

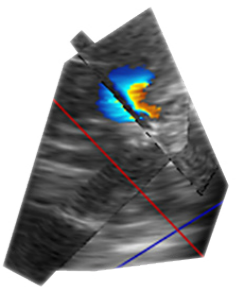
LIFE AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION: A CLINICAL AND ECHOCARDIOGRAPHIC APPRAISAL

ALEXANDRA GONÇALVES


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PORTO 2012



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Life after Transcatheter Aortic Valve Implantation: a Clinical and Echocardiographic Appraisal



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To my family
To Professor José Zamorano

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PART I

Introduction

INTRODUCTION

Aortic stenosis (AS) is the most frequent native valve disease of the elderly in western industrialized countries.¹ Once symptomatic it is responsible for serious disability, restrictions in the normal daily living and reduced life expectancy.² Until recently, the only effective treatment was surgical aortic valve replacement.³⁻⁴ However, surgery is associated with higher morbidity and mortality rates in the elderly compared with younger patients.⁵ It is estimated that about 31% of patients with severe AS, older than 75 years are not referred to surgery, or are refused by the cardiac surgeon because of co-morbidities and perceived high surgical risk.⁶ Transcatheter aortic valve implantation (TAVI) techniques have emerged as an alternative treatment for this group of patients.⁷⁻⁹ After the first human TAVI procedure, performed by Alain Cribier in April 2002¹⁰ the number of patients has increased exponentially and more than 40 000 patients had undergone TAVI worldwide.¹¹ Good procedural success and favourable clinical outcomes at short and midterm follow-up have been reported.¹²⁻¹⁵ Nevertheless, TAVI is a demanding procedure that requires a multidisciplinary team approach and still faces important safety issues, such as paravalvular leaks, vascular complications, stroke or conduction disorders. An additional challenge is the lack of operator direct visualization. Consequently, this technique greatly depends on imaging, especially on echocardiography, which plays an essential role in identifying patients suitable for the intervention, in providing intra-procedural monitoring and as primary modality for post-procedure follow-up.¹⁶ During peri-procedural guidance 2D and 3D transesophageal echocardiography (TEE) can contribute for balloon and prosthesis positioning, to confirm prosthesis normal functioning and to rapidly detect complications.¹⁷

Moreover, TEE guidance represents a unique opportunity to firstly assess left ventricle physiology and behavior following afterload release. Most patients referred for TAVI are elderly and present symptomatic AS with heart failure in NYHA class III-IV, in spite of preserved left ventricle (LV) systolic function.¹⁸⁻¹⁹ Immediate almost complete afterload normalization and significant clinical improvement at short-term follow-up have been reported.¹⁹⁻²¹ At medium-term, LV mass reduction and improvement in tissue Doppler velocities have also been described.²² In view of that we performed the first study evaluating the acute hemodynamic effects of TAVI in diastolic performance, immediately after aortic valvuloplasty and prosthesis deployment.²³

Aortic regurgitation is the most common complication after TAVI.^{14,8} It may occur as a consequence of incomplete expansion, incorrect positioning, restricted cusp motion, or inappropriate prosthetic size.²⁴ As a

result, in spite of low incidence of prosthesis-patient mismatch,²⁰ some degree of residual aortic regurgitation (AR) is common, mainly at the paravalvular location.^{12,25} The degree of AR appears to be minor in most patients, however in some it may be responsible for left ventricular remodelling and moderate/severe AR was shown to be a strong predictor of increased mortality and poor treatment response at midterm follow-up.²⁶⁻²⁷ Therefore, accurate evaluation and detailed description of AR are essential for proper identification of patients at risk and for appropriate follow-up, but up to now this remained challenging, as no systematic methodology had been proposed. Bearing these concerns in mind, we developed a new method for accurate description of paravalvular AR, based on three-dimensional (3D) transthoracic echocardiography evaluation, suitable for accurate identification of moderate AR and proper 3D echocardiographic follow-up.²⁸

Patients referred for TAVI are elderly and their expectations for the treatment are beyond procedural success and favourable clinical outcomes.^{19,29} Quality of life improvement is also a major concern for this elderly patient's profile.⁷ Clinical benefit and neurohormonal activation reduction has been reported at short term after TAVI,³⁰ but the midterm results of quality of life were scarce and the reports conflicting.³¹⁻³² Further than mortality and hemodynamic valve performance, quality of life assessment is crucial for the evaluation of procedure efficiency and to guide clinical decision-making. Therefore, we looked into changes in the quality of life of patients undergoing TAVI at a midterm follow-up.

Finally, considering the new demands placed by TAVI, a partnership between the European Association of Echocardiography and the American Society of Echocardiography, developed the recommendations for the use of echocardiography in new transcatheter interventions, providing an actual reference for echocardiographers participating in new transcatheter treatments for patients with valvular heart disease.¹⁶

Setting

This study included consecutive patients referred for TAVI at Hospital Clinico San Carlos, Madrid, from April 2009 to April 2010. All patients had severe aortic valve stenosis (aortic valve area ≤ 1 cm²) and were ineligible for conventional aortic valve replacement, due to an excessive surgical risk, estimated by the logistic EuroSCORE and/or clinical judgment of specific co-morbidities, such as porcelain aorta, severely reduced lung capacity or frailty.⁷

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PART II

Aims

AIMS

This research sought to improve the understanding of transcatheter aortic valve implantation (TAVI), focusing on the importance of the information provided by echocardiography. Additionally the effects of TAVI on quality of life were explored. The aims were:

- 1.** To describe the role of imaging in TAVI, from patient's selection to follow-up;
- 2.** To describe the role of echocardiography during TAVI, in terms of procedure guidance and assessment of complications;
- 3.** To determine the acute hemodynamic effects of TAVI in left ventricle diastolic performance, immediately after aortic valvuloplasty and prosthesis deployment;
- 4.** To illustrate an accurate methodology for paravalvular aortic regurgitation evaluation by echocardiography;
- 5.** To evaluate quality of life results at midterm follow-up after TAVI;
- 6.** To contribute for the elaboration of the recommendations for echocardiographers participating in any or all stages of TAVI.

PART III

Papers

CHAPTER I

Imaging For TAVI

CHAPTER I – IMAGING FOR TAVI

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Gonçalves A, Zamorano J. Chapter 10 - Imaging for TAVI. Valvular Medicine Textbook 2011, Springer US; in press

Introduction

Transcatheter aortic valve implantation (TAVI) is a recent technique for the treatment of patients with severe symptomatic aortic stenosis (AS), who are at high risk for conventional aortic valve replacement or considered inoperable.¹ It is a challenging procedure that requires a multidisciplinary team approach, involving interventional cardiologists, cardiac and vascular surgeons, anesthesiologists and imaging specialists. Currently the Edwards SAPIEN™ and CoreValve™ valve are the prosthesis approved for transcatheter aortic stenosis treatment, both with good clinical and hemodynamic results at short and midterm follow-up.²⁻⁴ Each valve has specific characteristics and different aortic anatomic requirements, in consequence, imaging plays an essential task for proper patient's selection, decision on procedure access route and also for procedure guidance and patients' follow-up.

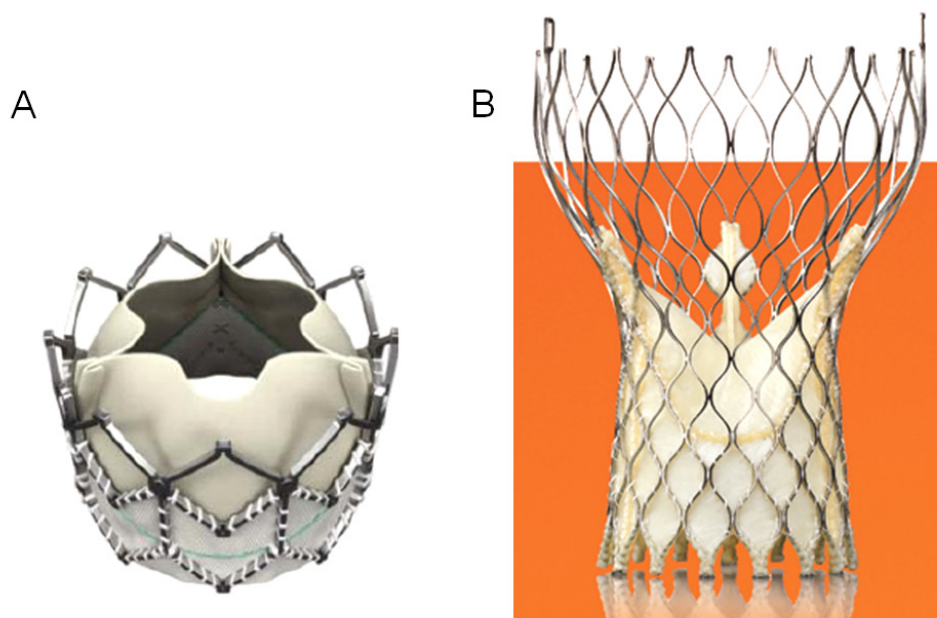


Figure 10.1 (A) The Edward Sapien-XT™ valve (Courtesy from Edwards Lifesciences) and (B) The CoreValve™ system (Medtronic copyright, used with permission)

Pre-procedure evaluation

At the time of patients' evaluation for TAVI the assessment of the anatomy of the aortic valve, aorta, and peripheral vasculature will determine the feasibility of the procedure, its best access approach and the prosthesis kind and size.

The Edwards SAPIEN™ valve is a cylindrical stainless steel balloon-expandable stent with three symmetric leaflets, made of bovine pericardium mounted inside (Figure 10.1 A). The stent also has a polyethylene terephthalate fabric skirt that decreases paravalvular leaks and it may be deployed via transfemoral or transapical route. The CoreValve™ ReValving system is a prosthesis made of porcine pericardial tissue sewn to form a trileaflet valve mounted within an asymmetrical self-expanding nitinol frame (Figure 10.1 B). The lower portion of the frame affixes the valve to the left ventricle outflow tract (LVOT), the mid-portion has a constrained waist that must be deployed at the level of the sinuses of Valsalva and coronary ostia and the upper section is designed to fix and stabilize the prosthesis in the ascending aorta. The Corevalve™ is designed for arterial access (femoral or subclavian), although there are case reports of deployment using a transapical route.⁵ Both valves are currently available in three sizes, as presented in Table 1.

Core Valve	Prosthesis size	AV annulus	S. Valsalva	Sino tubular junction
	26mm	20-23 mm	≥27 mm	≤40 mm
	29mm	23-27 mm	≥28 mm	≤43 mm
	31mm	26-29 mm	≥28 mm	≤43 mm
Edwards-Sapien				
	23mm	18-22 mm	-	-
	26mm	21-25 mm	-	-
	29mm	24-27 mm		

Table 1: Aortic anatomical requirements of contemporary transcatheter aortic valve prosthesis

TRANSTHORACIC ECHOCARDIOGRAPHY

The transthoracic echocardiography (TTE) evaluation provides anatomic and hemodynamic information. It establishes the presence of severe AS, which is defined by an aortic valve area of $\leq 1 \text{ cm}^2$ ($<0.6 \text{ cm}^2/\text{m}^2$) or a mean aortic valve gradient of $\geq 40 \text{ mmHg}$.^{6,7} The left and right ventricular dimensions, morphology and function are also evaluated by TTE. The presence of LV thrombus or a haemodynamically significant LVOT obstruction, due to basal septal hypertrophy should be excluded, as they represent contraindications for the procedure. Subaortic septal bulge may also create an obstacle to proper seating of the aortic prosthesis.⁸ The existence of a patch in the LV as well as significant pericardial calcification is a contraindication for TAVI using the transapical approach.¹ In addition, the presence of aortic regurgitation and the structure and function of the other

valves should be evaluated and described.

TTE is the first assessment of the aortic annular dimension and anatomic characteristics of the aortic valve. It can be used to describe the number of cusps, mobility, thickness and calcification. The presence of a bicuspid aortic valve is still a contra-indication for TAVI because of the risk of spontaneous aortic dissection or incorrect deployment of the aortic prosthesis due to the elliptical valvular orifice. However, successful TAVI in bicuspid AS has already been reported.⁹

As presented in Table I the aortic annulus dimension dictates the eligibility for TAVI and prosthesis size, which is determinant to the procedural success. Using TTE the aortic annular dimension is measured in systole, in a parasternal long-axis view, zoomed on the LVOT, at the point of insertion of the aortic valve cusps, from tissue–blood interface to blood–tissue interface—trailing edge to leading edge (Figure 10.2).¹⁰ 2D Transesophageal echocardiography (TEE) and even 3D TEE evaluation may be necessary when TTE measurements of the annulus are doubtful, particularly if they are near critical cut-offs for valve selection, or if the calcification extends from the aortic valve onto the anterior mitral leaflet or the septum.

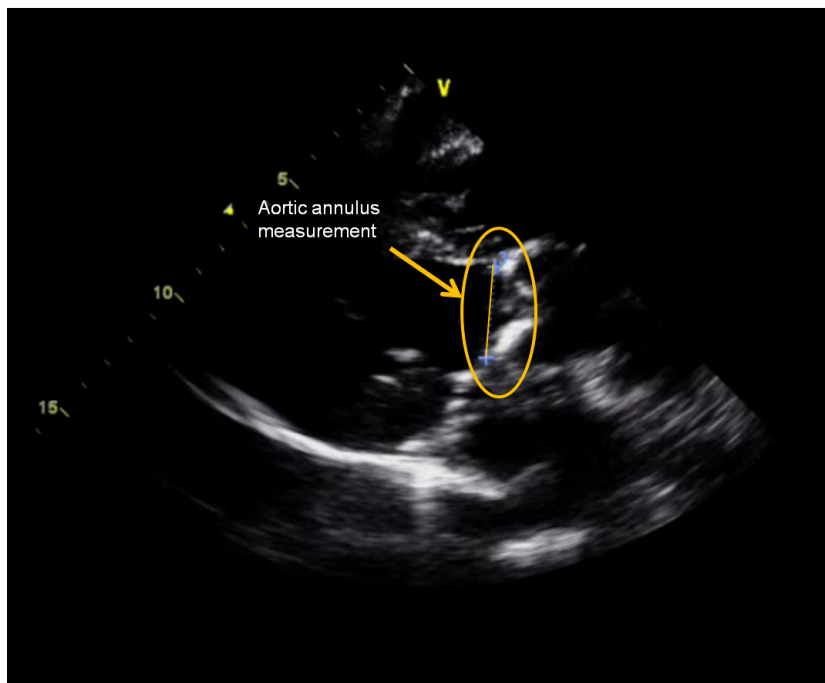


Figure 10.2 Transthoracic echocardiography parasternal long-axis view for measurement of aortic annular dimension.

TRANSESOPHAGEAL ECHOCARDIOGRAPHY

TEE is recommended prior to TAVI to a better evaluation of the aortic root anatomy, particularly if there are any concerns about the assessment of the aortic annular size and the number of cusps.

The annular diameter at the level of the basal attachment of the aortic valve cusps, measured in systole determines the size of the prosthesis, irrespective of the type of the valve inserted (Table I). There is a good correlation between TEE aortic annular measurements and TTE results; however TTE to some extent underestimates aortic annular size.¹¹

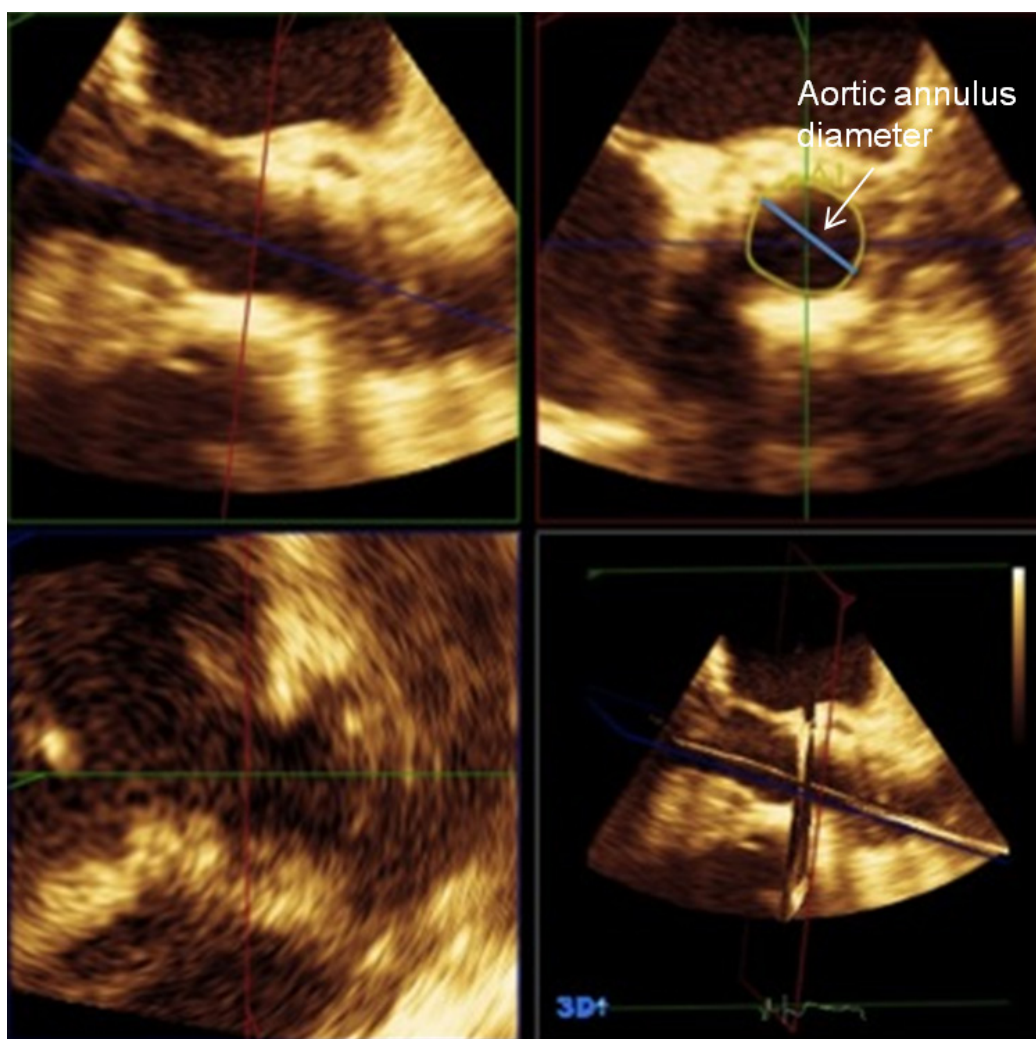


Figure 10.3 3D Transesophageal echocardiography assessing shape and measurements of the aortic annulus.

When measuring the annular diameter with 2D TEE, there is an assumption of annular circularity, which may result in erroneous measurements in patients whose annuli are more oval shaped. This limitation can be overcome using multiplanar tools of 3D TEE (Figure 10.3)¹⁰ or multidetector computed tomography (MDCT). The latter will be described in detail underneath in MDCT proper section. The final decision for the appropriate valve size mainly considers the annulus diameter, but in cases of borderline size decisions, the existence of large calcification in the native valve, may require a smaller prosthesis than the annular dimension alone would advise. Up to now there is no gold standard imaging technique for annular sizing for TAVI, but from the practical point of view, TTE complemented with TEE accomplishes good results in most patients.

Using short-axis views of the aortic valve the number of cusps can be precisely illustrated and its opening classified as central or eccentric. It is relevant to describe the severity and eventual asymmetry of calcification, as the differences in the tension–force across the valve may cause asymmetric deployment of the prosthesis and increase the risk of compression of the coronary arteries. However TEE presents constraints at the time of calcification evaluation, being MDCT the best method available.¹² The distance from the aortic annulus to the ostia of the coronary arteries should be measured, because patients with cusps length larger than annular-ostial distances are at risk of ostial coronary occlusion at time of valve deployment, as the native cusps will be crushed to the side. Only the right coronary annular-ostial distance

is possible to measure with 2D TEE, as the left coronary annular-ostial distance requires 3D TEE or MDCT.

Using TEE the characteristics of the ascending aorta, the aortic arch, and the descending thoracic aorta should be considered as the presence of large atheromas may increase the risk of peri-procedural embolization at the time of transfemoral approach.

MULTIDETECTOR COMPUTED TOMOGRAPHY (MDCT)

MDCT has a complementary role to echocardiography and angiography at the time of evaluation of patients before TAVI.¹³ It provides detailed anatomic visualization of the aortic root, thoraco-abdominal aorta and the iliofemoral access. Nevertheless, MDCT imaging is associated with the administration of iodinated contrast and exposure to ionizing radiation exposure, thus its use should be considered for individual patients based on risk and benefit.

Three-dimensional (3D) derived MDCT measurements provide precise dimensions for best prosthesis selection and sizing. Anatomically, the annulus is a crown-shaped 3-dimensional structure rather than a circular plane. However, 2D echocardiography and aortic angiography give the extent of a single diameter, making the assumption of annular orifice circularity. In contrast, 3D MDCT reconstruction of the annulus, orthogonal

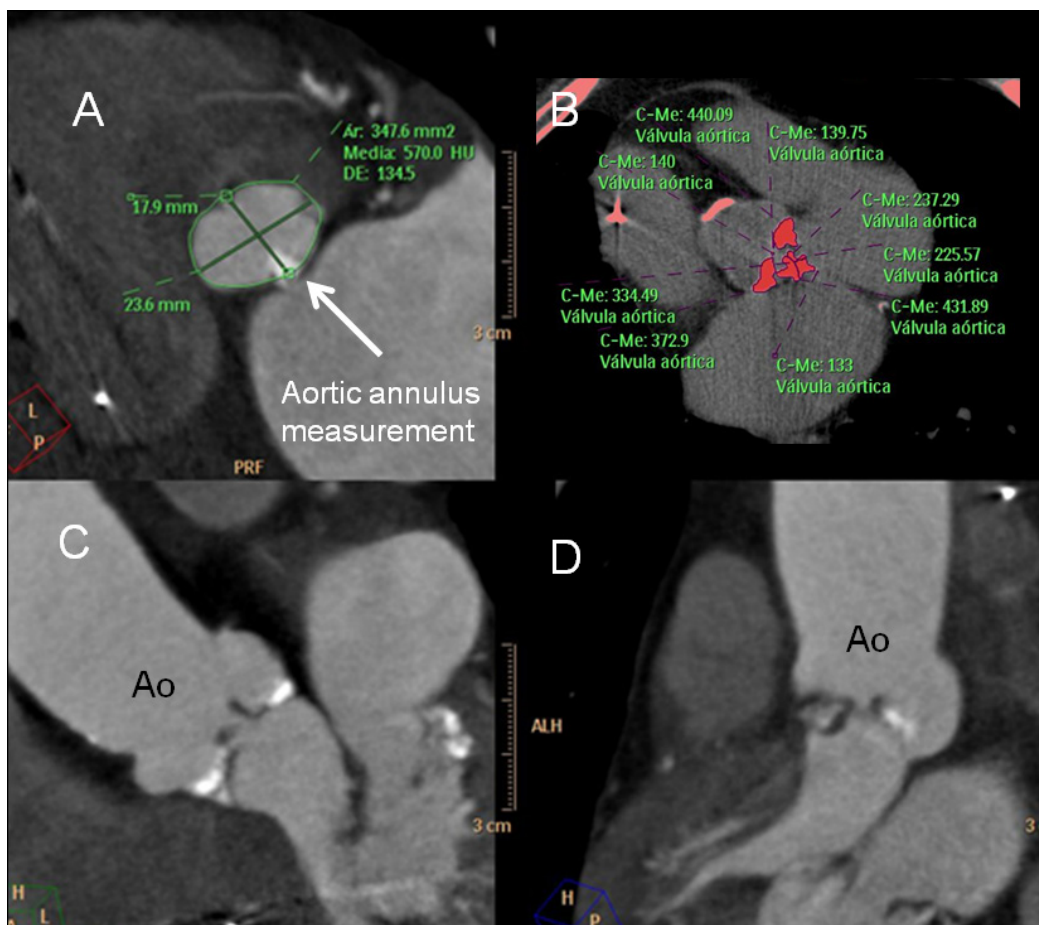


Figure 10.4 Multidetector computed tomography assessing aortic valve calcification (B) and reconstruction of the aortic root (A, C and D) measuring minimal and maximal diameters, circumference and area at the level of aortic annulus (A). Ao- Aorta. Courtesy of Dr. Pedro Marcos-Alberca

to the center-axis of the LVOT, allows the assessment of minimal and maximal diameters, circumference and area measurements (Figure 10.4). Although the use of 3D MDCT measurements for best prosthesis sizing may reduce the probability of error and present a more comprehensive definition of the annular size and shape, the mean of the maximum and minimum diameter measurements is comparable to 2D TEE measurement, remaining 2D TEE the most used technique.¹¹

Moreover, the aortic valve can be assessed in detail, and its morphology precisely described, regarding the number of cusps and the aortic valve area, measured by planimetry. Moreover, in comparison with echocardiography, MDCT has the ability to provide precise description of localization and extent of aortic cusps calcification. Relationships between aortic valve calcification and pos TAVI paravalvular aortic regurgitation have been described, being paravalvular aortic regurgitation associated with a larger aortic annulus and with more severe aortic root calcification.¹² Furthermore, dense aortic leaflet calcification measured on contrast MDCT discerned the need for an additional balloon post-dilatation, when using CoreValve™, for significant paravalvular regurgitation reduction.¹⁴

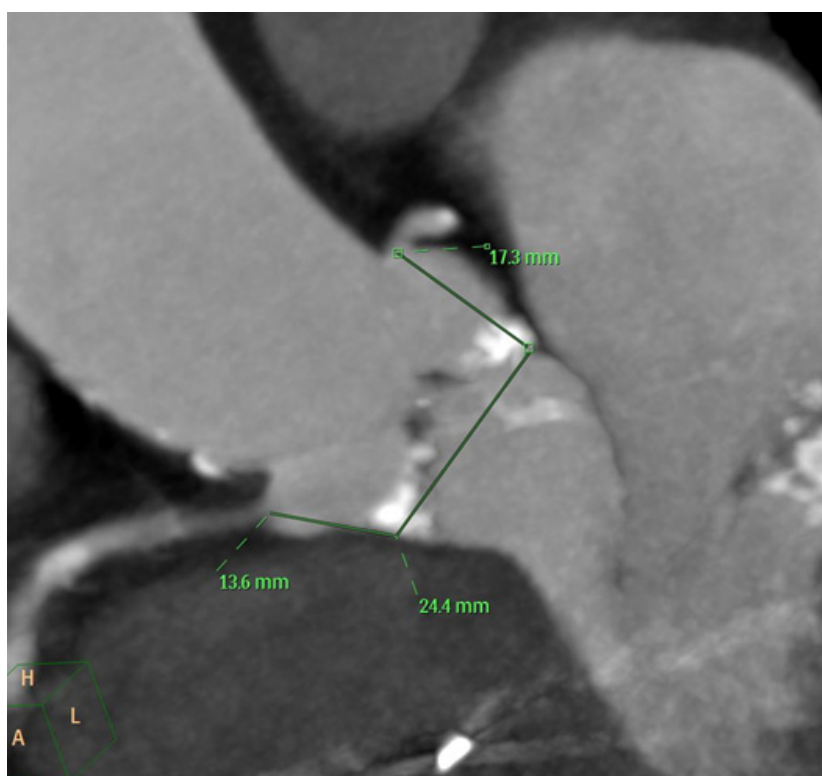


Figure 10.5 Multidetector computed tomography measuring the distance between annulus and coronary ostia.
Courtesy of Dr. Pedro Marcos-Alberca

At the time of pre-procedural evaluation, MDCT includes a complete assessment of coronary anatomy with conventional coronary angiography, which generally is limited by the advanced calcified disease. However, the relationship between leaflet height and distance between annulus and coronary ostia, can be accurately measured, identifying patients at higher risk for coronary occlusion during the procedure, when the annulus-coronary ostia distance is <11 mm (Figure 10.5).

The thoracic aorta evaluation is completed by the measurement of the aortic sinus diameter, sinotubular

junction and ascending and descending aorta, using centerline reconstructions. The occurrence of significant aneurismal dilatation is considered a contraindication for the use of CoreValve (Table I). Precise coaxial alignment of the prosthesis along the centerline of the aortic valve and aortic root is important during positioning to decrease the likelihood of complications as prosthesis embolization. MDCT offers the assessment of the aortic root in relation to the body axis and its pre-procedural angle prediction may decrease the number of aortograms required during the procedure, therefore shortening procedure time and contrast usage.¹⁵

Finally, MDCT allows the assessment of peripheral vasculature, considering caliber, tortuosity and calcification, being the minimum caliber of the common femoral artery dependent on the size of the prosthesis valve chosen. Using the previous Edward Sapien™ valve it was necessary a common femoral artery with a minimum of 8 mm of diameter, currently a minimum of 6 mm is required for both Edwards-XT™ and CoreValve™. Tortuosity and calcification are not prohibitive factors, but its combination is an adverse feature for site complications and central embolization. In addition the location of the bifurcation of the femoral artery and the degree of calcification have to be considered the time of deciding the feasibility of the transfemoral access or for choosing the alternative of subclavian or transapical approach.

ANGIOGRAPHY

Previously to the procedure, aortography produces images of the coronary arteries, thoracic and abdominal aorta. It allows the measurement of vessel diameters, tortuosity and excludes the presence of aorta aneurism. Nevertheless, at time of measuring vessels calcification, angiography presents limitations, being MDCT the best method.

Fluoroscopy is used for measurement of aortic annulus, at the time of definitive prosthesis sizing decision and to guide the procedure. The alignment of the three aortic sinuses in the same plane defines the optimal plane and angiography projection for TAVI.

Peri-procedural echocardiography during transcatheter aortic valve implantation

Peri-procedural 2D and 3D TEE can contribute for balloon and prosthesis positioning, to confirm prosthesis function immediately after implantation and to rapidly detect complications.

As in other intervention TEE guided procedures, the use of 3D, by its larger spacial resolution, presents advantages over 2D. It allows a better visualization of the guide wire path through the LV and around the mitral valve and subvalvular apparatus and permits a better evaluation of the prosthesis position on the balloon, relative to the native valve annulus and surrounding structures (Figure 10.6).

At the time of valvuloplasty, TEE guidance is especially useful when the valve is not very calcified, as those valves are difficult to image on fluoroscopy and easy observed by TEE. The balloon inflation is performed during rapid right ventricular pacing, though the balloon may accidentally migrate during inflation. TEE can be used to confirm a secure position during inflation and to monitor the behavior of the balloon and its effect on the calcified aortic cusps during inflation. During deployment of the prosthesis, 2D and 3D TEE confirm

the correct position of the valve and it is usually used in conjunction with fluoroscopy. The optimal position for the Edwards SAPIEN™ valve is with the ventricular side of the prosthesis positioned 2–4 mm below the annulus and for the CoreValve™, the ventricular edge of the prosthesis should be placed 5–10 mm below the aortic valve annular plane. After the deployment it is important to confirm that all the prosthetic cusps are moving well, that the valve stent has a circular configuration and to exclude significant valvular or paravalvular aortic regurgitation. Mild aortic regurgitation through the prosthesis, until the guidewire is removed and at the next few minutes after deployment is common. Small jets of paravalvular aortic regurgitation are frequent and it may occur even in a successful procedure, however severe aortic regurgitation is a serious complication and additional balloon inflation may be required.

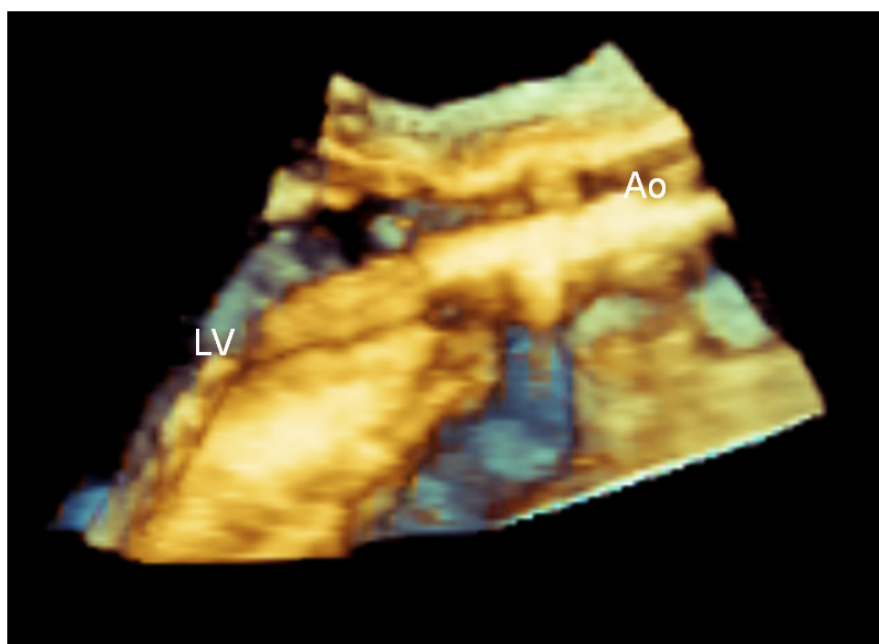


Figure 10.6 3D Transesophageal echocardiography showing the catheter and the balloon through the native aortic valve.
Ao- Aorta; LV- left ventricle.

ASSESSMENT OF COMPLICATIONS

Among the various complications assessable by TEE, aortic regurgitation is the most common (Figure 10.7).^{2,4} It may occur as a consequence of incomplete expansion, incorrect positioning, restricted cusp motion, or inappropriate prosthetic size.¹⁶ An undersized prosthesis may result in paravalvular aortic regurgitation. On the opposite, an oversized prosthesis has the risk of suboptimal stent expansion and central aortic regurgitation. Other mechanisms eventually responsible for aortic regurgitation are the presence of severe asymmetric calcification, causing paravalvular aortic leaks, or it may happen as a consequence of residual native aortic valve leaflet tissue prolapsing into the prosthesis, interfering with cusp motion and coaptation. The aortic regurgitation severity should be evaluated by the International recommended criteria.¹⁰

Furthermore, in result of prosthesis mismatch, or failed pacing capture, prosthetic embolism may occur. If the embolization happens towards the aorta, it might be resolved through successful transcatheter repositioning, but if it happens towards the LV, surgical removal is usually the only option.¹⁷

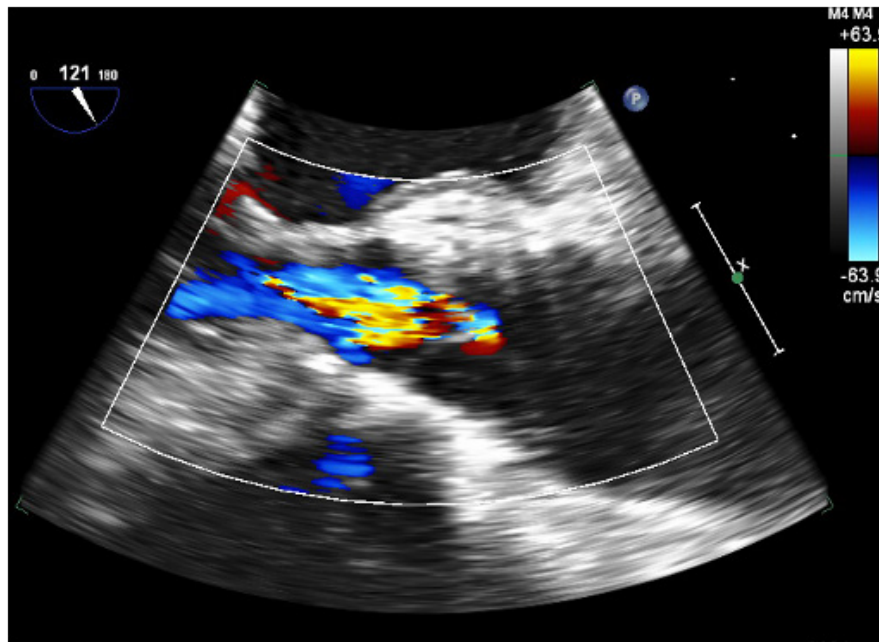


Figure 10.7 2D transesophageal echocardiography showing aortic prosthesis central regurgitation.

Other possible complications detectable by TEE are cardiac tamponade, secondary to wire perforation of the left or right ventricle and a new LV dysfunction, which may be secondary to ostial occlusion by fragment embolization or by an obstructive portion of the valve frame, sealing cuff or by native cusp.¹⁸

Moreover, sudden worsening of MR may occur due to right ventricular pacing, causing LV asynchrony, or as a consequence of prosthetic misplacement, towards the left ventricle outflow tract, with pressure exerted on the anterior mitral leaflet or by direct damage or distortion of the subvalvular apparatus.¹⁹ A tear or ruptures of the aortic root have been also observed during the procedure after balloon valvuloplasty or prosthesis deployment, especially in the presence of extensive annular calcification or prosthesis oversizing.²⁰

TEE is not mandatory during TAVI, as it usually requires general anesthesia and the probe may also partially obstruct the optimal fluoroscopic view, however it may be the main technique used for procedure guidance, particularly in patients with limited native valve calcification,¹⁰ providing the best guidance and rapid assessment of complications.

Post-implantation follow-up

The imaging follow-up evaluation of patients with transcatheter aortic valves is mainly based on TTE. It is usually performed at the time of hospital discharge, at one month follow-up and at 6 or 12 months, depending on each institution protocol. The echocardiographic evaluation is mostly similar to surgically implanted prostheses, as guided by previously published guidelines for prosthetic valves.²¹

Nevertheless, the accurate evaluation of aortic regurgitation severity is a main issue, as it may consist of central and paravalvular aortic regurgitation and the latter frequently includes multiple small jets. Colour flow qualitative evaluation is the method most commonly used for the assessment of the regurgitant jet size. The guidelines recommend using the following criteria for jet width based on the %LVOT diameter occupied:

≤25% suggests mild, 26–64% suggests moderate, and >65% suggests severe. These methods are limited in the setting of paravalvular jets which are frequently eccentric and irregular in shape. The ASE/EAE guidelines advise that for paravalvular jets, the proportion of the circumference of the sewing ring occupied by the jet gives a semi-quantitative guide to severity: <10% of the sewing ring suggests mild, 10–20% suggests moderate, and >20% suggests severe²¹. However, this concept assumes jet continuity, which may not be the case for transcatheter valves and therefore may overestimate the severity in presence of multiple small jets. For the quantitative approach the width of the vena contracta is a robust estimate of regurgitant severity, but in the setting of prostheses, portions of the sewing ring may not be imaged due to acoustic shadowing. In addition, there has been no validation for adding the vena contracta widths of multiple jets as it may be encountered post-TAVI. A new method using 3D TTE vena contracta planimetry has been recently described, showing an accurate alternative for quantitative evaluation and moderate AR recognition of paravalvular aortic regurgitation after TAVI.²² The quantitative methods for calculating regurgitant volume and effective regurgitant orifice area that rely on the comparison of stroke volumes across the aortic valve and a nonregurgitant valve may be also used for prosthetic valves evaluation.²¹ However, the final interpretation should follow the principle of comprehensive evaluation and integrated approach.

At the time of effective orifice area calculation, it is essential that the pre-valvular velocity is recorded proximal to the stent and the post-valvular velocity (typically recorded with continuous-wave Doppler) distal to the stented valve. If the LVOT velocity used in calculations is erroneously recorded within the stent but proximal to the cusps, the result will be an overestimation of valve area.¹⁰ Similarly the LVOT diameter should be measured immediately proximal to the stent.²³

In selected cases with suspicion of complications such as prosthesis malposition, MDCT by its higher spatial resolution is an appropriate technique, providing accurate information on the position and deployment of prosthesis.

Conclusion

Patient's evaluation for TAVI might require the use of multi-imaging modalities. Using echocardiography, MDCT and angiography, an accurate evaluation of aortic stenosis severity, annulus sizing, aortic morphology and peripheral vascular anatomy can be performed. These steps are decisive for appropriate patient selection. During TAVI, TEE along with fluoroscopy may be used for guidance, to evaluate possible complications and the final result. At time of patients' short and long-term follow-up, echocardiography represents the ideal technique for prosthesis hemodynamic characterization, being MDCT reserved for particularly complex conditions.

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CHAPTER 2

Echocardiography: guidance during valve implantation

Echocardiography: guidance during valve implantation

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KEYWORDS

Transcatheter aortic valve implantation, aortic valve stenosis, valvuloplasty, aortic prosthesis, three dimensional (3D) transesophageal echocardiography, procedure complications, transfemoral, transapical approach

Abstract

Transcatheter aortic valve implantation (TAVI) by percutaneous or transapical approach has emerged as an effective and less-invasive treatment for patients with severe symptomatic aortic valve stenosis and high surgical risk. Echocardiography is a fundamental tool in patients' selection for TAVI, for guiding the intervention as well as evaluating the position, deployment and function of the prosthesis. This review describes the role of echocardiography during the intervention, in procedure guidance and in the assessment of complications.

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Introduction

Transcatheter aortic valve implantation (TAVI) has recently emerged as an effective, less-invasive treatment for patients with severe symptomatic aortic valve stenosis and high surgical risk, either in its percutaneous or transapical approach.¹ Rates of success in device implantation of around 95%, and procedure-related mortality rates between 5 and 18% have been reported.²⁻⁴

Currently, two different systems are available either through transfemoral or transapical approach: the balloon-expandable Edwards SAPIEN® prosthesis (Edwards Lifesciences, Irvine, CA, USA), a trileaflet symmetrical bovine pericardial valve mounted within a stainless steel stent, and the self-expanding CoreValve ReValving® system (Medtronic, Minneapolis, MN, USA). The CoreValve prosthesis consists of a trileaflet bioprosthetic porcine pericardial tissue valve, which is sutured into a self-expanding nitinol frame with an asymmetric shape. For the CoreValve, the sizes of the developed delivery systems have been gradually reduced to 18 Fr, at the third generation, and recently, a new 18 Fr delivery system for the SAPIEN valve has been approved, facilitating the vascular access and deployment of the device. Presently, each system has two different sizes available, compliant with annulus dimensions from 19 to 27 mm. Both systems have been extensively described elsewhere.^{5,6} Echocardiography is a fundamental tool in patient selection for TAVI, for guiding the intervention and to evaluate the position, deployment and function of the prosthesis. The procedure is usually performed under fluoroscopic and transesophageal echocardiographic (TEE) imaging, but a fully echo-guided transapical aortic valve implantation has already been reported.^{7,8} This is an important step, considering the risk of acute postoperative renal failure following extensive use of contrast medium, which might reach 28%, according to recent reports.⁹

Transesophageal echocardiographic approach before valvuloplasty and prosthesis implantation

Before starting the procedure, the echocardiographer has to carefully describe the aortic valve anatomy and its anatomical landmarks, distribution of aortic valve calcification, geometry of the left ventricle outflow tract (LVOT) and its spatial relationships, the distance between coronary cusps insertion and coronary arteries ostium and also an eventual ectopic calcification of the basal portion of the anterior mitral leaflet and annulus. The aortic valve annulus diameter is measured, from the insertion of the non-coronary cusp to the insertion of the right coronary cusp in a 135° view (Figure 1). In the 45° view the orthogonal diameter of the aortic root is measured in an upper plane of the coronary arteries arisen. The precise distance of the coronary arteries to the annulus should be measured in order to minimise the risk of complications, namely myocardial ischaemia. It is advisable that at the time of deployment, coronary ostia should be minimally located 14 mm away from the leaflets insertion for the CoreValve and 11 mm for the Edwards SAPIEN prosthesis. Left and right ventricular systolic function, regional wall motion abnormalities, mitral or tricuspid regurgitation and thoracic aortic arch atheroma should also be evaluated.¹⁰ For the transapical aortic valve implantation approach, the echocardiographer can use transthoracic echocardiography to point the left ventricle apex position.¹¹

Although bi-dimensional (2D) echocardiography was the standard technique in TEE, currently three dimensional (3D) TEE is highly available and there is a common perception that it frequently shortens the learning curve of the procedure, which might influence early outcome. Moreover, the 3D transesophageal probe (X7-2t®, 7 MHz, Philips Medical Systems, Eindhoven, The Netherlands) has the capability of presenting two orthogonal bi-dimensional simultaneous plane views (e.g., 45° short-axis and 135°) which provides additional information, especially during the intervention (Figure 2). Throughout patient selection, and in the sensitive process of aortic annulus measurement, 3D imaging improves the assessment of valve anatomy and geometry of the LVOT (Figure 3), which was shown to be frequently elliptical instead of circular in form.^{12,13} Besides, the sectorial 3D image and amplified or zoom mode 3D acquisition allow the visualisation of the entire guidewires, catheters and prostheses throughout the process. This added value of 3D has become critical in the operating room, so fluoroscopy needs to be in a postero-anterior projection during transapical

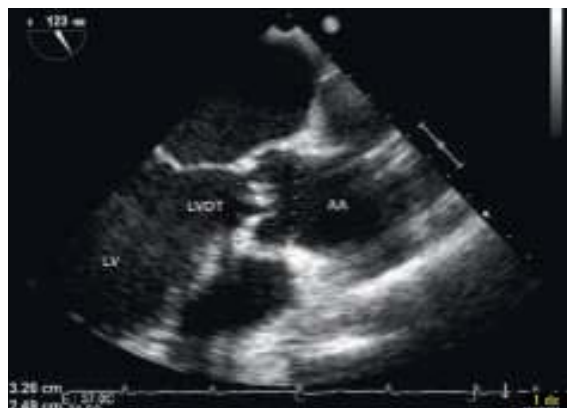


Figure 1. Two-dimensional TEE long axis view (123°) showing measurement of aortic valve annulus and sinotubular junction diameter. LV, left ventricle; AA, ascending aorta; LVOT, left ventricle outflow tract.

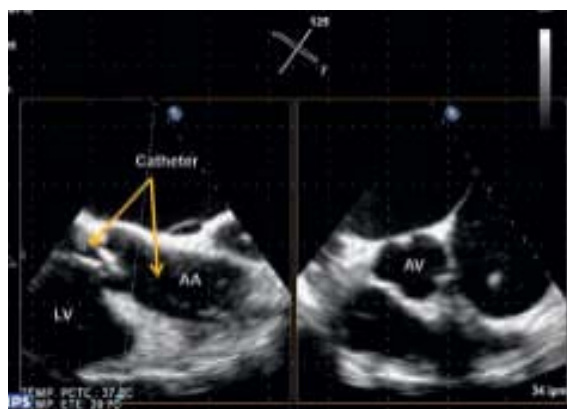


Figure 2. Two-dimensional TEE of two orthogonal simultaneous views (biplane or X-plane). LV, left ventricle; AA, ascending aorta; AV, aortic valve.

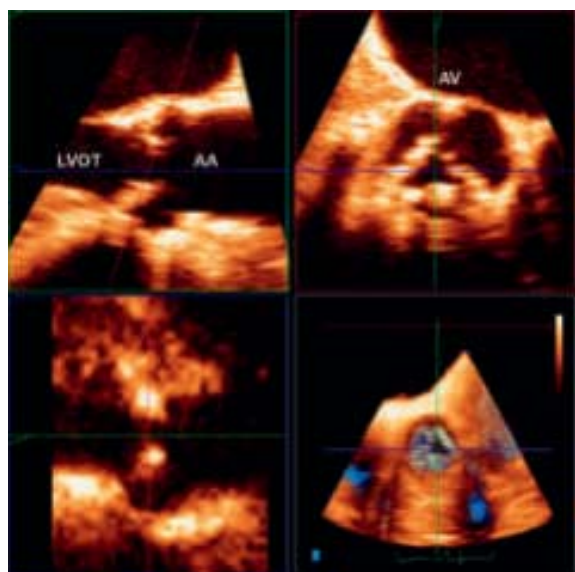


Figure 3. Post-processing of 3D volumetric acquisition using multiplanar reformatting or MPR showing valve anatomy and geometry of the LVOT. LVOT, left ventricle outflow tract; AA, ascending aorta; AV, aortic valve.

intervention. As a result, the calcified aortic annulus is positioned over the spine and the echocardiographic support is the only imaging technique which visualises and can guide, as well, the exact placement of the prosthesis.⁹ In the process of valve size selection, approximately 10% of oversizing is applied, based on these measurements. Although some oversizing is essential to avoid severe paravalvular leakage, however, in the presence of a rigid aortic root, too much oversizing entails a high risk of serious complications and should be avoided. In addition, it is wise to exclude patients with an annulus larger than the largest available prosthesis, in whom significant paravalvular regurgitation might be expected.¹⁴ In spite of the experience of the operators, the lack of congruence between the annulus and the device is related to significant paravalvular aortic regurgitation, thus the process of precise aortic annulus measurement is essential for better outcomes.¹⁵

Recent studies have also highlighted the value of multislice computed tomography to evaluate aortic valve annulus morphology and size, however TEE remains the reference technique due to its reliability, safeness and non radiation exposure.¹⁶

Valvuloplasty and prosthesis implantation

Balloon valvuloplasty is performed with a balloon filled with 1:4 diluted contrast placed in the aortic valve, during rapid ventricular pacing. Echocardiography is used to watch for antegrade or retrograde slippage of the balloon throughout its inflation. Inappropriate motion of the balloon towards the ventricle during inflation may happen due to axial motion of the heart, or to a small sinotubular junction. Conversely, an upward shifting of the balloon towards the aorta may be caused by the presence of a prosthetic mitral valve.¹⁷

Using the Live 3D mode, the dilatation of the valve with the valvuloplasty balloon and the anatomic results are accurately displayed (Video 1). Following pre-dilatation of the native aortic valve, the prosthesis is advanced and deployed within the aortic annulus. This is one of the most critical steps during the intervention, because of the possible misplacement and embolism of the device. After the valve is introduced into the annulus, the pusher is retrieved back into the delivery sheath.

A long-axis view of the aortic root with 2D TEE identifies the end of the delivery catheter through the aortic annulus and, joined with fluoroscopy imaging, allows observation of the initial position, deployment, and final placement of the prosthesis. However, the single plane of the 2D image has several constraints when looking for catheter alignment (Figure 2). Conversely, in spite of the relatively low temporal resolution of the 3D mode as compared to 2D TEE, using the Live 3D mode, the trajectory view is precisely identified (Figure 4). In addition, this discloses with detail the prosthesis deployment in relation to the aortic annulus (Video 2). Therefore, the 3D TEE approach provides relevant information to the interventional cardiologist during this decisive step, with an excellent visual agreement between the fluoroscopic and the 3D TEE images.

In order to accomplish correct position in the deployment process, the prosthesis should be oriented coaxially with the long axis of the ascending aorta and perpendicularly to the aortic annulus, as showed in Figure 5. An oblique position may lead to valve misplacement, particularly in patients with a calcified aortic root and/or narrow sinotubular junction, in whom restriction of balloon inflation may occur with consequent downward displacement of the valve into the ventricle.¹⁷

One of the issues of confronting TEE during the procedure, is to identify, in one imaging plane, the exact location of the valve stent in relation to the deployment balloon and its ventricular and aortic rims. The stent is recognised as an echogenic rectangular structure seen in bristly profile to the balloon (Figure 5). The image interpretation is easier if the echocardiographer is aware of its length and if 3D TEE is used. As the prosthesis can move up to 2 to 4 mm towards the ascending aorta with balloon inflation, the optimal position is achieved when the ventricular edge of the stent is

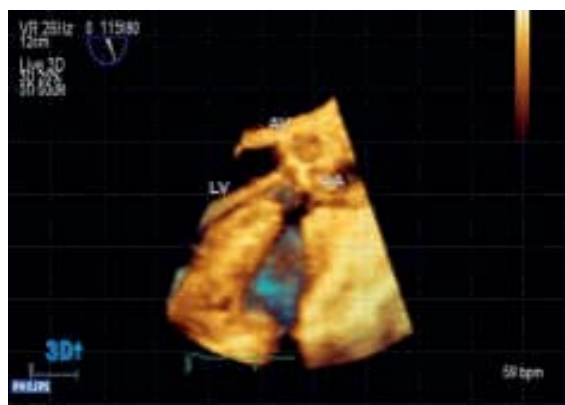


Figure 4. Real-time 3D transesophageal echocardiography showing the relative position of the catheter through aortic valve and ascending aorta. LV, left ventricle; AA, ascending aorta; AV, aortic valve.

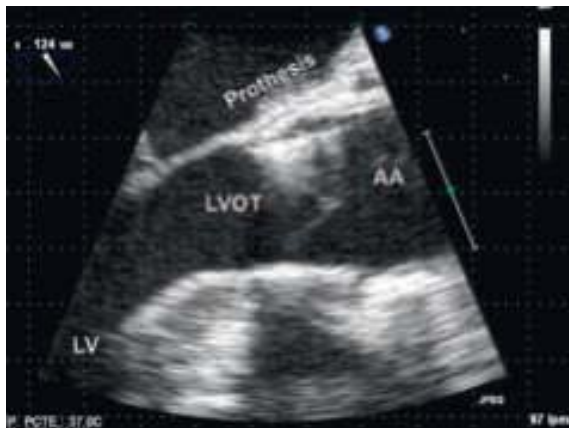


Figure 5. Two-dimensional transesophageal echocardiography long axis view showing the prosthesis, oriented coaxial with the long axis of the ascending aorta and perpendicular to the aortic annulus. LV, left ventricle; AA, ascending aorta; LVOT, left ventricle outflow tract.

positioned approximately 2 to 4 mm below the aortic valvular annular plane for the Edwards SAPIEN valve and 5–10 mm for the CoreValve ReValving system. The aortic rim of the stent should cover the upper limit of the native aortic leaflets, and the valve should be deployed when both echocardiographer and interventionist agree that is in the best position.

During deployment, the native aortic leaflets are compressed between the valve stent and the wall of the aortic root. To avoid an upper positioning of the prosthesis in the aorta upon deployment caused by left ventricular ejection flow, pacing is performed until the balloon is completely deflated.

After the permanent aortic prosthesis implantation, the correct positioning is confirmed and aortic regurgitation evaluated immediately after removal of the deployment catheter and guidewire. The aortic end of the valve stent should be below the level of the coronary ostia and the ventricular end of the valve stent should not interfere with anterior mitral leaflet function (Video 3).¹⁰ The prosthesis is expected to present a circular expansion, with native aortic leaflets perfectly contained and prosthesis leaflets moving amply, without significant aortic regurgitation (Videos 4 and 5). Finally, the transgastric window is used for Doppler interrogation of the aortic valve and to record the transaortic pressure gradient reduction and improvements in aortic valve area.

Assessment of results and detection of complications

One of the most common complications is aortic regurgitation, either perivalvular or central. It might be caused by severe asymmetric calcification of the native aortic valve (Figure 6 and Video 6), incomplete expansion of the device, incorrect positioning or inappropriate prosthesis size.¹⁵ An excessively small size might cause paravalvular aortic regurgitation (Figure 7). In contrast, a prosthesis implantation too large for the aortic root can cause suboptimal stent expansion, impaired leaflet mobility and central aortic regurgitation (Figure 8, Videos 7 and 8).

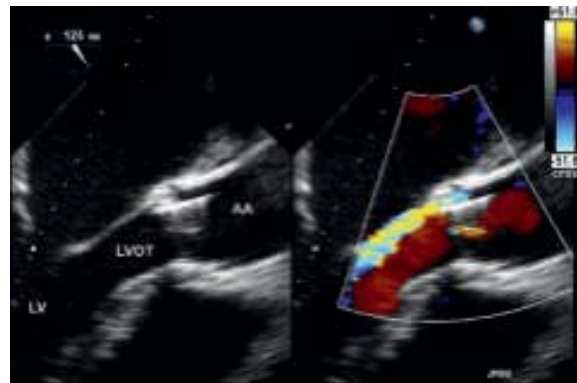


Figure 6. Two-dimensional transesophageal echocardiography long axis view showing moderate perivalvular regurgitation caused by asymmetric calcification. See Video 6 for viewing the entire sequence. LV, left ventricle; AA, ascending aorta; LVOT, left ventricle outflow tract.

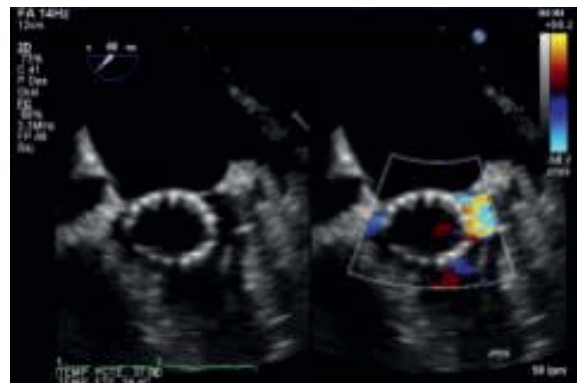


Figure 7. Two-dimensional transesophageal echocardiography short axis view showing perivalvular regurgitation.

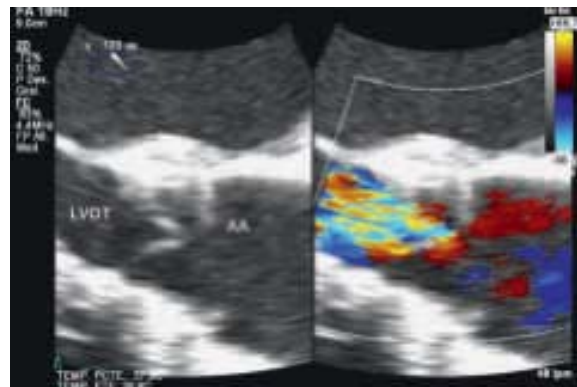


Figure 8. Two-dimensional transesophageal echocardiography long axis view showing central regurgitation. AA, ascending aorta; LVOT, left ventricle outflow tract.

Sometimes, mild to moderate aortic paravalvular regurgitations are seen due to minimal defects of sealing involving the posterior commissure, mainly when leaflets highly calcified. As a consequence of the accommodation of the struts to these calcified valves, frequently, after several minutes or several hours, the mild paravalvular regurgitations disappear.

Conventional criteria should be used to assess severity using colour Doppler to view the height and width of the regurgitant jet, but 3D TEE is also useful to evaluate the early functioning of the bioprosthesis, and classify the severity of perivalvular or central regurgitation (Video 7). In case of moderate severity, repeat dilation can be performed. However, primary valve dilatation and risk factors such as the amount of calcification, as a surrogate of risk of aortic rupture, have to be considered before proceeding to repeat dilatation. Furthermore, over dilatation of the stent is not recommended since, it might worsen central aortic insufficiency and potential leakage of the aortic wall. Concerning small paravalvular aortic regurgitation jets, their clinical significance is probably benign and not progressive in the majority of patients.¹⁸

In the context of acute and severe hypotension, cardiac effusion or cardiac tamponade secondary to wire perforations might be found, as well as left ventricular dysfunction and wall motion abnormalities secondary to an obstructive portion of the valve frame or the sealing cuff being placed directly over a coronary ostium. Conduction abnormalities might also be detected by the echocardiographer, more commonly in prostheses extending farther into the ventricle. Worsening of mitral regurgitation can occur, due to right ventricular pacing or due to the direct mechanical effect of the ventricular edge of the prosthesis on the anterior leaflet of the valve. Using the antegrade apical approach, direct damage or distortion in subvalvular apparatus might occur, leading to acute mitral regurgitation. Therefore, a careful monitoring of the mitral valve during and after implantation is needed. Stroke is also a potential complication of this procedure, with rates ranging from 0% to 10%.¹⁴ Even if potential causes of stroke, such as prolonged hypotension or air embolism from left ventricle apical cannulation cannot be assessed by echocardiography, other causes such as atheroembolism from the ascending aorta and aortic arch or aortic leaflet fragmented material embolisation, should be searched for and highlighted, in order to avoid this potentially lethal complication.¹⁹ Tear or rupture of the aortic root has been reported, with a risk of 0.5%, secondary to excessive balloon dilation or prosthesis oversizing in context of extensive annular calcification (Figure 9).²⁰ If this complication occurs, the procedure has to be converted to a conventional surgical technique.



Figure 9. Two-dimensional transesophageal echocardiography long axis view showing aortic root rupture during TAVI. LV, left ventricle; AA, ascending aorta; LVOT, left ventricle outflow tract.

Prosthetic embolism is the extreme complication that might occur in consequence of prosthesis mismatch. In case of valve embolisation towards the aorta, it might be resolved through successful transcatheter repositioning. However, if embolisation to the left ventricle occurs, surgical removal is usually the only option.^{21,22} Finally, procedural failure can take place. It may be caused by inability to cross the native aortic valve with the guidewire or with the device after valvuloplasty by the inability to pass the device through the aortic arch, upstream migration of the device or extreme malpositioning.¹⁰

Conclusion/future directions

The number of patients referred to TAVI is rapidly increasing and innovative advances, such as subclavian access or transapical approach, are being presented today for those with no conventional transfemoral access.²³

Good communications between the operating team and precise guidance are crucial to procedure success and early detection of potential complications.

In conclusion, 3D TEE monitoring should be used as a standard procedure during TAVI, in combination with 2D TEE. 3D TEE provides more accurate information to the interventional cardiologist during positioning, deployment as well as early functional evaluation of the prosthesis, and consequently makes the procedure safer.

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Online data supplement

Video 1. Real-time 3D transesophageal echocardiography showing aortic balloon valvuloplasty.

Video 2. Real-time 3D transesophageal echocardiography showing aortic prosthesis deployment.

Video 3. Full volume zoom 3D transesophageal echocardiography, showing restricted movement of the anterior leaflet of the mitral valve caused by the ventricular edge of aortic prosthesis.

Videos 4 and 5. Real-time 3D transesophageal echocardiography showing regular aortic prosthesis implantation.

Video 6. Two-dimensional transesophageal echocardiography long axis view showing moderate perivalvular regurgitation caused by asymmetric calcification.

Videos 7 and 8. Full volume 3D transesophageal echocardiography showing central aortic regurgitation jet caused by incomplete expansion of the device, which was too large for the aortic root.

CHAPTER 3

**Acute left ventricle diastolic function
improvement after transcatheter aortic
valve implantation**



Acute left ventricle diastolic function improvement after transcatheter aortic valve implantation

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Aims

Data regarding the effects of TAVI on LV after are scarce and conflicting results have been reported immediately after aortic valvuloplasty. This study aimed to determine the acute haemodynamic effects of transcatheter aortic valve implantation (TAVI) in left ventricle (LV) diastolic performance, immediately after aortic valvuloplasty and prosthesis deployment.

Methods and results

Sixty-one patients with severe aortic valve stenosis, and preserved LV systolic function submitted to successful TAVI, were included. All procedures were guided through transoesophageal echocardiography, and parameters of diastolic function were evaluated before and minutes after TAVI. The mean age was 83.5 ± 6 years and mean log EuroSCORE was 18.2 ± 9.4 . Before the procedure, all patients presented LV diastolic dysfunction. Immediately after TAVI, fewer patients presented a restrictive pattern [27 (44.3%), before the procedure, vs. 20 (34.4%), after TAVI ($P = 0.047$)], and an increase in E wave deceleration time (211.2 ± 75.5 vs. 252.7 ± 102.3 cm/s, $P = 0.001$), in E wave velocity (109.5 ± 41.2 vs. 120.3 ± 43.6 cm/s, $P = 0.025$), and in isovolumetric relaxation time (83 ± 36.5 vs. 97.1 ± 36.0 ms, $P = 0.013$) was observed. On multivariate analysis of covariance (ANCOVA), adjusting to LV systolic function, heart rate, blood pressure, and haematocrit values, the results remained significant. Patients referred to percutaneous approach had invasive haemodynamic data collected, showing a decrease in LV end-diastolic pressure after valve implantation [18.8 ± 5.7 vs. 14.7 ± 4.7 , mean difference -4.1 (95% CI: $-5.9; -2.9$)]. Patients with a restrictive pattern immediately after TAVI presented a smaller decrease in LV end diastolic pressure (-3.3 ± 4.7) than those with diastolic dysfunction grade I or II (-9.5 ± 4.7 ; $P = 0.017$).

Conclusion

This is the first study describing LV diastolic performance during TAVI. Our results show improvement in diastolic function parameters in patients with preserved LV systolic function, immediately after successful TAVI.

Keywords

Aortic valve stenosis • Aortic prosthesis • Diastolic dysfunction • Left ventricle (LV) • Transcatheter aortic valve implantation (TAVI)

Introduction

Transcatheter aortic valve implantation (TAVI) techniques have emerged as an alternative treatment for patients with severe aortic stenosis and high surgical risk.¹ Since the first-in-man

experience in 2002,² thousands of patients have been treated with this technique worldwide with procedural success rates of ~95%.^{1,3,4}

Most patients referred for TAVI are elderly and present symptomatic aortic stenosis with heart failure in NYHA classes III and IV,

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in spite of preserved left ventricle (LV) systolic function.^{1,5} Myocardial hypertrophy in consequence of cellular hypertrophy and cellular matrix hyperplasia occurs before the development of systolic dysfunction,⁶ being diastolic dysfunction the primarily responsible for heart failure symptoms. After aortic valve replacement (AVR), clinical improvement is expected and diastolic stiffness along with relaxation normalization is observed in late follow-up.⁷

In patients submitted to TAVI, several studies have already shown immediate almost complete normalization in afterload and a significant decrease in pressure gradient, between the aorta and the LV, as well as clinical improvement at short term.^{4,5,8} At medium-term follow-up, LV mass reduction and improvements in tissue Doppler velocities have been reported,⁹ and one study has described early regression of septal hypertrophy 1 month after TAVI.¹⁰ However, so far the acute changes in left ventricular diastolic performance after TAVI and its consequences in patients' clinical outcome are unknown. Conflicting results from invasive haemodynamic measurements after aortic balloon valvuloplasty have been reported and worsening of diastolic indexes was described.^{11,12} Nevertheless, the technique applied on TAVI is different, as well as the favourable clinical outcomes,¹ in opposition to the disappointing results after aortic valvuloplasty.^{13,14}

This study aimed to determine the acute haemodynamic effects of TAVI in LV diastolic performance, immediately after aortic valvuloplasty and prosthesis deployment.

Methods

Population

Sixty-one patients with severe aortic stenosis (aortic valve area ≤ 1 cm²) and preserved LV systolic function (ejection fraction $\geq 50\%$), submitted to successful TAVI in one tertiary centre from April 2009 to April 2010, were included. These patients were obtained from a series of 97 consecutive patients who underwent TAVI, after excluding those with LV systolic dysfunction (9 patients), atrial fibrillation or ventricular pacemaker rhythm (7 patients), concomitant moderate to severe mitral valve disease (6 patients), aortic regurgitation (3 patients), and those whose procedure was not totally guided through transoesophageal echocardiography¹⁵ (11 patients). Indications and contraindications for TAVI have been described previously elsewhere.^{1,5,16}

Patients were referred for TAVI due to an excessive risk for AVR, which was estimated using the logistic EuroSCORE and/or clinical judgement.¹⁷ Ten (16.4%) elderly patients were considered inoperable on the basis of comorbidities or risk factors such as pulmonary hypertension (defined as a pulmonary systolic pressure >50 mmHg as estimated by Doppler echocardiography or measured by cardiac catheterization) or frailty or porcelain aorta (5, 8.2% patients). No systematic tests were performed for the evaluation of frailty, being its conception based on medical criteria.¹⁸ Porcelain aorta was defined as wide circumferential calcification of the thoracic aorta when assessed by computed tomography and/or fluoroscopy.

Transthoracic echocardiography

On the previous day of the procedure, all patients performed a conventional transthoracic echocardiogram with bidimensional and Doppler assessment, which was completed with three-dimensional (3D) analysis (X4-1 probe, Philips Medical Systems, Andover, MA, USA). The following measurements were obtained in all patients: LV

mass calculated with the American Society of Echocardiography (ASE) recommended formula, mean transvalvular gradient calculated with the Bernoulli formula, aortic valve area measured by the continuity equation and early (*E'*) and late (*A'*) diastolic peak velocities from Doppler tissue imaging measured at septal and lateral mitral annulus. Considering the superior accuracy and reproducibility of 3D echocardiography, left atrium (LA) volume, LV systolic and diastolic volumes, and resulting ejection fraction were calculated with direct volumetric analysis.¹⁹ Valvular insufficiencies and diastolic function were graded according to international recommendations.^{20,21}

Transcatheter aortic valve implantation

TAVI was performed with fluoroscopy and TEE guidance, under general anaesthesia using techniques described in detail in previous reports.^{22,23}

Nineteen patients (31.1%) implanted an Edwards SAPIEN (Edwards Lifesciences, Irvine, CA, USA) aortic valve through anterograde transapical approach and 42 (68.9%) were submitted to the retrograde transfemoral approach. Among these, a CoreValve (Medtronic CoreValve Percutaneous System, Medtronic CV) was implanted in 23 (54.8%) patients and an Edwards SAPIEN valve in 19 (45.2%). Two valve sizes are available, 23- and 26-mm expanded diameters for Edwards SAPIEN valve and 26 and 29 mm for CoreValve. The aortic prosthesis size was decided according to the annulus diameter, measured with transoesophageal echocardiography.

Transoesophageal echocardiography protocol

During the procedure, data were recorded using TEE with real-time 3D capability (i.e. 33 echocardiography system, X7-2t probe, 7MHz, Philips Medical Systems, Eindhoven, the Netherlands). TEE was performed in the moments previously to intervention and it was repeated few minutes after aortic valve implantation (5.7 ± 2.4 min), for later comparison between TEE results before and after TAVI.

Pulsed wave spectral Doppler was recorded using mid-oesophageal views at four-chamber view, with the sample volume at the leaflet tips for transmitral inflow pattern assessment, and five-chamber view, with the sample volume between leaflet tips and LV outflow tract, for simultaneous imaging of mitral inflow and aortic valve closure clicks. Basal short-axis views were used to assess pulmonary veins flow and at least two pulmonary veins (one left and one right) were recorded. Colour M-mode Doppler in mid-oesophageal four-chamber view was used for recording transmitral flow for later measurement of propagation velocity. Transgastric mid short-axis view of the LV was recorded for LV systolic and diastolic area measurements. Deep transgastric long-axis view was used for continuous Doppler flow assessment through the aortic valve and pulsed Doppler recording at the LV outflow tract in order to calculate the effective aortic valve area before and after TAVI.

Off line analysis of the images captured was performed and using the average measurement of at least three consecutive cardiac cycles, the following measurements were obtained: transmitral E wave and A wave peak velocity, E wave deceleration time, isovolumetric relaxation time (IVRT), isovolumetric contraction time, ejection time (ET), pulmonary venous flow peak systolic velocity (*S*), peak diastolic velocity (*D*), peak atrial reversal (*Ar*) velocity and duration (*Adur*), and colour M-mode flow propagation velocity (*Vp*). Mean and maximum transvalvular gradients were calculated with the Bernoulli formula and the aortic valve area measured by the continuity equation. Subsequently, the *E/A* ratio, *S/D* ratio, and LV fractional area change were calculated. The latter was chosen for LV systolic function

estimation because of the best convenience at the acute scenario, using transoesophageal echocardiography. The probe used presents 3D echocardiography capabilities, which were regularly employed for guiding the procedure, but it has no tissue Doppler software included, consequently tissue Doppler measurements were not available during the procedure.

After aortic valve deployment, the presence of complications such as aortic regurgitation, cardiac effusion or cardiac tamponade, LV dysfunction or wall motion abnormalities, mitral valve damage or prosthesis misplacement were described.²⁰

In order to evaluate diastolic function from the beginning to the end of the procedure, modified ASE recommendations with the exclusion of tissue Doppler parameters were used.²¹ Mild diastolic dysfunction was defined by mitral *E/A* ratio <0.8 and *DT* >200 ms or *E/A* ratio <0.8 and *IVRT* ≥ 100 ms, along with predominant systolic flow in pulmonary venous flow ($S > D$); moderate diastolic dysfunction by mitral *E/A* ratio from 0.8 to 1.5 along with diastolic predominance in pulmonary venous flow ($S < D$) with at least one of the following: *DT* from 160 to 200 ms, *IVRT* <90 ms or *Ar* velocity >35 cm/s. Severe diastolic dysfunction/restrictive pattern was defined by *E/A* ratio ≥ 2 with *DT* ≤ 160 ms, or with *IVRT* ≤ 60 ms, along with diastolic predominance in pulmonary venous flow ($S < D$).²⁴

Data expected to interfere in diastolic function parameters namely heart rate, systolic and diastolic blood pressure, and haematocrit value were evaluated when starting the procedure and few minutes after valve implantation.

Invasive haemodynamic data

Patients referred for the percutaneous approach ($n = 42$) had invasive haemodynamic measurements performed. For the purpose of this study, LV end diastolic pressure measured immediately before and after implantation was considered.

This protocol was approved by the local ethics committee and all patients gave written informed consent for participation.

The authors are solely responsible for the design and conduct of this study, analyses, and its final contents.

Statistical analysis

Categorical variables were expressed as percentages and continuous variables as mean (SD) unless otherwise specified. Continuous variables were compared between groups using an unpaired *t*-test (for normally distributed variables) or the Mann–Whitney *U*-test (for non-normally distributed variables). Multivariate regression analysis of covariance (ANCOVA) was used to compare continuous variables and categorical variables relation with major outcomes. The confounders shown to present significant variation in univariate analysis (systolic and diastolic blood pressure, heart rate, haematocrit, and fractional area change of LV) were sequentially included in the model executed for each outcome variable.

For assessing the level of agreement, Cohen's kappa was used for categorical variables. All reported probability values are two-tailed, and $P < 0.05$ was considered statistically significant. Analyses were performed with the SPSS statistical software package (version 16.0) (SPSS Inc, Chicago, IL, USA).

Results

Patient characteristics

Among the 61 patients included in this prospective study, the mean age was 83.5 ± 6 years and mean log EuroSCORE was 18.2 ± 9.4 .

LV concentric hypertrophy was present in 44 (72%) patients, 45 (73.8%) had LA volume ≥ 34 mL/m² and 29 (47.5%) had *E/E'* ratio >15 . Only patients with preserved LV systolic function were included, but all patients presented LV diastolic dysfunction. Thirty-one (50.8%) showed a restrictive pattern when using the ASE recommendations²⁰ and 27 (44.3%), when the classification is modified, excluding tissue Doppler parameters (Cohen's kappa level of agreement = 0.679). Overall, and according to intervention, baseline patients' characteristics and echocardiography data are presented in Table 1. Most characteristics were similar in both groups, but patients referred to transapical approach were younger (78 ± 8 vs. 85 ± 4 , $P = 0.001$), presented more commonly dyslipidemia (89.5 vs. 50%, $P = 0.004$), peripheral vascular disease (63.2 vs. 14.3%, $P < 0.001$), and renal impairment (47.4 vs. 21.4% $P = 0.041$).

Echocardiographic haemodynamic parameters immediately after transcatheter aortic valve implantation

In the few minutes immediately after prosthesis deployment, mean aortic pressure gradient decreased to normal parameters (8 ± 3 mmHg). Mild aortic regurgitation, central or perivalvular was present in 30 (49.2%) patients after the procedure, but none ended with moderate or severe aortic regurgitation. There was a decrease in ET and an increase in E wave maximum velocity, E wave deceleration time, *E/A* ratio and *IVRT*. In spite of all patients having preserved LV systolic function, LV fraction area change significantly increased [difference of means 8.1 (95% CI: 4.4–11.8)] after the procedure. No significant variation was found in the comparative analysis of grade I or II of LV diastolic function (Figure 1); nevertheless, there was a significant reduction in a restrictive pattern after TAVI, as 27 (44.3%) patients presented a restrictive pattern before the procedure vs. 20 (34.4%) after TAVI ($P = 0.047$). Comparative results from univariate analysis of TEE and clinical parameters during TAVI are presented in Table 2. A significant decrease in blood pressure, heart rate, and haematocrit, as well as an increase in LV fractional area change, was observed after aortic valve implantation (Table 2).

Using the ANCOVA, we assessed the modification of the intervention effect on primary outcome variables and confounders during TAVI in the overall population. The results presented in Table 3 showed the absence of significant differences according to the type of procedure. However, a tendency for a smaller decrease in ET [percutaneous: -28.8 (95% CI: -46.5 ; -11.1) vs. transapical: -6.3 (95% CI: -27.5 ; -14.9)] and for a larger reduction in Vp slope [percutaneous: -0.095 (95% CI: -16.9 ; -16.8) vs. transapical: -10.8 (95% CI: -20.7 ; -0.97)] after prosthesis deployment could be observed in the transapical subgroup.

Subsequently, a multivariate ANCOVA was performed in order to assess the effect of potential confounders in main outcome variables variation. The modifications in the diastolic function parameters observed remained significant when adjusted in the multivariate models performed (Table 4). We found a significant increase in the E wave deceleration time [41.5 (95% CI: 18.0–65.1)] in the global population; however, the multivariate analysis with the ANCOVA model showed that it occurred mainly in

Table 1 Baseline characteristics of the study population

Variables	Overall (n = 61)	Percutaneous (n = 42)	Transapical (n = 19)	P-value
Age (years)	83 (6)	85 (4)	78 (8)	0.001
Female [n (%)]	38 (62.3)	29 (69.0)	9 (47.4)	0.154
Log EuroSCORE (%)	18.2 (9.4)	18.1 (7.8)	18.4 (12.4)	0.930
Body surface area (m ²)	1.6 (0.2)	1.7 (0.19)	1.9 (0.15)	0.680
Hypertension [n (%)]	52 (85.2)	36 (85.7)	16 (84.2)	1.0
Diabetes [n (%)]	15 (24.6)	8 (19.9)	7 (36.8)	0.199
Dyslipidemia [n (%)]	38 (62.3)	21 (50.0)	17 (89.5)	0.004
Coronary artery disease [n (%)]	22 (36.1)	15 (37.5)	7 (36.8)	1.0
Previous PCI or prior CABG [n (%)]	16 (26.2)	9 (21.4)	7 (36.8)	0.224
NYHA functional class				0.853
II	5 (8.2)	4 (9.5)	1 (5.3)	
III	53 (86.9)	36 (85.7)	17 (89.5)	
IV	3 (4.9)	2 (4.8)	1 (5.3)	
COPD [n (%)]	24 (39.3)	16 (38.1)	8 (42.1)	0.784
Renal impairment	18 (29.5)	9 (21.4)	9 (47.4)	0.041
Creatinine (mg/dL)	1.3 (0.7)	1.2 (0.7)	1.5 (0.7)	0.199
Peripheral vascular disease	18 (29.5)	6 (14.3)	12 (63.2)	<0.001
Nt-ProBNP (pg/mL) ^a	3208 (1794–6318)	3721 (2034–6529)	3200 (1319–8692)	0.739
Pulmonary hypertension	9 (14.8)	8 (25.0)	1 (14.3)	1.0
Mean aortic pressure gradient (mmHg)	54 (14)	56 (16)	51 (10)	0.221
Aortic peak pressure gradient (mmHg)	90 (22)	91 (24)	87 (20)	0.610
Aortic valve area (cm ²)	0.6 (0.1)	0.6 (0.1)	0.6 (0.1)	0.167
LV EF (%)	63 (9)	62 (10)	63 (9)	0.621
LA index volume (mL/m ²)	47 (24)	49 (28)	43 (12)	0.322
LV mass index (g/m ²)	132 (42)	137 (44)	121 (35)	0.197
E/E' ratio	21 (13)	23 (13)	17 (10)	0.210
Diastolic dysfunction				
Grade I	22 (36.1)	15 (35.7)	7 (36.8)	0.452
Grade II	8 (13.1)	3 (7.1)	5 (26.3)	0.212
Grade III	31 (50.8)	24 (57.1)	7 (36.8)	0.321

CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; LA, left atrium; LV, left ventricle; log EuroSCORE, logistic European System for Cardiac Operative Risk Evaluation; Nt-ProBNP, NT portion B-type natriuretic peptide; PCI, percutaneous coronary intervention.

^aPresented as median and interquartile range.

patients in whom the haematocrit value remained stable. In those with an important decrease in the haematocrit minutes after TAVI, the E wave deceleration time remained constant.

The baseline demographic and clinical characteristics presented in Table 1, as well as the type or size of prosthesis were individually tested for each diastolic parameter and confounders, but none had significant effect on the results obtained after the intervention.

Invasive haemodynamic parameters immediately after transcatheter aortic valve implantation

In the group of patients submitted to the percutaneous approach (n = 42), invasive haemodynamic measurements were performed and significant decrease in LV end-diastolic pressure, after valve implantation was found [18.8 ± 5.7 vs. 14.7 ± 4.7 , mean difference -4.1 (95% CI: -5.9 ; -2.9)]. Patients with a restrictive pattern

immediately after TAVI had a smaller decrease in LV end diastolic pressure (-3.3 ± 4.7) than those presenting diastolic dysfunction grade I or II after the procedure (-9.5 ± 4.7 ; $P = 0.017$).

Discussion

This is the first study describing acute haemodynamic changes regarding diastolic function parameters during TAVI. We present a representative group of patients among those being currently submitted to TAVI.²⁵ These elderly patients with degenerative aortic stenosis have severe heart failure symptoms, several comorbidities, high EuroSCORE, and multiple cardiovascular risk factors. The ones submitted to transapical approach have been considered by others as a particular group with more comorbidities and higher Logistic EuroScore.²⁵ Our patients referred to transapical approach had more frequently renal impairment and peripheral

vascular disease; however, they were younger and the mean Logistic EuroSCORE was similar to those referred to TAVI through percutaneous approach. This might be explained by the number of patients referred to transapical approach for porcelain aorta (5; 26.3%), which were younger and with fewer comorbidities, but still being refused for AVR.

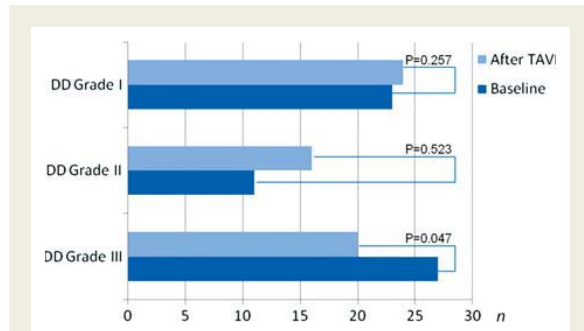


Figure 1 Patients' diastolic dysfunction classification at baseline and after transcatheter aortic valve implantation. Diastolic dysfunction²¹ definition according ASE recommendations modified by the exclusion of tissue Doppler parameters.

Left ventricle remodelling in severe aortic stenosis

In this study, the population was restricted to patients with preserved LV systolic function, which in fact represents most of the patients treated with TAVI.^{1,5} These patients, in addition to the age-related changes in diastolic function parameters, with increased passive stiffness and abnormal relaxation, also present LV hypertrophy, LA dilatation, and myocardium fibrosis in result of the chronic pressure overload.^{26,27} During the LV remodelling process, the myocytes and fibroblasts proliferation initially result in asymptomatic abnormal tissue Doppler velocities and diastolic dysfunction, in spite of normal ejection fraction. However, in the absence of treatment, global systolic dysfunction and/or symptoms eventually develop, leading to death unless the valve is replaced.²⁸

Immediate left ventricle diastolic response after transcatheter aortic valve implantation

Severe LV diastolic dysfunction prevailed at baseline, but it significantly improved after the procedure (Figure 1). This result was supported by the invasive measurement of LV end diastolic pressure. Analysing echocardiographic parameters, fewer patients presented severe LV diastolic dysfunction after the procedure, mostly because of the E wave deceleration time increase, which may be the result of increased relaxation and compliance and

Table 2 Overall univariate analysis of transoesophageal echocardiography and clinical parameters during transcatheter aortic valve implantation (n = 61)

Variables	Data at baseline	Data minutes after TAVI	Difference of means (95% CI)	P-value
Mean aortic pressure gradient (mmHg)	54 (14)	8 (3)	-46.4 (-50.3; -42.6)	<0.001
Aortic peak pressure gradient (mmHg)	90 (22)	16 (6)	-73.9 (-79.9; -68.1)	<0.001
E wave (cm/s)	109.5 (41.2)	120.3 (43.6)	10.5 (1.4; 20.2)	0.025
A wave (cm/s)	100.6 (40.7)	96.1 (38.9)	-3.7 (-14.3; -6.8)	0.482
E wave/A wave	1.2 (0.8)	1.5 (1.1)	0.29 (0.01; 0.57)	0.040
E wave deceleration time (ms)	211.2 (75.5)	252.7 (102.3)	41.6 (17.2; 65.9)	0.001
IVRT (ms)	83 (36.5)	97.1 (36.0)	14.1 (3.2; 25.1)	0.013
ET (ms)	314.9 (32.2)	293.1 (46.5)	-21.8 (-35.6; -8.0)	0.002
S/D	1.1 (0.8)	1.2 (0.5)	0.36 (-0.29; 0.37)	0.817
Ar (cm/s)	25.1 (11.1)	22.9 (10.5)	3.1 (1.2; 5.4)	0.092
Adur (ms)	124.3 (29.9)	121.8 (51.1)	2.9 (0.9; 6.8)	0.438
Vp (cm/s)	62.1 (20.0)	57.4 (28.9)	-4.6 (-14.9; -5.6)	0.366
LV diastolic area (cm ²)	17.9 (3.9)	17.8 (4.1)	-0.07 (-1.1; -0.9)	0.880
LV systolic area (cm ²)	8.4 (3.5)	7.0 (3.4)	-1.4 (-2.3; -0.5)	0.002
LV fractional area change (%)	54 (14)	62 (14)	8.1 (4.4; 11.8)	<0.001
Clinical parameters				
HR (b.p.m.)	79 (16)	75 (14)	-4.0 (-7.9; -0.07)	0.046
BP systolic (mmHg)	130 (19)	122 (17)	-7.9 (-13.2; -2.6)	0.004
BP diastolic (mmHg)	67 (11)	59 (11)	-8.5 (-11.1; -5.8)	<0.001
Haematocrit (%)	35.4 (4.7)	33.1 (3.8)	-2.5 (-3.8; -1.3)	<0.001

BP, blood pressure; D, pulmonary venous flow peak diastolic velocity; ET, ejection time; HR, heart rate; IVRT, isovolumetric relaxation time; LV, left ventricle; S, pulmonary venous flow peak systolic velocity; Vp, colour M-mode flow propagation velocity.

Table 3 Analysis of the intervention effect on primary outcome variables and confounders during transcatheter aortic valve implantation in the overall population (n = 61)

Variables	Difference of means (95% CI)		P-value
	Percutaneous (n = 42)	Transapical (n = 19)	
E wave (cm/s)	12.4 (0.6; 24.2)	7.3 (-9.4; 24.1)	0.624
E wave/A wave	0.3 (-0.05; 0.7)	0.3 (-0.21; 0.78)	0.954
E wave deceleration time (ms)	44.0 (15.6; 72.4)	36.2 (-14.9; 87.3)	0.770
IVRT (ms)	13.1 (-1.7; 28.0)	16.4 (1.5; 31.2)	0.788
ET (ms)	-28.8 (-46.5; -11.1)	-6.3 (-27.5; -14.9)	0.132
Vp slope (cm/s)	-0.095 (-16.9-16.8)	-10.8 (-20.7; -0.97)	0.303
LV fractional area change (%)	9.6 (4.9; 14.2)	4.8 (-1.4; 11.1)	0.232
HR (bpm)	-3.4 (-8.5; -1.7)	-5.4 (-11.7; -0.87)	0.630
BP systolic (mmHg)	-5.0 (-10.8; -0.79)	-14.2 (-25.5; -2.8)	0.108
BP diastolic (mmHg)	-7.8 (-11.0; -4.6)	-9.8 (-14.9; -4.7)	0.486
Haematocrit (%)	-2.2 (-3.7; -0.7)	-3.3 (-5.6; -1.0)	0.414

BP, blood pressure; ET, ejection time; HR, heart rate; IVRT, isovolumetric relaxation time; LV, left ventricle; Vp, colour M-mode flow propagation velocity.

Table 4 Analysis of covariance multivariate analysis of transoesophageal echocardiography and clinical parameters during transcatheter aortic valve implantation in the overall population (n = 61)

Variables	Baseline ^a	Minutes after TAVI ^a	Difference of means (95% CI)	P-value
E wave (cm/s)	109.5 (98.9; 120.1)	120.3 (109.2; 131.5)	10.8 (1.4; 20.2)	0.025 ^b
E wave/A wave	1.2 (0.9; 1.4)	1.5 (1.2; 1.8)	0.30 (0.03; 0.56)	0.002
E wave deceleration time (ms)	211.2 (191.7; 230.6)	252.7 (226.8; 278.7)	41.5 (18.0; 65.1)	<0.001
IVRT (ms)	83.0 (73.8; 92.8)	97.1 (87.9; 106.4)	14.2 (3.3; 25.0)	0.003
ET (ms)	314.9 (306.6; 323.2)	294.8 (284.2; 305.3)	-20.2 (-32.8; -7.5)	0.026

ET, ejection time; LV, left ventricle; IVRT, isovolumetric relaxation time; Vp, colour M-mode flow propagation velocity.

^aData presented as adjusted mean (95% CI).

^bUnivariate—none of the confounders had a significant effect on the mean E wave variation during the procedure.

LV end diastolic pressure reduction. Accordingly, the IVRT increase after TAVI suggests a significant reduction in LA pressure. In patients with major decline in the haematocrit during the procedure, the haemodynamic response with transient tachycardia in consequence of acute preload reduction may have constrained the deceleration time increase.

The increase in E wave maximum velocity may be explained by alterations in preload or in LV relaxation. During the intervention, the indirect parameters of preload evaluation were LV diastolic area, which remained constant, and haematocrit value, which did not significantly affect E wave velocity increase. Thus, we consider that the augmented LA LV pressure gradient during early diastole is consequence of an ameliorated LV relaxation, in response of immediate, complete, and sustained afterload release.

The diastolic function parameters presented similar results whether the procedure was performed by transapical or percutaneous approach. However, in patients submitted to TAVI through transapical approach, the Vp slope decline was evident (Table 3). This parameter has limitations in patients with

preserved LV systolic function, but it represents LV suction force and its slowing is consistent with an apical suction reduction.²¹ This is in accordance with the technical procedure, where the LV apex puncture is performed. Possibly, the reduced sample size of patients submitted to transapical approach may explain the absence of statistic difference in Vp slope between both groups. Therefore, this result should be expected in those patients and it should not be interpreted as lone criteria of abnormal LV filling pressures.

The acute improvement in diastolic function parameters found in our study is in agreement with the results obtained in patients with hypertrophic obstructive cardiomyopathy after septal ablation. In those patients, it was described an immediate improvement of diastolic function along with LV outflow tract pressure gradient reduction. However, after septal ablation, there is a reduction in systolic function, in opposition to LV ejection fraction improvement usually observed after TAVI.¹⁵ After aortic valvuloplasty, the immediate load-dependent responses reported have been inconsistent,^{11,12} which is not surprising given the limited and

often unsustained enlargement of aortic valvular area and the large variability of response after aortic valvuloplasty.¹¹ In contrast, almost complete normalization of afterload was found to occur after TAVI, without significant variability among patients.^{4,5,8} In what concerns to patients referred to AVR, limited assumptions can be made. Normalization of LV diastolic function⁷ and benefits in ejection fraction, volumes, and hypertrophy are seen at long-term follow-up,²⁹ but short-term results are limited by the effects of extracorporeal circulation, positive inotropic drugs administration, and the presence of a paradoxical septum.

TAVI represents a unique opportunity of LV diastolic function evaluation immediately after afterload release and the observed improvement is in concert with the expectations from the Frank–Starling law. Whether these results are persistent or transient is unknown and should be assessed in further studies.

Our results are in agreement with the study of Bauer *et al.*³⁰ that described improvement in myocardial velocities and strain, 24 h after aortic valve percutaneous implantation in a population of 19 patients. Gotzmann *et al.*⁹ have described diastolic function improvement at 6 months follow-up in patients with CoreValve prosthesis implanted by percutaneous approach. Even so, additional studies with longer follow-up regarding the different types of prosthesis and both techniques of implantation are needed, in order to clarify the relation of the acute changes in diastolic function with clinical outcomes among patients submitted to TAVI.

Limitations

The only form of comparison of degrees of diastolic dysfunction during TAVI was based on an adapted definition; however, an acceptable correlation between both classifications was found, allowing the assumption of an appropriate modified classification.

During the procedure, systolic function was assessed using fractional area change. This method has the limitation of measurement in one single plane, being its accurate assumption restricted to patients with symmetrically contracting ventricles. In this study, it may be considered an acceptable method since only patients with preserved LV systolic function were included, but in the eventual presence of wall motion abnormalities, it may have been misleading.

During TAVI, rapid pacing is performed, which may transiently change the diastolic properties of the LV. Consequently, echocardiography data were only acquired after rhythm stabilization in order to minimize the possible effect of the transient ventricular tachycardia.

Conclusion

Our results show the improvement of LV diastolic function in patients with preserved LV systolic function, immediately after successful TAVI. These results might corroborate to explain the remarkable clinical improvements in heart failure symptoms reported shortly after TAVI.

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CHAPTER 4

Three-Dimensional Echocardiography in Paravalvular Aortic Regurgitation Assessment after Transcatheter Aortic Valve Implantation

Three-Dimensional Echocardiography in Paravalvular Aortic Regurgitation Assessment after Transcatheter Aortic Valve Implantation

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Background: Paravalvular aortic regurgitation (AR) after transcatheter aortic valve implantation (TAVI) is common, but the evaluation of its severity by two-dimensional (2D) transthoracic echocardiography (TTE) presents several constraints. The aim of this study was to assess the usefulness of a new methodology, using three-dimensional (3D) TTE, for better assessment of paravalvular AR after TAVI.

Methods: Two-dimensional and 3D TTE was performed in 72 patients, 5 months after TAVI, using the X5-1 PureWave microbeamforming xMATRIX probe. The position and severity of the paravalvular AR jets were described using 2D and 3D TTE, and a model was designed for paravalvular AR systematic location description. Vena contracta width was measured using 2D transthoracic echocardiographic views, and the planimetry of the vena contracta was assessed after the perfect alignment plane was obtained using the multiplanar 3D transthoracic echocardiographic reconstruction tool. AR volume was calculated as the difference between 3D TTE-derived total left ventricular stroke volume and right ventricular stroke volume estimated using 2D TTE. Diagnostic efficiency for moderate AR was assessed using receiver operating characteristic curve analysis.

Results: Forty-three patients (57.4%) presented with AR; 10 (13.3%) had central AR, and 33 (44.0%) had paravalvular AR jets. Vena contracta widths were similar between patients with moderate and mild AR (2.1 ± 0.53 vs 1.9 ± 0.16 mm, $P = .16$), but vena contracta planimetry was larger in patients with moderate AR than in those with mild AR (0.30 ± 0.12 vs 0.09 ± 0.07 cm², $P = .001$). Vena contracta planimetry on 3D TTE was better correlated with AR volume than vena contracta width on 2D TTE (Kendall's $\tau = 0.82$ [$P < .001$] vs 0.66 [$P < .001$]). The areas under the receiver operating characteristic curves were 0.96 for vena contracta planimetry and 0.35 for vena contracta width.

Conclusions: This study proposes an alternative methodology for paravalvular AR assessment after TAVI. Using vena contracta planimetry on 3D TTE, an accurate methodology for paravalvular AR jet evaluation and moderate AR classification is described. (*J Am Soc Echocardiogr* 2012;25:47-55.)

Keywords: 3D transthoracic echocardiography, Paravalvular aortic regurgitation, Transcatheter aortic valve implantation, Vena contracta

Transcatheter aortic valve implantation (TAVI) techniques have been recently recognized as an alternative treatment for patients with severe aortic stenosis and high surgical risk.¹ Favorable hemodynamic results

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with a low incidence of prosthesis-patient mismatch have been demonstrated,² although some degree of residual aortic regurgitation (AR), particularly in the paravalvular region, is common.^{3,4} Paravalvular AR appears to be minor in most patients, but the hemodynamic impact and effect on cardiac chamber remodeling is unknown. Conversely, paravalvular leaks secondary to aortic valve replacement were found to be responsible for hemodynamic deterioration, left ventricular remodeling, or hemolysis.^{5,6} As a result, accurate evaluation and detailed description of AR after TAVI are essential for proper follow-up. However, until now, it has been challenging because no systematic methodology has been proposed. Moreover, the assessment of AR severity by two-dimensional (2D) transthoracic echocardiography (TTE) is demanding, and its limitations require the use of an integrative approach for an adequate evaluation of severity.^{7,8}

Vena contracta width by 2D TTE is one of the most robust measurements of AR in native valves, and it is well correlated with angiographic grading and regurgitant orifice area.^{9,10} However, its

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Abbreviations
AR = Aortic regurgitation
TAVI = Transcatheter aortic valve implantation
TEE = Transesophageal echocardiography
3D = Three-dimensional
TTE = Transthoracic echocardiography
2D = Two-dimensional

assessment might be difficult in the presence of a prosthesis. In the parasternal long-axis or apical view on 2D TTE, only one dimension of the AR jet is visualized. Consequently, the area can only be estimated using an assumption of its shape, commonly circular or elliptical, which is mostly an incorrect assumption.¹¹ In theory, using 2D transthoracic echocardiographic color Doppler in the short-axis view, the vena contracta shape could

be delineated either in a native valve or in a biologic prosthesis. However, it is impossible to ensure that the plane is exactly parallel to the vena contracta or that one is not measuring the jet size in a larger stream, particularly in presence of eccentric jets.⁵

Three-dimensional (3D) transthoracic echocardiographic color evaluation of AR is based on the acquisition of a pyramidal data set, with the aortic valve and paravalvular region inside it. Once performing the cropping to the correct angle, the precise location of an AR jet can be described and the real vena contracta shape planimeted.¹² Accordingly, 3D TTE represents an enhancement of 2D TTE. In the present study, we considered the usefulness of a new methodology using 3D TTE for the accurate assessment of paravalvular AR after TAVI.

METHODS

This study included 72 patients with severe aortic valve stenosis (aortic valve area ≤ 1 cm²) who underwent successful TAVI. All patients had degenerative aortic stenosis and tricuspid aortic valves. These patients were obtained from a series of 97 consecutive patients who underwent TAVI, after excluding those with concomitant moderate to severe mitral valve disease (six patients) and those not able to come to follow-up (19 patients).

Patients were referred for TAVI because of an excessive risk for aortic valve replacement, which was estimated using the logistic European System for Cardiac Operative Risk Evaluation score and/or clinical judgment.¹ The procedure was performed with fluoroscopic and transesophageal echocardiographic¹³ guidance (Philips iE33, X7-2t 7-MHz probe; Philips Medical Systems, Eindhoven, The Netherlands) using the techniques described in detail in previous reports.^{14,15} Two valve sizes are available, 23-mm and 26-mm expanded diameter for Edwards Sapien valves (Edwards Lifesciences, Irvine, CA) and 26 and 29 mm for CoreValve devices (Medtronic, Inc., Minneapolis, MN). The aortic prosthesis size was decided according to the annular diameter, measured with transesophageal echocardiography (TEE).

TTE

TTE was performed 5 months after TAVI, from June to October 2010, using the X5-1 PureWave microbeamforming xMATRIX probe (Philips Medical Systems). This probe presents all the facilities of the 2D S5-1 probe with 3D capabilities as full volume, Live 3D, and Live 3D color acquisitions, from one to four beats. The full volume combines a series of four subvolumes acquired with electrocardiographic gating to create the final reconstructed image. This acquisition mode is essential for the measurement of volumes and left ventricular ejection fraction by 3D volumetric assessment. Live 3D and Live 3D

color provide real-time 3D volumetric motion, without electrocardiographically gated reconstruction. However, these acquisition modes can be optimized for a higher frame rate by performing near-real-time images, with electrocardiographically gated reconstruction, with up to four heartbeats. In this study, we used Live 3D without electrocardiographically gated reconstruction and Live 3D color images acquired with four heartbeats. We used iCrop, a new flexible tool that allows direct analysis on Live 3D and Live 3D color images, for interpretation while performing the exams.

First, conventional 2D TTE was performed, in which the prosthesis area was calculated using the continuity equation. Apical five-chamber, three-chamber, and parasternal long-axis and short-axis color views were recorded, and AR jets were described following international standard recommendations.¹⁶ We systematically assessed the vena contracta width in the parasternal long-axis or apical long-axis view using a Nyquist limit of 50 to 60 cm/sec (Figure 1). AR volume was calculated as the difference between 3D TTE-derived total left ventricular stroke volume and stroke volume through the right ventricular outflow tract. The right ventricular outflow tract diameter and velocity-time integral at the site were measured in the short-axis parasternal view, and the right ventricular stroke volume was calculated by multiplication of the cross-sectional right ventricular outflow tract area by the velocity-time integral. AR was graded using an integrative approach considering the recommended semiquantitative Doppler parameters and the AR volume as mild (AR volume < 30 mL) or moderate (30 mL \leq AR volume \leq 59 mL), assessed as previously described.¹⁶

Full-volume and Live 3D color images were acquired from one to four heartbeats in the apical four-chamber view. At the time of acquisition, we used the 3D TTE and two orthogonal 2D transthoracic echocardiographic views for guidance, as illustrated in Figures 2A and 3. If necessary, we adjusted the lateral and the elevation width to be certain that all of the structures we intended to analyze were included in the volumetric images acquired. Full-volume acquisitions, obtained by combining four electrocardiographically gated subvolumes, were used to measure left ventricular volumes and ejection fraction by direct volumetric analysis (Figure 2). We assessed the aortic prosthesis using Live 3D views (Figure 4). Using Live 3D color images, with the narrowest sector possible for frame rate optimization, the aortic prosthesis was isolated with the iCrop tool. The entire circumference of the prosthesis, and the paravalvular region, were viewed from the aortic root and also from the ventricular aspect, as illustrated in Figure 3.

The iCrop tool constructs an image from two orthogonal square views, whose size can be adjusted for the proposed region of analysis. The anatomic findings can be viewed from each of the sides of the square (Figure 3); consequently, in the same acquisition, the prosthetic valve can be viewed from the left ventricular outflow tract and also from the aortic root. Depending on the cutting plane, the area of the regurgitant jet varies, because the view from the aortic root shows the isovelocity surface area proximal to the regurgitant orifice, while the view from the left ventricular outflow tract shows the beginning of the color jet as blood entrains and travels into the left ventricle. Consequently, iCrop allowed the identification and localization of the AR jet, but it was not used to measure AR jet size, which was performed using the multiplanar reconstruction tools. To describe AR localization systematically, we designed a reference diagram in which the parasternal short-axis view was chosen as a reference and the paravalvular region divided into 12 sections according to the hours of a clock face (Figure 5).

For AR vena contracta planimetry by 3D TTE, Live 3D color data sets were analyzed using the multiplanar reconstruction tool. First, the

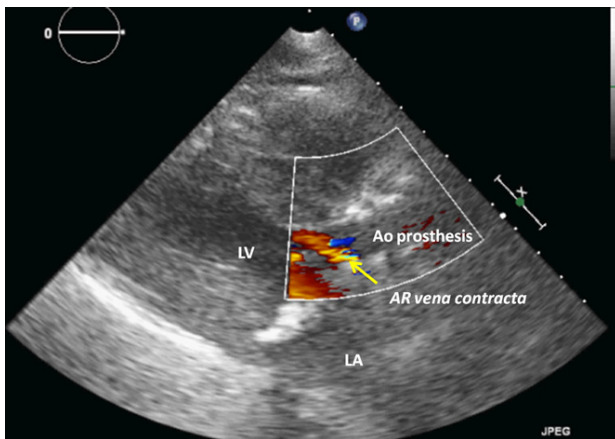


Figure 1 Paravalvular AR assessed by 2D echocardiography in the parasternal long-axis view. This image illustrates a vena contracta width of 2 mm. It was acquired from the same patient shown in Figure 6. Ao, Aorta; LA, left atrium; LV, left ventricle.

best frame for AR jet visualization in two orthogonal long-axis views was selected. Then we cropped the data set along the axis of the AR jet, from the aortic side to the level of the vena contracta, in a plane that was exactly perpendicular to the long axis of the AR jet. Subsequently, we performed planimetry (Figure 6) using the methodology previously validated by Fang *et al.*¹² In patients with more than one independent leak, the vena contracta was taken as the sum of all individual vena contracta areas.

This protocol was approved by the local ethics committee, and all patients gave written informed consent for participation.

Reproducibility

Two experienced operators blinded to 2D echocardiographic results analyzed separately 3D color data sets, worked through the multiplanar reconstruction tools, and performed the vena contracta planimetry in patients with AR.

Statistical Analysis

Categorical variables are expressed as percentages and continuous variables as mean \pm SD unless otherwise specified. Continuous variables were compared between groups using unpaired *t* tests (for normally distributed variables) or the Mann-Whitney *U* test (for variables not normally distributed). Kendall's τ (nonparametric test) was calculated for the assessment of correlations between vena contracta measurements by 3D TTE and 2D TTE and AR volume. The diagnostic efficiency of vena contracta width and planimetry was assessed using receiver operating characteristic curve analysis. All reported *P* values are two tailed, and *P* values $<$.05 were considered to indicate statistical significance. Analyses were performed using SPSS version 16.0 (SPSS, Inc., Chicago, IL).

RESULTS

Among the 72 patients included, 39 (54.2%) were women, the mean age was 82 ± 8 years, and the mean log European System for Cardiac Operative Risk Evaluation score was 19.2 ± 9.9 . Overall, and according to intervention, baseline patients' characteristics and echocardiographic

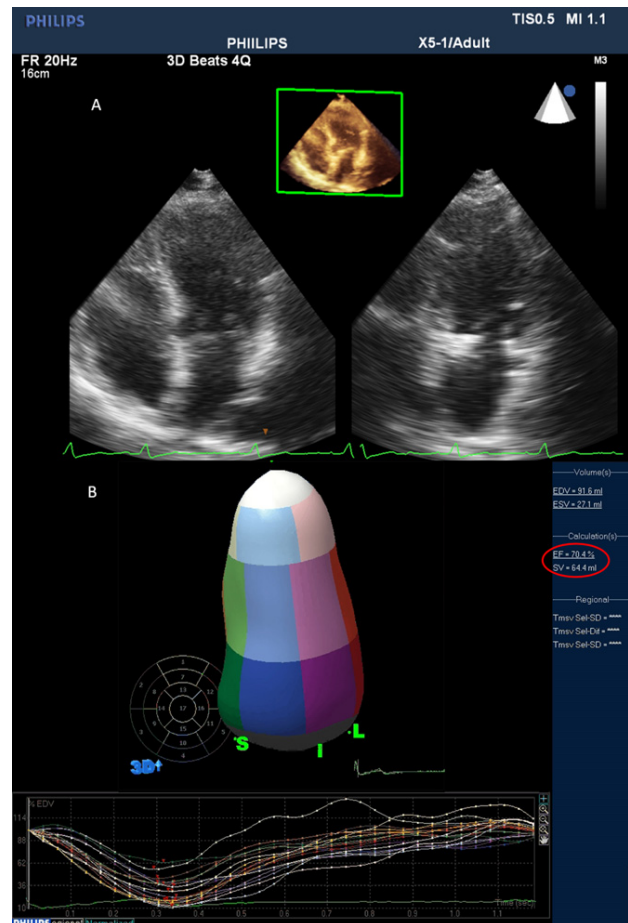


Figure 2 (A) Three-dimensional transthoracic echocardiographic four-heartbeat full-volume acquisition. (B) Left ventricular ejection fraction and stroke volume determination by direct volumetric analysis.

data are presented in Table 1. Most characteristics were similar in both groups, but patients who underwent a transapical approach were younger (77 ± 9 vs 84 ± 5 years, $P = .003$) and presented more commonly with peripheral vascular disease (65.2% vs 14.3%, $P < .001$).

A retrograde transfemoral approach was performed in 49 patients (68.1%). Among these, Edwards Sapien aortic valves were implanted in 28 (57.1%) and CoreValve devices in 21 (42.9%). All patients ($n = 23$) referred for TAVI using the transapical approach underwent implantation of Edwards Sapien valves.

TTE

Using AR volume for the accurate classification of AR severity, 43 patients (57.4%) demonstrated AR; 10 (13.3%) had central AR, and 33 (44.0%) had paravalvular AR jets. Moderate AR was present in eight patients (11.3%) and was restricted to patients with paravalvular AR. Thirty-six paravalvular jets were identified, as three patients had two independent leaks from different positions. The paravalvular region from 12 to 3 o'clock was the most common location for mild as well as for moderate paravalvular AR jets, but no correlation with aortic valve calcification severity or asymmetry was found.

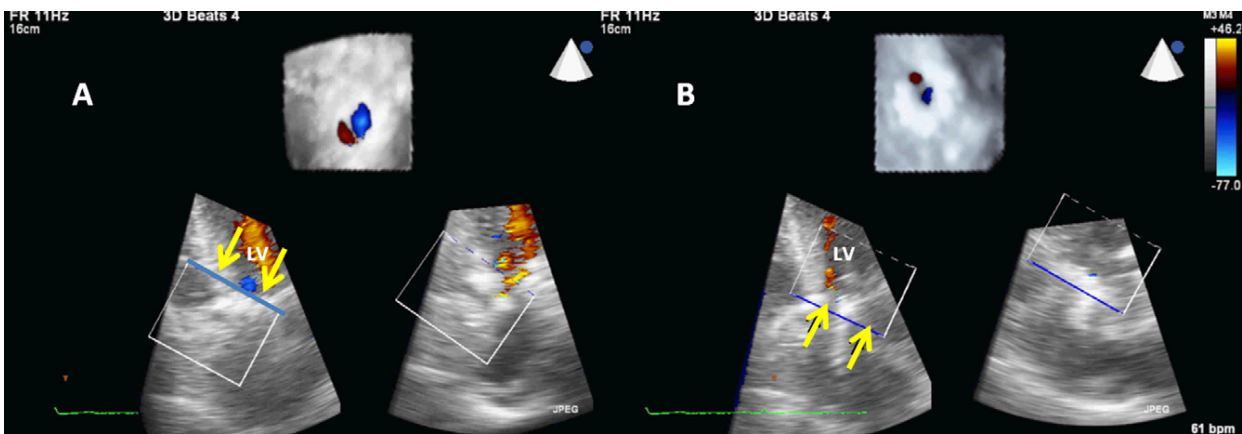


Figure 3 Paravalvular AR assessed with Live 3D color, using the iCrop tool. Two orthogonal 2D views and the 3D reconstruction are obtained simultaneously. **(A)** Paravalvular AR view from the left ventricle (LV) (arrows). **(B)** Paravalvular AR view from the aortic root (arrows). Depending on the location of the cut plane in relation to the aortic prosthesis, the area of the paravalvular AR jet varies as viewed in the short-axis orientation.

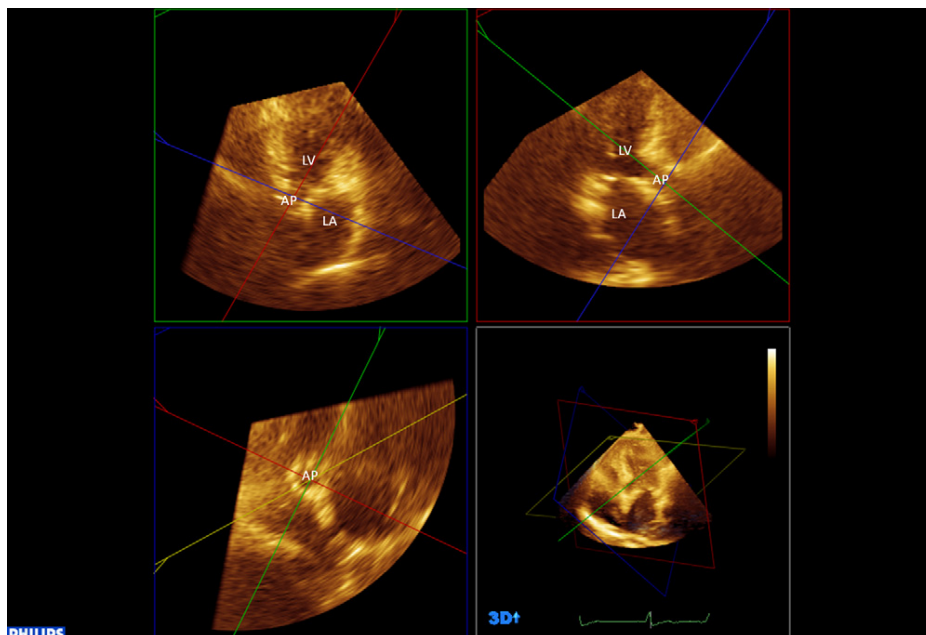


Figure 4 Live 3D transthoracic echocardiographic multiplanar reconstruction for aortic prosthesis (AP) ring assessment. LA, Left atrium; LV, left ventricle.

Transthoracic echocardiographic data at follow-up are presented in Table 2. Left ventricular ejection fraction, left ventricular mass, and aortic valve area were similar between all groups of patients, regardless of AR presence or severity, but patients with moderate AR had larger end-diastolic volumes than those with mild AR (66.1 ± 18.6 vs 48.4 ± 21.9 mL/m², $P = .044$). Vena contracta widths were similar between patients with moderate and mild AR (2.1 ± 0.53 vs 1.9 ± 0.16 mm, $P = .16$), but vena contracta planimetry by 3D TTE was larger in patients with moderate AR than in those with mild AR (0.30 ± 0.12 vs 0.09 ± 0.07 cm², $P = .001$). Vena contracta planimetry on 3D TTE was better correlated with AR volume than vena contracta width on 2D TTE (Kendall's $\tau = 0.82$ [$P < .001$] vs 0.66 [$P < .001$]). The area under the receiver operating characteristic curve

for moderate AR assessment also showed better accuracy of vena contracta planimetry (area under the curve, 0.96; 95% confidence interval, 0.91–1.0) than vena contracta width (area under the curve, 0.35; 95% confidence interval, 0.15–0.55) (Figure 7).

Reproducibility

Vena contracta planimetry was traced by two blinded independent operators, and a low absolute difference of 0.005 ± 0.075 between the two measurements was observed. Absolute interobserver variability was $12.4 \pm 11.5\%$, and Pearson's correlation was significant between observers ($r = 0.86$, $P < .001$).

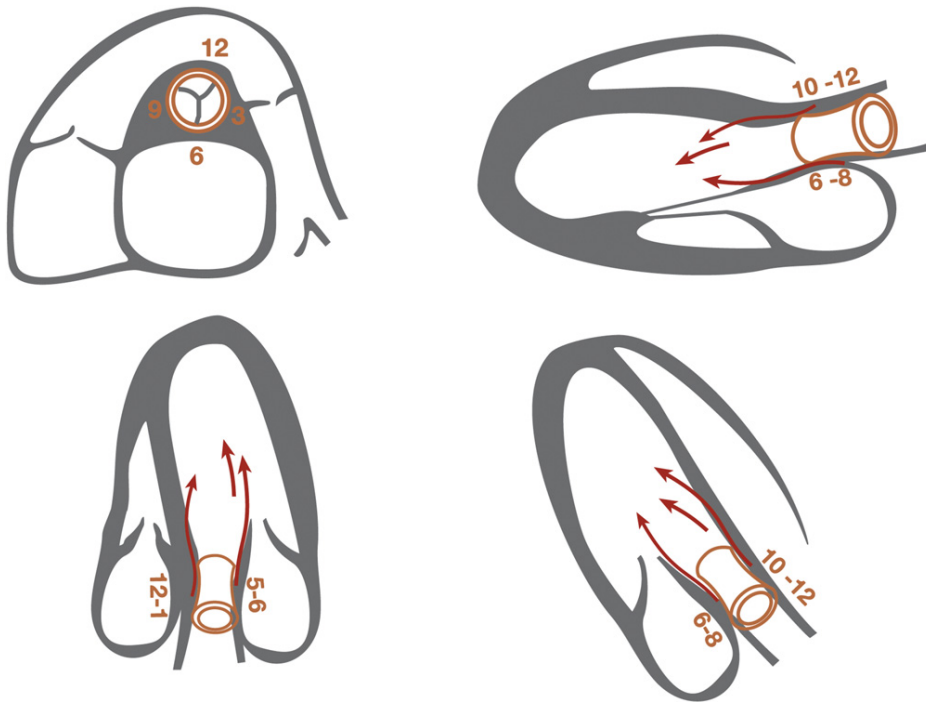


Figure 5 Representation of paravalvular AR jets location according to the face of a clock. Conventional 2D transthoracic echocardiographic views are represented. **(A)** Parasternal short-axis view. **(B)** Parasternal long-axis view. **(C)** Apical five-chamber view. **(D)** Apical three-chamber view.

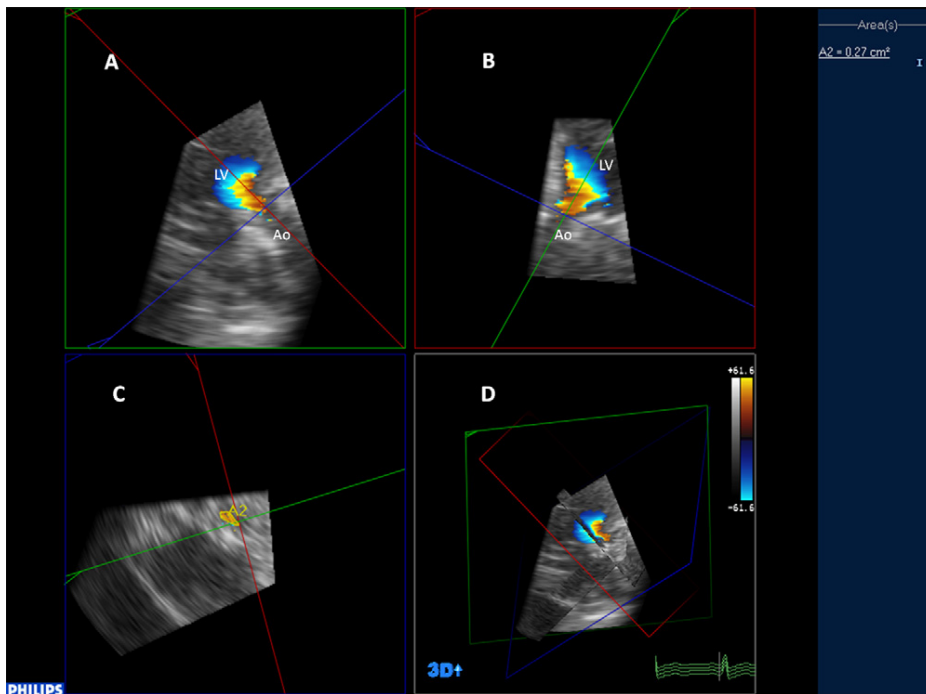


Figure 6 AR Live 3D color analysis using multiplanar reconstruction tools. After selecting the best frame for AR jet visualization in two orthogonal long axis views **(A,B)**, the data set was cropped through the perpendicular plane of the AR jet long axis, from the aortic side to the level of the vena contracta **(C)**. **(A)** Coronal axis view. **(B)** Sagittal axis view. **(C)** Axial axis view, with planimetry of the vena contracta. **(D)** Multiplanar simultaneous axis view. Ao, Aorta; LV, left ventricle.

Table 1 Baseline characteristics of the study population

Variable	Overall (n = 72)	Percutaneous (n = 49)	Transapical (n = 23)	P
Clinical characteristics				
Age (y)	82 ± 8	84 ± 5	77 ± 10	.003
Women	39 (54.2%)	30 (61.2%)	9 (39.1%)	.133
Log EuroSCORE (%)	19.1 ± 9.9	19.2 ± 8.2	18.8 ± 13.0	.544
Hypertension	59 (81.9%)	41 (83.7%)	18 (78.3%)	.820
Diabetes	20 (27.8%)	11 (22.4%)	9 (39.1%)	.234
Dyslipidemia	44 (61.1%)	25 (51.0%)	19 (82.6%)	.021
Coronary artery disease	30 (41.7%)	19 (38.8%)	11 (47.8%)	.638
Previous PCI or prior CABG	24 (33.3%)	13 (26.5%)	11 (47.8%)	.129
COPD	29 (40.3%)	19 (38.8%)	10 (43.5%)	.903
Renal impairment	20 (27.8%)	11 (22.4%)	9 (39.1%)	.234
Peripheral vascular disease	22 (30.6%)	7 (14.3%)	15 (65.2%)	<.001
Echocardiographic characteristics				
Mean aortic pressure gradient (mm Hg)	52 ± 16	54 ± 16	47 ± 13	.073
Aortic peak pressure gradient (mm Hg)	86 ± 24	88 ± 24	81 ± 24	.198
Aortic valve area (cm ²)	0.6 ± 0.1	0.6 ± 0.1	0.6 ± 0.1	.465
LVEF (%)	59 ± 13	58 ± 14	59 ± 13	.865
Systolic aortic annular diameter (mm)	21.2 ± 2.4	21.2 ± 2.5	21.2 ± 2.3	.972
Device				
Edwards Sapien valve				
23 mm	24 (47.1%)	16 (57.1%)	8 (34.8%)	.105
26 mm	27 (52.9%)	12 (42.9%)	15 (65.2%)	
CoreValve				
26 mm	19 (90.5%)	19 (90.5%)	0	—
29 mm	2 (9.5%)	2 (9.5%)	0	

CABG, Coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; EuroSCORE, European System for Cardiac Operative Risk Evaluation; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention. Data are expressed as mean ± SD or as number (percentage).

Table 2 Transthoracic echocardiographic results at follow-up (n = 72)

Variable	AR				P [†]
	None (n = 29)	Mild (n = 35)	P*	Moderate (n = 8)	
Left ventricular ejection fraction (%)	63.9 ± 11.4	60.4 ± 10.6	.227	58.6 ± 13.2	.696
Left ventricular mass (g/m ²)	121.9 ± 39.1	125.4 ± 42.6	.769	130.0 ± 27.7	.784
Aortic peak pressure gradient (mm Hg)	17.6 ± 10.0	14.9 ± 7.4	.245	17.4 ± 7.8	.437
Mean aortic pressure gradient (mm Hg)	8.4 ± 4.5	7.5 ± 3.4	.418	9.0 ± 5.1	.395
Left ventricle end-diastolic volume (mL/m ²)	44.0 ± 16.3	48.4 ± 21.9	.477	66.1 ± 18.6	.044
Aortic valvular area (cm ²)	1.9 ± 0.6	2.0 ± 0.6	.605	1.9 ± 0.6	.680
AR volume (mL)	—	22.2 ± 5.5	—	41.3 ± 6.4	<.001
Vena contracta width (mm)	—	2.3 ± 0.6	—	2.0 ± 0.5	.139
Vena contracta planimetry (cm ²)	—	0.09 ± 0.06	—	0.29 ± 0.1	.001

Data are expressed as mean ± SD.

*No versus mild AR.

†Mild versus moderate AR.

DISCUSSION

AR After TAVI

This study shows an additional contribution of 3D TTE to 2D TTE for the accurate evaluation of AR after TAVI, using AR volume as a reference standard.

We found an AR prevalence of 57.4% at midterm follow-up, which was mainly caused by paravalvular AR. Among all, most patients pre-

sented with mild AR (48.6%), and moderate AR was restricted to patients with paravalvular AR. This result is consistent with data reported from studies assessing AR immediately after TAVI³ or at midterm follow-up.^{17,18} Favorable outcomes are expected in patients with mild AR,^{5,19} but paravalvular AR severity can change over time, as observed in patients with AR after aortic valve replacement.⁶ Significant AR may cause hemodynamic deterioration, and it was shown that mild paravalvular leaks after TAVI cause

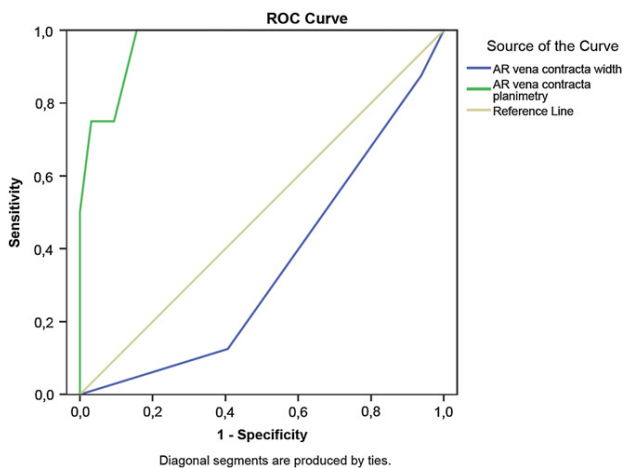


Figure 7 Receiver operating characteristic (ROC) curves for vena contracta width by 2D TTE (area under the curve, 0.35; 95% confidence interval, 0.15–0.55) and vena contracta planimetry by 3D TTE (area under the curve, 0.96; 95% confidence interval, 0.91–1.0) for the diagnosis of moderate AR.

a significantly higher workload on the left ventricle than in an equivalently sized surgically implanted bioprosthesis.²⁰

The presence of postprocedural significant AR (defined as $\geq 2/4$) was described as strong independent predictor of in-hospital death after TAVI,²¹ and long-term follow-up is essential to further define the impact of AR on clinical outcomes. Accordingly, at 5-month follow-up, our study showed larger end-diastolic volumes in patients with moderate AR than in those with mild AR, which can be interpreted as the direct consequence of left ventricular remodeling caused by the chronic volume overload.

Three-Dimensional Echocardiography

The feasibility of visualizing valvular regurgitant jets with 3D color flow imaging has been previously demonstrated, and a better correlation between 3D transthoracic echocardiographic AR vena contracta planimetry and aortography, compared with conventional 2D transthoracic echocardiographic AR width, was shown.¹² Moreover, 3D TEE¹³ is superior to 2D TEE in the evaluation of paravalvular prosthetic regurgitation. It provides more information regarding the location and a more accurate estimate of aortic and mitral valve prosthetic paravalvular defect size compared with 2D TEE.^{22,23} Nevertheless, until now, no data regarding the evaluation of aortic paravalvular leaks with 3D TTE have been presented.

The methodology proposed in this study allowed the precise localization of AR jets. By acquiring 3D color volumes from apical windows and analyzing views cropped in short-axis orientation, we found that the paravalvular region from 12 to 3 o'clock (corresponding to the usual location of the commissural junction between the left and right aortic cusps) was the most common location for paravalvular AR. This systematized description is fundamental once the prosthesis is implanted, as the native aortic cusps are smashed into the paravalvular region and the native references are partially lost. However, in this study, we did not find a correlation between the aortic valve calcification severity or leaflet asymmetry and the presence of paravalvular AR, which is consistent with previous results using computed tomography.²⁴

Using one 3D image acquisition, instead of the views in single 2D cut planes, it is possible to analyze the complete morphology of the

AR color flow stream in the region of its origin. Consequently, the view from any level can be obtained, and the direction and extension of paravalvular AR jets can be assessed objectively, overcoming the assumptions needed to analyze AR jet extension, direction, and vena contracta shape using 2D imaging.⁸ Figure 3 shows an example of paravalvular AR viewed simultaneously from the aortic root and from the left ventricular outflow tract; this figure demonstrates that depending on the location of the cut plane in relation to the aortic prosthesis, the area of the paravalvular AR jet varies as viewed in the short-axis orientation. This highlights the potential errors inherent to the analyses in single short-axis views from 2D imaging, in which the image orientation relative to the axis of the jet is unknown. Simultaneously, Figure 3A depicts a short-axis view of the color jet cross-sectional area and left ventricular outflow tract cross-sectional area, which is also a semiquantitative measure of AR severity. At the same time, from the aortic root (Figure 3B), we can visualize the proximal isovelocity surface.

AR volume was used for quantitative AR severity classification by the difference between 3D TTE-derived left ventricular stroke volume and the right ventricular stroke volume. Left ventricular volumes assessed by 3D TTE have higher accuracy and better concordance with cardiac magnetic resonance compared with 2D TTE²⁵; consequently, we used 3D volumetric calculation of left ventricular stroke volume. This method overcame the risk for AR volume overestimation, when measuring the flow integral in the left ventricular outflow tract, because when the sample volume is placed too close to the prosthetic valve, proximal acceleration may lead to overestimation of velocity and consequently an overestimation of AR volume.

Considering vena contracta measurements, our results showed a better correlation of 3D transthoracic echocardiographic vena contracta planimetry with AR volume than vena contracta width assessed by 2D TTE (Kendall's $\tau = 0.82$ $P < .001$ vs 0.66 [$P < .001$]). Consistently, a better accuracy for moderate AR diagnosis by vena contracta planimetry was shown by the area under the receiver operating characteristic (Figure 7). In fact, vena contracta width by 2D TTE provides a robust estimation of the size of the effective regurgitant orifice area in native valves, but once the jet presents an irregular shape, as frequently found in paravalvular leaks, its value is restricted and may not reflect AR severity.^{7,12} Moreover, the vena contracta width was similar between patients with moderate and mild AR, while vena contracta planimetry was larger in patients with moderate AR than in those with mild AR. These results support the use of vena contracta planimetry as an additional tool for quantitative measurement of paravalvular AR. Indeed, vena contracta area by 3D transthoracic echocardiographic sequential cropping has been previously validated in patients with AR in native aortic valves.¹² However, until now, widespread 3D color echocardiography has been limited by restricted temporal resolution and a narrow color sector. Besides, the 3D color image could only be reconstructed from several heartbeats, which often causes stitching artifacts.²⁶ In this study, we used Live 3D color from the X5-1 PureWave microbeam-forming xMATRIX probe. Even if 3D color frame rates are still lower than 2D rates, a considerable improvement from the previous X4 transthoracic echocardiographic probe could be observed. We were able to acquire the 3D color image with four heartbeats, minimizing stitching artifacts, and with all paravalvular area inside of the same volume acquisition. Consequently, the assessment of the real shape of the vena contracta and its planimetry was confidently performed. Nevertheless, despite the improvement in 3D images, a satisfactory acoustic window is still a fundamental requirement for proper visualization and interpretation. In this study, we had four patients with

unacceptable apical windows. These patients were part of the group without AR, and consequently there was no interference with AR results obtained, but limitations may occur when trying to apply 3D transthoracic echocardiographic analysis in patients with inadequate acoustic windows. Once a patient presents a poor window on 2D TTE, there is no expectation of improvement using 3D TTE. In those cases, TEE is the technique that can provide secure information. Because this study was performed 5 months after TAVI, we were able to include patients in whom TAVI was performed through a transapical route. It would have been impossible to study these patients immediately after the TAVI procedure, because image quality would have been reduced by the subcutaneous hematomas that result from left anterolateral minithoracotomy. Moreover, we must consider that a certain level of expertise is necessary for proper image acquisition, interpretation, and reproducibility of results. When using this methodology for paravalvular AR analysis in clinical practice, it may increase the time devoted to the transthoracic echocardiographic study, specially until achieving confidence with the method, but if we consider that we are adding significant information for appropriate quantification of paravalvular AR, we will be dedicating time to a higher standard in the performance of echocardiography. Further studies will certainly assess its clinical impact.

Limitations

In this study, moderate AR was restricted to patients with paravalvular AR, so the interpretation of vena contracta planimetry results can be applied only to patients with paravalvular AR.

Our results are based on the latest 3D transthoracic echocardiographic technology available for clinical practice, but 3D echocardiography still has lower frame rates than 2D echocardiography, which may present restrictions on flow data interpretation and require a higher level of expertise at the time of data acquisition and image interpretation.

We are presenting a single-time frame evaluation of patients with paravalvular AR. Additional studies are required for the assessment of the clinical benefit of this methodology at long-term follow-up.

CONCLUSIONS

In this study, we have proposed an alternative methodology for paravalvular AR assessment after TAVI. Using vena contracta planimetry by 3D TTE, we have described an accurate methodology for paravalvular AR jet evaluation and moderate AR classification.

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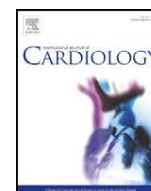
CHAPTER 5

**Quality of life improvement at midterm
follow-up after transcatheter aortic
valve implantation**



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Quality of life improvement at midterm follow-up after transcatheter aortic valve implantation[☆]

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ABSTRACT

Background: Transcatheter aortic valve implantation (TAVI) techniques have been presenting good procedural success and favorable clinical outcomes. However, optimal management of aortic valve disease in elderly patients depends on quality of life (QoL) improvement. In this study we aimed to evaluate changes in QoL in patients referred for TAVI.

Methods and results: Prospective analysis of 74 consecutive patients (34 male), aged 81.6 ± 8 years with symptomatic severe aortic valve stenosis (AS) ineligible for conventional aortic valve replacement, referred to TAVI in one tertiary center. For the assessment of QoL, the Minnesota Living with Heart Failure Questionnaire (MLHFQ) was used before the procedure and at 6.5 months. The mortality was 9.5% at 30 days and 20.2% at 6.5 months follow-up. Fifty three (71.6%) patients completed MLHFQ at baseline and at follow-up. All patients showed good hemodynamic results and no signs of prosthesis dysfunction were observed on transthoracic echocardiography. The New York Heart Association (NYHA) class (2.9 ± 0.4 to 1.4 ± 0.7 ; $p < 0.001$), and the MLHFQ scores [overall (37.0 ± 14.7 vs. 14.4 ± 10.1 ; $p < 0.001$), physical dimension (23.2 ± 9.5 vs. 8.6 ± 5.9 ; $p < 0.001$) and emotional dimension (5.4 ± 4.2 vs. 2.6 ± 3.0 ; $p < 0.001$)] were significantly improved 6.5 months after TAVI. Patients with peripheral vascular disease (PVD) had an inferior improvement in QoL caused by a lower enhancement in physical dimension MLHFQ score (mean difference: -17.0 ± 10.2 vs. -10.1 ± 11.5 ; $p = 0.036$).

Conclusion: TAVI significantly improves symptoms and QoL in patients with severe AS and high surgical risk. Patients with PVD might be expected to have a less impressive improvement in QoL after TAVI.

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1. Introduction

Aortic stenosis is the most frequent native valve disease of the elderly, in western industrialized countries [1]. Once symptomatic it is responsible for serious disability, restrictions in the normal daily living and reduced life expectancy [2]. Until recently, the only effective treatment was surgical aortic valve replacement [3,4]. However, surgery is associated with higher morbidity and mortality rates in the elderly compared with younger patients [5]. It is estimated that about 31% of patients with severe AS, older than 75 years are not referred to surgery, or are refused by the cardiac surgeon because of co-morbidities and perceived high surgical risk [6]. At this stage of the disease patients commonly

present severe heart failure symptoms, in spite of optimal medical treatment.

Transcatheter aortic valve implantation (TAVI) techniques have emerged as an alternative treatment for this group of patients. Good procedural success and favorable clinical outcomes at short and midterm follow-up have been reported [7–9]. Nevertheless, quality of life (QoL) improvement is a major expectation for this elderly patient's profile [10]. Clinical benefit and neurohormonal activation reduction at short term after TAVI were shown [11], but midterm follow-up results of QoL are scarce and conflicting results were reported for the mental evaluation component when using the Short Form 36-Item Health Survey [12,13].

Further than mortality and hemodynamic valve performance, QoL assessment is crucial for the evaluation of these procedures' efficiency and to guide clinical decision-making. The Minnesota Living with Heart Failure Questionnaire (MLHFQ) is a well-documented and widely used disease-specific health-related QoL questionnaire for heart failure [14]. Therefore, the objective of our study was to evaluate changes in the QoL of patients undergoing TAVI using the MLHFQ.

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2. Methods

This study included 74 consecutive patients referred for TAVI in one tertiary center, from April 2009 to April 2010. All patients had severe aortic valve stenosis (aortic valve area $\leq 1 \text{ cm}^2$) and were ineligible for conventional aortic valve replacement (AVR), due to an excessive surgical risk, estimated by the logistic EuroSCORE and/or clinical judgment of specific co-morbidities, such as porcelain aorta, severely reduced lung capacity or frailty[10]. Pre-procedure assessment included medical history, physical examination, trans-thoracic and transesophageal echocardiography, coronary angiography, aortography, iliac-femoral arteriography and when necessary, computed tomography (CT) angiography. The patients' clinical characteristics were self reported or recorded from medical records. Peripheral vascular disease (PVD) was defined by documented history of a clinical syndrome consistent with PVD as well as confirmatory imaging (duplex ultrasound, arteriography or CT angiography) and/or physiologic study (ankle brachial index) or a history of peripheral arterial surgery or angioplasty.

For the purpose of this prospective study the QoL assessment was performed before the procedure (baseline) and at midterm follow-up. In order to be included in this cohort, patients had to be able to understand Spanish and to answer the questionnaire by them or with minor familiar help.

2.1. Transcatheter aortic valve implantation

The procedure was performed under fluoroscopy and transesophageal echocardiography (TEE) guidance using the techniques described in detail in previous reports [15,16].

Among all, 25 (33.8%) patients were implanted with an Edwards SAPIEN (Edwards Lifesciences, Irvine, CA, USA) aortic valve through anterograde transapical approach and 28 (37.8%) through retrograde transfemoral approach. The CoreValve (Medtronic CoreValve Percutaneous System, Medtronic CV) was implanted in 21 (28.3%) patients exclusively by retrograde transfemoral approach. Two valve sizes are available, 23- and 26-mm expanded diameter for Edwards SAPIEN valve and 26- and 29-mm for CoreValve. The aortic prosthesis size was decided according to annulus diameter,

Table 1
Baseline characteristics of the study population.

Variables	Overall (n=74)	Percutaneous (n=49)	Transapical (n=25)	P value
<i>Clinical characteristics</i>				
Age, years	82 (8)	84 (5)	77 (10)	0.001
Female, n (%)	40 (54.1)	30 (61.2)	10 (40.0)	0.137
Log EuroSCORE (%)	19.3 (9.9)	19.2 (8.3)	19.6 (12.8)	0.5899
Hypertension, n (%)	61 (82.4)	41 (83.7)	20 (80.0)	0.944
Diabetes, n (%)	21 (28.4)	11 (22.4)	10 (40.0)	0.190
Dyslipidemia n (%)	46 (62.2)	25 (51.6)	21 (84.0)	0.012
Coronary artery disease, n (%)	31 (41.9)	19 (38.8)	12 (48.0)	0.609
Previous PCI or prior CABG, n (%)	25 (33.8)	13 (26.5)	12 (48.0)	0.113
COPD, n (%)	30 (40.5)	19 (38.8)	11 (44.0)	0.855
Renal impairment n (%)	22 (29.7)	11 (22.4)	11 (44.0)	0.099
Peripheral vascular disease n (%)	24 (32.4)	7 (14.3)	17 (68.0)	<0.001
NYHA functional class n (%)				
II	7 (9.5)	5 (10.2)	2 (8.0)	0.649
III	61 (82.4)	41 (83.7)	20 (80.0)	
IV	6 (8.1)	3 (6.1)	3 (12.0)	
Angina n (%)	35 (47.3)	20 (40.8)	15 (62.5)	0.136
Syncope n (%)	10 (13.5)	7 (14.3)	3 (12.5)	0.835
<i>Echocardiography characteristics</i>				
Mean aortic pressure gradient (mm Hg)	51 (16)	55 (16)	46 (13)	0.050
Aortic peak pressure gradient (mm Hg)	85 (25)	89 (24)	80 (26)	0.128
Aortic valve area (cm ²)	0.6 (0.1)	0.6 (0.2)	0.6 (0.1)	0.569
LV EF (%)	58 (14)	59 (14)	58 (14)	0.766
Systolic aortic annulus diameter (mm)	21.1 (2.5)	21.2 (2.5)	20.9 (2.4)	0.700
<i>Procedure data</i>				
Edward SAPIEN				
Number 23 n (%)	25 (33.8)	16 (57.1)	9 (36.0)	0.206
Number 26 n (%)	28 (37.8)	12 (42.9)	16 (57.1)	
CoreValve				
Number 26 n (%)	19 (25.7)	19 (90.5)	0	-
Number 29 n (%)	2 (2.7)	2 (9.5)	0	

logEuroSCORE, logistic European System for Cardiac Operative Risk Evaluation; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; LV, left ventricle; EF, ejection fraction.

measured by transesophageal echocardiography. The deployment was performed under the agreement of the interventionalist and the echocardiographer. Device success was defined as stable device placement and function as assessed by angiography and echocardiography. All patients with developing new grade III atrioventricular block were implanted with a permanent pacemaker within 3 days after valve implantation.

2.2. Quality of life assessment

QoL was assessed using MLHFQ[14]. At hospital admission for TAVI, all patients were clinically evaluated and completed the baseline questionnaire, which was administered by a 5-minute interview. Patients were invited to come to follow-up, when the MLHFQ was repeated and an additional questionnaire was applied to evaluate the individual living condition. The subject perception of QoL improvement and the reaffirmation of the decision to have TAVI were assessed by two further questions that should be answered with yes or no.

The MLHFQ15 is a 21-item structured questionnaire that measures patient perceptions about the effects of symptoms, functional limitations and psychological distress of an individual's QoL[14]. The questionnaire can be self-administered or applied in a 5-minute interview, which was the chosen methodology[17]. Respondents were asked to rate the degree to each heart failure related item that prevented them from living as they wanted, during the previous four weeks. It is evaluated using a 6-point Likert scale ranging from 0 (no impact/not applicable (best score)) to 5 (severe impact (worst score)). The MLHFQ produces a total score (21 items, range: 0 to 105) and physical and emotional dimension scores (ranges: 0 to 40 (8 items) and 0 to 25 (5 items), respectively). Lower scores indicate better HQoL and a change ≥ 5 points in total score is considered clinically meaningful[18].

This protocol was approved by the local ethics committee and all patients gave written informed consent for participation.

The authors are solely responsible for the design and conduct of this study, analyses and its final contents.

2.3. Statistical analysis

Categorical variables were expressed as percentages and continuous variables as mean and standard deviation (SD) unless otherwise specified. Fisher exact test was used for comparisons between dichotomous variables and continuous variables were compared between groups using an unpaired *t* test or the Mann-Whitney *U* test, as appropriated. All reported probability values are 2-tailed, and *p* values <0.05 were considered statistically significant.

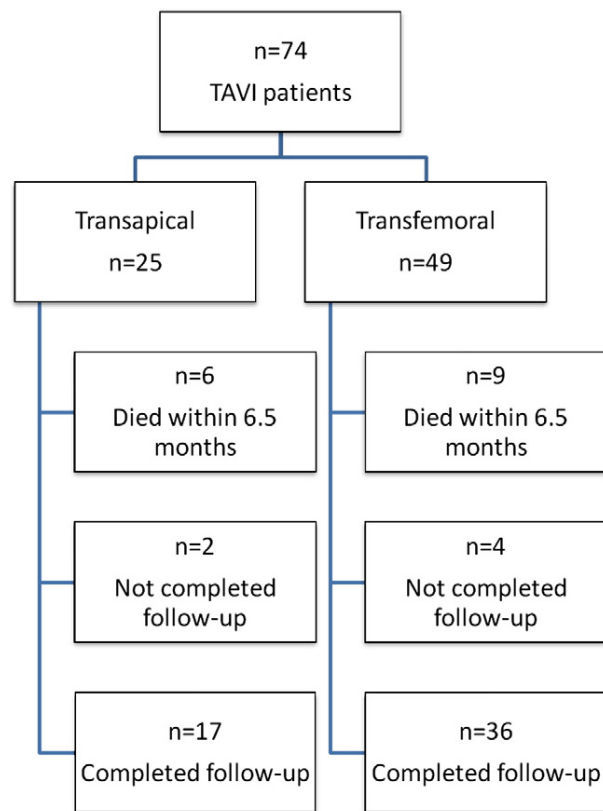


Fig. 1. Flowchart showing the follow-up of the 74 patients included in this study.

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Table 2
Echocardiography results at baseline, immediately after TAVI and at midterm follow-up (n = 53).

Parameter	Baseline	After TAVI	P value	Follow-up	P value ^a
Aortic peak pressure gradient (mm Hg)	84.2 (21.5)	15.3 (6.5)	<0.001	16.1 (7.6)	0.533
Mean aortic pressure gradient (mm Hg)	49.1 (13.0)	7.4 (3.5)	<0.001	8.2 (3.6)	0.970
Aortic valvular area (cm ²)	0.6 (0.1)	1.9 (0.6)	<0.001	1.7 (0.4)	0.096
Aortic regurgitation	–	32 (60.4)	–	33 (62.3)	0.074
Left ventricle ejection fraction (%)	57.8 (13.2)	63.5 (12.3)	0.564	61.0 (11.2)	0.625
Left ventricle mass (g/m ²)	220.9 (67.2)	–	–	218.2 (64.2)	0.833

^a P value result from a comparison between results immediately after TAVI and at follow-up.

All statistical analyses were performed with the SPSS statistical software package (version 16.0) (SPSS Inc, Chicago, IL).

3. Results

This study included 74 patients, 40 (54.1%) were female, the mean age was 81.6 ± 8 years and mean log EuroSCORE was 19.3 ± 9.9 . Baseline patients' characteristics and echocardiography data are presented in Table 1. Patients referred to transapical approach were younger (77 ± 10 vs. 84 ± 5 years; $p = 0.001$) and presented more commonly dyslipidemia (84.0% vs. 51.6%; $p = 0.012$) and PVD (68.0% vs. 14.3%; $p < 0.001$). The remaining characteristics were similar in both groups.

3.1. Clinical outcome

Among all, 53 (71.6%) patients completed the MLHFQ at baseline and 6.5 months after TAVI. The 30-day mortality was 9.5% and 15 (20.2%) patients had died at 6.5 months follow-up (transfemoral – 9 (18.4%); transapical – 6 (24.0%); $p = 0.791$). In the all cohort 11 (73.3%) patients died for cardiovascular causes, 2 (13.3%) for infections, 1 (6.6%) for multiorgan failure and 1 (6.6%) for unknown etiology. The remaining 6 (8.1%) patients were not able or willing to return to follow-up. At last, 14 (26.4%) patients required permanent pacemaker implantation. The length of in hospital stay after the procedure was 11.4 ± 5.8 days, which was similar in both interventions. Fig. 1 shows the follow-up of the entire cohort.

The 53 patients who attended to follow-up had a mean age of 82 ± 8 years, 29 (54.7%) were female and the mean log EuroSCORE was 18.4 ± 9.3 . Among these the mean New York Heart Association (NYHA) class significantly improved from 2.9 ± 0.4 before the procedure, to 1.4 ± 0.7 ($p < 0.001$) at 6.5 months after TAVI (Fig. 2).

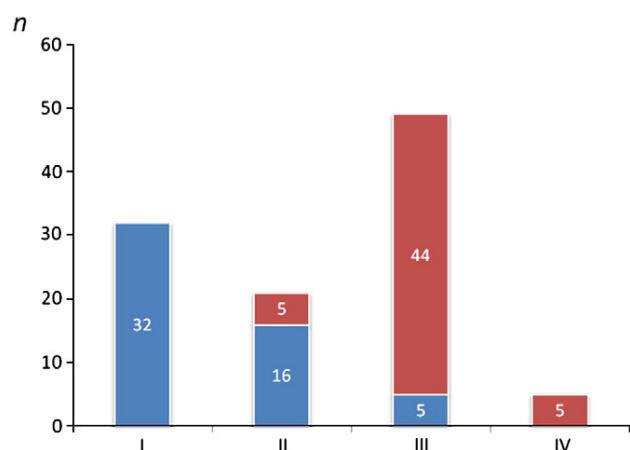


Fig. 2. New York Heart Association class at baseline (red columns) and at 6.5 months after TAVI (blue columns). Data presented in absolute numbers (n = 53). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

3.2. Echocardiography data

The procedure was successful in all patients, which was confirmed by a significant increase of the effective orifice area (before: 0.6 ± 0.1 ; after: 1.9 ± 0.6 ; $p < 0.001$) and a decrease in peak (before: 84.2 ± 21.5 ; after: 15.3 ± 6.5 ; $p < 0.001$) and mean (before: 49.1 ± 13.0 ; after: 7.4 ± 3.5 ; $p < 0.001$) aortic valve pressure gradients. Thirty-two (60.4%) patients ended with aortic prosthesis regurgitation that was mild in 27 (50.9%) and moderate in 5 (9.4%) patients.

At follow-up no patient showed signs of prosthesis dysfunction. Aortic regurgitation severity, as well as mean transvalvular gradients, remained similar to the collected data immediately after prosthesis deployment. No differences in left ventricle (LV) ejection fraction or LV mass were found. Echocardiography parameters at baseline and at follow-up are given in Table 2.

3.3. Quality of life assessment

The global MLHFQ score (37.0 ± 14.7 vs. 14.7 ± 10.1 ; $p < 0.001$), the physical dimension score (23.2 ± 9.5 vs. 8.6 ± 5.9 ; $p < 0.001$) and the emotional dimension score (5.4 ± 4.2 vs. 2.6 ± 3.0 ; $p < 0.001$) significantly improved at 6.5 months after TAVI (Fig. 3). No single patient presented an increase in any score after TAVI and all patients showed a clinically meaningful change in total score [18]. No differences in MLHFQ scores were found according to gender, age or echocardiography characteristics at baseline. The effect of the type of intervention in QoL results was assessed and no differences between percutaneous or transapical approach were found (Fig. 4). However, when the effect of baseline clinical characteristics on QoL improvement was considered, patients with PVD presented a lower improvement in QoL. This result was a consequence of an inferior decrease in the physical dimension MLHFQ score (mean difference: -17.0 ± 10.2 in patients

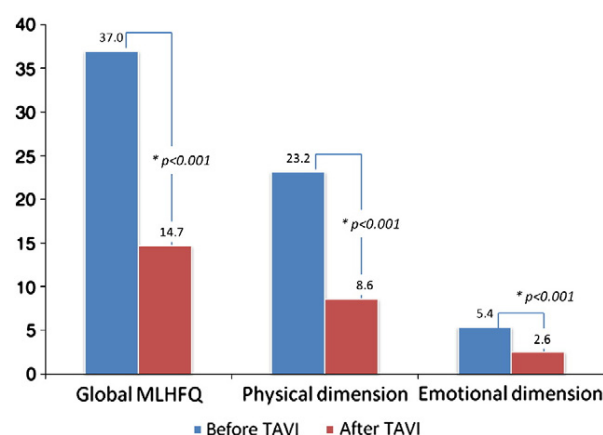


Fig. 3. Representation of the global MLHFQ score, physical dimension score and emotional dimension score at baseline (blue columns) and at midterm follow-up after TAVI (red columns) of all the population studied (n = 53). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

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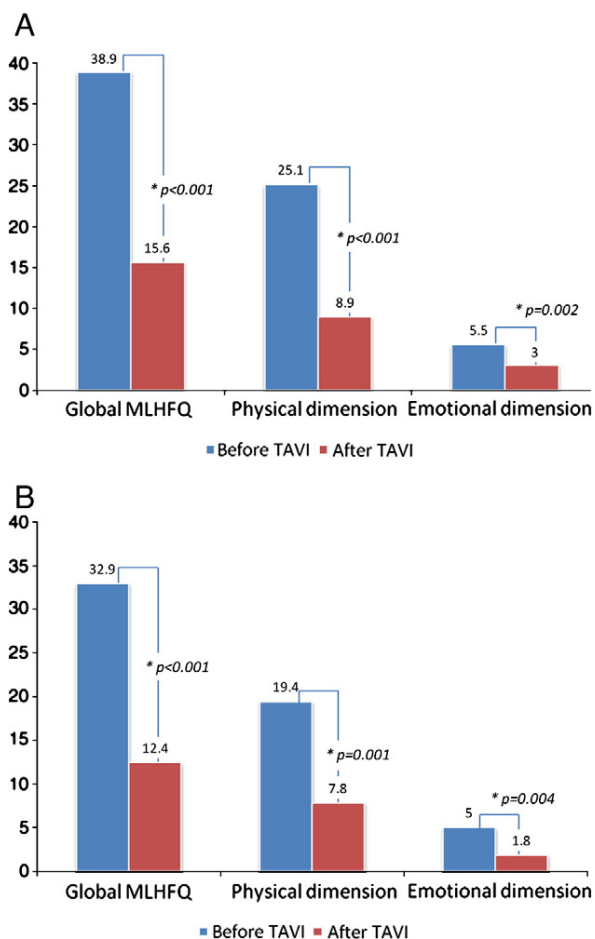


Fig. 4. Representation of the global MLHFQ score, physical dimension score and emotional dimension score at baseline (blue columns) and at midterm follow-up after TAVI (red columns), from patients (n=53) referred to transfemoral (A) and to transapical approach (B). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

without PVD vs. -10.1 ± 11.5 in patients with PVD; $p=0.036$) (Fig. 5). When considering the other clinical characteristics assessed at baseline (Table 1), or the requirement of definitive pacemaker implantation, no significant effect on MLHFQ scores was found.

The individual subjective perception of QoL improvement occurred in 50 (94.3%) patients, who reaffirmed their decision to have TAVI 6.5 months after the procedure. Finally, 3 (5.6%) patients lived independently before TAVI in contrast to 47 (88.6%) that reported to live independently 6.5 months after the procedure ($p<0.001$).

4. Discussion

This study shows that TAVI significantly improves QoL in patients with severe AS ineligible for conventional AVR. It was observed as a striking improvement in global MLHFQ score as well as in physical and psychological dimensions. Moreover, the large majority of patients lived independently and reaffirmed their decision to have TAVI 6.5 months after the procedure.

In absence of an effective conservative treatment for symptomatic severe AS, TAVI has become an appropriate alternative for elderly patients with high surgical risk[10]. At the time these patients are referred for intervention, they present reduced life expectancy and severe heart failure symptoms with consequent restrictions in the normal daily living. Good procedural success and favorable clinical outcomes have been reported, however TAVI may be followed by

meaningful complications and it is a main issue to assess if the short term improvement in NYHA class [19,20] is equivalent to significant improvement in QoL.

4.1. Clinical outcome and QoL assessment

Our study showed a rate of death from any cause of 9.5% at 30-days and 20.2% at 6.5 months follow up. These results are in agreement with preceding reports[8], considering that we studied a population including transfemoral [20] and transapical patients[15]. The latter have been recognized in SOURCE Registry to suffer more comorbidities than the transfemoral patients, therefore a less favorable outcome can be expected[8]. In our population the logistic EuroSCORE was similar between the two groups. However, patients referred to transapical delivery presented more frequent PVD, which can significantly contribute for a poorer outcome. Nevertheless, we could not find significant differences between transapical and transfemoral patients' clinical outcomes on QoL results.

Quality of life improvement is a major concern in these patients. The partner trial showed a significant reduction in the rates of death, as well as cardiac symptoms improvement, at one year follow-up, among patients who had undergone TAVI, compared to those who had received standard therapy. However, TAVI patients suffered more major vascular events and major strokes and QoL consequences of the procedure were unknown[21]. Conversely, besides symptoms improvement, an improvement in QoL was demonstrated in elderly patients referred for AVR [22] thus, similar results might be expected in patients referred to TAVI.

Gotzmann M. et al. has showed clinical benefit and a reduction of neurohormonal activation 30 days after TAVI[11]. Other studies have reported benefit in quality of life on the first month [11] and 3 months after TAVI[12], but midterm follow-up QoL results are scarce[13,23]. Moreover, according to our knowledge this is the first study using the MLHFQ for midterm follow-up of TAVI patients. The MLHFQ score is widely used for heart failure patients, has well-documented validity, reliability and sensitivity and is also validated in patients referred to valvular surgery[24]. The SF-36[®] is broadly used in cardiac patient population but, it contains 36 items which is a considerable burden for patients and investigators. The SF-12v2 Health-Survey is a subset of SF-36 that has been applied in 30 patients referred to percutaneous

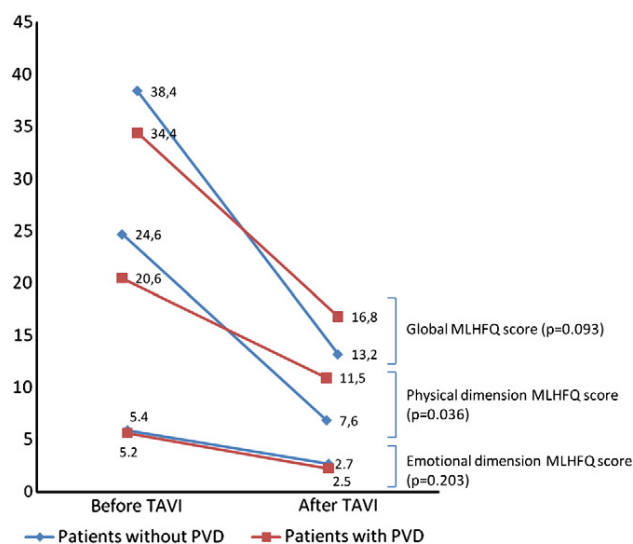


Fig. 5. Representation of the global MLHFQ score, physical dimension score and emotional dimension score change from baseline to midterm follow-up after TAVI (n=53), among patients with peripheral vascular disease (PVD) and those without PVD.

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aortic valve implantation. The authors reported marked short-term improvement in functional status and physical and mental health in those patients[23]. Though, the SF-12v2 Health-Survey is less sensitive than MLHFQ for detecting clinically important changes in heart failure patients and has only been considered a satisfactory alternative to the SF-36® when using large samples[25]. The MLHFQ is a short and easy to understand questionnaire, reducing respondent time and improving response rates.

The pre-procedural MLHFQ total score of this cohort (37 ± 5) demonstrated a severe impairment in perceived QoL, considering that the average total scores of 27.7 and 42.7 were shown by others to correspond to NYHA functional class II and III, respectively, among patients with chronic heart failure[26]. This is according with the severity of heart failure symptoms, as most patients presented NYHA functional class III (Fig. 2)[26]. However, after TAVI, besides the significant improvement in NYHA functional class an impressive enhancement in QoL was found, regarding both physical and psychological dimensions of the MLHFQ. The physical dimension score results from direct effects on symptoms and the psychological dimension improvement may be justified by the reduction in social activities constrains, caused by severe heart failure symptoms. Nevertheless, Krane M et al. studied TAVI patients within 3 months after valve implantation and in spite of the global improvement in QoL, SF-36® mental health summarized score showed no changes. This can be explained by currently unidentified differences in the population selected or by the shorter follow-up performed[12].

Regarding clinical characteristics in view of best patient selection, we found that patients with PVD presented a lower improvement in QoL, than those without PVD. This result was a consequence of an inferior difference from baseline to follow-up in the physical dimension score in patients with PVD. Health-related QoL has been previously shown to be significantly impaired in individuals with PVD, by pain, sleep disturbance and restrictions in daily living activities [27], but it is interesting to notice its significant effect in patients submitted to TAVI. Remarkably, even being more patients with PVD referred to transapical aortic valve implantation, no differences in QoL outcomes were found between the techniques, remaining the presence of PVD the single characteristic related to less impressive QoL improvement.

4.2. Limitations

This study has no control group to compare the outcome following TAVI with the outcome under medical therapy. However, the dismal prognosis of severe aortic stenosis is well known, therefore a comparison group on medical therapy would be hard to find and ethically difficult to justify. In accordance, no accurate accounts on life expectancy improvement after TAVI can be accessed from the study results. However, our aim was to assess QoL improvement after TAVI, thus our results are not dependent on a comparison group.

We have to consider a potential selection bias caused by the 15 patients who died within the follow-up period and the 6 who failed to complete the questionnaire 6.5 months after TAVI.

Finally, in spite of significant results at 6.5 months, a longer interval will be certainly interesting to assess in future studies.

5. Conclusion

TAVI significantly improves symptoms and QoL in patients with severe AS ineligible for conventional AVR. Using the MLHFQ, impressive improvement in physical and psychological dimensions was shown at 6.5 months follow-up. Moreover, the majority of patients were living independently and reaffirmed their decision to have TAVI. Patients with PVD might be expected to have a less impressive improvement in QoL after TAVI; however, predictors for best patient selection remain to be determined.

Disclosures

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The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [28].

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ATTACHMENT

**EAE/ASE recommendations for
the use of echocardiography in new
transcatheter interventions for valvular
heart disease**

EAE/ASE recommendations for the use of echocardiography in new transcatheter interventions for valvular heart disease

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The introduction of devices for transcatheter aortic valve implantation, mitral repair, and closure of prosthetic paravalvular leaks has led to a greatly expanded armamentarium of catheter-based approaches to patients with regurgitant as well as stenotic valvular disease. Echocardiography plays an essential role in identifying patients suitable for these interventions and in providing intra-procedural monitoring. Moreover, echocardiography is the primary modality for post-procedure follow-up. The echocardiographic assessment of patients undergoing transcatheter interventions places demands on echocardiographers that differ from those of the routine evaluation of patients with native or prosthetic valvular disease. Consequently, the European Association of Echocardiography in partnership with the American Society of Echocardiography has developed the recommendations for the use of echocardiography in new transcatheter interventions for valvular heart disease. It is intended that this document will serve as a reference for echocardiographers participating in any or all stages of new transcatheter treatments for patients with valvular heart disease.

Keywords

Transcatheter aortic valve implantation • Transcatheter mitral repair • Transcatheter paravalvular leak closure • Echocardiography

Introduction

Until recently, transcatheter therapy for valvular heart disease was limited to balloon valvuloplasty. However, the introduction of devices for transcatheter aortic valve implantation (TAVI), mitral repair, and closure of prosthetic paravalvular leaks has led to a greatly expanded armamentarium of catheter-based approaches to patients with regurgitant as well as stenotic valvular disease.

Echocardiography plays an essential role in identifying patients suitable for these interventions and in providing intra-procedural

monitoring. Moreover, echocardiography is the primary modality for post-procedure follow-up. The echocardiographic assessment of patients undergoing transcatheter interventions places demands on echocardiographers that differ from those of the routine evaluation of patients with native or prosthetic valvular disease. Consequently, anticipating growing use of transcatheter valve therapies and, along with it, an expanding need for informed echocardiographic evaluation, the European Association of Echocardiography in partnership with the American Society of Echocardiography has developed these recommendations. It is intended that this document

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will complement the earlier ASE guideline for Echocardiography-guided interventions¹ and will serve as a reference for echocardiographers participating in any or all stages of new transcatheter treatments for patients with valvular heart disease.

Transcatheter aortic valve implantation

TAVI is a new technique with the potential for transforming the treatment of patients with aortic stenosis (AS). The technology is currently being evaluated in patients with severe symptomatic AS who are at high risk for conventional open heart surgery or considered inoperable. In the future, however, there may be expanded indications for TAVI. At this stage of development, TAVI remains a challenging technology that requires a multidisciplinary team approach involving interventional cardiologists, surgeons, anaesthesiologists, and imaging specialists. Imaging indeed plays a central role in successfully implementing TAVI as it is needed at each step of the procedure including patient selection, choice of procedural access, prosthetic choice and sizing, procedural guidance, and detection of early and late complications.

Introduction

In April 2002, Cribier *et al.*² reported the first successful implantation of a bovine pericardial bioprosthesis mounted within a stainless steel balloon-expandable stent in a patient with severe AS who presented in cardiogenic shock. After this first-in-man implantation, the procedure was attempted on a compassionate basis in several other patients with an equine pericardial modification of the original valve design. Valve placement was initially done via an antegrade transseptal approach. This was a challenging procedure, owing to the need for transseptal puncture, the tortuous navigation of the valve assembly across the mitral and aortic valves, and the guide wire interaction with the mitral valve apparatus, which often caused severe mitral regurgitation (MR). These limitations prompted technical improvements in the size and steerability of the delivery system which allowed for the development of the more practical retrograde transfemoral approach. Additional changes in the structure of the valve (processed bovine pericardium and extended skirt height) resulted in the Edwards SAPIEN™ valve. For patients with poor peripheral vascular access, a transapical approach was subsequently developed.³ The SAPIEN™ valve received European approval (CE Mark) for both transfemoral and transapical approaches in 2007.

In 2005, Grube *et al.*⁴ first reported the use of a different type of percutaneous valve system designed for the aortic position, the CoreValve™ system. This received CE mark in 2007. The CoreValve™ valve is self-expandable and offers the advantage of being self-centring and partially repositionable.

Expansion and refinement of transcatheter approaches for aortic valve implantation is an area of active research and development with a variety of devices in the pipeline, but only the SAPIEN™ and CoreValve™ valves have been approved. Both have been reported to have excellent flow characteristics with core-lab-adjudicated mean aortic valve area (AVA) and mean gradient at 1 year of 1.5 cm² and 11 mmHg, respectively, for the SAPIEN™ valve,⁵ and

site-reported mean gradients of 8 mmHg at 1 year for the CoreValve™.⁶

Current status of Edwards SAPIEN™ and CoreValve™ systems in Europe and North America

European approval of both the Edwards SAPIEN™ and CoreValve™ valves was granted in 2007, in the absence of a randomized trial and depending on data from a series of relatively small studies and registry reports. A newer generation modification of the Edwards valve, the Edwards SAPIEN™ XT, received CE mark in 2010. Both the SAPIEN™ and CoreValve™ valves are available in Canada for compassionate use for the treatment of patients with severe AS who are considered inoperable or at very high surgical risk. Although neither of these valves has been approved for commercial or compassionate use in the USA, the Edwards SAPIEN™ valve was approved for use as an investigational device in a pivotal trial (PARTNER US; Placement of AoRTic traNscatheterER valves) and results were recently published.^{5,7} A US randomized multicentre trial evaluating the CoreValve™ valve is underway, and a US randomized multicentre trial evaluating the SAPIEN™ XT valve has been approved.

Transcatheter aortic valve prostheses

Echocardiographers need to be familiar with the design of the two available prostheses, the Edwards SAPIEN™ valve and the Medtronic CoreValve™ valve. Each valve has specific characteristics and different aortic anatomic requirements. Thus, a precise echocardiographic evaluation is essential for appropriate patient selection

'The Edwards SAPIEN™ valve' is a balloon-expandable valve based on Cribier's original design.² The current-generation valve is composed of a cylindrical stainless steel balloon-expandable stent into which three symmetric leaflets made of bovine pericardium are mounted (*Figure 1A*). The stent also has a polyethylene terephthalate fabric skirt that decreases paravalvular leaks. The valve is available in two sizes, oversized in relation to the aortic annulus to reduce the degree of paravalvular regurgitation (PVR); a 23 mm prosthesis for transverse aortic annular diameters of 18–21 mm (measured at the level of aortic cusp insertion) and a 26 mm prosthesis for aortic annular diameters of 22–25 mm. The valve may be deployed via a transfemoral or transapical route. Because of the large valve size, sheath size is a significant factor with respect to procedural complications.

A newer generation valve, the Edwards SAPIEN™ XT as well as NovaFlex™ transfemoral and Ascendra™ transapical delivery systems, has recently received CE mark in Europe. The delivery system has a smaller calibre (18 F) and the valve stent is thinner and comprised a cobalt-chromium frame (*Figure 1B*), providing improved radial strength and enhanced circularity.

Transfemoral 'retrograde' delivery technique

Transfemoral placement is undertaken using an introducer sheath with an internal calibre of 22 or 24 F depending on the valve size.^{8,9} After femoral artery vascular access is achieved, a balloon aortic valvuloplasty is performed during rapid right ventricular pacing. Subsequently, the stented valve, crimped onto the delivery

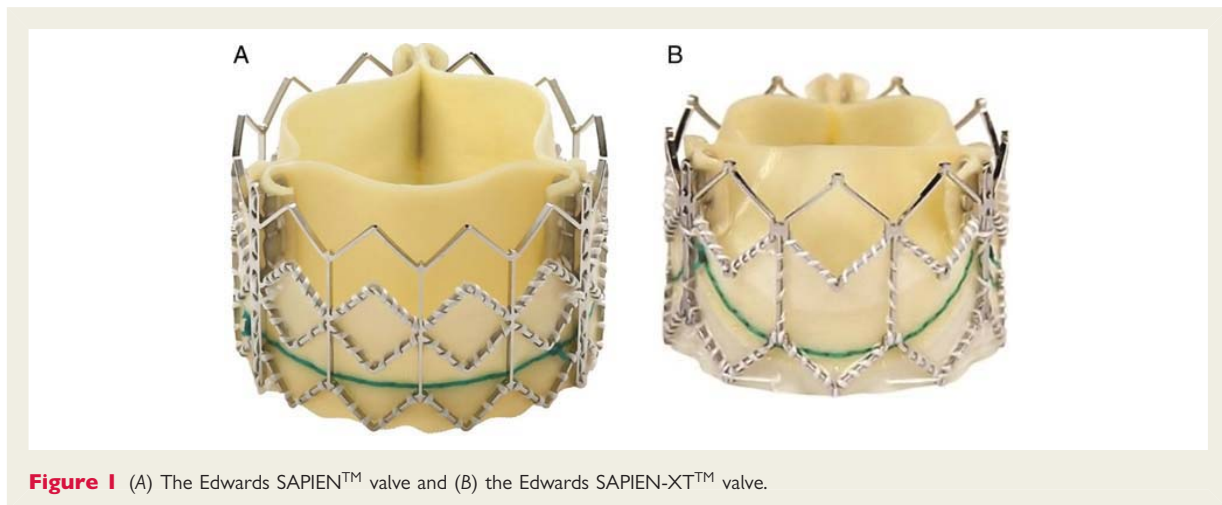


Figure 1 (A) The Edwards SAPIEN™ valve and (B) the Edwards SAPIEN-XT™ valve.

balloon, is advanced under fluoroscopic guidance, using a manually deflectable-guiding catheter that facilitates atraumatic navigation of the valve around the aortic arch and centring the guide wire through the native valve commissures. The valve is then positioned in a subcoronary position using fluoroscopic and/or transoesophageal echocardiography (TEE) guidance. Once the proper position has been achieved, the valve is deployed under rapid right ventricular pacing.

Transapical delivery technique

This more invasive approach requires an anterolateral mini-thoracotomy, ideally performed in a hybrid operative suite. Prior to the creation of a sterile field, the location of the apex is identified by palpation and confirmed by transthoracic echocardiography (TTE). Subsequently, the pericardium is opened near the left ventricular (LV) apex, a sheath is inserted directly into the LV cavity, and a guide wire is used to cross the aortic valve under fluoroscopic and TEE guidance. Aortic balloon valvuloplasty is then performed during rapid pacing after which the 26 F sheath is inserted permitting deployment of the prosthetic valve.

Procedural success and early clinical outcomes

Recent preliminary data reported from the SAPIEN™ Aortic Bioprosthesis European Outcome SOURCE Registry,¹⁰ a clinical post-commercialization 'real-world' registry of patients undergoing TAVI with the Edwards SAPIEN™ valve, included 1038 consecutive patients (575 apical and 463 transfemoral) from 32 sites. Overall short-term procedural success was 93.8%. The incidence of valve embolization and coronary obstruction was 0.6 and 0.3%, respectively. Thirty-day mortality was 6.3% in transfemoral patients and 10.3% in transapical patients. Illustrating the steep learning curve with the procedure, Webb *et al.*,¹¹ reporting a single institution's experience of 113 patients noted that mortality fell from 12.3% in the initial half to 3.6% in the second half of the experience. In the report of 1-year results for Cohort B of the PARTNER trial (inoperable patients randomized to either TAVI or medical therapy including valvuloplasty), 1-year survival was 50.7% in the TAVI arm vs. 30.7% in the medical arm.⁵ This is the only randomized trial to date comparing



Figure 2 The CoreValve™ ReValving system.

TAVI with surgery or medical therapy. The results of Cohort A [699 high-risk surgical patients, Society of Thoracic Surgeons (STS) score ≥ 10 or a predicted operative mortality $\geq 15\%$, randomized to either surgery or transfemoral/transapical valve implantation, depending on vascular access] were recently presented,⁷ showing non-inferiority with regard to mortality at 1 year. In both PARTNER and the 1-year SOURCE reports, vascular complications at the time of intervention were associated with reduced survival.

'The CoreValve™ ReValving system' prosthesis consists of porcine pericardial tissue sewn to form a trileaflet valve mounted within an asymmetrical self-expanding nitinol frame (Figure 2). Once deployed, the point of coaptation of the leaflets is supra-annular. The current-generation nitinol frame is >50 mm in length and is hourglass-shaped. The lower portion of the frame affixes the valve to the LV outflow tract (LVOT) and

has the greatest radial strength, but care must be taken not to impinge on the anterior mitral leaflet. The mid-portion of the prosthesis has a constrained waist that must be deployed at the level of the sinuses of Valsalva and the coronary ostia, so as not to jeopardize coronary flow. It has a high radial force to firmly anchor the prosthesis and prevent migration or paravalvular leakage. Finally, the upper section (outflow) has the lowest radial force and is designed to fix and stabilize the prosthesis in the ascending aorta.

The prosthetic size is determined by the external diameter of the ventricular end; the 26 and 29 mm prostheses have mid-portion diameters of 22 and 24 mm, aortic end-diameters of 40 and 43 mm, and prosthetic lengths of 55 and 53 mm, respectively. The 26 mm prosthesis is designed for patients with aortic annular diameters of 20–23 mm, whereas the 29 mm prosthesis is suitable for patients with 24–27 mm aortic annuli. However, the design of this prosthesis, with a broader upper segment to secure it to the ascending aortic wall, mandates that the height and width of the aortic sinuses and the ascending aortic diameter be carefully measured. In the presence of ascending aortic diameters >45 mm and/or aortic annular diameters <20 or >27 mm, this device should not be implanted. The delivery system of the CoreValve™ has evolved from an initial 25 F to the current 18 F device, which allows completely percutaneous arterial access and the possibility of avoiding general anaesthesia.

CoreValve™ delivery technique

The CoreValve™ is designed for retrograde delivery through arterial access, although there are case reports of deployment using a transapical route.¹² Vascular access can be obtained with or without standard surgical cut down of the common iliac, common femoral, or subclavian arteries. The procedure can be performed under general anaesthesia or with local anaesthesia in combination with mild systemic sedation/analgesia. After femoral artery access has been secured, a balloon aortic valvuloplasty of the calcified stenotic aortic valve is performed during rapid right ventricular pacing. After this valvular dilation, the prosthesis is deployed and implanted retrogradely over a stiff guide wire. Post-dilation of the CoreValve™ prosthesis can be performed at the discretion of the operator depending on the perceived proper placement of the device angiographically and the degree of aortic regurgitation.

Procedural success and early clinical outcomes

Recently, Piazza et al.¹³ reported procedural success and outcomes at 30 days in 636 patients with symptomatic AS, who underwent implantation with the third-generation CoreValve™ during the first year of the multicentre expanded CoreValve™ evaluation registry. Procedural success was achieved in 97.2% patients. Procedural death occurred in 1.5% of the patients. The combined incidence of procedural death, myocardial infarction, and stroke was 2.5%. At 30 days, all-cause mortality was 8%, one half of these deaths being judged to be procedure-related. Permanent pacemaker implantation was needed in 9.3% of the patients. TTE performed prior to discharge demonstrated a significant reduction in mean transaortic pressure gradients (from 49 ± 14 to 3 ± 2 mmHg).

Patient selection for transcatheter aortic valve implantation

Appropriate screening and patient selection, based on clinical criteria and careful analysis of cardiovascular anatomy, is crucial for the success of TAVI. Selection of candidates is complex and involves a multidisciplinary team evaluation and the use of multiple imaging modalities in order to fully delineate the anatomy of the aortic valve, aorta, and peripheral vasculature. Although not the focus or scope of these recommendations, the clinical criteria for patient selection are briefly described below.

Clinical criteria

The consensus statement on TAVI from 2008 recommends the use of this procedure in high-risk patients or those with contraindications for surgery.¹⁴ Risk evaluation is usually performed using the Logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) and/or the STS Predicted Risk of Mortality Score. High surgical risk is defined by a logistic EuroSCORE of ≥ 15 –20% or an STS mortality risk score of $\geq 10\%$. However, these scores have clear limitations and their predictive capacity may be reduced in high-risk patients who represent a small proportion of the population from which the scores were constructed. Moreover, the suitability of these scores for assessing risk during TAVI has been questioned¹⁵ since co-morbidities that are less significant for TAVI considerably increase the risk of surgical aortic valve replacement (AVR), especially in elderly patients.

Patient characteristics that might favour TAVI over AVR include prior cardiac surgery with grafts and/or adhesions, previous chest radiation therapy, porcelain aorta, liver cirrhosis, pulmonary hypertension, right ventricular failure, or marked patient frailty.^{16,17} Nevertheless, TAVI is not recommended for patients whose life expectancy is less than 1 year or who cannot expect significant improvement in quality of life.¹⁴ In clinically suitable patients for TAVI, the evaluation of the size, tortuosity, and calcification of peripheral arteries by angiography, multislice computed tomography (MSCT), or magnetic resonance imaging assists in choosing between transfemoral and transapical approaches.¹⁸

Echocardiographic evaluation

Echocardiography is critical in the assessment of candidates for TAVI, providing both anatomic and haemodynamic information.

Transthoracic echo

Transthoracic echo plays a key role in establishing the presence of severe AS with Doppler assessment of peak and mean transaortic gradients as well as AVA calculation by the continuity equation.¹⁹ According to the current guidelines, severe AS is defined by an AVA of ≤ 1 cm² (<0.6 cm²/m²) or a mean aortic valve gradient of ≥ 40 mmHg.^{20,21} However, the requirements for SAPIENT™ implantation as defined in the PARTNER trial are a valve area of <0.8 cm², a peak transvalvular velocity of ≥ 4 m/s and/or a mean gradient of ≥ 40 mmHg, targeting patients with particularly severe (critical) stenosis.

Although a full discussion of the pitfalls in diagnosing severe AS is beyond the scope of this document, two groups where the diagnosis of severe AS may be challenging should be noted. Patients

may present with low gradients, despite valve areas within the severe range in the presence of severe LV systolic dysfunction. This may pose the dilemma of distinguishing between true severe AS and pseudo-severe AS in which reduced LV systolic function contributes to the reduction in calculated valve area. Dobutamine stress echocardiography has been shown to distinguish between the two and provide useful information concerning contractile reserve.²² Additionally, attention has recently been focused on patients with low gradients and normal LV ejection fraction but low flow AS²³ for whom calculation of projected valve area under normal flow states may be useful. Cardiac catheterization is no longer recommended for determining the severity of AS, except in exceptional cases with conflicting data on echocardiography.^{20,21}

Once the diagnosis of severe valvular AS is clear, echocardiography must determine whether the patient's anatomy is suitable for TAVI. Using TTE, assessing the annular dimension and detailed anatomic characteristics of the aortic valve, including the number, mobility, and thickness of cusps, as well as the extent and distribution of calcification should be described. Currently, bicuspid aortic valve is an exclusion criterion for TAVI because an elliptical valvular orifice may predispose to an increased risk of incomplete and incorrect deployment of the aortic prosthesis. Moreover, the risk of aortic complications, such as spontaneous aortic dissection, may be increased, due to abnormal arterial wall structure.¹⁷ That said, cases of successful TAVI in bicuspid AS have been reported.¹⁸

Accurate sizing is critical to TAVI procedural success. Annular dimension is a key measurement as this determines eligibility for TAVI and guides the selection of valve type and size. Prior sections have described criteria for selecting valve size based on aortic annular, sinus of Valsalva, and ascending aortic dimensions.

Undersizing the prosthesis can result in device migration or significant paravalvular aortic regurgitation. Moreover, even if severe procedural complications do not occur, prosthesis mismatch may result. Oversizing predisposes to complications related to vascular access or to difficulties when crossing the native aortic valve with the delivery system. There is also the risk of under-expansion with consequent redundancy of leaflet tissue, creating folds that will generate regions of compressive and tensile stress that may cause central aortic regurgitation or reduction in valve durability.²⁴

Annular diameter is typically measured in systole, in a parasternal long-axis view, zoomed on the LVOT. The measurement is taken at the point of insertion of the aortic valve cusps, from tissue–blood interface to blood–tissue interface—trailing edge to leading edge (*Figure 3A*), regardless of the degree of calcification of the aortic cusps. When transthoracic two-dimensional (2D) echocardiographic measurements of the annulus are uncertain, particularly if measurements are near critical cut-offs for valve selection or if calcification extends from the aortic valve onto either the anterior mitral leaflet or the septum, TEE ± 3D evaluation may be necessary. The resolution of 3D TTE is currently inadequate for assistance in annular measurements in most subjects.

LV and right ventricular dimensions and function, aortic regurgitation, and the structure and function of the other valves should be evaluated.²⁵ The presence of haemodynamically significant LVOT obstruction due to basal septal hypertrophy represents a

contraindication as septal hypertrophy is a potential cause of prosthesis displacement during or after implantation. These patients are potential candidates for myomectomy. The presence of an LV thrombus must be excluded, as it represents a contraindication to the procedure. The presence of a patch in the LV as well as significant pericardial calcification is a contraindication for TAVI using the transapical approach.¹⁴

Transoesophageal echo

TEE is recommended prior to TAVI if there are any concerns about the assessment of the aortic root anatomy, aortic annular size, or number of cusps. Since patients with symptomatic AS tolerate hypotension poorly, sedation should be performed carefully with an emphasis on effective topical anaesthesia.

The aortic root is a direct continuation of the LVOT and extends from the basal attachment of the aortic valvular cusps to the level of the sinotubular junction.²⁴ The diameter of the root varies considerably along its length, but it is the annular diameter at the level of the basal attachment of the aortic valve cusps, measured in systole, that dictates the size of the prosthesis, irrespective of the type of the valve inserted (*Figure 3B*).

TEE aortic annular measurements correlate well with TTE, although the latter underestimates TEE-measured aortic annular size with a mean difference of 1.36 mm (95% confidence interval, 1.75–4.48 mm).²⁶ There is concern that the assumption of annular circularity made by 2D echo may result in erroneous annular measurements in patients whose annuli are more oval-shaped. However, a strategy based on 2D TEE measurements has been shown to provide good clinical results when compared with MSCT.²⁷

Currently, there is no consensus regarding the gold standard imaging technique for annular sizing, although, from a practical perspective, TTE performs this task adequately in most patients.

Transoesophageal echocardiography protocol

The pre-procedure TEE evaluation may be performed as part of screening or as the initial step of intra-procedural monitoring.

Using the long-axis view (usually around 110–130°), the LVOT and upper septum should be assessed since the presence of a sub-aortic septal bulge may create an obstacle to proper seating of the aortic prosthesis.²⁴

Using short-axis views, the opening of the aortic valve should be classified as central or eccentric and the severity, location, and symmetry of aortic valve calcification accurately described. During TAVI, the prosthesis anchors according to the resistance of the subleaflet tissue. During implantation, the native cusps are crushed against the aortic wall and the differences in the tension–force across the valve may cause asymmetric deployment of the prosthesis and contribute to the risk of compression of the coronary arteries during TAVI.⁸

In order to minimize the risk of coronary occlusion, it is essential to know the distance from the aortic annulus to the ostia of the coronary arteries and to compare this with the length of the cusps measured in a long-axis view. Although the cusps are typically shorter than the annular-ostial distances, patients in whom the cusp length exceeds the annular-ostial distances are at risk of ostial coronary occlusion when the valve is deployed and the

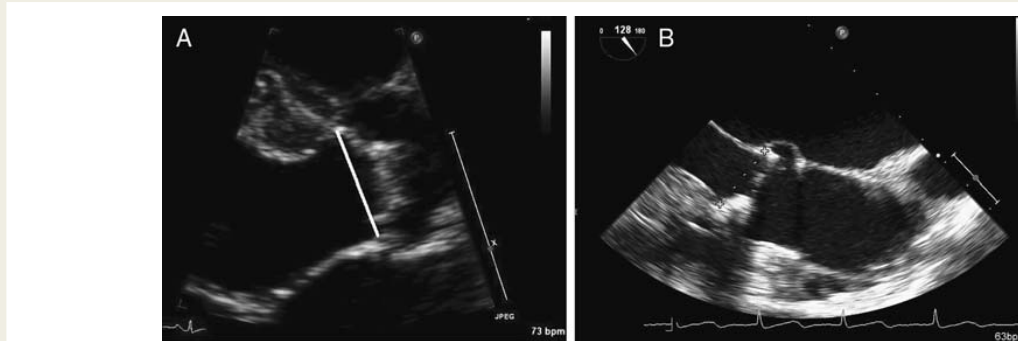


Figure 3 Annular sizing with two-dimensional transthoracic echocardiography (A) and transoesophageal echocardiography (B). The image should be aligned to avoid oblique measurements.

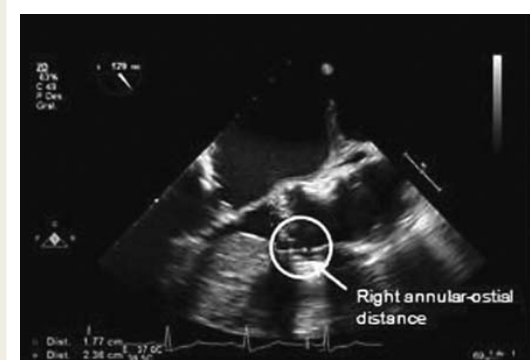


Figure 4 The ostium of the right coronary artery can be identified using a long-axis view of the left ventricular outflow tract permitting the measurement of the annular-ostial distance and the length of the right coronary cusp.

native cusps crushed to the side. Although the determination of the right coronary annular-ostial distance should be possible with 2D TEE (Figure 4), measurement of the left coronary annular-ostial distance requires 3D TEE (see below) or MSCT.

It is also important to assess the characteristics of the ascending aorta, the aortic arch, and the descending thoracic aorta since the presence of aortic arch atheromas may increase the risk of peri-procedural embolization and therefore favour a transapical approach.

Peri-procedural echocardiography during transcatheter aortic valve implantation

Two-dimensional echocardiography

Although TTE clearly plays an important role in patient selection for TAVI, its role during the actual procedure is limited. In patients undergoing TAVI via a transapical approach, TTE can be helpful in locating and marking the position of the LV apex in order to guide the thoracotomy. However, there are a number of points to remember when doing this: (i) it is important to use two

orthogonal TTE apical views; (ii) the apex should be located with the surgeon and echocardiographer on the same side of the patient so that both can agree on the optimum intercostal space; and (iii) once the skin is marked with the optimal position, it is essential that the patient and/or the skin not be moved. Such movement may occur as surgical drapes are being applied and may change the position of the skin mark relative to the ribs.

The use of peri-procedural TEE is variable. The technique can aid balloon positioning during valvuloplasty, detect post-valvuloplasty aortic regurgitation, aid prosthesis positioning during implantation, confirm prosthesis function immediately post-implantation, and rapidly detect complications. However, the use of peri-procedural TEE usually requires general anaesthesia and the probe may also partially obstruct the optimal fluoroscopic view. Therefore, some operators feel that these disadvantages outweigh the many advantages of peri-procedural TEE. However, it should be noted that the transapical approach will always require general anaesthesia anyway and some centres have reported transfemoral implantation with TEE guidance using only moderate sedation. Moreover, to avoid obstructing the fluoroscopic view, the TEE probe may be retracted during the actual valve implantation and be rapidly repositioned following deployment.

Transnasal TEE is a relatively new technique^{28,29} that can be used to monitor TAVI. Although its image quality is not quite as good as conventional TEE and transnasal TEE does not currently have 3D capability, this approach could be considered in patients where general anaesthesia is not deemed appropriate. Some sites have also adapted intracardiac echo (ICE) for TAVI, although ICE poses additional challenges in securing adequate windows.

As described more fully in a subsequent section, 3D TEE conveys certain advantages over 2D TEE during TAVI. For example, the 3D depth perspective makes it easier to visualize the position of the prosthesis on the balloon relative to the native valve annulus and surrounding structures. It also facilitates appreciation of the guide wire path through the LV and around the mitral valve subvalvular apparatus.

Both transapical and transfemoral TAVI procedures commence with balloon valvuloplasty. This is designed to split the valve commissures and make subsequent valve implantation easier. TEE can be used to guide positioning of the balloon relative to

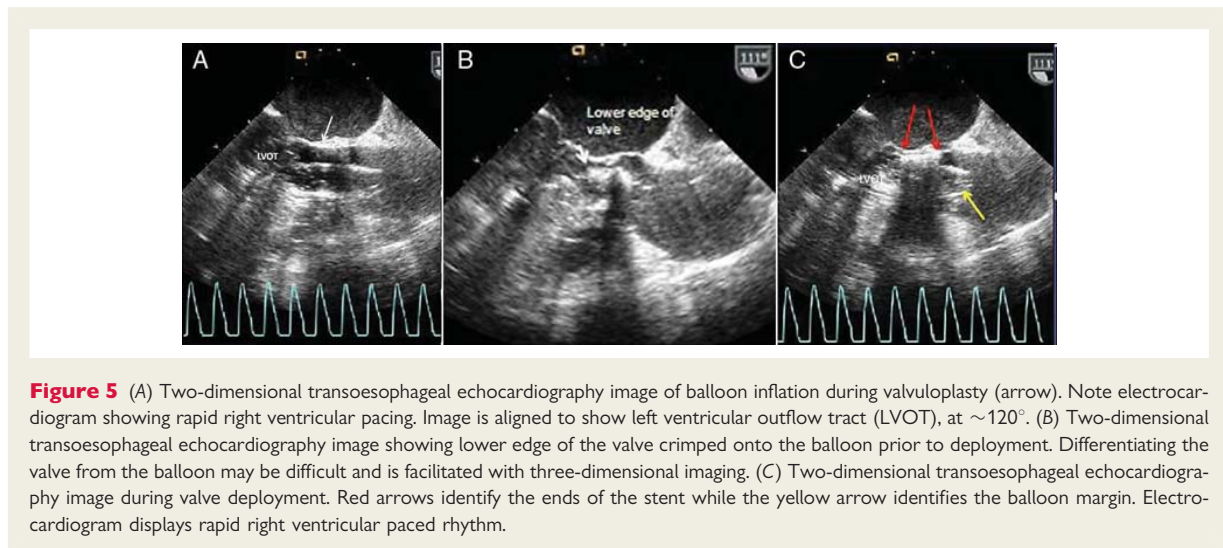


Figure 5 (A) Two-dimensional transoesophageal echocardiography image of balloon inflation during valvuloplasty (arrow). Note electrocardiogram showing rapid right ventricular pacing. Image is aligned to show left ventricular outflow tract (LVOT), at $\sim 120^\circ$. (B) Two-dimensional transoesophageal echocardiography image showing lower edge of the valve crimped onto the balloon prior to deployment. Differentiating the valve from the balloon may be difficult and is facilitated with three-dimensional imaging. (C) Two-dimensional transoesophageal echocardiography image during valve deployment. Red arrows identify the ends of the stent while the yellow arrow identifies the balloon margin. Electrocardiogram displays rapid right ventricular paced rhythm.

the aortic valve and is especially useful when the valve is not very calcified and, consequently, difficult to image on fluoroscopy. It may also help in the final decision-making concerning the appropriate valve size, because a valve with bulky calcification and small sinuses may require a smaller prosthesis than the annular dimension alone would suggest.

Although balloon inflation is normally performed during rapid right ventricular pacing to reduce cardiac output, the balloon may still migrate during inflation, particularly in patients with extensive subaortic septal hypertrophy or a small sinotubular junction. Loss of right ventricular capture and premature restoration of the native rhythm may also result in balloon migration. TEE may be used to confirm a stable position during inflation and to monitor the behaviour of the calcified aortic cusps during inflation as they are pushed back into the sinuses and towards the coronary ostia (Figure 5A)

During deployment of the prosthesis, TEE is very helpful in confirming the correct position of the valve and is usually used in conjunction with fluoroscopy for this purpose. In patients with limited native valve calcification or for valve-in-valve procedures where TAVI is used in the setting of another bioprosthesis, TEE may be the main technique used for guidance.

The optimal position for the Edwards SAPIEN™ valve is with the ventricular side of the prosthesis positioned 2–4 mm below the annulus in the LVOT. Examples of 2D TEE imaging during prosthesis positioning and deployment are shown in Figure 5B and C. Since the CoreValve™ has a different structure, the ventricular edge of the prosthesis should be placed 5–10 mm below the aortic valve annular plane. A normally positioned CoreValve™ is shown in Figure 6.

Immediately following deployment, TEE is used to confirm satisfactory positioning and function of the prosthesis (Figure 7A and B). This requires a combination of 2D imaging and Doppler evaluation with 3D also used if available. When the prosthesis is positioned too low, it may impinge on the mitral valve apparatus (Figure 8) or it may be difficult to stabilize in patients with marked subaortic septal hypertrophy. The native valve cusps may also fold over the

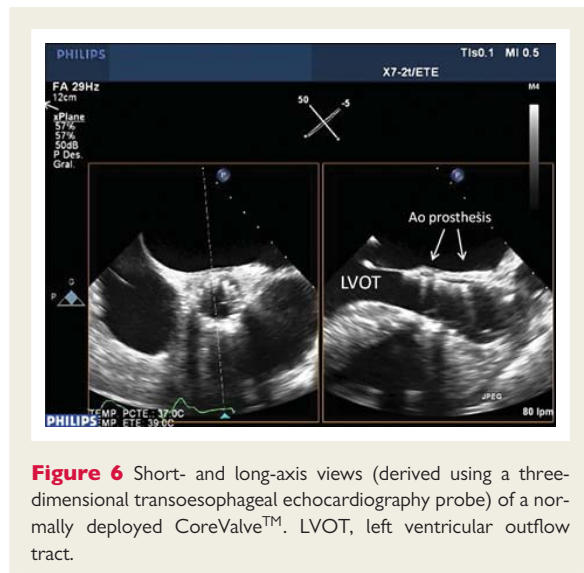


Figure 6 Short- and long-axis views (derived using a three-dimensional transoesophageal echocardiography probe) of a normally deployed CoreValve™. LVOT, left ventricular outflow tract.

top of the prosthesis and impede its function. If the prosthesis is implanted too high, it may migrate up the aorta, obstruct the coronary ostia, or be associated with significant PVR.

It is important to confirm that all the prosthetic cusps are moving well, that the valve stent has assumed a circular configuration (using 2D or 3D views), and that there is no significant valvular or PVR. Some regurgitation through the prosthesis will be common, whereas the delivery apparatus and/or guide wire remain across the valve and may persist, to a lesser degree, after their removal as it may take a few minutes post-implant for the leaflets to completely recover from being crimped for deployment. Until this occurs, the cusps may not coapt completely and mild valvular regurgitation may be transiently observed. Transgastric TEE views with continuous-wave, pulsed-wave, and colour Doppler should be used to confirm satisfactory prosthetic

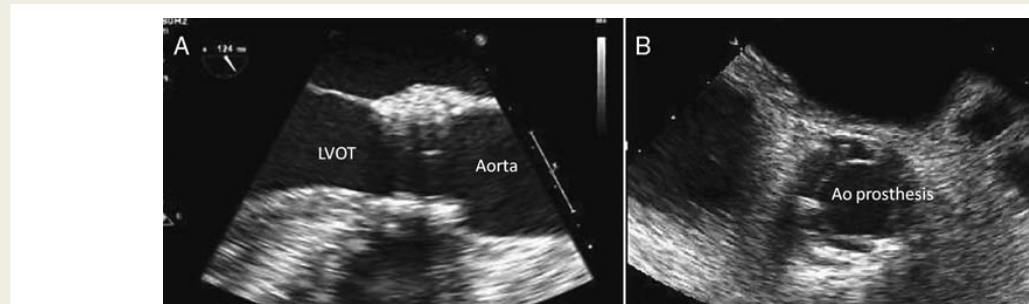


Figure 7 Two-dimensional transoesophageal echocardiography images showing an optimally implanted SAPIEN™ valve in (A) a diastolic long-axis view and (B) a systolic short-axis view, LVOT, left ventricular outflow tract.

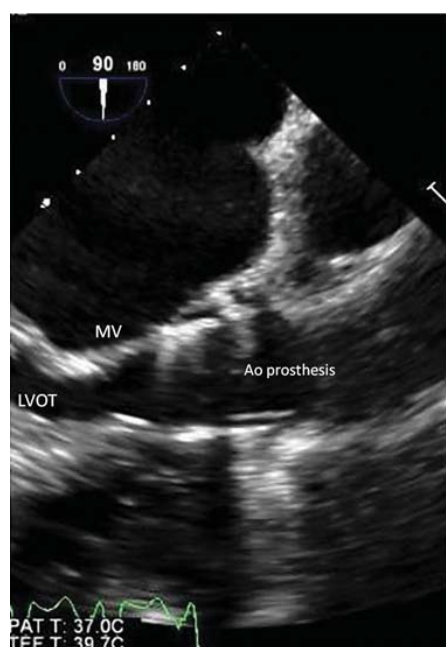


Figure 8 Two-dimensional transoesophageal echocardiography long-axis view of a SAPIEN™ valve that has been implanted too low. Note the position of the strut adjacent to the anterior mitral leaflet. LVOT, left ventricular outflow tract; MV, mitral valve.

functioning before the probe is finally removed. This window is essential to ensure that all regurgitant jets are detected (Figure 9).

PVR, not infrequently with multiple jets, is common following TAVI, though trace to mild and with a benign stable course in the majority of patients.³⁰ On the other hand, severe aortic regurgitation may occur as a consequence of incomplete expansion or incorrect positioning of the device, restricted cusp motion, or inappropriate prosthetic size.³¹ An undersized prosthesis is expected to be associated with paravalvular aortic regurgitation. In contrast, an oversized prosthesis may result in suboptimal stent expansion,

impaired cusp mobility, and central aortic regurgitation. Moreover, in the presence of severe asymmetric calcification of the native aortic valve, deficient (asymmetric) accommodation of the stent may occur, causing PVR of varying severity. The approach to assessing post-TAVI aortic regurgitation is discussed in detail in a later section. However, in the context of the immediate post-implantation assessment, conventional criteria including using colour jet dimensions, vena contracta, pressure half-time, and quantitative Doppler may all be helpful.^{32,33} Three-dimensional TEE is an additional tool to evaluate the early function of the bio-prosthesis and define the severity and precise location of paravalvular and/or central regurgitation.³⁴ Additionally, the patient's haemodynamic status and aortography may all help identify the patient with excessive regurgitation.

In the case of moderate paravalvular aortic regurgitation, supplementary balloon dilation can be performed. However, the risk of aortic rupture, cusp trauma, and over dilatation of the stent, all of which might worsen central aortic insufficiency, must be considered. Aortic regurgitation has also been reported as a consequence of residual native aortic valve leaflet tissue prolapsing into the prosthesis, interfering with cusp motion and coaptation. This may result from deficient containment of residual native aortic tissue by the prosthesis³⁵ and/or positioning the valve too low.

The extreme consequence of prosthesis mismatch (or failed pacing capture) is prosthetic embolism. If the embolization occurs towards the aorta, it might be resolved through successful transcatheter repositioning, but if it happens towards the LV, surgical removal is usually the only option.^{36,37}

During the procedure, the echocardiographer may be alerted to acute, severe hypotension. Possible explanations identifiable by TEE are cardiac tamponade secondary to wire perforation of the left or right ventricle, LV dysfunction, or severe aortic regurgitation. Left ventricular dysfunction with acute wall motion abnormalities may be secondary to ostial occlusion by fragment embolization or by an obstructive portion of the valve frame, sealing cuff, or native cusp.⁸ Although this complication may be fatal, successful management of ostial occlusions with percutaneous angioplasty or bypass surgery has been reported.³⁸

Another possible complication of TAVI is sudden worsening of MR. This may occur due to right ventricular pacing (LV asynchrony) or as a consequence of prosthetic misplacement with

pressure exerted on the anterior mitral leaflet from the ventricular edge of the prosthesis (Figures 10 and 11) or by direct damage or distortion of the subvalvular apparatus. The latter is more common with the antegrade apical approach, as the catheter might trap the subvalvular apparatus when passing through the LV towards the outflow tract. This may cause temporary or, in the case of chordal or leaflet rupture, permanent distortion and severe MR. Careful echocardiographic monitoring of the mitral valve during and after implantation can help avoid this complication.^{39,40}

Rarely, (frequency 0–4%),^{39,40} a tear or rupture of the aortic root may be observed during the procedure after balloon

valvuloplasty or prosthesis deployment, especially in the presence of extensive annular calcification or prosthesis oversizing.⁴¹ Inspection of the ascending aorta and aortic arch may also detect aortic cusp fragment embolization or atheroembolism. These complications, along with thrombo-embolism from catheters, air embolism, prolonged hypotension, or arch vessel dissection, may cause stroke which occurs with rates ranging from 0 to 10%.⁴⁰

Most of the peri-procedural complications just described may arise with either the SAPIEN™ valve or CoreValve™ (Table 1). However, because the CoreValve™ extends into the LV with close proximity of the skirt of the valve to the membranous septum where the atrioventricular (AV) node is located, conduction abnormalities are more common with the CoreValve™ than with the SAPIEN™ valve.⁴² Optimal deployment of the valve can decrease the risk of this complication. Additionally, the CoreValve™ can be repositioned during deployment and its format and larger length make stable positioning more independent of valvular calcification than the SAPIEN™ valve.

Three-dimensional echocardiography

A complete understanding of the 3D anatomy of the aortic and mitral valves by interventionalists and imagers has become the foundation for accurate placement of new transcatheter devices. Although 3D TTE imaging is undergoing dramatic improvements and the development of real-time 3D colour Doppler imaging will simplify quantification of valvular regurgitation, the current TTE technology plays a limited role in TAVI. Therefore, this section will focus on the utility of 3D TEE in TAVI.

Although 3D TEE may be helpful in distinguishing between tricuspid and bicuspid valves,⁴³ this is rarely an indication for 3D TEE. However, defining the aortic valve annulus is a particularly important aspect of pre-implantation TEE and an area where 3D can be extremely helpful. Piazza *et al.*²⁴ has described the AV complex as being composed of four rings: the virtual annulus, the anatomic annulus, the sinotubular junction, and a crown-like ring from the cusps. The anatomic annulus is located where the muscular arterial aortic root joins the myocardium of the septum anteriorly and the fibrous tissue of the mitral valve posteriorly. Two-thirds of the ring abuts the septum and one-third of the

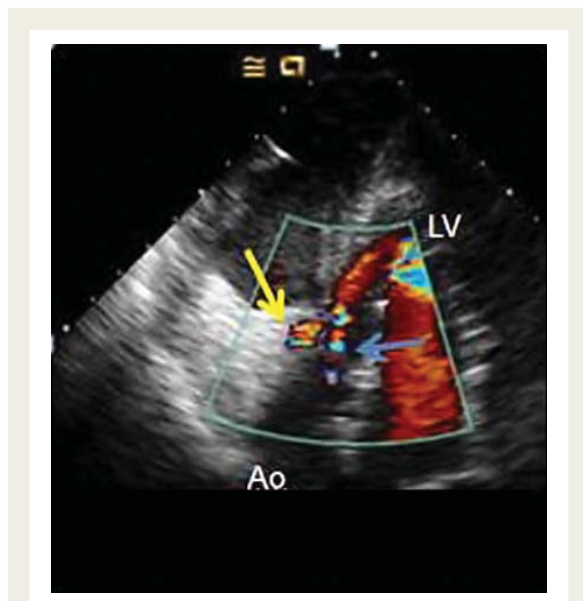


Figure 9 Deep transgastric transoesophageal echocardiography view of a newly implanted SAPIEN™ valve showing both paravalvular (yellow arrow) and valvular (blue arrow) regurgitation. Ao, aorta; LV, left ventricle.

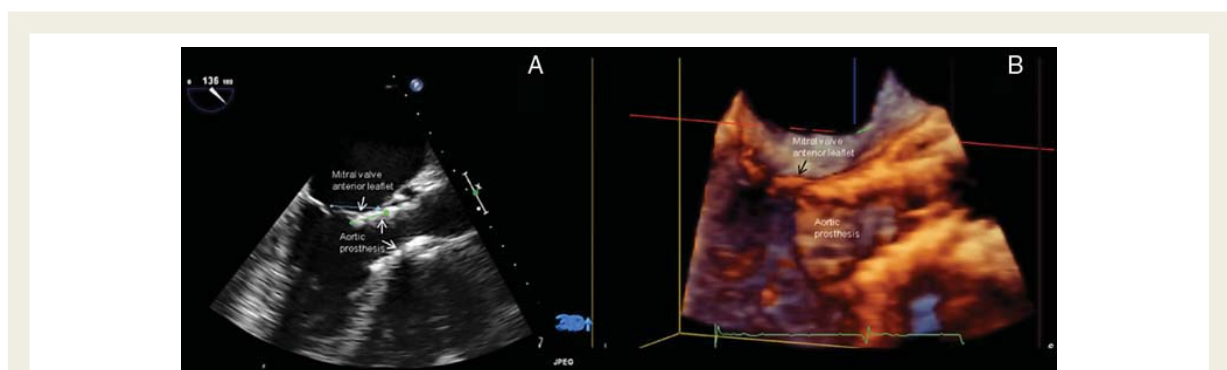


Figure 10 Two-dimensional (A) and three-dimensional transoesophageal echocardiography (B) images of a CoreValve™ which has been implanted low, distorting the anterior mitral leaflet and causing mitral regurgitation (data not shown).

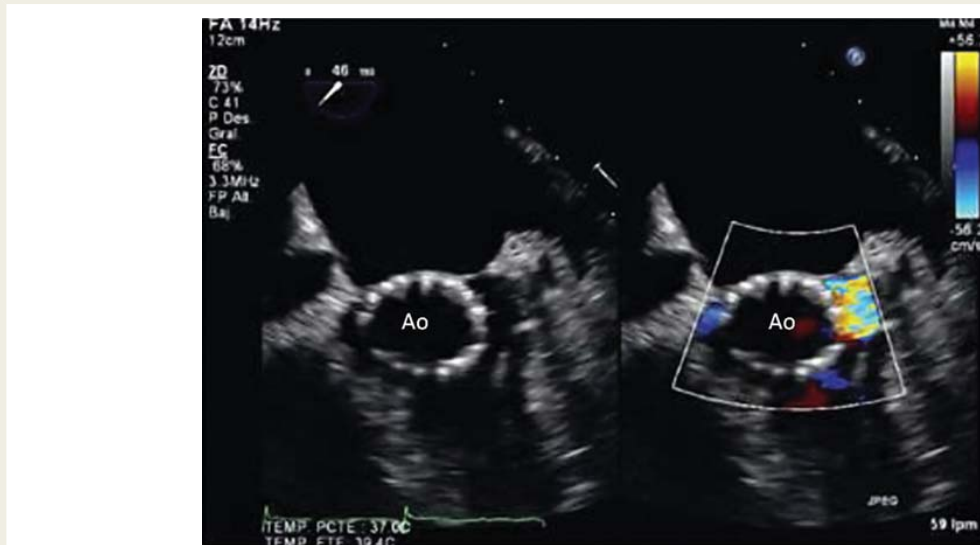


Figure 11 Two-dimensional transoesophageal echocardiography image of a CoreValve™ associated with paravalvular regurgitation. Ao, lumen of the aortic prosthesis. Reprinted with permission from Gonçalves *et al.*³⁴

Table 1 Peri-procedural complications of transcatheter aortic valve implantation assessable by echocardiography

Aortic prosthesis misplacement
Embolization towards the aorta or left ventricle
Deployed valve is positioned too high (towards the aorta) or too low (towards the mitral valve apparatus)
Aortic regurgitation
Central
Paravalvular
Mitral regurgitation
Aortic prosthesis impinges on the anterior mitral leaflet
Left ventricle asynchrony caused by right ventricular pacing
Damage or distortion of the subvalvular mitral apparatus by delivery system
New left ventricular wall motion abnormalities
Acute coronary ostial occlusion
Cardiac tamponade
Perforation of the left or right ventricle
Dissection or rupture of the aortic root

ring the anterior mitral valve (*Figure 12*). What we measure as the AV annulus is the virtual ring which is also the hinge point of the AV cusps. Because the AV typically has three equal cusps, bisecting the aortic annulus to measure the maximum diameter will typically result in an image where the immobile, calcified right coronary cusp is anterior and the commissure between the left and non-coronary cusps is posterior. As shown in *Figure 13*, the orientation of the typical 2D parasternal long-axis view that

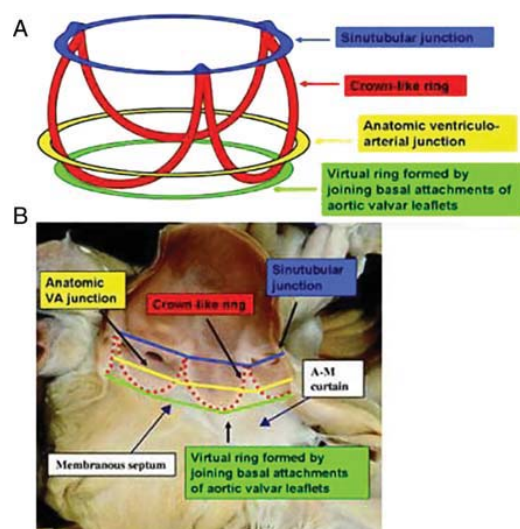


Figure 12 Schematic showing three-dimensional structure of a native aortic valve. Reprinted with permission from Piazza *et al.*²⁴

displays the commissure between right and non-coronary cusps (red arrow) does not show the maximum diameter of the annulus (blue arrow). Three-dimensional TEE can be very useful in accurately sizing the annulus because aligning the short-axis view of the AV to present the true annulus allows the assessment of its circularity and the measurement of the maximum diameters (*Figure 14*).

Although 2D TEE is able to define the annular-ostial distance for the right coronary, measurement of the distance from the annulus to the left main coronary ostium requires 3D TEE as the left main coronary artery ostium lies in the coronal plane which cannot be acquired by standard 2D imaging. However, using 3D full-volume acquisition of the aortic valve and multiplanar reconstruction allows a rapid intra-procedural derivation of the coronal plane for measurement of the annulus-to-left main distance and for imaging the left coronary cusp length (Figure 15). In general, a distance of >10 mm is desirable for the 23 mm balloon-expandable valve and a distance of >11 mm is desirable for the 26 mm valve. This measurement is not necessary for the self-expanding prosthetic aortic valve.

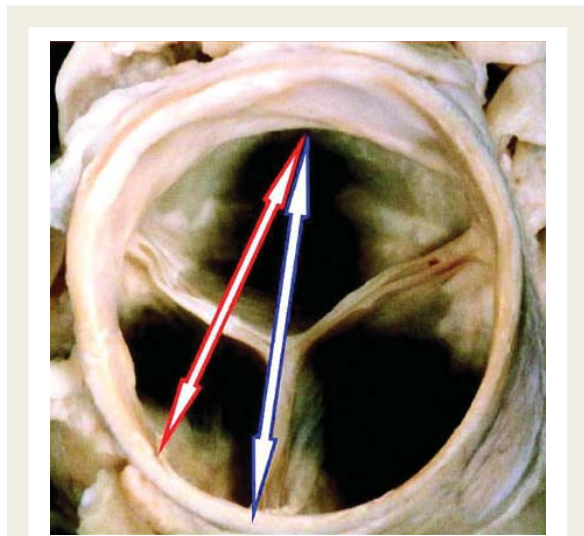


Figure 13 Anatomic short axis of the aortic valve illustrating the disparity between annular diameter as measured by the two-dimensional parasternal long-axis view (red arrow) vs. the true anatomic transverse diameter (blue arrow). Reprinted with permission from Piazza *et al.*²⁴

Live 3D (narrow sector) may also be useful when positioning the transcatheter valve across the annulus. Although the 2D TEE long-axis ($\sim 120^\circ$) view may be adequate for positioning, severe calcification of the AV and annulus, as well as dystrophic calcification of the anterior mitral leaflet, may cause significant acoustic shadowing of the transcatheter valve and make it difficult to distinguish the valve from the balloon. Live 3D imaging, however, increases the 'field of view' and frequently improves localization of the crimped valve margins within the aortic valve apparatus (Figure 16). The biplane view that provides complementary 2D planes is also very helpful in monitoring valve positioning and deployment (Figure 17).

Three-dimensional TEE is probably most useful immediately following valve deployment when the echocardiographer must rapidly and accurately assess the position and function of the valve including identifying the presence/severity of aortic regurgitation (Figures 18 and 19). Significant regurgitation may be an indication for repeat balloon inflation to attempt maximal expansion of the valve. Biplane colour Doppler imaging allows a rapid, accurate assessment of PVR from simultaneous long- and short-axis views. Finally, 3D colour Doppler volume sets obtained from deep gastric and/or mid-oesophageal views may allow direct planimetry of the regurgitant orifice(s).

Post-implantation follow-up

The echocardiographic follow-up evaluation of transcatheter valves is, in most ways, the same as that for surgically implanted prostheses as guided by previously published guidelines for prosthetic valves.³³ However, two areas provide challenges that are somewhat unique to transcatheter valves.

First is the calculation of effective orifice area or other indices of valve opening that are founded in the ratio of post- to pre-valvular velocities. Since there is flow acceleration within the transcatheter stents proximal to the valve cusps and then additional flow acceleration at the level of the cusps, it is essential that the pre-valvular velocity be recorded proximal to the stent and the post-valvular velocity (typically recorded with continuous-wave Doppler) reflect that distal to the stented valve. If the LVOT velocity used in calculations is erroneously recorded within the stent but

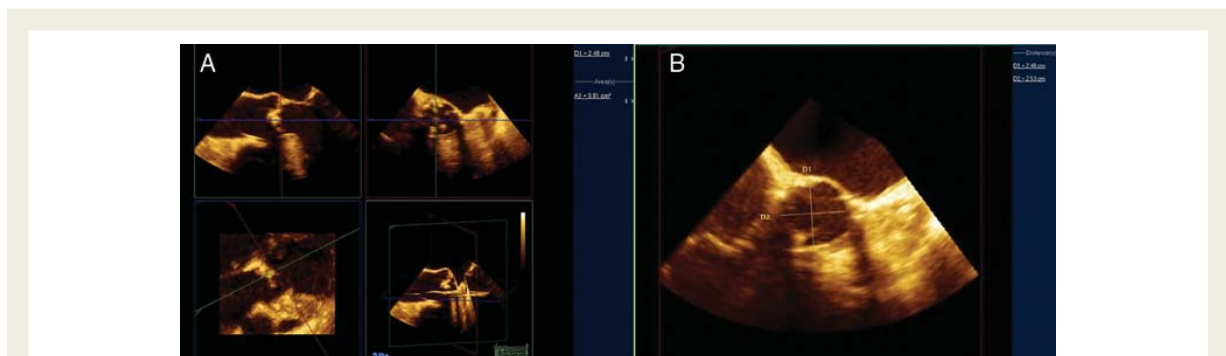
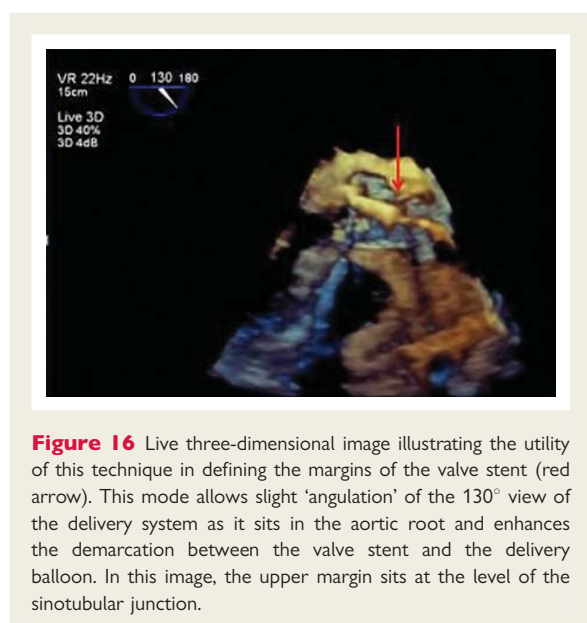
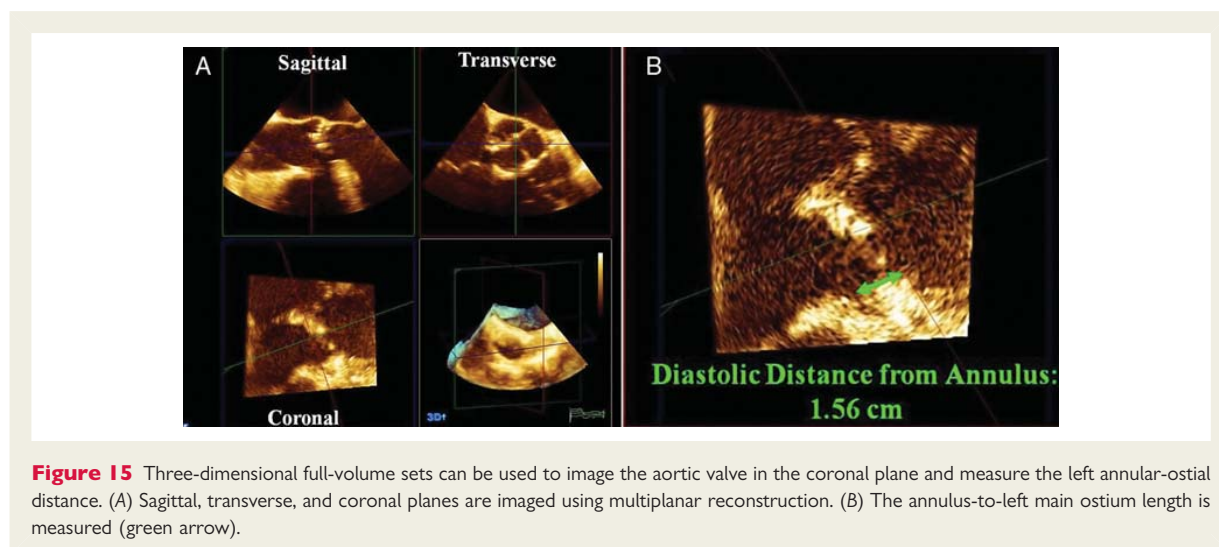


Figure 14 Three-dimensional transoesophageal echocardiography provide an accurate assessment of the shape and maximum diameters of the aortic annulus. Note (A) that the red plane is positioned so that it provides an optimized on-axis view of the annulus (B).



proximal to the cusps, the result will be an overestimation of valve area.⁴⁴

A second area of difficulty arises with the accurate quantification of aortic regurgitation which may consist of central and PVR, the latter not infrequently including multiple small jets. Accurate assessment of the severity of post-TAVI aortic regurgitation is difficult in the absence of validated methods to quantify PVR. Qualitative methods for assessing native valvular regurgitation have been well described⁴⁵ and can be applied to the assessment of prosthetic valve regurgitation.³³ Colour-flow Doppler is most commonly used to assess the regurgitant jet size. The length of the jet is an unreliable indicator of severity and the proximal jet width or cross-sectional area of the jet beneath the prosthesis (within the LVOT) is preferred for central jets. Although colour-flow Doppler

assessment typically relies on visual estimates of severity, the guidelines suggest using the following criteria for jet width based on the %LVOT diameter occupied: $\leq 25\%$ suggests mild, 26–64% suggests moderate, and $> 65\%$ suggests severe. These methods are limited in the setting of paravalvular jets which are frequently eccentric and irregular in shape.

The size of the jet vena contracta is an estimate of the effective regurgitant orifice area (EROA) and, as such, is a more robust estimate of regurgitant severity. Unfortunately, in the setting of prostheses, portions of the sewing ring may not be imaged due to acoustic shadowing. In addition, there has been no validation for adding the vena contracta widths of multiple jets as may be encountered post-TAVI. The ASE/EAE guidelines³³ suggest that for paravalvular jets, the proportion of the circumference of the sewing ring occupied by the jet gives a semi-quantitative guide to severity: $< 10\%$ of the sewing ring suggests mild, 10–20% suggests moderate, and $> 20\%$ suggests severe. However, this assumes continuity of the jet which may not be the case for transcatheter valves and therefore may overestimate the severity when there are multiple small jets. This approach also does not consider that the radial extent of paravalvular jets may vary and in the case of transcatheter valves may be very small. Attempting to add the degrees of involvement when jets are small is equally challenging.

Quantitative methods for calculating regurgitant volume and EROA rely on the comparison of stroke volumes across the aortic valve (representing total stroke volume) and a non-regurgitant valve (either mitral or pulmonary) and can be used for prosthetic valves.³³ Although total stroke volume (regurgitant and forward volumes) can be measured by subtracting LV end-systolic volume from end-diastolic volume, the more common method is to calculate the stroke volume across the LVOT. Three-dimensional echocardiography may become the method of choice for assessing aortic regurgitant volume and EROA. Validation of this technology for quantitating native aortic regurgitation is growing,⁴⁶ although the utility of 3D echocardiography for the assessment of prosthetic regurgitation has yet to be determined.

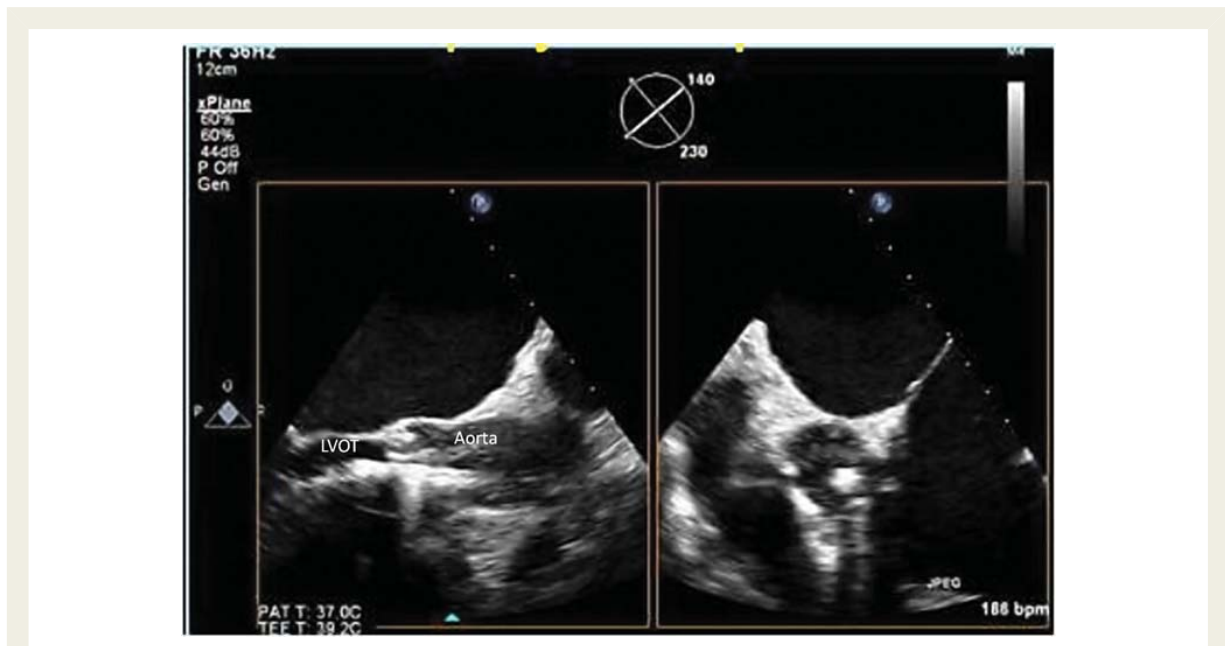


Figure 17 Simultaneous biplane images made possible with three-dimensional transoesophageal echocardiography probes show valve positioning across the native valve in long and short axis. LVOT, left ventricular outflow tract.



Figure 18 Normal three-dimensional transoesophageal echocardiography diastolic short-axis image of a SAPIEN™ valve.

Secondary signs supporting the diagnosis of significant prosthetic regurgitation include excessive rocking of the prosthesis (associated with >40% dehiscence), a short pressure half-time of the continuous-wave Doppler signal of aortic regurgitation, a dense spectral display, or diastolic flow reversal in the descending aorta (pulsed-wave Doppler from the suprasternal notch) and/or abdominal aorta (subcostal view). Sometimes, however, it remains impossible to be confident about whether aortic prosthetic regurgitation is moderate or severe and a comprehensive integrated approach must always be used.



Figure 19 Three-dimensional diastolic colour Doppler image revealing valvular aortic regurgitation following SAPIEN™ valve implantation. LVOT, left ventricular outflow tract.

Future directions

Despite the success and rapid technical advances of transcatheter AVR procedures,^{47,48} limitations remain. In addition to the SAPIEN™ and CoreValve™ valves that are currently available, other new valve and deployment systems are in development.⁴⁹ The future holds much promise, requiring alternatives for patients with difficult vascular access, expansion of target patient

populations, more accurate prosthesis deployment, and establishment of long-term prosthetic durability.

The future of TAVI will also include imaging improvements. Currently, it is challenging to place echocardiographers and echocardiography machines in a position that allows free movement of fluoroscopy cameras, ensures patient access by interventionalists, surgeons, and anaesthesiologists, and minimizes radiation exposure to the echocardiographers. Integrated, small imaging consoles would be helpful as would be improved intracardiac ultrasound devices, ideally with 3D capability, that might ultimately reduce the need for TEE.

Percutaneous transcatheter repair of paravalvular regurgitation

Introduction

PVR after surgical valve replacement is typically associated with dehiscence of sutures and may result from infection, annular calcification, friable/weak tissue at the site of suturing, or technical factors at the time of implantation. Most commonly encountered with mitral prostheses, paravalvular leaks may be associated with haemodynamically significant regurgitation causing heart failure and/or haemolysis. Because reoperation for PVR is associated with an increased likelihood of a recurrent leak as well as surgical morbidity and mortality, transcatheter closure is appealing.

Transcatheter closure of paravalvular leaks was first reported in 2003 using a ductal coil.⁵⁰ Since then, various devices, including the Rashkind umbrella, the CardioSeal device, Amplatzer septal occluder, and Amplatzer duct occluder, have been used with varying degrees of success.⁵¹ More recently, devices specifically designed for the treatment of PVR have been developed.⁵² Although there has been growth in these procedures, successful closure is limited by the anatomy of the defects which tend to be irregular and may be multiple, technical challenges in positioning closure devices and the limitations of available devices and imaging modalities. Finally, even small haemodynamically insignificant residual defects may cause clinically significant haemolysis so that device closure may be a haemodynamic success but an overall medical failure. Despite the associated technical challenges, the use of multiple smaller devices may be preferable to a single large device and the concept of implantation of a device at the time of surgical implantation (for example when exuberant annular calcification limits suturing) has been introduced.

Echocardiography has proven essential in paravalvular leak closure with both TEE and intracardiac echocardiography (ICE)⁵³ used to guide these procedures. Three-dimensional TEE^{54–56} is now considered the preferred TEE imaging modality as it is uniquely capable of demonstrating the irregular (frequently crescentic) shape of the defects and is better able to identify multiple defects and provide accurate sizing.

Echocardiographic evaluation of paravalvular regurgitation

The approach to assessing prosthetic PVR is similar to that used for native valve regurgitation but is technically more demanding

and limited by artefacts from the highly reflective components of the prosthetic valve that can mask part or all of a regurgitant jet. This is particularly problematic when TTE is used to evaluate mechanical mitral prostheses. With TEE, the left atrium becomes the near-field chamber and MR can be more readily assessed. Patients with aortic prosthetic valves can usually be adequately assessed by TTE because the aortic prosthesis does not obscure aortic regurgitation to the same extent. However, even in this setting, TEE should be considered because it provides high-quality images and allows for a more precise determination of the location and severity of PVR.^{33,57,58}

In assessing PVR in mitral prostheses, the actual area of dehiscence can be detected by TEE as an area of echo drop-out outside the sewing ring (Figure 20A). This must be confirmed by the presence of the paravalvular regurgitant jet on colour-flow imaging.³³ In order to facilitate communication between the echocardiographer and the interventionalist, the location of the dehiscence is best described in relation to internal landmarks such as the left atrial appendage, aortic valve, and crux of the heart (Figure 21).

Colour-flow imaging is used to localize the paravalvular regurgitant jet as well as to assess the severity. Commonly used parameters of MR severity in this setting are jet width and jet area. Although the proximal isovelocity surface area (PISA) approach has not been validated in the setting of PVR, the presence of a large PISA shell is consistent with more severe regurgitation. The quantitative Doppler method is not suitable for assessing PVR since the prosthesis confounds the measurement of antegrade transvalvular flow. Pulsed Doppler assessment of the pulmonary vein pattern can be useful, and the detection of systolic retrograde flow is a specific sign of severe MR.³³

The entire sewing ring should be examined by meticulously sweeping the mitral prosthesis from 0° to 180°, quantitating the circumferential extent of dehiscence by noting the angle at which the jet(s) is(are) first detected to the point of disappearance. Multiple regurgitant jets can be identified by the presence of intervening areas where the attachment of the sewing ring is intact. Although not obtainable in all cases, the transgastric view with colour-flow imaging showing the valve ring in short axis should always be attempted because it provides an *en face* view of the entire circumference of the valve ring.

Real-time 3D TEE imaging is a major advance in the localization and quantification of paravalvular MR, because it can consistently provide an *en face* view of the mitral prosthesis allowing the accurate determination of the number and location(s) of areas of paravalvular dehiscence (Figure 22A). The location and orientation of the paravalvular regurgitant jets can be further delineated using 3D colour-flow imaging (Figure 23).^{57,59} Although 3D TEE may permit the planimetry of the regurgitant orifice(s), the resolution may be limited when the areas of dehiscence (and associated regurgitant orifices) are slit-like.

Assessment of aortic prosthetic PVR with 2D TEE is less consistently successful. The aortic prosthesis may not be imaged adequately due to distortion of the aortic valve plane that may occur in patients with aortic valve disease and a proper short-axis *en face* view of the aortic prosthesis may be difficult to obtain, particularly for mechanical valves. The anterior aspect of the valve ring, which is located in the far field, is frequently obscured by

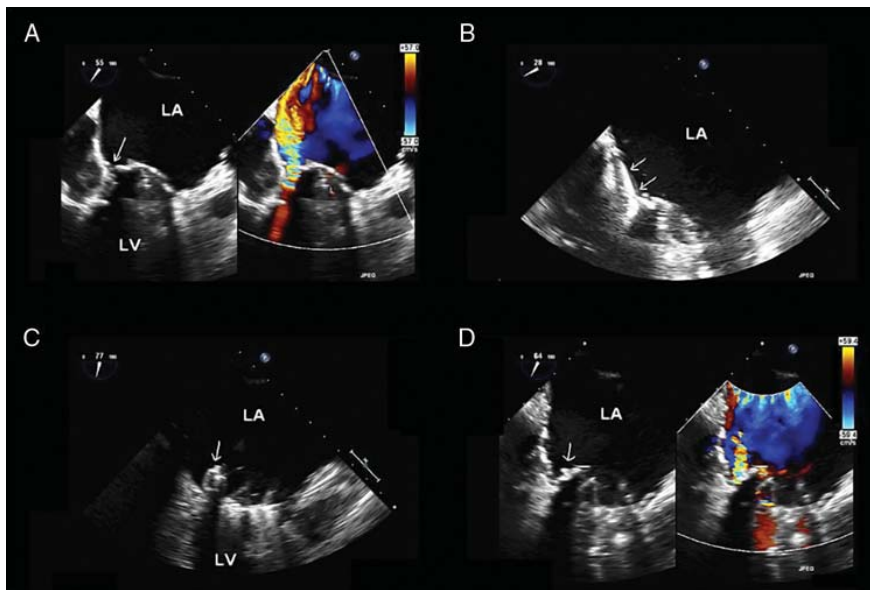


Figure 20 Two-dimensional transoesophageal views in a patient with a mechanical mitral bileaflet prosthetic valve and paravalvular regurgitation. (A) The area of dehiscence is visualized as a defect (arrow) at the posterior aspect of the valve ring with demonstration of paravalvular regurgitation by colour-flow imaging. (B) The guide wire (arrows) has been passed through the defect. (C) The closure device (arrow) is open. (D) The closure device is positioned securely in the defect and colour-flow imaging shows only mild residual paravalvular regurgitation. LA, left atrium; LV, left ventricle.

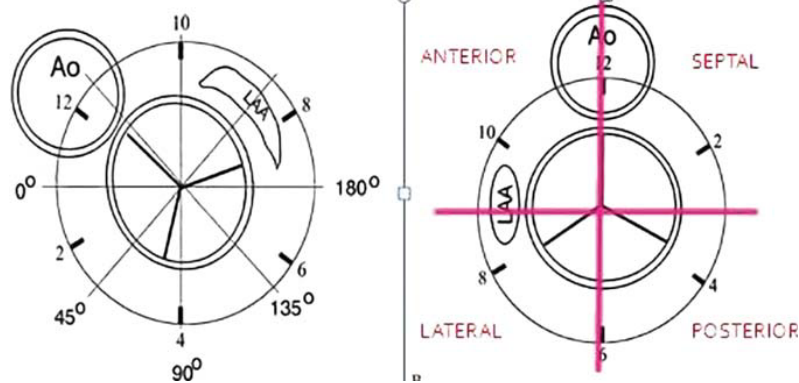


Figure 21 Schematic diagram for use in describing the location and extent of sites of paravalvular regurgitation using as main references the aorta (Ao) and the left atrial appendage (LAA). On the left is the echocardiographic view and on the right the anatomic view. Reprinted with permission from Luigi M.⁸⁰

reverberation artefact/acoustic shadowing from the posterior valve ring, such that anteriorly located PVR may be difficult to identify. These technical difficulties also limit 3D TEE imaging, which is not as helpful as in the setting of mitral prostheses. In addition to mid-oesophageal long- and short-axis views (Figure 24A and B), the transgastric view should be routinely attempted and a good display of the LVOT can be obtained by using a longitudinal imaging plane at about 100–120° with leftward flexion of the

transducer (Figure 24C). A zero-degree deep transgastric view with anteflexion and leftward angulation may also be helpful (Figure 24D). Paravalvular aortic regurgitation can usually be appreciated using these views, although the spatial resolution of images from this window may be inadequate to provide accurate localization of the paravalvular jet(s).

In assessing aortic prosthetic valves, the location of the coronary arteries should be routinely assessed. A coronary ostium low in

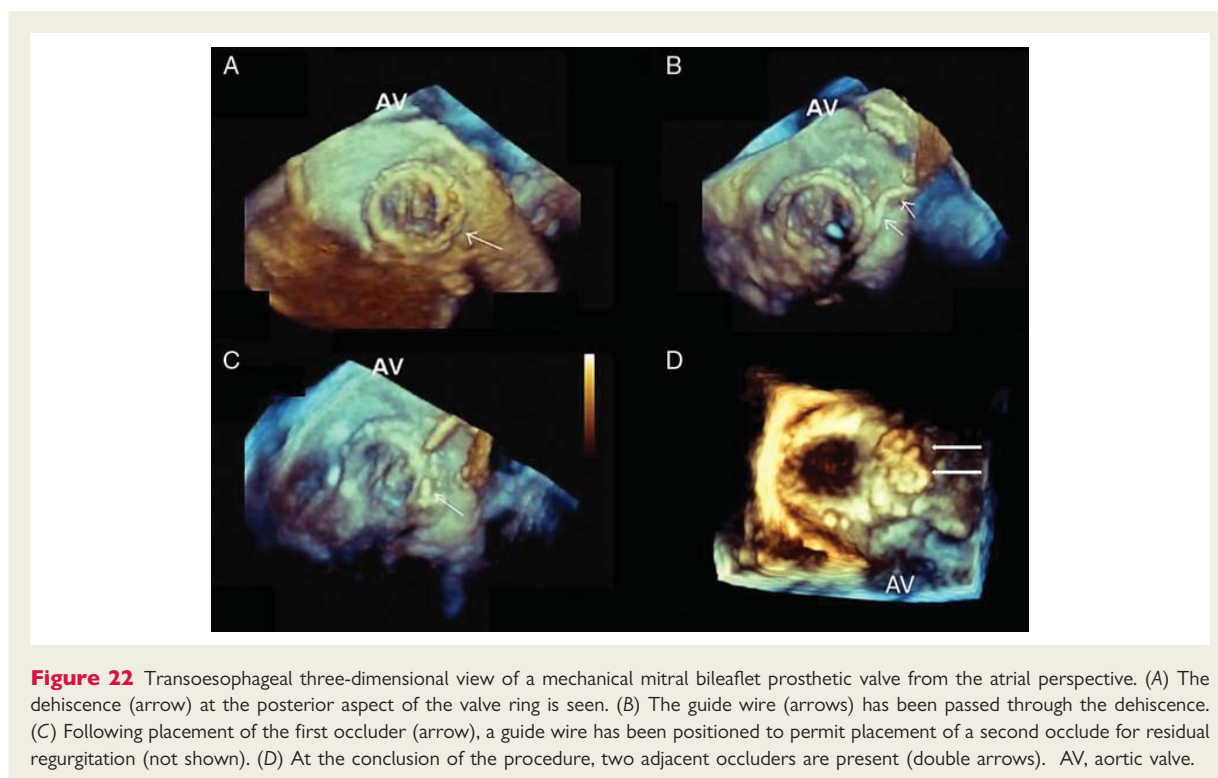


Figure 22 Transoesophageal three-dimensional view of a mechanical mitral bileaflet prosthetic valve from the atrial perspective. (A) The dehiscence (arrow) at the posterior aspect of the valve ring is seen. (B) The guide wire (arrows) has been passed through the dehiscence. (C) Following placement of the first occluder (arrow), a guide wire has been positioned to permit placement of a second occlude for residual regurgitation (not shown). (D) At the conclusion of the procedure, two adjacent occluders are present (double arrows). AV, aortic valve.

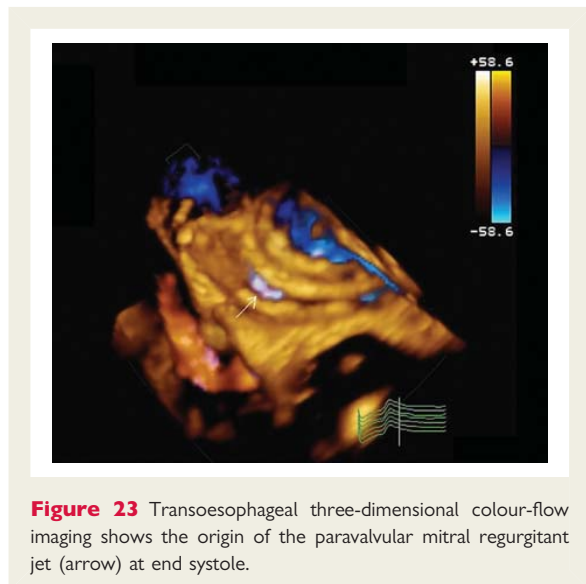


Figure 23 Transoesophageal three-dimensional colour-flow imaging shows the origin of the paravalvular mitral regurgitant jet (arrow) at end systole.

the aortic sinus close to the valve ring may pose a significant technical problem in transcatheter paravalvular leak closure and affect the choice of closure device.^{59,60} The left main ostium can usually be imaged with the transverse plane at the aortic sinus level with the aortic root in the short axis, although, as previously noted, measuring the annular-ostial distance requires 3D imaging. The proximal 1–2 cm of the right coronary artery can usually be

visualized by slowly sweeping the aortic sinus from the annulus to the sinotubular junction using the transverse plane at 0–45° or in the long-axis view of the aortic root (120°) where it is seen to leave the aorta at ~6 o'clock. The locations of the coronary ostia and orientation of the aortic sinuses (right coronary, left coronary, and non-coronary) serve as useful internal landmarks when communicating the location of the paravalvular jet(s) to the interventionalist. In addition to the jet width and jet area, a flow convergence area in the aortic root should be carefully sought. The presence of a clearly defined flow convergence not only pinpoints the location of dehiscence but also indicates that the regurgitation is significant.³³

Peri-procedural echocardiography during transcatheter repair of paravalvular regurgitation

Although there is some experience in performing aortic paravalvular leak closure with ICE, TEE is considered to be an integral part of transcatheter closure of PVR^{57,58,61–63} and has a role in the selection of appropriate patients, facilitation of the procedure, and assessment of the results (Table 2). Since most patients should already have had a comprehensive TEE before being accepted for the procedure, usually only a brief goal-oriented pre-procedure TEE is performed to confirm the location(s) and severity of PVR. A real-time 3D image using the zoom option can be acquired to provide the interventionalist with a display of the paravalvular defect, particularly in the mitral position.^{57,59} However, care must be taken to avoid misdiagnosing areas of echo

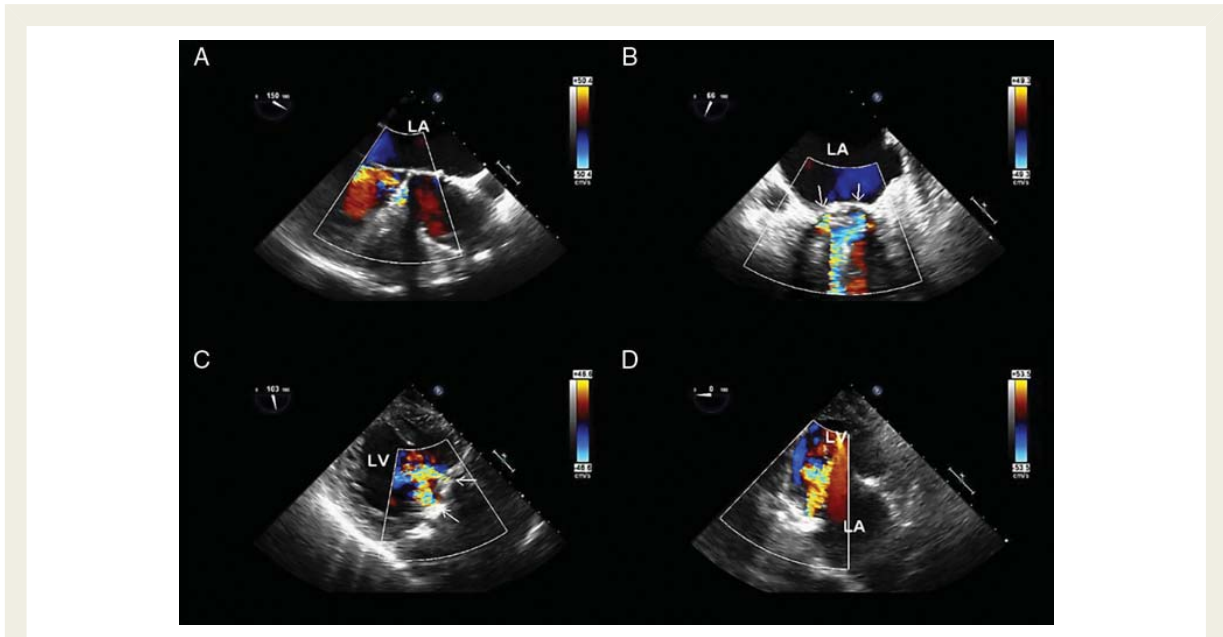


Figure 24 Transesophageal mid-oesophageal long- (A) and short-axis (B) views of an aortic mechanical bileaflet valve show two paravalvular aortic regurgitant jets (arrows), best seen in the short-axis view. The transgastric view with leftward flexion confirms the presence of the two jets (arrows) (C), but the deep transgastric view shows only one jet (D). LA, left atrium; LV, left ventricle.

Table 2 Role of peri-procedural transesophageal echocardiography in device closure for paravalvular regurgitation

Confirm location(s) and severity of paravalvular regurgitation
Exclude prosthetic and intracardiac thrombi or vegetations
Facilitate guide wire and catheter placement
Assess seating of the closure device
Ensure proper functioning of the prosthetic valve
Assess residual paravalvular regurgitation
Detect complications such as air embolism or tamponade

drop-out as paravalvular defects and confirmation with colour mapping should be performed. In addition, volume sets are needed to measure the areas of dehiscence for device sizing and to display the associated regurgitant jet(s). If the dehiscence is large (exceeding 25% of the circumference), a single device is unlikely to be sufficient. Additionally, when the defect is larger than 25% of the circumference, the prosthesis may rock and it may be inadvisable to proceed with device closure because of the high risk of device embolization.^{58,60} With small defects where closure may be contemplated to correct haemolysis, smaller and less bulky devices such as coils can be used for closure.^{57,58} Since anticoagulation may have been withheld in these patients, thrombus formation on the prosthetic valve or within the cardiac chambers should be excluded. The presence of intracardiac thrombus increases the risk of thrombo-embolic events during the procedure and mandates that the procedure be postponed.

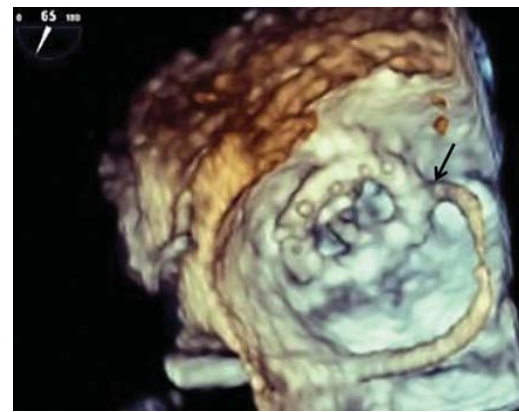
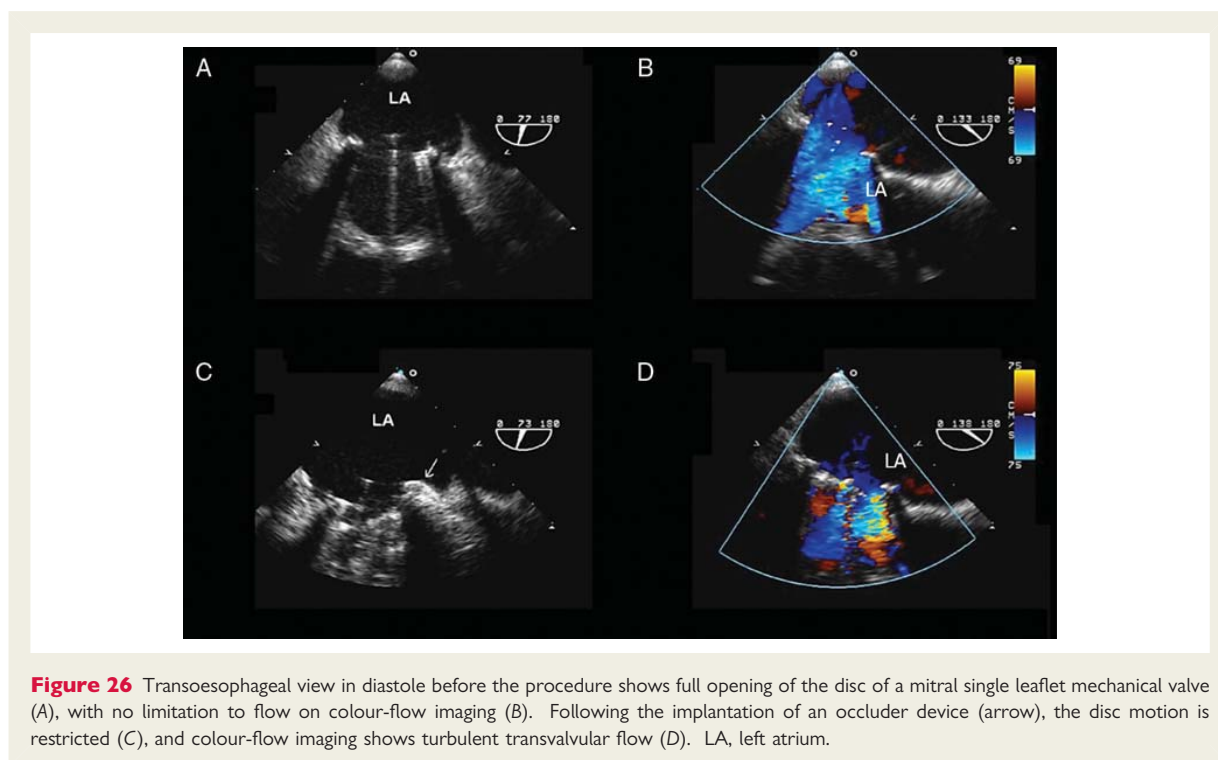


Figure 25 Real-time three-dimensional image from a left atrial perspective showing the path of the guide wire (arrow) as it passes through the interatrial septum (left), across the left atrium and through the paravalvular defect.

When the antegrade approach is used, TEE may be used to guide the transeptal puncture and help minimize the risk of inadvertent puncture of the aorta or atrial wall. TEE also can help guide the passage of the guide wire and catheter through the defect (Figure 20B). Real-time 3D TEE has been shown to be particularly helpful in this regard (Figure 22B and Figure 25). Injection of contrast has also been used to identify the position of the tip of the catheter in relation to the defect.⁵⁸ During deployment of the



closure device, TEE helps to ensure proper positioning of the opened occluder over the paravalvular defect and proper seating of the device (Figure 20C and D). Simultaneously, function of the prosthetic valve, particularly if this is a mechanical prosthesis, should be assessed to ensure that the occluder does not impede proper opening and closing of the prosthetic leaflets/discs (Figure 26). With mechanical prosthetic valves, fluoroscopy should also be used to assess the motion of the leaflet(s).^{58,62} The occluder device is not released until proper device seating and prosthetic valve function are assured. After release of the device, TEE is performed to assess residual PVR, which is not uncommon after the procedure (Figure 27D). If the residual regurgitation is severe, placement of additional devices can be considered (Figure 28). Other complications such as air embolism and haemopericardium can also be readily detected by TEE.^{57,58}

Percutaneous mitral valve intervention

Introduction

MR is an important cause of morbidity and mortality in developed countries.^{64,65} The most common causes of MR are degenerative and functional (ischaemic and non-ischaemic), with an age-related epidemiological burden consisting of a peak incidence in patients over 70 years of age.⁶⁴ Open surgical correction, using mitral valve repair or replacement, is currently accepted as the best available treatment of MR.²¹ However, there is a need for alternative treatment options. For example, a significant number of patients

with severe MR are denied surgery on the basis of age, LV dysfunction, and/or co-morbidities.⁶⁶ The survival rate of these non-operated patients is lower than that of those who undergo surgery. In addition, patients with less-than-severe MR that is uncorrected at the time of first cardiac surgery may develop significant MR over time and be denied reoperation on the basis of increased risk. In clinical practice, the presence of severe MR has favoured surgical over percutaneous revascularization in those with coronary artery disease, because of the need to perform concomitant mitral repair/replacement but access to transcatheter treatment of MR might permit simultaneous transcatheter revascularization and mitral repair as an alternative to surgery. Finally, some patients might need prophylactic MR correction in order to tolerate potentially high-risk therapies for non-cardiac disease. Thus, substantial efforts have been made to carry out less invasive mitral valve repair using various percutaneous strategies with the goals of decreasing morbidity and mortality and offering repair to patients at high risk for surgery.⁶⁷

As with surgical mitral repair, the echocardiographic assessment of mitral functional anatomy and the determination of the mechanism of MR are mandatory to select patients who can benefit from percutaneous intervention and to tailor the repair strategy. Both degenerative and functional/ischaemic MR can be suitable for percutaneous valve repair through a variety of approaches including those that offer direct leaflet repair, direct or indirect annular remodelling, and ventricular remodelling. Two-dimensional echocardiography supplemented by a real-time 3D imaging is also essential to guide and evaluate the effectiveness of the chosen percutaneous repair technique.

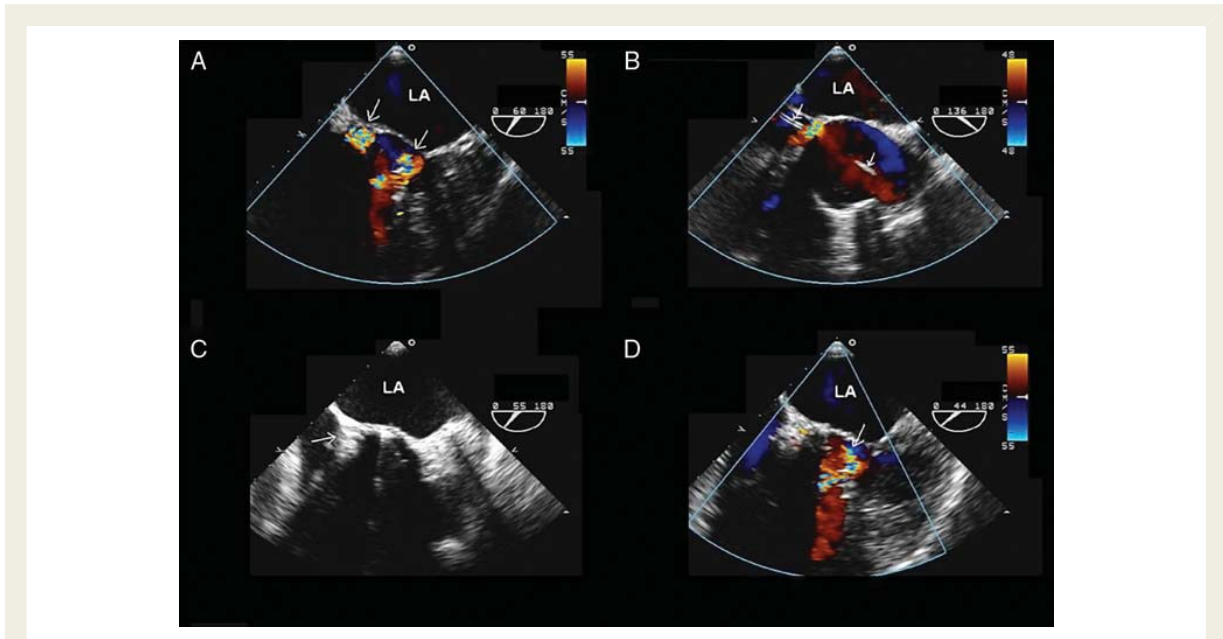


Figure 27 (A) Transoesophageal colour-flow imaging of an aortic mechanical bileaflet valve in short-axis shows two paravalvular regurgitant jets (arrows). (B) The guide wire (arrows) has been passed through the posterior dehisence. (C) The occluder device (arrow) is deployed. (D) The posterior paravalvular regurgitant is no longer present, but the anterior regurgitant jet is again detected. LA, left atrium.

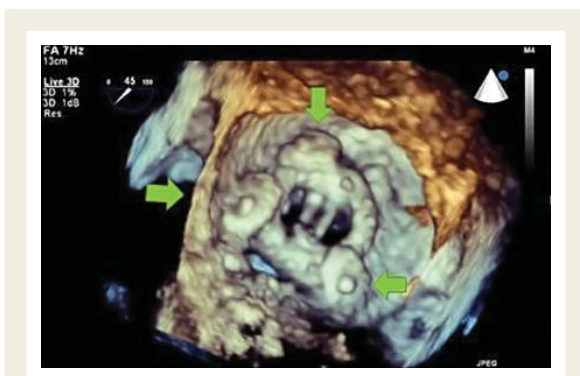


Figure 28 Three-dimensional transoesophageal echocardiography image from a left atrial perspective demonstrating three closure devices (arrows) surrounding a bileaflet mitral prosthesis.

Percutaneous therapies and current experience

Percutaneous repair techniques can be categorized into four general approaches, the majority patterned on surgical interventions:

- (i) Indirect annuloplasty-coronary sinus techniques
- (ii) Direct annuloplasty
- (iii) Leaflet repair
- (iv) Ventricular remodelling

Table 3 summarizes the clinical experience with available devices for percutaneous mitral valve repair. However, it should be noted that this is a rapidly changing field with the frequent introduction of new devices and withdrawal/redesign of existing devices. Thus, subsequent paragraphs will focus on general principles of echocardiographic evaluation of the mitral valve that are applicable to all devices with a detailed discussion of procedural echocardiography limited to the MitraClip™. This device has been most extensively evaluated and is, consequently, the only device with CE mark and the only device (while still investigational) that has completed pivotal trial evaluation and is available for compassionate use in the USA.

Percutaneous annuloplasty techniques

Percutaneous annuloplasty techniques mimic surgical annular remodelling in order to reverse mitral leaflet coaptation abnormalities and related MR. This approach is targeted to selected patients with functional/ischaemic MR and may be more effective when annular dilation/deformation is predominant. Based on surgical annuloplasty experience, common MR mechanisms that might be corrected by percutaneous annuloplasty include symmetrical leaflet tethering due to LV remodelling or leaflet coaptation loss arising from annular dilation. Hypothetically, patients with extreme asymmetrical tethering (especially when the posterior leaflet shows a tethering angle $\geq 45^\circ$) might not be suitable for percutaneous annuloplasty.⁶⁸ However, an analysis of treatment failures with individual devices using detailed 3D echocardiographic imaging will be essential to identify better the subset of patients for whom device therapy might be most suitable. MR arising from structural mitral valve abnormalities, including prolapse/flail

Table 3 Approaches to percutaneous mitral repair

Approach	Device	Manufacturer	Clinical experience
Coronary sinus annuloplasty ⁶⁹	MONARC CARILLON PTMA	Edward Lifesciences Cardiac Dimension Viacor	EVOLUTION I and II trials with core-lab evaluation ^a AMADEUS trial PTOLEMY trial
Direct annuloplasty ⁷⁰	QuantumCor Accucinch Percutaneous Annuloplasty System	QuantumCor Guided Delivery Mitralign	Pre-clinical testing Pre-clinical testing First-in-man cases performed
Ventricular remodelling ^{71,72,75}	iCoapsys	Myocor	First-in-man cases performed
Leaflet repair ⁷⁷	MitraClip Mobius	Evalve Edwards Lifesciences	EVEREST I–II trial with core-lab evaluation Clinical studies without core-lab evaluation

^aEVOLUTION II trial suspended.

for ruptured chordae tendinae, fibrotic or calcified leaflet restriction, or annular calcification, should not be considered for this procedure.

Indirect annuloplasty-coronary sinus techniques

Coronary sinus annuloplasty attempts to re-shape the anteroposterior annular dimension to correct the mitral leaflet apposition-coaptation abnormality underlying the MR. The rationale of this approach is based on the anatomical relationship between the coronary sinus/great cardiac vein and the posterior annulus. Several techniques (Table 3) have been proposed that involve placing a device within the coronary sinus/great cardiac vein to attempt septal-lateral diameter reduction and/or mitral annulus 'cinching'. To achieve therapeutic goals, transcatheter approaches should provide an appropriate degree of tension to reduce MR without slipping and fracturing. The variable distance between the coronary sinus and the mitral annulus, as demonstrated by CT studies, may affect procedural success. In some patients, the coronary sinus is located above the annular level in contact with the left atrial wall. Annular devices in these patients theoretically would cinch the left atrial wall without annular re-shaping and therefore might not reduce MR. An additional concern of indirect annuloplasty is the risk of coronary ischaemic events due to the close but variable relationship between the coronary sinus and the left circumflex artery.⁶⁹ Finally, these devices pose at least a theoretical risk of coronary sinus thrombosis or rupture.

Direct annuloplasty

Some devices have proposed to remodel the annulus using a direct ventricular approach. Approaches used, to date, have included collagen shrinkage through the application of radiofrequency,⁷⁰ and transventricular suture annuloplasty.

Mitral leaflet repair

Percutaneous mitral leaflet repair aims to reproduce surgical techniques of improving leaflet coaptation and reducing/eliminating MR. The tested edge-to-edge Alfieri surgical technique^{71,72} is mimicked by the percutaneous MitraClip™ system. Other experimental approaches, including chordal replacement or cutting, are currently under development.



Figure 29 MitraClip™ device for mitral repair. Arms of the device are in the open position.

The MitraClip™ system is a polyester fabric-covered cobalt-chromium implant with two arms which can be opened and closed with a steerable-guiding mechanism (Figure 29).

The MitraClip™ is easily imaged with TEE permitting reliable step-by-step procedural guidance as detailed below. Under general anaesthesia, an antegrade (transseptal) approach is used with the device aligned at the A2–P2 interface perpendicular to the commissure using a sophisticated guiding/positioning system and echocardiographic/fluoroscopic guidance. The device is deployed after successfully grasping the regurgitant target zone of the mitral leaflet. If needed, an additional clip may be placed to achieve satisfactory reduction in MR. The MitraClip™ system

is effective in selected patients with either degenerative or functional MR.

In degenerative MR, the percutaneous clip anchors the flail and/or prolapsed leaflet, whereas, in patients with functional MR, it improves coaptation of the tethered leaflet(s) to reduce the time and force required to close the valve. Additionally, the clip creates a tissue bridge between the two mitral leaflets. As a result, it limits annular dilatation and supports the durability of the repair. Finally, the clip restrains the LV wall by restricting LV dilatation and induces reverse LV remodelling, which, in patients with functional/ischaemic MR, may further reduce tethering and resultant regurgitation.

The procedure has been tested in the safety–feasibility EVEREST I trial that reported procedural success, defined as successful implant with reduced MR $\leq 2+$, in 79 of 107 (74%) patients.⁷³ All results were core-lab-adjudicated. The core-lab-adjudicated randomized controlled EVEREST II trial, comparing percutaneous vs. surgical repair, has recently been reported.⁷⁴ In the per-protocol analysis, MitraClip™ therapy was able to reduce MR in 72.4% of patients vs. 87.8% of patients treated surgically. The overall 30-day major adverse event rate (designed to show superiority) in the MitraClip™ arm was similar for both functional and degenerative MR patient subgroups, and both lower than the surgical control group. In addition, the MitraClip™ system demonstrated consistent results in both functional and degenerative MR patients with significant improvement at 1 year from baseline measures of heart function, symptoms, and quality of life, thus meeting the goal of the study to show non-inferiority to surgery. Other recent clinical experiences have been published, providing additional support to the EVEREST data. In a two-centre study, Tamburino *et al.*⁷⁵ reported 97% successful implantations in 31 high-risk patients with ischaemic or degenerative MR as defined by the EVEREST criteria. In a single-centre study of 51 subjects at high surgical risk, Franzen *et al.*⁷⁶ reported clinical improvement in 49 successfully implanted patients. However, unlike the EVEREST trials, neither of these studies had core-lab evaluation of MR.

Long-term observational studies are needed to confirm the stability of MitraClip™ implantation, sustained MR reduction, and clinical improvement.

Ventricular remodelling

Devices based on the concept of ventricular remodelling have been designed in recognition of the fact that abnormal ventricular geometry with displacement of the papillary muscles is an important element in the pathogenesis of functional MR. Although a surgical approach to ventricular remodelling as a treatment for functional MR (Coapsys™) has been evaluated in a core-lab-adjudicated trial and shown to have improved survival and fewer adverse events (although more MR) than the control surgical approach,⁷⁷ this and other ventricular remodelling devices remain experimental with meaningful extrapolation to transcatheter approaches yet to come.

Assessment of the functional anatomy of mitral valve for percutaneous repair

The mitral valve apparatus is a complex anatomic structure composed of the mitral annulus, two discrete leaflets (anterior and

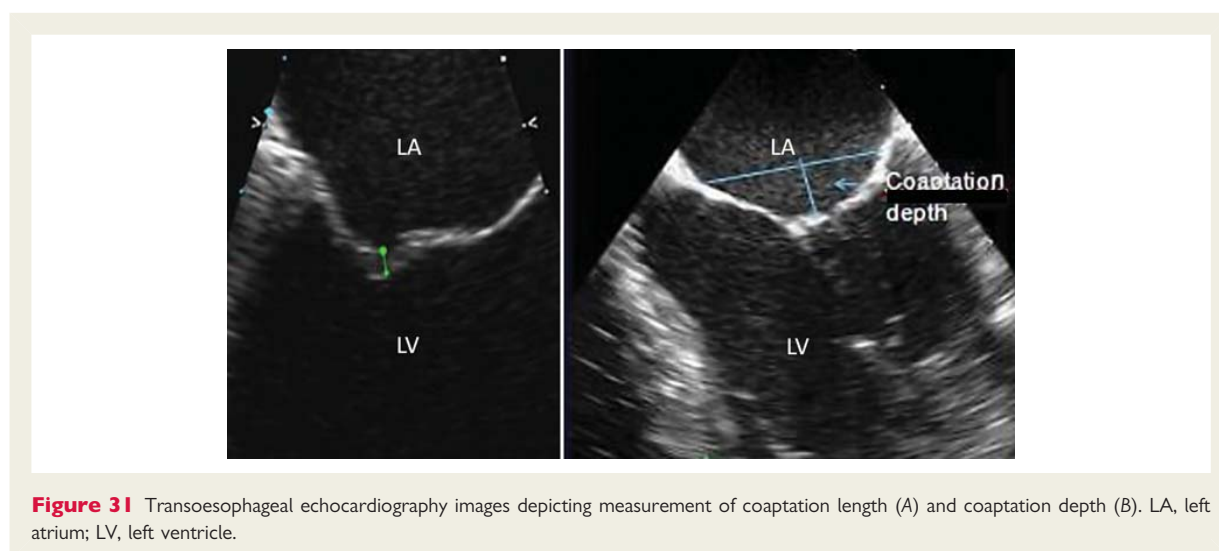
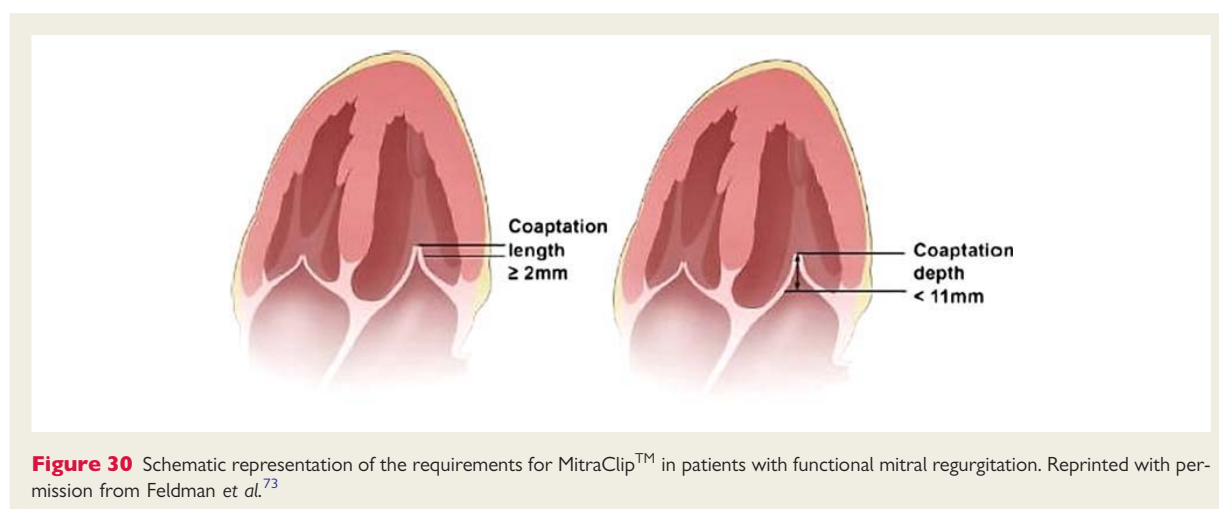
posterior), and chordae which attach both leaflets to anterolateral and posteromedial LV papillary muscles. Importantly, mitral geometry and function are also influenced by the geometry and function of the left atrium and LV. The posterior leaflet is further separated into three discrete, named scallops P1, P2, and P3 (from lateral to medial). Although the anterior mitral leaflet is typically not anatomically divided, its segments are named A1–A3 to mirror the segmentation of the opposing posterior leaflet scallops.

The mitral annulus is a complex saddle-shaped structure with peaks anteriorly and posteriorly, and nadirs medially and laterally. The anterior aspect of the mitral annulus is a rigid fibrous band that is shared with the aorta (aorto-mitral fibrosa or curtain), whereas the remaining medial, lateral, and posterior aspects are more vulnerable to remodelling and distortion of shape.

MR may occur due to diverse clinical and anatomic processes. The pathophysiological triad, a concept first described by Carpentier, separates the 'disease' that produces a mitral valve lesion, from the resulting 'anatomic lesion' that ensues from that disease, and the subsequent 'type of valve dysfunction' that results. Furthermore, Carpentier classified MR into three basic but distinct types of valve dysfunction. Type I dysfunction is characterized by normal mitral leaflet motion and is typically seen in atrial fibrillation with atrial and mitral annular dilation, as well as in endocarditis with valve perforation. Type II dysfunction is characterized by excessive systolic leaflet motion and is seen in degenerative mitral valve disease with prolapse and/or flail of the mitral leaflets. Type IIIa dysfunction is characterized by reduced leaflet motion in both systole and diastole as is seen in rheumatic mitral disease and Type IIIb dysfunction is characterized by reduced systolic leaflet motion, as is typically seen in patients with dilated cardiomyopathy or MR due to ischaemic LV remodelling.

Considerations for edge-to-edge repair

Percutaneous edge-to-edge repair may be accomplished with an implantable clip MitraClip™ that approximates the middle scallops of the mitral valve, creating a double orifice mitral valve. As such, the predominant mechanism of MR must originate from the central mitral scallops, A2 and P2. The guidelines for selection of patients for MitraClip™ mirror the selection criteria used in the two EVEREST trials. Patients with degenerative MR (Carpentier Type II dysfunction) with either prolapse or flail of the A2 and/or P2 scallops are candidates for the MitraClip™, and in EVEREST II, represented approximately two-thirds of those evaluated. Similarly, patients with functional MR, either due to dilated cardiomyopathy or ischaemic LV remodelling, are also candidates provided the dominant MR jet arises from A2 to P2. In EVEREST II, these patients accounted for one-third of those enrolled. In EVEREST II, patients with significant MR originating from the medial or lateral aspects of the valve were excluded, as were those with rheumatic disease, endocarditis, and a mitral valve area of $<4 \text{ cm}^2$. Relative contraindications also include abnormal thickness of the leaflets or calcification that would impede grasping by the device arms. Additional functional anatomic exclusions for percutaneous MitraClip™ repair exist. In patients with functional MR, those with a coapting surface length $<2 \text{ mm}$ and/or a coaptation depth of $>11 \text{ mm}$ are excluded. In patients with degenerative



MR, those with a flail height of >10 mm and a flail width of >15 mm are excluded (Figures 30–33).

Echocardiography for edge-to-edge clip repair

Patient selection

At present, patient selection involves a consensus between the patients and treating physicians as well as agreement that the patient is anatomically eligible based on TTE and TEE findings.

Clinical indications include:

- (i) Patients who are at high risk for surgery (excessive comorbidity). This may include patients with advanced chronic obstructive airway disease, renal failure, diabetes mellitus, etc.
- (ii) Patients with previous cardiac surgery for whom any re-do operation increases the peri-operative risk. This includes patients with functional MR after CABG surgery.
- (iii) Patients who decline surgery.

In addition to confirming the presence of 3–4+ MR using the combined approach recommended by ASE/EAE guidelines,⁴⁵ echocardiography is used to determine anatomic suitability for the device. TTE is typically used as an initial screen but TEE, ideally with 3D, is necessary to confirm eligibility.

For patients with functional MR, there needs to be sufficient leaflet tissue for mechanical coaptation. This is evaluated by TEE from the four-chamber view by measuring the coaptation length and depth. As previously noted, for optimal results, coaptation length must be ≥ 2 mm and coaptation depth ≤ 11 mm (Figure 30). Although an initial assessment may be performed with TTE, these parameters, particularly coaptation length, typically require TEE for precise measurement (Figure 31).

For patients with flail mitral valves, the TEE view should be aligned to demonstrate the maximal excursion of the flail segment [typically mid-oesophageal zero degree angulated to show the A2–P2 scallops and/or the long-axis view of the LVOT

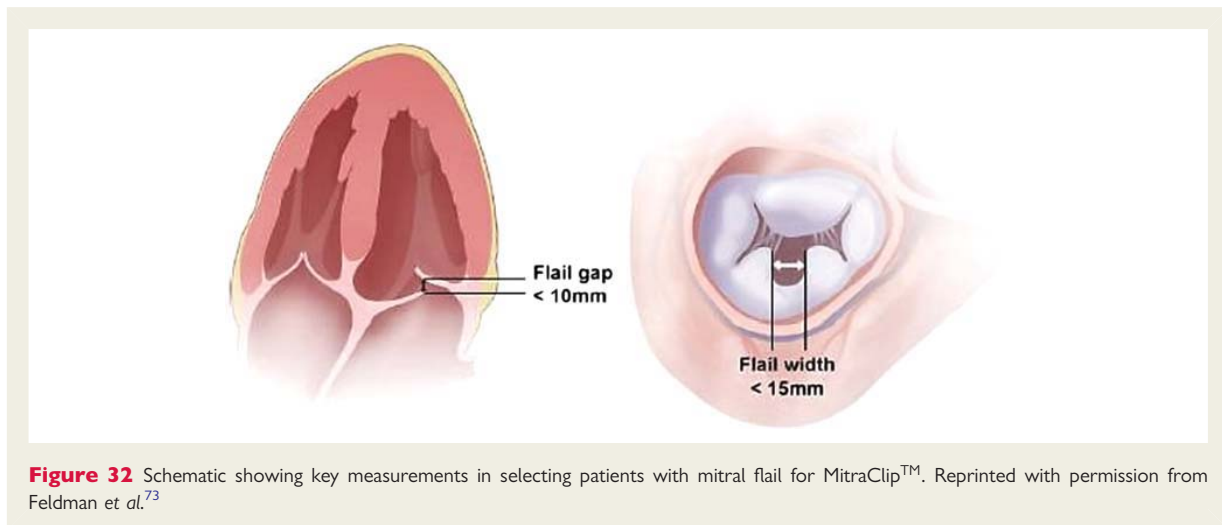


Figure 32 Schematic showing key measurements in selecting patients with mitral flail for MitraClip™. Reprinted with permission from Feldman et al.⁷³

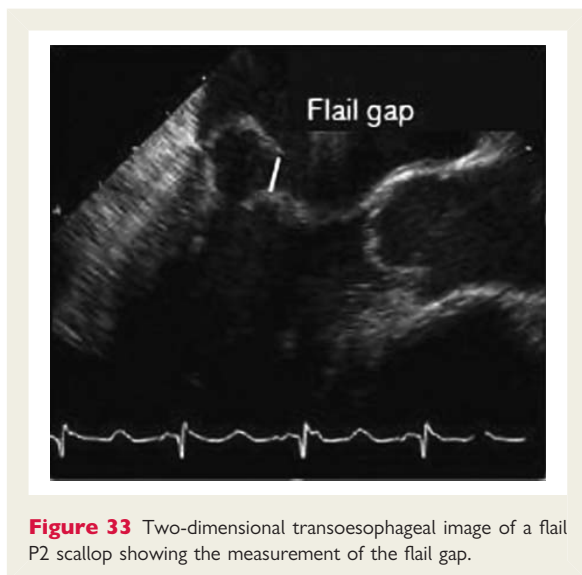


Figure 33 Two-dimensional transoesophageal image of a flail P2 scallop showing the measurement of the flail gap.

(100–160°) that also shows these scallops]. The inter-commissural view (55–75°) may also be helpful. The distance separating the tip of the flail segment from its opposing normally coapting leaflet is termed as the flail gap. Leaflet grasping is facilitated when this distance is <10 mm (Figures 32 and 33). This measurement is readily accomplished with 2D TEE.

Although 3D TEE provides the clearest delineation of the involved segment with *en face* views from the left atrial perspective, 3D quantitation is limited since there is no calibration of these views. However, adequate sizing can be achieved using the inter-commissural 2D view with complementary information available in some patients using the transgastric short-axis view of the valve. The flail/prolapse width should be <15 mm.

TTE ± TEE will also identify patients whose regurgitation is on the basis of rheumatic disease or endocarditis or who have other anatomic exclusions as described previously.

Peri-procedural echocardiography

Echocardiography is the primary imaging modality used at all stages of the percutaneous mitral clip procedure, complementing fluoroscopy.⁷⁸

Transseptal catheterization

During the transseptal puncture, TEE is helpful in guiding precise positioning of the transseptal catheter, first in puncturing the atrial septum and second in positioning the MitraClip™ guiding catheter. The primary views are the mid-oesophageal short-axis view (30–60°) and bicaval 90° view at the level of the aortic valve. These can be simultaneously displayed with biplane imaging using 3D probes. The transseptal puncture should be performed through the posterior-mid aspect of the fossa in a posterior and superior direction. This is to facilitate the ultimate positioning of the clip delivery system. During transseptal puncture, TEE identifies the position of the needle tip by detecting the tenting it creates on the adjacent septum rather than on the basis of directly imaging the needle tip. The puncture site should sit 3.5–4.0 cm above the leaflets. If the position of the catheter is suboptimal, the needle may be repositioned prior to puncturing the septum.

Advancing the clip delivery system towards the mitral leaflets

Once the correct transseptal puncture has been made, the mitral clip delivery system is angled down towards the mitral leaflets, aiming for A2–P2. Correct positioning can be ascertained from the inter-commissural (55–75°) projection demonstrating medial–lateral alignment and the LV outflow (100–160°) projection demonstrating posterior–anterior alignment. Three-dimensional TEE (3D zoom with a large field of view) greatly facilitates this part of the procedure as it provides an *en face* view of the mitral leaflets and approaching clip (Figure 34).

Positioning the clip above the regurgitant orifice and orientation of the clip arms

The optimal position of the clip delivery system is immediately above the regurgitant orifice, which will be the target of the clip. The target orifice is chosen using the maximal PISA effect. The clip should be oriented perpendicular to the commissure, something easily assessed with 3D zoom imaging. However, if 3D is not available, the transgastric short-axis view may be used for this purpose.

Entry into the left ventricle and pull-back to grasp the leaflets

As viewed from the LVOT position (100–160°), the clip with the arms closed will cross the mitral leaflets and enter the LV. Here, 3D echo (or alternatively the transgastric short-axis view)

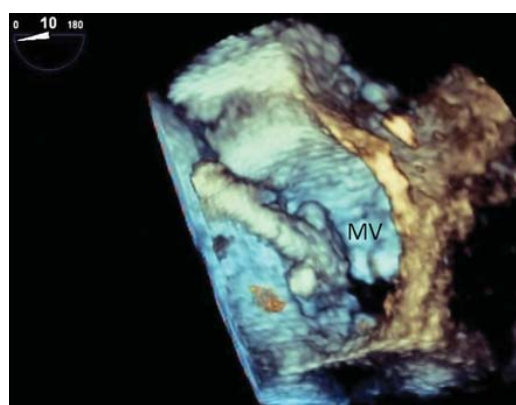


Figure 34 Three-dimensional transoesophageal echocardiography image from the left atrial perspective showing the MitraClip™ delivery system directed towards the mitral orifice. Real-time three-dimensional imaging greatly facilitates the process of ensuring that the clip is appropriately directed/aligned. MV, mitral valve.

permits a rapid check that the arms of the mitral clip device are still perpendicular to the line of coaptation as the delivery system may rotate as it is advanced.

Once the delivery system is in the LV, the clip arms open and the device is pulled back towards the left atrium, simultaneously grasping both leaflets with the device grippers (Figure 35). Using the LV outflow and inter-commissural views (60–70°), capture of both leaflets must be verified and the clip closed. If either leaflet is inadequately captured, the clip is reopened and re-advanced into the LV and the process is repeated. Once both leaflets have been satisfactorily clipped, a quick assessment of residual MR with colour Doppler is performed. Additionally, it is essential to exclude mitral stenosis, particularly if two clips have been deployed. This is accomplished by measuring the transvalvular gradient with continuous-wave Doppler and planimetry of the two orifices using ideally 3D or alternatively transgastric short-axis views. If MR reduction is satisfactory and the degree of stenosis is acceptable (mean gradient ≤ 5 mmHg), the clip is fully deployed by detaching it from the delivery system. At this point, a final assessment of MR is performed.⁷⁹

If there is significant residual regurgitation and the source of the residual regurgitation is amenable to correction with a second clip, a second clip may be placed using a similar overall approach but using the first clip as a reference point. In assessing the degree of residual MR, it is important that the systolic blood pressure approximate normal values for the patient as functional MR, in particular, is afterload-dependent.

Using 3D echocardiography, it is possible to observe the repaired valve *en face* from both atrial (Figure 36) and ventricular perspectives, documenting the eccentricity, if any, of the dual orifices created by the device. Moreover, 3D colour displays also provide good definition of the site(s) of any residual regurgitation (Figure 37).

Detection of complications

TEE provides a method for early detection of many of the potential complications of clip placement including perforation of the atrial wall, resulting in pericardial effusion, partial dehiscence of the

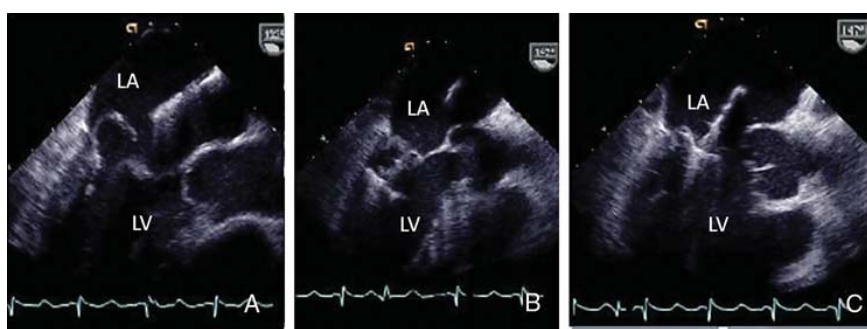


Figure 35 Two-dimensional transoesophageal echocardiography images showing the left ventricular outflow tract view used to monitor advancement of the MitraClip™ delivery system across the mitral valve (A), opening of the clip arms (B), and pull back across the valve with closure of the device arms to grasp the free edges of A2 and P2 (C). LA, left atrium; LV, left ventricle.



Figure 36 Three-dimensional transoesophageal echocardiography view of the typical double orifice appearance of a mitral valve that has undergone successful MitraClip™ placement (atrial perspective).

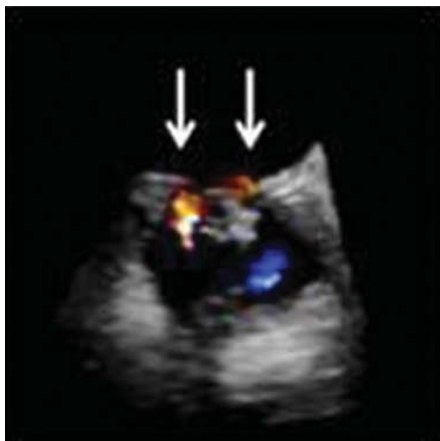


Figure 37 Three-dimensional transoesophageal echocardiography view from the left atrial perspective showing two small jets of residual mitral regurgitation (arrows).

clip after initial seating and leaflet or chordal tears caused by repeated attempts to grasp the leaflets.

Echocardiography for outpatient follow-up

Follow-up of patients after successful mitral clip placement is important. Key elements of echocardiographic follow-up are described below.

Assessing the presence of residual/recurrent mitral regurgitation

Although TEE is best suited for assessing MR, a careful transthoracic examination may be sufficient. Quantitation of any residual MR may be difficult as the mitral valve will now have two orifices and the mitral inflow volume needed for volumetric (quantitative) Doppler calculations cannot be obtained. Additionally, the PISA approach has not been validated for multiple jets as may exist post MitraClip™ or for the double orifice geometry created with this device. Theoretically, in the absence of aortic regurgitation, LV forward flow can be calculated as flow through the outflow tract using the continuity equation and LV stroke volume calculated from 3D determinations of end-diastolic and end-systolic volumes. The difference between the two (stroke volume – forward flow) = regurgitant volume. In practice, colour Doppler echocardiography using semi-quantitative techniques based on regurgitant jet dimensions and/or the use of 3D TEE to planimeter regurgitant orifices may be best suited for long-term follow-up. As with native valve regurgitation, an integrated approach is essential.⁴⁵

Assessment of reverse left ventricular remodelling

Following reduction in MR, it is expected that the LV dimensions and volumes will be reduced. Although the timing of LV remodelling in this setting is unclear, a 6-month assessment with TTE is reasonable.

Representative images from transthoracic studies performed after successful MitraClip™ placement are shown in Figure 38.

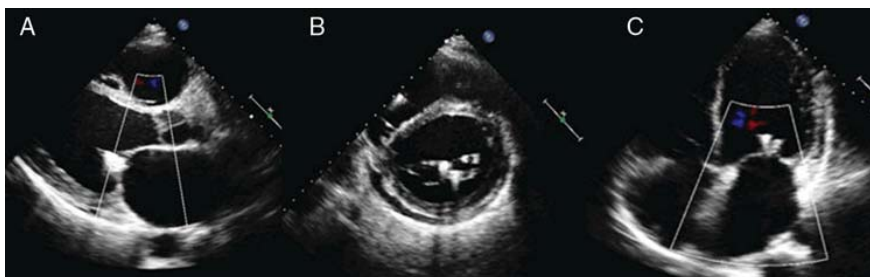


Figure 38 Parasternal long-axis (A), parasternal short-axis (B) and apical four-chamber (C) views showing successfully placed MitraClip™. In this case, two clips were needed to eliminate the mitral regurgitation.

Conclusions

Although transcatheter intervention for valvular heart disease is a rapidly evolving field, echocardiography has played and will continue to play a pivotal role. It is notable that the history of echocardiographic imaging during cardiac interventions has been characterized by a transition of responsibility for imaging from echocardiographers to interventionalists (transcatheter procedures) or anaesthesiologists (surgical procedures) with cardiologist–echocardiographers ultimately serving a more consultative, supportive role during the actual procedures. Improved ICE devices would facilitate ultrasound imaging by interventionalists and reduce the demand for general anaesthesia. However, it is notable that when there are intra-procedural complications, patients may need the undivided attention of interventionalists and anaesthesiologists and it may be beneficial to have other physicians available who can focus on imaging. Although these recommendations have been designed with the non-invasive cardiologist–echocardiographer in mind, they should be equally valuable to anaesthesiologists and interventionalists who may become involved in imaging patients undergoing transcatheter valve procedures.

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PART IV

Conclusions

CONCLUSIONS

- Patient's evaluation before TAVI may require the use of multi-imaging modalities, namely echocardiography, multidetector computed tomography and angiography.
- During TAVI, 2D and 3D transesophageal echocardiography, along with fluoroscopy can be used for procedure guidance, to identify possible complications and the final result.
- Patients referred for TAVI commonly present severe left ventricular diastolic dysfunction, but it significantly improves immediately after the procedure.
- Paravalvular aortic regurgitation is common at midterm follow-up after TAVI.
- We proposed an alternative new methodology for paravalvular aortic regurgitation assessment after TAVI. Using *vena contracta* planimetry by 3D transthoracic echocardiography, we described an accurate methodology for paravalvular aortic regurgitation jet evaluation and severity classification.
- TAVI significantly improves symptoms and quality of life in patients with severe aortic stenosis ineligible for conventional aortic valve replacement. Using the Minnesota Living with Heart Failure Questionnaire, we found an impressive improvement in physical and psychological dimensions at 6.5 months follow-up.
- Patients with peripheral vascular disease had a less impressive improvement in quality of life after TAVI.
- The echocardiographic assessment of patients undergoing TAVI places demands on echocardiographers that differ from those of the routine evaluation. In a partnership from the European Association of Echocardiography with the American Society of Echocardiography we presented the recommendations for the use of echocardiography in new transcatheter interventions, from patient's selection to procedure guidance and follow-up.

PART V

Abstract

ABSTRACT

Transcatheter aortic valve implantation (TAVI) has been recently recognized as an alternative treatment for patients with severe aortic stenosis ineligible for conventional aortic valve replacement. However, it is a demanding procedure that requires a multidisciplinary team approach, in which proper clinical evaluation and imaging play an essential part.

This research was intended to improve the knowledge on transcatheter aortic valve implantation (TAVI), with a particular focus on the importance of the information provided by echocardiography. We aimed to describe the role of echocardiography on this procedure, to determine the acute hemodynamic effects of TAVI in left ventricular diastolic performance and to describe a new accurate methodology for paravalvular aortic regurgitation evaluation. Additionally we evaluated the results on quality of life at midterm follow-up after the procedure.

We followed a cohort of patients referred for TAVI at Hospital Clínico San Carlos, Madrid, included from April 2009 to April 2010. Pre-procedure assessment included medical history, physical examination, transthoracic and transesophageal echocardiography, coronary angiography, aortography, iliac-femoral arteriography and when necessary, computed tomography angiography. 2D and 3D Transesophageal echocardiography was performed during the procedure. Quality of life assessment was performed before the procedure and at midterm follow-up, in conjunction with 2D and 3D transthoracic echocardiography.

We described that 2D and 3D transesophageal echocardiography is useful for patients' selection, procedure guidance and to evaluate possible TAVI complications. We found that patients referred for TAVI commonly present severe left ventricle diastolic dysfunction and it significantly improves immediately after the procedure. We created a new alternative methodology for paravalvular aortic regurgitation assessment. Using 3D transthoracic echocardiography, the vena contracta planimetry accurately recognizes moderate paravalvular aortic regurgitation. We found that TAVI, either transfemoral or transapical, significantly improves quality of life at midterm follow-up and that patients with peripheral vascular disease have a less impressive improvement in quality of life after TAVI.

RESUMO

A implantação de válvula aórtica transcater (TAVI) foi recentemente reconhecida como tratamento alternativo para doentes com estenose aórtica severa não elegíveis para substituição valvular aórtica convencional. Porém, a TAVI é um procedimento complexo que requer uma abordagem multidisciplinar e em que a avaliação clínica e imagiológica apropriada é fundamental.

Esta tese teve como objectivo ampliar o conhecimento médico sobre TAVI, com enfoque particular na importância da ecocardiografia. Pretendemos descrever o papel da ecocardiografia, determinar os efeitos hemodinâmicos agudos da TAVI na função diastólica do ventrículo esquerdo, descrever uma nova metodologia para avaliação de insuficiência paravalvular aórtica e avaliar os resultados sobre a qualidade de vida a médio prazo após o procedimento.

Efectuamos o seguimento de uma coorte de doentes referenciados para TAVI no Hospital Clínico San Carlos, Madrid, incluídos desde Abril 2009 a Abril 2010. A avaliação pré-procedimento incluiu história clínica completa, ecocardiograma transtorácico e transesofágico, angiografia coronária, aortografia, angiografia ilíaco-femoral e quando necessário angiotomografia cardíaca. Durante o procedimento efectuamos monitorização ecocardiográfica 2D e 3D. O questionário de qualidade de vida foi aplicado antes do procedimento e na avaliação aos 6 meses, data que o ecocardiograma transtorácico 2D e 3D foi repetido.

Neste trabalho descrevemos a relevância da ecocardiografia transesofágica 2D e 3D na selecção dos doentes para TAVI, na monitorização durante o procedimento e na avaliação de possíveis complicações. Verificamos que os doentes propostos para TAVI apresentam frequentemente disfunção diastólica severa, mas que esta melhora significativamente imediatamente após o procedimento. Sugerimos uma metodologia alternativa para avaliação precisa da insuficiência paravalvular aórtica, utilizando a planimetria da *vena contracta*, adquirida por ecocardiografia transtorácica 3D.

Finalmente, verificamos que a TAVI, por abordagem transfemoral ou transapical melhora significativamente a qualidade de vida a médio prazo e que os doentes com insuficiência vascular periférica apresentam uma melhoria de qualidade de vida menos marcada.

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