was 77, 83, 85 and 81%, respectively (Table 2). The sensitivity and specificity were 57 and 89% for inflow stenosis, 80 and 84% for outflow stenosis, 12 and 97% for co-existing inflow–outflow stenosis and 86 and 79% for AVF thrombosis, respectively (Table 2). There was a moderate agreement beyond chance between PE by general nephrologists and angiography for the assessment of AVF dysfunction (κ = 0.49, 95% CI 0.40–0.57; Table 3). More specifically, there was a moderate agreement between PE and angiography in the diagnosis of AVF inflow and outflow stenosis and AVF thrombosis (κ = 0.49, 95% CI 0.34–0.64; κ = 0.58, 95% CI 0.44–0.73; κ = 0.52, 95% CI 0.38–0.65, respectively;

**Table 1.** Diagnostic elements of the PE used in the evaluation of AVF dysfunction [7, 8][a]

| Diagnosis | Thrill | Pulse | Arm elevation test | Pulse augmentation test |
|---|---|---|---|---|
| Inflow stenosis | Weak, discontinuous | Weak | Excessive collapse | Failure of the pulse to increase |
| Outflow stenosis | Strong, systolic | Strong | No partial vein collapse | n.a. |
| Co-existing inflow–outflow stenosis | Weak, discontinuous | n.a. | No partial vein collapse | Failure of the pulse to increase |
| Fistula thrombosis[b] | Absent | Strong or absent | n.a. | n.a. |

[a]n.a., not applicable.
[b]Additional physical examination finding was the presence of a palpable clot.

**Table 2.** Diagnostic accuracy of PE in the detection of AVF dysfunction by general nephrologists (GNs) and nephrology resident (NR)[a]

| Diagnosis | | ACC | SEN | SPE | PPV | NPV | PREV |
|---|---|---|---|---|---|---|---|
| Inflow stenosis | GN | 0.77 (0.62–0.89) | 0.57 (0.45–0.68) | 0.89 (0.82–0.94) | 0.76 (0.65–0.84) | 0.78 (0.70–0.85) | 0.37 |
| | NR | 0.92 (0.87–0.96) | 0.98 (0.92–1) | 0.88 (0.81–0.93) | 0.83 (0.80–0.91) | 0.99 (0.95–1) | |
| Outflow stenosis | GN | 0.83 (0.78–0.89) | 0.80 (0.71–0.90) | 0.84 (0.77–0.90) | 0.67 (0.58–0.75) | 0.91 (0.81–0.96) | 0.28 |
| | NR | 0.97 (0.91–0.99) | 0.96 (0.87–0.99) | 0.97 (0.92–0.99) | 0.92 (0.89–0.98) | 0.98 (0.94–1) | |
| Co-existing inflow–outflow stenosis | GN | 0.85 (0.77–0.94) | 0.12 (0.04–0.30) | 0.97 (0.92–0.99) | 0.43 (0.30–0.55) | 0.87 (0.72–0.93) | 0.14 |
| | NR | 0.92 (0.87–0.96) | 0.44 (0.27–0.63) | 0.99 (0.96–1) | 0.92 (0.87–0.96) | 0.92 (0.89–0.98) | |
| Fistula thrombosis | GN | 0.81 (0.71–0.89) | 0.86 (0.72–0.94) | 0.79 (0.72–0.85) | 0.52 (0.44–0.55) | 0.95 (0.89–0.99) | 0.21 |
| | NR | 0.99 (0.98–1) | 0.97 (0.86–1) | 1 (0.97–1) | 1 (0.96–1) | 0.99 (0.97–1) | |

[a]ACC, accuracy; NPV, negative predictive value; PPV, positive predictive value; PREV, prevalence of diagnosis by angiography; SEN, sensitivity; SPE, specificity.

Table 3) and a poor agreement between PE and angiography in the diagnosis of co-existing inflow–outfllow stenosis (κ = 0.14, 95% CI 0.02–0.26; Table 3). Analysis of the forearm and upper-arm AVF findings revealed a fair-to-moderate agreement between the PE and angiography for the assessment of dysfunctional forearm and upper-arm AVFs, respectively (κ = 0.34, 95% CI 0.19–0.41 versus κ = 0.60, 95% CI 0.51–0.71; Table 4).

The accuracy of PE by the trained nephrology resident for the detection of inflow, outflow, co-existing inflow–outflow stenosis and AVF thrombosis was 92, 97, 92 and 99%, respectively (Table 2). The sensitivity and specificity were 98 and 88% for inflow stenosis, 96 and 97% for outflow stenosis, 44 and 99% for co-existing inflow–outflow stenosis and 97 and 100% for AVF thrombosis, respectively (Table 2). There was a near-perfect agreement beyond chance between PE by the trained nephrology resident and angiography for the assessment of AVF dysfunction (κ = 0.86, 95% CI 0.77–0.95; Table 3). More specifically, there was a near-perfect agreement between the PE and angiography in the diagnosis of inflow and outflow stenosis and AVF thrombosis (κ = 0.84, 95% CI 0.69–0.98; κ = 0.92, 95% CI 0.77–1.0; κ = 0.98, 95% CI 0.84–1.0, respectively; Table 3) and a moderate agreement between PE and angiography in the diagnosis of co-existing inflow–outflow stenosis (κ = 0.55, 95% CI 0.42–0.69; Table 3). Analysis of the forearm and upper-arm AVFs revealed no significant difference in the level of agreement between PE and angiography (κ = 0.82, 95% CI 0.70–0.91 versus κ = 0.89, 95% CI 0.78–0.92, respectively; Table 4).

## Discussion

By comparing PE to the gold standard (angiography), the current study objectively assessed the accuracy of PE when performed by general nephrologists and a trained nephrology resident in the diagnosis of various types of disorder responsible for AVF dysfunction. Our results showed that PE by general nephrologists had a poor-to-moderate accuracy for the assessment of AVF dysfunction. The sensitivity was low for the diagnosis of AVF inflow stenosis, particularly for co-existing inflow–outflow lesions. On the other hand, the sensitivity and specificity of PE performed by general nephrologists were relatively high for the diagnosis of AVF outflow stenosis and AVF thrombosis. These findings are consistent with other recent data suggesting that AVFs with outflow stenosis are easier to assess by PE than AVFs with inflow stenosis [8]. With respect to the accuracy of PE in the hands of a trained nephrology resident, we observed a high level of agreement between PE and angiography for the diagnosis of AVF dysfunction, particularly for inflow and outflow stenosis and AVF thrombosis. Our results agree well with the previous findings by Asif *et al.* [13] confirming that PE performed by trained physicians is an accurate diagnostic tool for the detection of stenosis in a great majority of dysfunctional AVFs.

With respect to the location of the AVFs, general nephrologists did better with upper-am AVFs compared with forearm AVFs, whereas the trained nephrology resident presented a same level of agreement similar results with both upper-arm and forearm AVFs (Table 4). The discrepancy observed among the general nephrologists may be explained by the fact that outflow stenosis was the most common type of disorder in upper-arm AVF, whereas inflow stenosis was the most frequent one in forearm AVFs.

The value of PE in the detection of AVF stenosis has recently been compared with angiography and Doppler ultrasound [8, 13–15]. Asif *et al.* [13] and Campos *et al.* [15] determined the accuracy of PE in the detection of stenosis in AVFs, with excellent results. However, PE was

**Table 3.** κ value for PE in the diagnosis of various types of disorder by general nephrologists and nephrology resident

| Diagnosis | General nephrologists (κ) | Nephrology resident (κ) |
|---|---|---|
| Inflow stenosis | 0.49 [0.34–0.64] (P < 0.001) | 0.84 [0.69–0.98] (P < 0.001) |
| Outflow stenosis | 0.58 [0.44–0.73] (P < 0.001) | 0.92 [0.77–1] (P < 0.001) |
| Co-existing inflow–outflow stenosis | 0.14 [0.02–0.26] (P = 0.021) | 0.55 [0.42–0.69] (P < 0.001) |
| Fistula thrombosis | 0.52 [0.38–0.65] (P < 0.001) | 0.98 [0.84–1] (P < 0.001) |
| Overall | 0.49 [0.40–0.57] (P < 0.001) | 0.86 [0.77–0.95] (P < 0.001) |

**Table 4.** κ values for PE of dysfunctional forearm and upper-arm fistulae by general nephrologists and nephrology resident

| Diagnosis | | General nephrologists (κ) | Nephrology resident (κ) |
|---|---|---|---|
| Inflow stenosis | Forearm | 0.31 (P = 0.003) | 0.80 (P < 0.001) |
| | Upper arm | 0.63 (P < 0.001) | 0.87 (P < 0.001) |
| Outflow stenosis | Forearm | 0.43 (P < 0.001) | 0.91 (P < 0.001) |
| | Upper arm | 0.65 (P < 0.001) | 0.93 (P < 0.001) |
| Co-existing inflow–outflow stenosis | Forearm | 0.15 (P = 0.12) | 0.59 (P < 0.001) |
| | Upper arm | 0.02 (P = 0.20) | 0.50 (P < 0.001) |
| Fistula thrombosis | Forearm | 0.43 (P < 0.001) | 1.0 (P < 0.001) |
| | Upper arm | 0.60 (P < 0.001) | 0.97 (P < 0.001) |
| Overall | Forearm | 0.34 (P < 0.001) | 0.82 (P < 0.001) |
| | Upper arm | 0.60 (P < 0.001) | 0.89 (P < 0.001) |

performed by only one physician with experience in this field. In addition, Campos *et al.* [15] determined the accuracy of PE in the detection of AVF stenosis in comparison with Doppler ultrasound and Asif *et al.* [13] with angiography (albeit in a restricted manner because only still images were evaluated). Leon *et al.* [14] reported a similar accuracy of PE performed by an experienced interventionalist and a trained nephrology fellow (however, the two examiners performed the PE in different populations). Recently, Tessitore *et al.* [8] reported that the level of agreement of PE in the detection of AVF stenosis was fair-to-moderate among nephrologists with different expertise on vascular access monitoring. Our results agree well with the previous findings of Tessitore *et al.* [8] and further suggest that the accuracy of PE in the assessment of AVF dysfunction depends on the specific training of the examiner rather than on the cumulative experience in dialysis clinical practice. In addition, by assessing the accuracy of PE performed by general nephrologists in their own daily clinical practice, our study allows us to examine the quality of AVF monitoring in 'real practice in a real world'.

The fundamental concept of vascular access monitoring and surveillance is that stenosis develops over varying intervals in the great majority of AVFs and, if detected and corrected in time, maturation can be promoted, underdialysis minimized or avoided and thrombosis avoided or reduced [17, 18]. There are several factors that can suggest the presence of AVF dysfunction, such as low access blood flow, elevated intra-access pressure, unexplained decreases in delivered dialysis dose or access recirculation. However, they do not detect the cause of AVF dysfunction. PE provides a means of access evaluation that incurs no extra cost and is readily available. Moreover, PE provides additional information that is of the utmost importance for the interventionalist since different endovascular approaches are used for AVFs with inflow, outflow, co-existing inflow–outflow problems or AVF thrombosis. Detection of AVF dysfunction therefore requires an accurate diagnosis of its cause.

We are aware that our study has its limitations. This is not a randomized clinical study; the order of the assessors was not random and, for logistic (and cost) reasons, one rater always performed later and this may have introduced a bias. The results obtained by the general nephrologists may have been influenced by the fact that the PE was conducted in their own dialysis patients, and different interpretations of the PE findings used for the evaluation of AVF dysfunction may have occurred. Also, the results of this study apply only to a cohort of dysfunctional AVFs and may not apply to unselected AVF populations. In addition, the analysis did not address any variability in the interpretation of the angiography.

## Conclusion

PE of AVFs is non-invasive, incurs no extra cost and may provide an accurate means by which to diagnose AVF dysfunction. However, nephrologists in haemodialysis units may need to improve their skills in performing PE. Theoretical and hands-on training in PE should therefore be provided for nephrologists in-training and for the dialysis staff.

*Acknowledgements*. The authors thank Prof João Frazão for his assistance in manuscript preparation and Ms Doreen Raine for editing this article in English.

*Conflict of interest statement*. None declared.

## References

1. Tordoir J, Canaud B, Haage P *et al.* EBPG on vascular access. *Nephrol Dial Transplant* 2007; 22 (Suppl 2): ii88–ii117
2. Vascular Access 2006 Work Group. NKF-DOQI clinical practice guidelines for vascular access: update 2006. *Am J Kidney Dis* 2006; 48 (Suppl 1): S176–S276
3. Tonelli M, Jindal K, Hirsch D *et al.* Screening for subclinical stenosis in native vessel arteriovenous fistulae. *J Am Soc Nephrol* 2001; 12: 1729–1733
4. Schwab SJ, Oliver MJ, Suhocki P *et al.* Hemodialysis arteriovenous access: detection of stenosis and response to treatment by vascular access blood flow. *Kidney Int* 2001; 59: 358–362
5. McCarley P, Wingard RL, Shyr Y *et al.* Vascular access blood flow monitoring reduces access morbidity and costs. *Kidney Int* 2001; 60: 1164–1172
6. Tessitore N, Bedogna V, Gammaro L *et al.* Diagnostic accuracy of ultrasound dilution access blood flow measurement in detecting stenosis abd predicting thrombosis in native forearm arteriovenous fistulae for hemodialysis. *Am J Kidney Dis* 2003; 42: 331–341
7. Tessitore N, Lipari G, Poli A *et al.* Can blood flow surveillance and pre-emptive repair of subclinical stenosis prolong the useful life of arteriovenous fistulae? A randomized controlled study. *Nephrol Dial Transplant* 2004; 19: 2325–2333
8. Tessitore N, Bedogna V, Melilli E *et al.* In search of an optimal bedside screening program for arteriovenous fistula stenosis. *CJASN* 2011; 6: 819–826
9. Tessitore N, Bedogna V, Lipari G *et al.* Bedside screening for fistula stenosis should be tailored to the site of the arteriovenous anastomosis. *CJASN* 2011; 6: 1073–1080
10. Besarab A, Ravani P, Spergel LM *et al.* The native arteriovenous fistula in 2007. Research nedds. *J Nephrol* 2007; 20: 668–673
11. Beathard GA. Physical examination of the dialysis vascular access. *Semin Dial* 1998; 11: 231–236
12. Beathard GA. An algorithm for the physical examination of early fistula failure. *Semin Dial* 2005; 18: 331–335
13. Asif A, Leon C, Orozco-Vargas LC *et al.* Accuracy of physical examination in the detection of arteriovenous fistula stenosis. *Clin J Am Soc Nephrol* 2007; 2: 1191–1194
14. Leon C, Asif A. Physical examination of arteriovenous fistulae by a renal fellow: does it compare favorably to an experienced interventionalist? *Semin Dial* 2008; 21: 557–560
15. Campos RR, Chula DC, Perreto S *et al.* Accuracy of physical examination and intra-access pressure in the detection of stenosis in hemodialysis arteriovenous fistula. *Semin Dial* 2008; 21: 269–273
16. McGinn T, Wyers PC, Newman T *et al.* Tips for learners of evidence-based medicine: measures of observer variability/kappa statistics. *CMAJ* 2004; 171: 1369–1373
17. Campos R, Riella MC. Challenge for the interventional nephrologist: monitoring the arteriovenous fistula. *Contrib Nephrol* 2008; 161: 12–22
18. Besarab A, Asif A, Roy-Chaudhury P *et al.* The native arteriovenous fistula in 2007. Surveillance and monitoring. *J Nephrol* 2007; 20: 656–667

*Received for publication: 9.6.11; Accepted in revised form: 9.8.11*

# Percutaneous Treatment of Thrombosed Arteriovenous Fistulas: Clinical and Economic Implications

Luís Coentrão,*† Pedro Bizarro,* Carlos Ribeiro,‡ Ricardo Neto,* and Manuel Pestana*

**Nephrology Research and Development Unit, Hospital S. João, and †Institute of Pharmacology and Therapeutics, Faculty of Medicine, University of Porto, Porto, Portugal; and ‡Financial Management Unit, Hospital S. João, Porto, Portugal*

**Background and objectives: Maintenance of previously thrombosed arteriovenous fistulas (AVFs) as functional vascular accesses can be highly expensive, with relevant financial implications for healthcare systems. The aim of our study was to evaluate the costs and health outcomes of vascular access care in hemodialysis patients with AVF thrombosis.**

**Design, setting, participants, & measurements: A retrospective, controlled cohort study was performed among local hemodialysis patients with completely thrombosed AVFs between August 1, 2007, and July 1, 2008. Detailed clinical and demographic information was collected and a comprehensive measure of total vascular access costs was obtained. Costs are reported in 2009 U.S. dollars.**

**Results: A total of 63 consecutive hemodialysis patients with thrombosed AVFs were identified—a cohort of 37 patients treated with percutaneous thrombectomy and a historic cohort of 25 patients with abandoned thrombosed AVFs. The mean cost of all vascular access care at 6 months was $2479. Salvage of thrombosed AVFs led to a near two-fold reduction in access-related expenses, per patient-month at risk ($375 *versus* $706; $P = 0.048$). The costs for access-related hospitalizations ($393 *versus* $91; $P = 0.050$), management of access dysfunction ($106 *versus* $28; $P = 0.005$), and surgical interventions ($35 *versus* $6; $P = 0.001$) were also significantly lower in the percutaneous treatment group. At 6 months, most of these patients had a functional AVF as permanent vascular access (91% *versus* 33%, $P = 0.0001$).**

**Conclusions: Salvage of thromboses AVF is a highly efficient procedure; therefore, intensive efforts should be undertaken to universalize these interventions.**

*Clin J Am Soc Nephrol* 5: 2245–2250, 2010. doi: 10.2215/CJN.03070410

Functional vascular access is a prerequisite for adequate hemodialysis treatment in patients with ESRD. Autogenous arteriovenous fistulas (AVFs) are considered superior to synthetic grafts as a hemodialysis vascular access; however, AVFs are not without problems (1). In the last decade, management of thrombosed AVFs has been largely accomplished by surgical or endovascular interventions. Despite the existence of well established endovascular procedures to declot a thrombosed AVF (2–10), attempts to salvage these accesses are not universally used.

Percutaneous treatment of thrombosed AVFs is a relatively highly successful procedure. However, repeated interventions are usually required to achieve long-term access survival (11). Therefore, maintenance of a previously thrombosed AVF could be a highly expensive policy. Published data regarding the economic value of vascular access surveillance and prophylactic angioplasty to prevent AVF thrombosis are controversial (12,13), and information about the cost-effectiveness of AVF salvage procedures has been limited.

In the study presented here, we performed a retrospective analysis among adult maintenance dialysis patients with thrombosed AVFs to estimate the costs and health outcomes of vascular access care during the first 6 months post-thrombosis.

## Patients and Methods

### *Patient Population*

The Hospital S. João, Porto, is a university hospital center that serves a large population on regular hemodialysis (approximately 1600 patients). Until the last few years, hemodialysis patients with thrombosed AVFs were referred for surgical revision of the clotted AVF or to our nephrology department for central venous catheterization pending creation of a new AVF. By 2008, endovascular treatment of thrombosed AVFs became a standard procedure in our unit.

Patients were recruited from the Nephrology Unit, Hospital S. João, Porto. All adult maintenance dialysis patients with completely thrombosed AVFs between August 1, 2007 and July 31, 2008, were included in this study. From August 1 and December 31, 2007, patients were referred for central venous catheterization pending creation of a new AVF. From January 1 to July 31, 2008, patients were referred for consideration of a percutaneous thrombectomy.

Sixty-three adult maintenance dialysis patients fulfilled the study criteria. Thirty-seven patients were treated with percutaneous thrombectomy (group A) and 25 patients underwent central venous catheterization to bridge the interval until a new AVF was suitable for

Received April 7, 2010. Accepted July 14, 2010.

*Published online ahead of print. Publication date available at www.cjasn.org.*

**Correspondence:** Dr. Luís Coentrão, Nephrology Research and Development Unit, Faculty of Medicine, University of Porto, Alameda Prof. Hernâni Monteiro, 4200-319 Porto, Portugal. Phone: +35-191-053-8824; Fax: +35-122-551-2228; E-mail: coentrao@med.up.pt



ISSN: 1555-9041/512–2245

cannulation (group B). In only one patient the interventionalist deemed that endovascular intervention was not advisable because of the presence of long segmental aneurysms with an extremely large clot burden. This patient underwent central venous catheterization. Three patients were lost to follow-up. In the final analysis, group A included 35 patients and group B included 24 patients ($n = 59$).

The study was approved by the Ethics Committee for Health of the Hospital S. João, Porto.

### *Procedures*

In our unit, we used the method of manual catheter-directed thromboaspiration (2). If a hemodynamically significant lesion was encountered, a conventional angioplasty balloon, rated burst pressure of 15 atm (Cordis Corporation, Johnson & Johnson Medical N.V/S.A., Waterloo, Belgium), was inflated at the level of the stenotic site. Patients were referred within 72 hours of thrombosis. The only contraindications for percutaneous declotting were infection and the presence of long segmental aneurysms with extremely large clot burdens. Percutaneous thrombectomy was performed as an outpatient procedure.

Tunneled cuffed catheter (TCC) placement (Retro, Spire Biomedical, Inc., Bedford, MA) was performed with ultrasound guidance, as recommended by Dialysis Outcomes Quality Initiatives (14). Postprocedure chest radiography was performed in all patients.

Clinical success was defined as the resumption of dialysis with a blood flow >300 ml/min at the first dialysis session after the intervention (15). Primary (unassisted) patency of the vascular access was calculated from the date of the index procedure to the first subsequent access intervention. Access primary patency ended when any of the following occurred: (*1*) there was an intervention for the treatment of stenosis or thrombosis anywhere within the AVF; (*2*) there was an intervention for the treatment of intracatheter thrombosis, catheter malposition, or kinking; or (*3*) there was an intervention for the treatment of access-related bacteriaemia requiring catheter removal or AVF closure.

### *Cost Analysis*

Our study took the perspective of the healthcare purchaser including direct vascular access care-related costs. All resource use was valued at prices in 2009. All costs were converted to U.S. dollars using an exchange rate of 1 Euro (€) equal to 1.41 U.S.$.

A direct access care-related cost was estimated for each procedure, including all expenses for creation of a new AVF (unitary cost, $420), placement of TCC (unitary cost, $605), and hospitalization for vascular access-related complications (unitary cost for in-hospital care of vascular access infection, $2075). Costs for correcting the AVF stenosis or thrombosis by endovascular means were assessed to be $1401. The cost per procedure was established from the Ministry of Health and Welfare Ordinance Legislation - Diário da República (1st series, no. 147, July 31, 2009, ordinance no. 839 and 2nd series, no. 81, April 5, 2000, dispatch no. 7376/2000).

Information on all vascular access surgeries was captured from our nephrology unit database, which collects surgical data for all patients who undergo vascular access surgery. Information on hospital admissions for management of vascular access-related problems (*e.g.*, local or metastatic infection, limb ischemia, hemorrhage, or thrombosis), endovascular procedures (*i.e.*, all radiology procedures performed as part of access-related care), and catheter placements/local thrombolytic therapy, was collected from our hospital database. Patient's transport costs required for the vascular access care were also included in the analysis. They principally used a taxi or ambulance for hospital visits ($0.66 for 1 km). In addition, we did not collect information on costs specifically related to outpatient use of intravenous antibiotics for access-related infection.

### *Follow-Up*

Patient follow-up started on the day the vascular access intervention was first performed and continued for 6 months. Clinical and demographic data, as well as data on access type, were collected from hospital and satellite unit records. Demographic information was assessed by means of a questionnaire. The presence of comorbid illness was assessed by a physician as of the enrolment date by complete review of patient's records. Information was collected for the 19 variables that constitute the Charlson comorbidity index (16), which has been validated for use in patients with ESRD. Follow-up was censored for patient death or transplant.

### *Study Endpoints*

The primary endpoint of this analysis was to determine the economic effect of endovascular intervention in hemodialysis patients with thrombosed AVF. Secondary outcomes of the study included all access-related clinical adverse events (*e.g.*, bacteriaemia, access dysfunction, surgical interventions, hospital admissions, and death).

### *Statistical Analyses*

Data are given as percentages and mean ± SD. Normally distributed continuous variables were analyzed using Student's unpaired *t* test and categorical variables using Fisher's exact test. Rates were calculated for each of the patients by dividing the number of events/procedures by the duration of follow-up in months. Vascular access patency was analyzed using the Kaplan–Meier method and differences between groups were evaluated by log-rank tests. All tests were two sided, and differences were considered significant at $P < 0.05$. All statistical analyses were performed using the SPSS software, version 11 (SPSS, Inc., Chicago, IL).

## Results

Approximately two thirds of the patients were male. Diabetes, hypertension, and vascular disease were commonly present in both study groups. There were no relevant differences between the two treatment groups at baseline with respect to demographic characteristics and medical history (Table 1).

Percutaneous thrombectomy was successfully performed in 34 patients, with prompt restoration of a thrill and bruit. No stent was deployed. Angioplasty was not feasible in one patient with an upper-arm AVF because of the inability to pass the guidewire through a tight stenotic lesion. This patient underwent TCC placement. Clinical success was observed in 34 patients (success rate = 97%). Twenty-four patients (69%) presented with a radial-cephalic AVF (an underlying stenosis lesion was present in the draining vein in 11 patients and concurrent stenoses at the arterial anastomosis and in the draining vein in 13 patients). Eleven patients (31%) presented with a brachial-cephalic AVF (an underlying stenosis lesion was present in the draining vein in five patients and in the arterial anastomosis in six patients). One patient with upper-arm AVF developed steal syndrome and myocardial infarction, approximately 2 weeks postprocedure, requiring hospitalization and further access surgery. Six patients experienced AVF thrombosis during follow-up (five patients with an upper-arm AVF and one patient with a forearm AVF): three patients were treated

*Table 1.* Baseline characteristics of patients overall and according to treatment group

| Characteristics | Overall ($n$ = 59) | Group A ($n$ = 35) | Group B ($n$ = 24) | $P$ |
|---|---|---|---|---|
| Age, years | 66 ± 13,4 | 64 ± 14 | 69 ± 11.8 | 0.07 |
| Gender, $n$ (%) male | 39 (66%) | 25 (71%) | 14 (58.3%) | 0.29 |
| Previous fistulas, $n$ (%) | 24 (40.7%) | 13 (37%) | 11 (45.8%) | 0.21 |
| Previous dialysis catheter, $n$ (%) | 34 (57.6%) | 21 (60%) | 13 (54.2%) | 0.29 |
| Time on dialysis, years | 3.3 ± 2.6 | 3.9 ± 2.8 | 2.4 ± 1.8 | 0.02 |
| Charlson comorbidity index | 4.7 ± 2.3 | 4.6 ± 2.3 | 4.8 ± 2.3 | 0.4 |
| Comorbid conditions, $n$ (%) | | | | |
| coronary heart disease | 11 (18.60%) | 7 (20%) | 4 (16.70%) | 0.76 |
| congestive heart failure | 19 (32.20%) | 11 (31.40%) | 8 (33.30%) | 0.86 |
| peripheral vascular disease | 14 (23.70%) | 9 (25.7%) | 5 (20.8%) | 0.65 |
| previous stroke | 11 (18.60%) | 5 (14.3%) | 6 (25%) | 0.31 |
| diabetes | 16 (27.10%) | 12 (34.30%) | 4 (16.70%) | 0.14 |

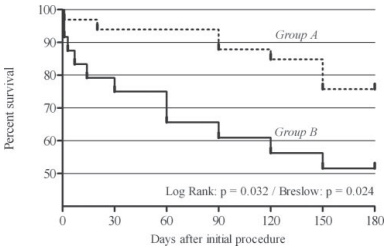


*Figure 1.* Percentage of freedom from subsequent interventions at 6 months. The graph shows the primary patency as of enrollment according to the Kaplan–Meier analysis.

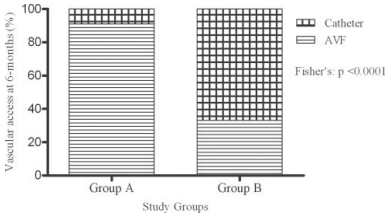


*Figure 2.* Permanent vascular access type at 6 months of follow-up for each study group. At the end of follow-up, a significantly higher number of group A patients had a functioning AVF as a permanent vascular access.

with further percutaneous thrombectomy, two patients were given a TCC placement, and one patient underwent a new AVF creation in the same arm. Two patients died during follow-up because of acute pancreatitis and respiratory infection, respectively. At 6 months, the primary patency rate of the vascular access was 75% (Figure 1). At the end of follow-up, 30 patients (91%) presented a functional AVF as a permanent vascular access (Figure 2).

TCC placement was successfully performed in 24 patients. Nevertheless, clinical success was observed in 22 patients (success rate = 92%). Twenty-two patients (92%) presented with an internal jugular catheter. During follow-up, hospitalization because of catheter-related bacteriaemia ($n$ = 4) or central venous thrombosis ($n$ = 2) was required in six patients. Local catheter thrombolysis (total = 16) was necessary in six patients. Thereafter, four patients underwent catheter removal because of late dysfunction. Nine patients underwent a second TCC placement. At 6 months, the primary patency rate of the vascular access was 51% (Figure 1). Although 22 patients underwent a new AVF creation, only eight patients (33%) were performing dialysis with a functional AVF at the end of follow-up (Figure 2). The mean time for the construction of a new AVF was 33 days (3 to 180 days). Table 2 shows the mean values of secondary outcomes for both study groups.

The cost of vascular access care was substantial, with a mean cost per patient at 6 months of $2479 (median $1455; interquartile range [IQR] $647 to $18,848). The total cost for patient-month at risk was lowest for the endovascular group (mean $374; median $241; IQR $228 to $3146 *versus* mean $706; median $379; IQR $108 to $3018; $P$ = 0.048; Table 3). Furthermore, the mean access-related surgical costs, costs for access-related hospital admissions, and management of access dysfunction were significantly higher for group B patients. The largest expenses for patients treated with central venous catheterization were related with hospitalizations. On the other hand, percutaneous thrombectomy itself was responsible for approximately two thirds of the costs spent with group A patients (Table 3).

*Table 2.* Secondary outcomes at 6 months of follow-up according to study group (median ± SD)

| Outcome | Group A ($n$ = 35) | Group B ($n$ = 24) | $P$ |
|---|---|---|---|
| Access-related surgery | 0.08 ± 0.27 | 0.33 ± 0.47 | 0.01 |
| Access-related hospital admissions | 0.05 ± 0.32 | 0.25 ± 0.43 | 0.047 |
| Management of access dysfunction[a] | 0.16 ± 0.43 | 0.96 ± 1.45 | 0.004 |
| Management of access-related infection | 0 | 0.17 ± 0.47 | 0.036 |
| Patient death, access-related | 0 | 0.08 ± 0.48 | 0.072 |

[a]Includes all radiology procedures performed as part of access-related care, catheter placements, and local thrombolytic therapy.

*Table 3.* Cost analysis in U.S. dollars/patient-month overall and according to treatment group (mean ± SD)

| | Overall ($n$ = 59) | Group A ($n$ = 35) | Group B ($n$ = 24) | $P$ |
|---|---|---|---|---|
| Index procedure | $182 ± 45 | $232 ± 3 | $109 ± 20 | <0.001 |
| Surgical interventions | $18 ± 25 | $6 ± 14 | $35 ± 32 | 0.001 |
| Hospital admissions | $211 ± 428 | $91 ± 327 | $393 ± 50 | 0.050 |
| Management of access dysfunction[a] | $60 ± 75 | $28 ± 54 | $106 ± 88 | 0.005 |
| Patient's transport | $22 ± 22 | $8 ± 3 | $45 ± 29 | 0.002 |
| Total cost | $510 ± 466 | $375 ± 355 | $706 ± 563 | 0.048 |

[a]Includes all radiology procedures performed as part of access-related care, catheter placements, and local thrombolytic therapy.

## Discussion

Vascular access care is responsible for a significant proportion of healthcare costs in prevalent hemodialysis patients (17). Manns *et al.* (18) have shown that the high access-related costs of incident hemodialysis patients with primary AVF failure were partially due to the increased number of diagnostic imaging and radiologic interventions. For healthcare systems with strict economic barriers, this issue may be extremely relevant.

Bittl *et al.* (12) recently published an economic analysis concluding that preemptive angiographic management of AVF dysfunction may represent a less efficient use of healthcare resources than increasing the number of patients with AVF. In the study presented here, we have demonstrated that salvage of clotted AVF by percutaneous thrombectomy rather than waiting for a new mature AVF, was associated with a reduction in access-related costs (Table 2).

Study groups were relatively well matched for baseline parameters and length of follow-up. Despite the relative short time on hemodialysis, near a half of the patients had a previous history of dialysis catheters and vascular access surgeries (Table 1). As such, salvage of the clotted AVF would be of an utmost importance.

Among the previous series (2–10), clinical success and primary patency at 6 months of thrombosed AVFs treated with interventional thrombectomy has ranged between 73% to 96% and 38% to 81%, respectively. For TCC placement, primary patency rates are approximately 60% at 6 months (19). The outcomes of the current series, for endovascular procedure (clinical success 97%, primary patency 75%) and catheter placement (clinical success 92%, primary patency 51%), were at the higher end of these ranges (Figure 1).

In 2006, Allon *et al.* (20) reported that change in vascular access had relevant clinical implications in hemodialysis patients. In the study presented here, 91% of group A patients had a functioning AVF as a permanent vascular access at 6 months. In contrast, we have found only 33% of group B patients with a functional AVF at the end of follow-up. As a consequence, group B patients presented a higher percentage of hospitalizations and comorbidity (Table 2). Local practice patterns may have been responsible for the observed low rate of functioning AVF in group B patients. However, these results are not surprising because even incident hemodialysis patients (without a previous history of failed AVF) with a timely referral to a nephrologist and subsequently to a vascular surgeon still may not have a functioning AVF, as result of a delay in procedure scheduling or failure of the AVF to mature (21).

We found that vascular access care in the first 6 months post-thrombosis was cumbersome, with patients selected for central venous catheterization pending the creation of a new AVF incurring the highest costs. Cost-effectiveness analysis showed that AVF salvage by endovascular therapy led to a near two-fold reduction in access-related expenses per patient-month at risk; the added costs associated with the

procedure itself was completely offset by the saving associated with lower surgical visits, access dysfunction, and hospitalizations (Table 3). In fact, management of access dysfunction and access-related hospitalizations was nearly 4 times higher in group B patients (Table 3), reflecting the lower access survival and the subsequent comorbidity associated with TCC placement. Interestingly, the usual forgotten patient's transport cost required for the establishment and management of the vascular access had a relevant economic effect in group B patients (Table 3). Therefore, the guarantee of a functional AVF with a high primary patency rate is an utmost important issue in hemodialysis patients, with obvious economic benefits.

Although patients were followed-up for only 6 months, we were able to find clinical and economic disparities between the two different approaches. Probably, if a long-term follow-up was performed, differences between cohorts would have been similar because both groups would require more vascular-access interventions to establish or maintain a functional vascular access.

Our study had several limitations. First, as a retrospective study, it shares all of the limitations of that approach. Selection of candidates for AVF salvage therapy and the type of procedure performed may differ among centers and countries, and this may have an effect on the external generalizability of our results. Also, the patient population consisted mainly of Caucasian Europeans, which makes it impossible to draw conclusions for other ethnicities. The cost of certain healthcare procedures has been reported to differ between countries (22). However, the relative amount of resources required for intervention and the determinants of vascular access costs are likely to be similar between centers. We are aware that our study cannot provide a definitive answer regarding the efficiency of percutaneous thrombectomy in AVF thrombosis and that further prospective cost-effectiveness analysis comparing endovascular and surgical procedures needs to be undertaken.

In conclusion, the cost of vascular access care is high among patients with AVF thrombosis and highest for patients selected for central venous catheterization pending the creation of a new AVF. Our study suggests that salvage of thrombosed AVFs by percutaneous thrombectomy is a safe and cost-effective policy; therefore, intensive efforts should be undertaken to universalize these procedures.

## Acknowledgments

We thank the clinical directors from hemodialysis clinics who kindly agreed to collaborate in this study: A. Baldaia Moreira M.D., A. Caldeira Gomes M.D., A. Castro Henriques M.D., Antunes de Azevedo M.D, Eva Xavier M.D., João C. Fernandes M.D., João M. Frazão M.D., Ph.D., Jorge P. Baldaia M.D., José M. Madureira M.D., José Pinheiro M.D., Odete Pereira M.D., Sofia Pedroso M.D., Susana Sampaio M.D., and Vasco Miranda M.D.

## Disclosures

None.

## References

1. Beathard GA: Fistula salvage by endovascular therapy. *Adv Chronic Kidney Dis* 16: 339–351, 2009
2. Turmel-Rodrigues L, Sapoval M, Pengloan J, Billaux L, Testou D, Hauss S, Mouton A, Blanchard D: Manual thromboaspiration and dilation of thrombosed dialysis access: Mid-term results of a simple concept. *J Vasc Interv Radiol* 8: 813–824, 1997
3. Turmel-Rodrigues L, Pengloan J, Rodrigues H, Brillet G, Lataste A, Pierre D, Jourdan JL, Blanchard D: Treatment of failed native arteriovenous fistulae for hemodialysis by interventional radiology. *Kidney Int* 57: 1124–1140, 2000
4. Moossavi S, Regan JD, Pierson ED, Kasey JM, Tuttle AB, Vachharajani TJ, Bettmann MA, Russell GB, Freedman BI: Nonsurgical salvage of thrombosed arterio-venous fistulae: A case series and review of the literature. *Semin Dial* 20: 459–464, 2007
5. Haage P, Vorwerk D, Wilberger JE, Piroth W, Schurmann K, Gunther RW: Percutaneous treatment of thrombosed primary arteriovenous hemodialysis access fistulae. *Kidney Int* 57: 1169–1175, 2000
6. Liang HL, Pan HB, Chung HM, Ger LP, Fang HC, Wu TH, Wu MT, Lai PH, Chen CK, Yang CF: Restoration of thrombosed Brescia-Cimino dialysis fistulas by using percutaneous transluminal angioplasty. *Radiology* 223: 339–344, 2002
7. Rajan DK, Clark T, Simons ME, Kachura JR, Sniderman K: Procedural success and patency after percutaneous treatment of thrombosed autogenous arteriovenous dialysis fistulas. *J Vasc Interv Radiol* 13: 1211–1218, 2002
8. Shatsky JB, Berns JS, Clark TW, Kwak A, Tuite CM, Shlansky-Goldberg RD, Modschein JI, Patel AA, Stavropoulos SW, Soulen MC, Solomon JA, Kobrin S, Chittams JL, Trerotola SO: Single-center experience with the Arrow-Trerotola percutaneous thrombectomy device in the management of thrombosed native dialysis fistulas. *J Vasc Interv Radiol* 16: 1605–1611, 2005
9. Beathard GA, Litchfield T: Physician Operators Forum of RMS Lifeline, Inc: Effectiveness and safety of dialysis vascular access procedures performed by interventional nephrologists. *Kidney Int* 66: 1622–1632, 2004
10. Jain G, Maya ID, Allon M: Outcomes of percutaneous mechanical thrombectomy of arteriovenous fistulas in hemodialysis patients. *Semin Dial* 21: 581–583, 2008
11. Jan H. M. Tordoir JHM, Bode AS, Peppelenbosch N: Surgical or endovascular repair of thrombosed dialysis vascular access: Is there any evidence? *J Vasc Surg* 50: 953–956, 2009
12. Bittl JA, Cohen DJ, Seek MM, Feldman RL: Economic analysis of angiography and preemptive angioplasty to prevent hemodialysis-access thrombosis. *Catheter Cardiovasc Interv* 75: 14–21, 2010
13. Tessitore N, Bedogna V, Poli A, Mantovani W, Lipari G, Baggio E, Mansueto G, Lupo A: Adding access blood flow surveillance to clinical monitoring reduces thrombosis rates and costs, and improves fistula patency in the short term: A controlled cohort study. *Nephrol Dial Transplant* 23: 3578–3584, 2008
14. National Kidney Foundation-Disease Outcomes Quality Initiative: Clinical practice guidelines and clinical practice recommendations for vascular access 2006. *Am J Kidney Dis* 48: S176–S322, 2006

15. Sidawy A, Gray R, Besarab A, Henry M, Ascher E, Silva M Jr: Recommended standards for reports arteriovenous hemodialysis accesses. *J Vasc Surg* 3: 603–610, 2002
16. Charlson ME, Pompei P, Ales KL: A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *J Am Soc Nephrol* 7: 198–207, 1996
17. Lee H, Manns BJ, Taub K, Ghali WA, Dean S, Johnson D, Donaldson C: Cost analysis of ongoing care of patients with end-stage renal disease: The impact of dialysis modality and dialysis access. *Am J Kidney Dis* 40: 611–622, 2002
18. Manns B, Tonelli M, Yilmaz S, Lee H, Laupland K, Klarenbach S: Establishment and maintenance of vascular access in incident hemodialysis patients: A prospective cost analysis. *J Am Soc Nephrol* 16: 201–209, 2005
19. Lee T, Barker J, Allon M: Tunneled catheters in hemodialysis patients: Reasons and subsequent outcomes. *Am J Kidney Dis* 46: 501–508, 2005
20. Allon M, Daugirdas J, Depner T, Greene T, Ornt D, Schwab SJ: Effect of change in vascular access on patient mortality in hemodialysis patients. *Am J Kidney Dis* 47: 469–477, 2006
21. Lok CE: Fistula First Initiative: Advantages and pitfalls. *Clin J Am Soc Nephrol* 2: 1043–1053, 2007
22. World Bank: *World Development Indicators* 2000, Washington DC, World Bank, 2001

Catheterization and Cardiovascular Interventions 77:1065–1070 (2011)

# Endovascular Treatment of Thrombosed Dialysis Fistulae: A Cumulative Cost Analysis

**Pedro Bizarro,[1] MD, Luís Coentrão,[1,2*] MD, Carlos Ribeiro,[3] BA, Ricardo Neto,[1] MD, and Manuel Pestana,[1] MD, PhD**

**Objectives: In the present study, we determined the cumulative costs and outcomes of endovascular treatment of thrombosed autogenous arteriovenous fistulae (AVF) at our medical center. Background: Previous studies examining the salvage procedures of thrombosed AVFs have focused exclusively on clinical outcomes, and, in the absence of costing data, current guidelines do not take into consideration economic issues. Methods: A retrospective cohort study was performed among local hemodialysis patients with completely thrombosed AVFs receiving endovascular treatment in our institution between January 1 and December 31, 2008. Forty-four patients were enrolled and followed-up for 1 year. Success and complications were recorded according to consensus definitions, and a comprehensive measurement of total vascular access care-related costs was obtained. Costs are reported in 2010 in U.S. dollars. Results: Clinical success was achieved in 95% of cases. The primary and secondary patency rates were 63 and 78% at 1 year, respectively. Primary patency rate at 12 months was significantly better for radiocephalic AVFs (70% vs. 43%; *P* = 0.047). The mean cumulative cost of all vascular access care during year 1 was $2,504 (median $1,484; range, $1,362–$18,279; Table V) per patient-year at risk. The mean cumulative cost for maintaining radiocephalic and brachiocephalic AVFs was $1,624 (median $1,381; range, $1,130–$3,116) and $3,578 (median $2,092; range, $1,470–$18,279) per patient-year at risk, respectively (*P* = 0.022). Conclusion: The cost of maintenance of a thrombosed AVF by endovascular intervention is high, with patients with clotted radiocephalic fistulae incurring the lowest costs and achieving higher survival times.** © 2011 Wiley-Liss, Inc.

**Key words: autogenous arteriovenous fistulae; percutaneous thrombectomy; economic analysis**

## INTRODUCTION

Thrombosis of the vascular access is a relatively infrequent complication of autogenous arteriovenous fistulae (AVF) [1,2]. However, as current clinical practice guidelines recommend that at least 65% of the end stage renal disease (ESRD) population should have a functional AVF as a permanent dialysis access [1,2], AVF thrombosis has become a clinical challenge in our nephrology practice, with relevant clinical implications for dialysis patients. Several studies have reported on the feasibility and relatively high-clinical success rate of the endovascular approach to thrombosed AVF in recent years [3–12], and salvage procedures have therefore been recommended in the recently published guidelines in order to re-establish the functionality of failed vascular accesses [1,2].

Published findings regarding the economic value of vascular access surveillance revealed that adding access blood flow surveillance to clinical monitoring of AVFs reduces thrombosis rates and costs [13]. Bittl et al. [14] recently reported, in a large observational economic analysis, that preemptive angiographic management of malfunctioning nonthrombosed hemodialysis accesses may represent a less efficient use of healthcare resources than increasing the number of

[1]Nephrology Research and Development Unit, Faculty of Medicine, University of Porto, Hospital S. João, Porto, Portugal
[2]Institute of Pharmacology and Therapeutics, Faculty of Medicine, University of Porto, Portugal
[3]Financial Management Unit, Hospital S. João, Porto, Portugal

Conflict of interest: Nothing to report.

Pedro Bizarro and Luís Coentrão contributed equally to the work.

*Correspondence to: Luís Coentrão, MD, Nephrology Research and Development Unit, Faculty of Medicine, University of Porto, Al. Prof. Hernâni Monteiro, 4200-319 Porto, Portugal.
E-mail: coentrao@med.up.pt

Received 6 October 2010; Revision accepted 22 November 2010

DOI 10.1002/ccd.22913
Published online 16 March 2011 in Wiley Online Library (wileyonlinelibrary.com)

patients with AVFs. Cost-effective analyses of endovascular interventions for thrombosed hemodialysis accesses have been performed only in patients with clotted prosthetic grafts [15–18], and most of these studies have used patient charges rather than actual costs for financial analysis [16–19]. In this regard, reporting standards for percutaneous interventions on dialysis accesses recommend that the cumulative costs per patient should be measured over months or years whenever possible for more insightful comparisons [19].

In the present study, we determined the cumulative costs and outcomes of endovascular treatment of clotted AVFs during the first-year post-thrombosis, at our medical center.

## SUBJECTS AND METHODS

### Patient Population

This investigation was reviewed and approved by the Hospital S. João Institutional Review Board. The Hospital S. João is a tertiary-care University Hospital that carries out interventional procedures for patients from our hospital hemodialysis center and satellite hemodialysis units. The patients in these hemodialysis units were monitored for clinical signs of access dysfunction. On the basis of clinical changes, the patients were referred for diagnostic fistulography and endovascular treatment as appropriate. The exclusion criteria for endovascular treatment were an infected AVF and the presence of old wall-adherent thrombi. Patients with nonthrombosed failing AVFs (low thrill) were excluded from the study. Forty-eight patients with totally occluded AVFs were consecutively referred for the consideration of percutaneous thromboaspiration from January 1 to December 31, 2008. In one patient, the interventionalist deemed that endovascular intervention was not advisable due to the presence of old wall-adherent thrombi. Three patients were excluded from the study due to insufficient data collection. The final analysis included 44 patients.

### Procedures

The method used in our unit was manual catheter-directed thromboaspiration [3]. When a hemodynamically significant lesion was encountered, a conventional angioplasty balloon [(Cordis Corporation, Johnson & Johnson Medical N.V/S.A., Waterloo, Belgium), burst pressure = 15 atm] was inflated at the level of the stenosed site. The intervention was performed as an outpatient procedure. Cases were referred within 96 hr of the detection of the loss of a thrill or bruit in the access. Systematic low-molecular weight heparin was recommended for 2 weeks post-thrombectomy, as previously reported by Turmel-Rodrigues et al. [3,4]. All procedures were performed by the same nephrologist.

Patients with thrombosed AVF for whom the endovascular approach was either unsuccessful or contraindicated underwent tunneled dialysis catheter placement and/or creation of a new AVF, as an outpatient procedure. Tunneled cuffed catheter placement (Retro, Spire Biomedical, Bedford, MA) was performed by a nephrologist and with ultrasound guidance, as recommended by Dialysis Outcomes Quality Initiatives [2]. Postprocedure chest radiography was performed in all patients. Surgical construction of a new AVF was performed by local vascular surgeons as an outpatient procedure.

### Follow-Up

Clinical information was collected retrospectively from both hospital and satellite unit records. Data were assessed by means of a questionnaire. The presence of comorbidity at the enrolment date was assessed by a physician by complete review of patients' records. Information was collected for the 19 variables that constitute the Charlson Comorbidity Index [20], which has been validated for use in patients with ESRD. Follow-up was based on clinical surveillance by the attending nephrologists in the 14 referring hemodialysis centers. Recurrence of abnormalities, such as increased venous pressure, increased time to hemostasis and arm edema, led to further angiography with subsequent intervention. Acute thrombosis was treated percutaneously by aspiration thrombectomy [3]. During follow-up, patients with thrombosed AVF for whom the endovascular approach was either unsuccessful or contraindicated underwent ambulatory dialysis catheter placement and/or creation of a new AVF. Patient follow-up started on the day the vascular access intervention was first performed and continued for 1 year. Follow-up ceased at patient death, renal transplantation, or switching to peritoneal dialysis.

### Definitions

Success, complications, and secondary interventions were recorded according to consensus definitions [19]. Clinical success was defined as the resumption of dialysis with a blood flow $> 300$ ml/min on the first three dialysis sessions after the intervention. Primary patency was considered to begin on the day of declotting (index procedure) and to end on the day of access failure or further reintervention (either radiological or surgical). Secondary patency included all further radiological treatments (dilation, new percutaneous declotting) but ended with surgical revision.

Catheterization and Cardiovascular Interventions DOI 10.1002/ccd.
Published on behalf of The Society for Cardiovascular Angiography and Interventions (SCAI).

### Cost Analysis

Our study was performed from the perspective of the health care purchaser and included direct vascular access care-related costs. All resource use was valued at prices in 2010. All costs were converted to U.S. dollars using an exchange rate of 1 Euro (€) equal to $1.31US.

The data concerning the hospital costs and professional fees for physicians and nurses were obtained from the Information Management Division. The professional fee per intervention was determined from the average fee charged by Nephrology professionals per year divided by the number of procedures and time spent in the angiography suite. The average technical costs per intervention included the supplies, pharmacy and radiology costs, and additional overhead expenses. The total expense for each procedure represents the sum of the average technical costs and the average professional fees. The cost of hospital admissions for which the primary reason for admission (as defined by the discharge diagnosis [*International Classification of Diseases Ninth Revision codes*]) was related to access care was obtained from the Information Management Division. The vascular access surgical data (outpatient creation of autogenous arteriovenous fistula) in this study are more similar to "charges" than to "costs" in that they were extracted from the Ministry of Health and Welfare Ordinance (unitary cost, $393). Patient's transport costs required for the vascular access care were also included in the analysis. They principally used a taxi or ambulance for hospital visits ($0.66 for 1 km). The cumulative cost represents the sum of all access-related procedures, hospitalizations, and patient's transport required to establish or to maintain a functional vascular access during follow-up. Initial failures and dialysis catheter placements before attempted thrombectomy were included in the analysis.

### Statistical Analysis

Data are given as percentages and mean ± standard deviation. Normally, distributed continuous variables were analyzed using Student's unpaired *t*-test and categorical variables using Fisher's exact test. Rates were calculated for each of the patients by dividing the number of events/procedures by the duration of follow-up. Fistula patency was analyzed using the Kaplan–Meier method, and differences between groups were evaluated by log-rank tests.

## RESULTS

Patient characteristics are summarized in Table I. The average time on dialysis was 3.9 years (range, 0.5–28 years), and mean fistula age was 4.6 years (range, 0.3–28 years). Clotted accesses included 24 (55%) radiocephalic AVFs and 20 (45%) brachiocephalic AVFs (Table I). The mean age was 63.7 ± 8 (SD) years in the radiocephalic fistula group compared to 63.3 ± 4 years in the brachiocephalic fistula group ($P$ = NS), and there were relatively higher number of men in the radiocephalic fistula group (87% in radiocephalic fistula group, 65% in brachiocephalic fistula group, and $P = 0.07$). Twenty-nine percent of patients in the radiocephalic fistula group were diabetic and 25% in the brachiocephalic fistula group ($P$ = NS). Three patients were referred for percutaneous thrombectomy 96 hr after the detection of AVF thrombosis. These patients underwent dialysis catheter placement before the endovascular treatment of the clotted fistula.

**TABLE I. Patient Characteristics at Baseline**

| | |
|---|---|
| Age (years) | 63.6 ± 14.5 |
| Sex, *N* (%) male | 32 (73%) |
| Previous fistulae, *N* (%) | 19 (44%) |
| Previous catheters, *N* (%) | 23 (52%) |
| Mean time on dialysis (years) | 3.9 ± 3.0 |
| Mean fistula age (years) | 4.6 ± 6.1 |
| Fistula location, *N* (%) | |
| Radiocephalic | 24 (55%) |
| Brachiocephalic | 20 (45%) |
| Charlson comorbidity index | 4.7 ± 2.3 |
| Comorbid conditions (%) | |
| CAOD | 19% |
| Congestive heart failure | 32% |
| PAOD | 24% |
| Previous stroke | 18% |
| Diabetes | 27% |
| Hypertension | 71% |
| Cause of ESRD (%) | |
| Unknown | 39% |
| Diabetes | 25% |
| Hypertension | 14% |
| ADPKD | 12% |
| Glomerulonephritis | 10% |

ADPKD, autosomal dominant polycystic kidney disease; ESRD, end-stage renal disease; CAOD, coronary artery occlusive disease; PAOD, peripheral artery occlusive disease.

Manual catheter-directed thromboaspiration was technically successful in 42 patients, with prompt restoration of a thrill and bruit (clinical success rate = 95%). The most frequent lesions are shown in Table II. Stent placements or blood transfusions were not required during the procedure. Angioplasty was not feasible in two patients due to the impossibility of passing the guidewire through a tight stenotic lesion. Both patients underwent tunneled catheter placement. One patient with a brachiocephalic AVF developed steal syndrome and myocardial infarction ~2 weeks postprocedure and required hospitalization and further access surgery. Eleven patients experienced AVF

Catheterization and Cardiovascular Interventions DOI 10.1002/ccd.
Published on behalf of The Society for Cardiovascular Angiography and Interventions (SCAI).

**TABLE II. Location of Stenosis and Thrombectomy Outcomes**

| | Radiocephalic fistulae | Brachiocephalic fistulae | *P*-value |
|---|---|---|---|
| *N* pts | 24 | 20 | n.a. |
| Location of stenosis | | | |
| Venous outlet | 10 (40%) | 11 (55%) | 0.363 |
| Arterial anastomosis | 16 (65%) | 9 (45%) | 0.142 |
| Central vein | 0 (0%) | 2 (20%) | 0.147 |
| Number of stenotic lesions | | | |
| 1 | 16 (65%) | 10 (50%) | 0.261 |
| ≥2 | 8 (35%) | 12 (60%) | 0.068 |
| "Short-segment thrombus" | 14 (58%) | 5 (25%) | 0.028 |
| Clinical success | 23 (96%) | 19 (95%) | 1 |
| Primary patency rate at year 1[a] | 17 (70%) | 8 (43%) | 0.047 |

[a]Initial failures are included.

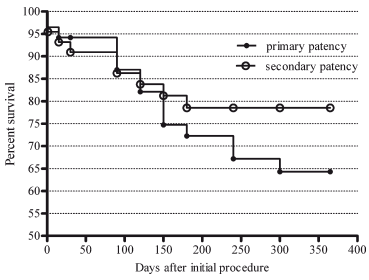


**Fig. 1. Primary and secondary patency rates at 1 year, according to the Kaplan–Meier analysis.**

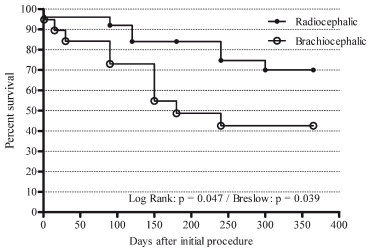


**Fig. 2. Primary patency rates after declotting for radiocephalic and brachiocephalic fistulae, showing better results in radiocephalic fistulae.**

**TABLE III. Mean Expense (in US$) for Each Component of the Procedure**

| | |
|---|---|
| Professional fees | |
| Percutaneous transluminal angioplasty | $220 (range, $110–$450) |
| Manual catheter-directed thromboaspiration | $489 (range, $220–$550) |
| Placement of tunneled cuffed catheter | $194 (range, $150–$400) |
| Technical costs | |
| Percutaneous transluminal angioplasty | $565 (range, $453–$901) |
| Manual catheter-directed thromboaspiration | $892 (range, $596–$1,187) |
| Placement of tunneled cuffed catheter | $307 (range, $261–$554) |

rethrombosis during follow-up (8/3, brachiocephalic/radiocephalic AVF): six patients (4/2, brachiocephalic/radiocephalic AVF) underwent further aspiration thrombectomy; the remaining five patients (4/1, brachiocephalic/radiocephalic AVF) underwent tunneled catheter placement and/or new AVF creation. Three patients developed venous hypertension due to recurrent stenosis, successfully treated with balloon angioplasty. Three patients died during follow-up due to acute pancreatitis, mesenteric infarction, and respiratory infection, respectively. Two patients received a kidney transplant, and one patient switched to peritoneal dialysis. Including the initial failures, the primary and secondary patency rates of all AVF were 63 and 78% at 1 year, respectively (Fig. 1). Primary patency rate at the end of follow-up was significantly better for radiocephalic AVFs (70% vs. 43%; $P = 0.047$; Fig. 2).

The mean expense for each component of the two procedures is presented in Table III. The mean technical cost for the manual catheter-directed thromboaspiration procedure was $892 (range, $596–$1,187). The mean nephrology professional fee was $489 (range, $200–$550). Therefore, mean total expense of the percutaneous thrombectomy procedure was $1381 (range, $1,036–$1,627; Table IV). The mean cumulative cost of vascular access care at year 1 was $2,504 (median $1,484; range, $1,362–$18,279; Table V) per patient-year at risk. The mean cost per patient-year at risk was greatest for patients with brachiocephalic AVFs $3,578 (median $2,092; range, $1,470–$18,279) versus mean $1,604 (median $1,381; range, $1,130–$3,116; $P = 0.022$; Table V).

## DISCUSSION

The present study provides a different perspective on vascular access maintenance and presents the cumulative costs and resources required to treat hemodialysis patients with thrombosed AVF by endovascular means. This study is, to our knowledge, the first study estimating the cumulative cost of percutaneous thrombectomy of autogenous AVF during 1 year of follow-up.

Catheterization and Cardiovascular Interventions DOI 10.1002/ccd.
Published on behalf of The Society for Cardiovascular Angiography and Interventions (SCAI).

**TABLE IV. Costs of Invasive Examinations, Central Venous Catheter Implantation, and Hospitalizations**

| | Average cost per intervention (US$) |
|---|---|
| Percutaneous transluminal angioplasty | $785 (range, $673–$1,121) |
| Manual catheter-directed thromboaspiration | $1381 (range, $1,036–$1,627) |
| Placement of tunneled cuffed catheter | $501 (range, $454–$748) |
| Daily cost of hospitalization in the general ward of the Department of Internal Medicine | $415 |

**TABLE V. Cumulative Cost Analysis in US$/Patient-Year at Risk**[a]

| | Overall ($n = 44$) | Radiocephalic fistulae ($n = 24$) | Brachiocephalic fistulae ($n = 20$) | *P*-value |
|---|---|---|---|---|
| Index procedure (mean ± SD) | $1,381 ± 54 | $1,332 ± 83 | $1,431 ± 94 | N.S. |
| Outpatient access-related surgery (mean ± SD) | $45 ± 150 | $66 ± 185 | $20 ± 86 | N.S. |
| Access-related hospital admissions (mean ± SD) | $702 ± 3,231 | – | $1,545 ± 4,655 | 0.060 |
| Management of access dysfunction[b] (mean ± SD) | $310 ± 535 | $153 ± 381 | $498 ± 624 | 0.017 |
| Patient's transport (mean ± SD) | $66 ± 51 | $53 ± 23 | $84 ± 67 | 0.021 |
| Total cost (mean ± SD) | $2,504 ± 3,219 | $1,604 ± 511 | $3,578 ± 4,518 | 0.022 |

[a]Initial failures are included.
[b]Includes all radiology procedures performed as part of access-related care, dialysis catheter placements, and local catheter thrombolytic therapy.

Among the previous series [3–11], clinical success and primary and secondary patency rates of percutaneous thrombectomy of clotted AVF at 1 year have ranged from 73 to 96%, 18 to 70%, and 27 to 81%, respectively. The outcomes of the current series were at the higher end of these ranges (clinical success, 95%; primary patency rate, 63%; secondary patency rate, 78%; Fig. 1), and the clinical success of percutaneous thromboaspiration was similar in both radiocephalic and brachiocephalic AVFs (Table IV). However, the Kaplan–Meier log-rank analysis showed that manual catheter-directed thromboaspiration of radiocephalic AVFs had better long-term outcome (Fig. 2), as previously reported by Turmel-Rodrigues et al. [4]. This might be explained by the higher percentage of cases with "short-segment thrombus" observed in the radiocephalic fistula group (Table IV). This issue was also addressed by Wu et al. [21] who separated "long segment thrombus" from "short segment thrombus" and showed significant differences in survival, with poorer patency associated with the larger clot burden.

Cost analysis revealed that manual catheter-directed thromboaspiration of totally occluded AVFs is more expensive than percutaneous transluminal angioplasty (Tables III and IV). Although similar results have previously been reported by Bittl et al. [14], procedure costs were approximately two times higher in this study (angioplasty, $1,939 vs. $785; percutaneous thrombectomy, $3,336 vs. $1,381). Professional fees and technical costs might have been responsible for the differences observed between these two cost analyses. First, physician billing has been reported to differ among countries [22], and, second, the amount of resources required for endovascular interventions is likely to vary among vascular access centers with different endovascular salvage procedures. In the present study, a 9-F catheter (Cordis, Miami, FL) and a 50-mL syringe were the mainstay devices for endovascular salvage therapy. Bittl et al. [14] used a rheolytic thrombectomy device (AngioJet, Possis Medical, MN) for thrombosed AVFs. In addition, stents were not used in our patients, whereas Bittl et al. [14] placed stents for several indications.

Although fistula salvage by endovascular means remains a successful approach for the maintenance of a functional vascular access, it is responsible for a significant financial burden on the ongoing care of ESRD patients. The U.S. Renal Data System estimated the cost of vascular access care for prevalent hemodialysis patients as being 8.4% of total Medicare ESRD spending [23]. In our country, the public health care system reimbursement for the ongoing care in outpatient dialysis (equipment costs, staff, consumable items, reverse-osmosis water, regular laboratory and radiology tests, and medications) is $37,335 per patient-year. In the present study, economic analysis revealed that endovascular treatment of thrombosed AVF carries an additional cost of 6.5% on the outpatient dialysis expenses ($2,504 per patient-year at risk, Table V). In addition, we observed that treatment and maintenance of thrombosed radiocephalic AVFs was half as expensive as in brachiocephalic AVFs, representing an additional cost of ~4.3 and 9.6% on the outpatient dialysis expenses, respectively ($1,604 vs. $3,578 per patient-year at risk, respectively; Table V). Access-related hospitalizations, ambulatory management of access dysfunction (including

all radiology procedures performed as part of access-related care, catheter placements/local thrombolytic therapy), and patient's transport were responsible for the higher financial burden observed in the brachiocephalic fistula group (Table V). In fact, few resources were required to maintain the functional patency of a radiocephalic AVF at 1 year, because ~85% of the total expenses were related with the index procedure (Table V). In contrast, ~60% of the expenditure was spent in secondary interventions in patients with brachiocephalic AVFs.

We recognize that this is a retrospective study and thus has all the limitations of such an approach. We are also aware that our study does not provide a definitive answer regarding the efficiency of endovascular treatment of AVF thrombosis and that further prospective cost-effectiveness analyses comparing different thrombectomy procedures (endovascular vs. surgery) and distinct approaches for the maintenance of a functional AVF (pre-emptive angioplasty vs. percutaneous thrombectomy) need to be carried out.

In conclusion, our results indicate that the cumulative cost of maintenance of a thrombosed AVF by endovascular means is high, with patients with clotted radiocephalic AVFs incurring the lowest costs and achieving higher survival times.

## ACKNOWLEDGEMENTS

The authors thank Ms. Doreen Raine for editing the English and the clinical directors from hemodialysis clinics who kindly agreed to collaborate in this study: A. Baldaia Moreira M.D., A. Caldeira Gomes M.D., A. Castro Henriques M.D., Antunes de Azevedo M.D., Eva Xavier M.D., João C. Fernandes M.D., João M. Frazão M.D., PhD, Jorge Baldaia M.D., José Madureira M.D., José Pinheiro M.D., Odete Pereira M.D., Sofia Pedroso M.D., Susana Sampaio M.D., and Vasco Miranda M.D.

## REFERENCES

1. Tordoir J, Canaud B, Haage P, et al. EBPG on vascular access. Nephrol Dial Transpl 2007;22(Suppl 2):ii88–ii117.
2. KDOQI: Clinical practice guidelines and clinical practice recommendations for vascular access. Am J Kidney Dis 2006;48: S176–S247.
3. Turmel-Rodrigues L, Sapoval M, Pengloan J, et al. Manual thromboaspiration and dilation of thrombosed dialysis access: Mid-term results of a simple concept. J Vasc Interv Radiol 1997; 8:813–824.
4. Turmel-Rodrigues L, Pengloan J, Rodrigue H, et al. Treatment of failed native arteriovenous fistulae for hemodialysis by interventional radiology. Kidney Int 2000;57:1124–1140.
5. Moossavi S, Regan JD, Pierson ED, et al. Nonsurgical salvage of thrombosed arterio-venous fistulae: A case series and review of the literature. Semin Dial 2000;20:459–464.
6. Haage P, Vorwerk D, Wilberger JE, et al. Percutaneous treatment of thrombosed primary arteriovenous hemodialysis access fistulae. Kidney Int 2000;57:1169–1175.
7. Liang HL, Pan HB, Chung HM, et al. Restoration of thrombosed Brescia-Cimino dialysis fistulas by using percutaneous transluminal angioplasty. Radiology 2002;223:339–344.
8. Rajan DK, Clark T, Me S, et al. Procedural success and patency after percutaneous treatment of thrombosed autogenous arteriovenous dialysis fistulas. J Vasc Interv Radiol 2002;13: 1211–1218.
9. Shatsky JB, Berns JS, Clark TW, et al. Single-center experience with the Arrow-Trerotola percutaneous thrombectomy device in the management of thrombosed native dialysis fistulas. J Vasc Interv Radiol 2005;16:1605–1611.
10. Beathard GA, Litchfield T. Physician Operators Forum of RMS Lifeline Inc: Effectiveness and safety of dialysis vascular access procedures performed by interventional nephrologists. Kidney Int 2004;66:1622–1632.
11. Jain G, Maya ID, Allon M. Outcomes of percutaneous mechanical thrombectomy of arteriovenous fistulas in hemodialysis patients. Semin Dial 2008;21:581–583.
12. Bittl JA. Percutaneous therapy of dialysis access failure. Catheter Cardiovasc Interv 2002;56:157–161.
13. Tessitore N, Bedogna V, Poli A, et al. Adding access blood flow surveillance to clinical monitoring reduces thrombosis rates and costs, and improves fistula patency in the short term: A controlled cohort study. Nephrol Dial Transpl 2008;23:3578–3584.
14. Bittl JA, Cohen DJ, Seek MM, et al. Economic analysis of angiography and preemptive angioplasty to prevent hemodialysis-access thrombosis. Catheter Cardiovasc Interv 2010;75: 14–21.
15. Vesely TM, Idso MC, Audrain J, et al. Thrombolysis versus surgical thrombectomy for the treatment of dialysis graft thrombosis: Pilot study comparing costs. J Vasc Interv Radiol 1996;7:507–512.
16. Sands JJ, Patel S, Plaviak DJ, et al. Pharmacomechanical thrombolysis with urokinase for treatment of thrombosed hemodialysis access grafts. ASAIO J 1994;40:M886–M888.
17. Schuman E, Quinn S, Standage B, et al. Thrombolysis versus thrombectomy for occluded hemodialysis grafts. Am J Surg 1994;167:473–476.
18. Summers S, Drazan K, Gomes A, et al. Urokinase therapy for thrombosed hemodialysis access grafts. Surg Gynecol Obstet 1993;176:534–538.
19. Gray R, Sacks D, Martin L, et al. Reporting standards for percutaneous interventions in dialysis access. J Vasc Interv Radiol 2003;10:1405–1415.
20. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Am Soc Nephrol 1996;7:198–207.
21. Wu CC, Wen SC, Chen MK, et al. Radial artery approach for endovascular salvage of occluded autogenous radial-cephalic fistulae. Nephrol Dial Transpl 2009;24:2497–2502.
22. World Bank: World Development Indicators 2000. Washington DC: World Bank; 2001.
23. USRDS: The economic cost of ESRD, vascular access procedures, and medicare spending for alternative modalities of treatment. Am J Kidney Dis 1997;30:S160–S17.

Catheterization and Cardiovascular Interventions DOI 10.1002/ccd.
Published on behalf of The Society for Cardiovascular Angiography and Interventions (SCAI).

U.PORTO
FMUP FACULDADE DE MEDICINA
UNIVERSIDADE DO PORTO

LUÍS COENTRÃO | 2013