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Meniscal transplantation as a therapeutic option in symptomatic patients after meniscectomy

Bárbara Luís Neves Pinheiro Monteiro

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Bárbara Luís Neves Pinheiro Monteiro
barbara_monteiro_@hotmail.com

Dissertação de Mestrado Integrado em Medicina
Instituto de Ciências Biomédicas Abel Salazar – Universidade do Porto

Orientador: Adélio Vilaça
Assistente Graduado de Ortopedia
Serviço de Ortopedia, Centro Hospitalar e Universitário do Porto
Assistente Convidado, Instituto de Ciências Biomédicas Abel Salazar – Universidade do Porto

Coorientador: Pedro Cardoso
Assistente Graduado de Ortopedia
Serviço de Ortopedia, Centro Hospitalar e Universitário do Porto
Professor Auxiliar Convidado, Instituto de Ciências Biomédicas Abel Salazar – Universidade do Porto

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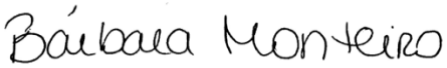
Estudante:



(Bárbara Luís Neves Pinheiro Monteiro)

Orientador:

(Adélio Vilaça)

Coorientador:

(Pedro Cardoso)

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Abstract

Knee pain is an inevitable consequence for many patients that were previously submitted to a partial or total meniscectomy. Meniscal transplantation started as a symptomatic treatment, with the prospect of being an ideal replacement to the native meniscus, able to decrease or even avoid the accelerated progression to osteoarthritis.

Currently there are numerous criteria the define an ideal candidate for this procedure, with the most agreeable on are young and active patients, under 50 years old, with chronic and incapacitating knee pain, refractory to conservative management, and, if there is any coexisting pathology of the surrounding structures that may cause malalignment or joint instability, this ought to be amenable to surgical correction during or prior to the transplant. Although not ideal, cartilage damage or degeneration is not a formal contraindication for the transplant, but it will negatively affect the outcome of the surgery.

There are three graft options for the transplant, and the allotransplant is by far the most used one, consequently becoming the most studied and the safest option. There are some areas where experts disagree regarding the protocols of the sizing method of the graft, its preservation techniques, and the fixation of the graft during surgery. The technique each surgeon uses depends purely on their experience and preference as there is no clear superiority of one method versus the other, each has their own benefits and limitations. In regard to the preservation technique, the two most used ones are the cryopreservation and the fresh-frozen one. The sizing of the graft is mostly done using the Pollard method based on X-rays, although others are increasing in popularity. The fixation of the graft can be achieved through suture-only or through bone-plugs or bone-bridge. The most used one is the suture-only method as it is the less technically demanding and the fastest one to perform, however it causes more complications and is linked to a higher transplant failure rate.

The goal of a meniscal transplant, besides the reduction of the knee pain and improving joint function, is to prevent the rapid onset of osteoarthritis, inevitable consequence of a meniscectomy. In fact, the transplant shows good clinical outcomes as a symptomatic treatment, successfully relieving knee pain in medium and long-term outcomes studies. However, there is lack of evidence regarding the effectiveness of the transplant in the chondroprotection of the knee, which is why there is a need for more studies and investigation in this field.

Keywords: meniscus; meniscal transplantation; allograft; functional outcomes; chondroprotection.

Resumo

Gonalgia é uma consequência inevitável para muitos doentes previamente submetidos a uma meniscectomia, quer parcial que total. Os transplantes meniscais surgiram como tratamento sintomático, com a perspetiva de poderem substituir o menisco nativo de tal forma que a rápida progressão para gonartrose também seria evitada ou desacelerada.

Atualmente existem diversos critérios que constituem um candidato ideal a ser submetido a esta cirurgia, sendo os mais consensuais a idade jovem, inferior a 50 anos, população ativa, com gonalgia crónica incapacitante, refratária a terapêutica conservadora, e, caso tenha algum tipo de patologia das estruturas circundantes que afetem a estabilidade e alinhamento da articulação, estas deverão ser passíveis de correção cirúrgica aquando ou previamente ao transplante. Atualmente, apesar de não ser o ideal, alterações degenerativas da cartilagem não constituem uma contraindicação formal para o transplante, mas têm um impacto negativo significativo no futuro.

Dentro das três opções que existem de enxertos, o alo enxerto é o mais comumente utilizado e, consequentemente, o mais estudado e seguro. Ainda assim, existem algumas áreas de desacordo em relação ao protocolo ou método de escolha da medição pré-operatória do enxerto, da sua preservação e da sua fixação na articulação. A técnica que cada cirurgião utiliza acaba por depender da sua experiência e preferência já que nenhum método é superior aos restantes, tendo cada um deles os seus benefícios e as suas limitações. No que diz respeito à técnica de conservação do enxerto, as duas mais utilizadas são a criopreservação e congelado fresco. A medição do enxerto pré-operatório é maioritariamente feita através do método de Pollard à base de raios X, apesar de outros estarem a ganhar seguidores. A fixação do enxerto pode ser feita atrás de apenas suturas ou com a utilização de osso, em pontes ou dois pequenos enxerto de osso. O mais usado é o método das suturas uma vez que tecnicamente é mais fácil e mais rápido, no entanto está ligado a mais complicações e maior taxa de falência do transplante.

O objetivo de submeter um doente a um transplante meniscal é, para além da redução da dor articular e melhoria da função, a prevenção do rápido desenvolvimento de gonartrose, consequência inevitável de uma meniscectomia. De facto, o transplante tem boa evidência como tratamento sintomático, aliviando eficazmente a gonalgia com bons resultados a médio e longo prazo. No entanto, há pouca evidência de que o enxerto possa ter alguma condroproteção ou intenção curativa, sendo necessários mais estudos a avaliar este ponto.

Palavras-chave: menisco; transplante meniscal; aloenxerto; desfechos funcionais; condroproteção.

List of Abbreviations

3D-CT	Three-dimensional computed tomography
ACL	Anterior cruciate ligament
BMI	Body mass index
MAT	Meniscal allograft transplantation
MRI	Magnetic resonance imaging

Table of contents

List of tables

Introduction

The menisci are fibrocartilaginous structures with a hight water content (60-70%) that are crucial for maintaining and preserving the normal function and nutrition of the knee joint.[1–4] There are two menisci in each knee joint, the medial one is more c-shaped, covering approximately 60% of the surface area, whereas the lateral one is responsible for covering approximately 80% of the plateau. [3–5] The menisci play an essential role in shock absorption and load distributing. Moreover, there are several peripheral anchor points connecting the meniscus to the tibial plateau which contributes not only to the stability of the joint, but also to the overall proprioception. Additionally, both menisci help lubricate the joint and facilitate congruity, as they spread the synovial fluid on the articular surface. [2–4,6–12]

Meniscal tears are the most common knee injury, with an incidence of approximately 61 per 100,000 every year, which, consequently, leads to meniscal resections being the most common surgical procedure in orthopaedics. [4,5,11–13] A meniscus tear is most often degenerative or irreparable due to unfavourable conditions, type or location of the tear, and conservative treatment failure, which makes total or partial meniscectomy sometimes inevitable. [10,14,15] Even though a meniscectomy may provide patients a short-term relief from pain and mechanical symptoms, the loss of a meniscus will, in time, lead to articular cartilage degeneration, with studies claiming a 14 times higher risk of developing osteoarthritis and knee pain after this procedure, as a total meniscectomy increases contact stress in the tibial-femoral joint by over 130%.[1,2,6,7,9] As a consequence, the removal of a meniscus in a young and active person can severely damage the entire knee compartment, altering its biomechanical and biological conditions, leading to progressive knee pain, loss of function and premature symptomatic osteoarthritis, which accounts for an estimated 4% cartilage loss per year. [5,8,9,11,14,16–20]

The first meniscal allograft transplantation (MAT) was performed in 1984 as a potential treatment option in a painful meniscectomized knee. The clinical trial that followed reported the experimental and short-term results of this technique, stating it is a viable treatment option available for patients with symptomatic knees after meniscectomy. [2,9,11,20,21] The goal of the MAT is to recreate the native meniscus and its properties regarding load distribution, restoring the normal contact mechanics of the knee joint, relieving symptoms, and ultimately preventing or delaying the progression of cartilage degeneration. [1,2,4,20,22]

In recent years, MAT has become the state-of-the-art treatment for selected groups of patients with persistent pain after meniscectomy after failure of non-operative management. Although many benefits have been shown by many studies, the chondroprotective effect of the

MAT is yet to be completely established, which, in addition to its relatively high complication and reoperation rate, make this procedure not universally accepted. [1,4,7,22]

Objectives

This review aims to gather the most recent insight on meniscal transplant, focusing on the optimal candidates to undergo this procedure, the different grafts used worldwide for this purpose, the planning necessary for this technique, including how to harvest the graft, discussing different preservation methods and the most used sizing systems, a brief comparison between several surgical techniques, a consensus on the rehabilitation process, the current debate whether patients should return to physical activity, as well as the most reported complications in long term studies and possible future developments in this area. In order to write this review numerous sources were confronted and compared, which highlighted the differences and similarities between studies.

Methods

To develop this review, an extensive search on relevant literature concerning meniscal transplant was performed. Several databases were used for the research, in particular PubMed, Elsevier, Google Scholar and Medline. The consulted scientific articles were mostly original articles, metanalysis and systematic reviews, although some bibliographic reviews were also included.

The keywords meniscus, transplantation, meniscectomy, allograft, meniscal scaffold, fixation, preservation, rehabilitation and chondroprotection were used for this research, alone and combined in various ways. Some articles from the references of original scientific articles were also read and included when relevant, and the “similar articles” option was also used in PubMed and Elsevier.

Based on the title and abstract, 167 scientific articles were analysed, in order to select 95 references for this review, with publication date between 1985 and 2022. No relevant articles were excluded purely based on the publication date, although the ones published in the last decade were favoured.

Patient selection for meniscal transplantation

Ideal candidates: indications and limits of this procedure

Meniscal transplantation requires certain criteria to be filled in order for a patient to become a candidate for this procedure. The indications for meniscal transplantation that most specialists agree upon are young and active patients that developed chronic pain in the meniscus-

deficient compartment, consequence of a total or partial meniscectomy, that have been experiencing recurrent effusions, decreased knee function and instability of the knee joint, after failure of a satisfactory trial of conservative management. [1,4,7–10,22,23] Ideally, the patient should be under 50 years old, have debilitating pain localized to the tibiofemoral articular joint, but also have a stable and well-aligned knee joint, without advanced degenerative cartilage damage (table I). [8,9,23–26]

The presence of cartilage degeneration is a strong predictor for meniscal transplant failure, as well as cartilage wear which appears to reduce the survival of the graft. [4,8,27,28] Initially, patients with Outerbridge grade II cartilage defects were excluded from meniscal transplantation, but with the development of cartilage restoration procedures (e.g. osteochondral allograft transplantation and autologous chondrocyte implantation), the outcomes between those who underwent a meniscal transplantation with or without concomitant cartilage restoration were similar, allowing patients with cartilage damage up until Outerbridge grade IV to be considered as candidates. [7,12,29–31]

Prior to a meniscus transplant, every patient should be evaluated for any concurrent pathology on the lower limbs. Firstly, when meniscal transplantation started to be performed, any patient with malalignment or instability of the knee joint was automatically excluded from the procedure, whereas in recent years these conditions are assessed to understand if they are amenable to surgical correction during the transplantation process.[4,9,11,22,23,31] Ligamentous instability, especially an anterior cruciate ligament (ACL) tear, should be addressed surgically prior to or in combination with the meniscal transplantation, as both procedures (ACL reconstruction and meniscal transplantation) have a protective effect on each other. [4,10,23,32,33] When malalignment is detected, it should be surgically corrected with osteotomy prior to the meniscal transplantation surgery, as a valgus-aligned lower limb, for example, can compromise the outcome of the transplant. [4,10,23]

Equally important is that any patient who undergoes a meniscus transplant ought to have a hight potential for a successful follow-up and compliance with the rehabilitation protocols, since it was shown that compliant patients have significantly less likelihood of needing a transplant revision or progress to a total knee arthroplasty, increasing the overall success of the procedure. [7,34]

Therefore, the indications continue to be refined as new techniques are developed, the existing limitations of meniscal transplantation are far less significant and controversial. [2,31] Recent studies suggest patients older that 50 years, a body mass index (BMI) higher than 35 kg/m^2, radiographic evidence of osteophytes or other high-grade chondral lesions, inflammatory arthritis, synovial disease, prior joint infection, non-operative joint malalignment or instability and skeletal

immaturity as possible contraindications for a meniscus transplantation. [7,22,23,35–37] Nevertheless, the decision whether to perform a meniscus transplant should be made on a case-by-case basis, allowing surgeons and patients to decide if the risk of failure is acceptable when a transplantation is performed on less optimal candidate. [22,31]

Choosing a graft

Autograft – historical usage

The usage of autografts started to gain some attention forty years ago as a solution for the costs and the logistical problems with the storage of allografts, as well as to mitigate the transmission of infectious diseases.[38,39] The first clinical trials testing different autografts happened in Germany where fat pad and quadriceps tendon autografts were used to substitute the meniscus tissue.[4,40,41] This and other studies concluded that autografts definitely solved the cost and storage problems, as they are readily available, affordable, do not require storage and, depending on the surgical circumstances, free of infection.[38,39] Despite being successful in lessening knee pain, the majority of the autografts lack resemblance to a meniscus on arthroscopy, and its properties are inferior to those of the allografts, which lead to the autografts being abandoned for this purpose. [38,42]

Allograft

An allograft of the meniscus is currently the preferred graft to use in transplantation as it is the most researched and the safest alternative between the three. Several advances have been made in order to enhance its sizing and preservation methods, improving the outcome and decreasing its complications and morbidity. As new techniques are developed, the controversy between experts increases, leading to a disagreement in the ideal preservation technique or sizing system.

Scaffold – future usage

Further options for the traditional allograft have been evolving as they gain the attention of bioengineers, trying to develop synthetic or acellular xenogenic grafts for meniscal transplantation to replace the native one.[4,43,44] The increased concern regarding the complications shown with the use of allografts made scaffold appealing, with scientists turning their focus to how to make them safe for humans. [44] This type of graft is being studied as synthetic collagen scaffolds that allowed the ingrowth of fibrochondrocytes for the last three decades, as scientists try to overcome its biggest flaw, the lack of a matrix to orientate the cell growth, resulting in immature

tissue.[4,38,45] Currently, many advances and clinical trials have been made in this area, however the mechanical characteristics of available scaffolds still have a long way to improve to a point where they will resemble the native meniscus. [4,46] The most recent studies now explore the role of a mechanical stimulus in cell maturation and differentiation, hypothesising that the scaffold should be more biomimetic, with the possible usage of bone marrow for this end. [4,38]

Preservation techniques

The menisci are avascular structures capable of surviving up until 12 hours at room temperature or 24 hours at low temperatures, tolerating being the last organ harvested in the operation room. [4,23,38] This limits fresh grafts viability, which, depending on the chosen protocol, can only be used in a few hours gap, or, when cooled down to 4ºC, remains viable for three-to-four weeks after harvesting.[38,47] Fresh grafts are the ideal ones when it comes to viability as they have alive cells that improve the mechanical properties of the transplanted meniscus. [23] In regard to logistics, these are probably the most difficult to use, not only because of the short viable interval of the grafts, but also for the limited availability, increased risk of infectious diseases transmission and unlikelihood of finding a perfect match in size (table II).[38,47]

Apart from the fresh grafts, there are three storage methods currently used for transplantation of the menisci that allow a long-term preservation, as well as a complete donor screening and grant the opportunity for the establishment of donor banks for an increased number of meniscus transplantations. [23,38] The allografts can be fresh-frozen, cryopreserved or lyophilized, all of which can be used for meniscus transplantation according to the surgeon preference, as any of these methods have their advantages and weaknesses to be considered. [22,23]

The first aspect that should be taken into consideration is how aggressive the preservation and sterilization procedures are to the graft, as the purpose of the storage method should be to produce minimal change in the menisci's collagen architecture, as it can impact the graft survival. [1,4,38] Both lyophilized and cryopreserved put the menisci through extremely low temperatures, consequently leading to an increased likelihood of deleterious effects on the mechanical properties of the allograft, higher risk of transplant failure, logistical problems and higher cost, which account for their lack of popularity when compared to fresh-frozen grafts. [1,22,23,47]

Lyophilized was the first storage technique being used, as it was chosen for the first allograft transplantation in 1984.[4,21] Since then, this method has progressively been abandoned due to its high rates of failure and excessive tissue deformation when compared to the alternatives. [8–10]

Currently there is a lot of debate among experts about the superior method between cryopreserved and fresh-frozen.[22] Until the beginning of the decade, in 2010, both cryopreserved

and fresh-frozen were used in similar numbers, whereas more recent studies have directed their focus to fresh-frozen grafts as they seem to be the preference of most orthopaedic surgeons. [11,24] Although the majority prefers to use the fresh-frozen technique, freezing has been shown to cause an abnormal collagen network in the graft, which does not seem to occur in the cryopreserved method.[1,7,10,22,23] Regarding the cell viability, the fresh-frozen technique prevents any cell to survive during the process, whereas the cryopreservation method enables some degree of cell survival, with recent studies reaching percentages of 4 to 54% of cell survival after cryopreservation. [1,4,10,23,38,48] Additionally, cryopreserved grafts require certain logistic procedures to be ensure, such as a controlled temperatures of -196ºC with the meniscus bathed in cryoprotectant and strict thawing protocols that guarantee the integrity of the meniscus allograft, all of which may be challenging to achieve in the clinical environment and have a greater cost attached. [7,11,23]

Overall, after the lyophilized method was abandoned, two techniques remained in practice until current days, fresh-frozen and cryopreserved.[8–10] While many recent studies claim that no method is superior to the other, fresh-frozen remain the surgeons' favourite.[4,10,23,38] The growth in popularity of these long-term preservation procedures allows for the grafts to be storage for years, making them immediately available when an organ bank for menisci is present. [23,38]

Sizing methods

When meniscal transplants first started to be performed, little attention was given to the graft size, whereas now it is recognized by most experts to be one of the most important preoperative evaluations for a successful outcome. [1,4,9] Many studies demonstrate the importance of an accurate sizing, showing a severe decrease of the graft survival mainly when it is undersized by more than 5 mm in width. [7,49] On the other hand, clinical trials have also shown that an oversized and extruded graft will result in a suboptimal biomechanical joint with an inadequate distribution of the weight and an added load to the joint. An undersized graft, though able to decrease the contact pressures in the joint, will be exposed to increased strain and shear forces, causing early graft failure and rupture of the meniscus. [1,4,7,22,50,51] Ideally, the allograft size ought to be matched to within 5 to 10% of the native meniscus size, enabling it to produce a contact surface similar to a healthy knee joint. [1,4,22] Most specialists advise to opt for an oversized rather than an undersized graft, as it can be partially amenable surgically, where the surgeon can reduce its dimensions. [4,7,49]

Numerous matching and sizing protocols were suggested in the past, but most were unreliable, such as trying to match the anthropometric data of the recipient to the donor, including age, sex, height and weight.[1] The gold standard method of measurement is far from consensual among professionals, although the Pollard method seems to be the most commonly used

worldwide. [4,9,22,52] This technique was first published in 1995 and relies on X-rays of the knee in order to estimate the size of the native meniscus. [9,22,52] The width of the meniscus is determined by measuring the distance between the peak of the tibial eminence and the periphery of the tibial metaphysis using an antero-posterior X-ray of the knee. A lateral view is used to determine the length of the meniscus, which corresponds to 80% of the sagittal length of the tibial plateau. [4,7,52]

Most radiographic measurements have a margin of error of about 10%, whereas by means of the Pollard method this percentage is reduced to less than 8.4%, making it more reliable. [1,22,52] Nevertheless, this method still presents with some flaws, mostly affecting the accuracy of the lateral allograft sizing. [4,52] As a consequence of the usage of plain X-rays to determine the size of the meniscus, there is seen a significant interindividual variability between the medial and lateral compartment, mainly in the antero-posterior direction, with some mathematical models being developed to increase the accuracy of this process. [4,53]

Other imaging methods, such as three-dimensional computed tomography (3D-CT) and magnetic resonance imaging (MRI), are now growing in popularity as a sizing technique for meniscal transplant, although the great cost associated can be an issue. [10,22,54] Most studies on this matter reach encouraging results in regard to the usage of 3D-CT for this end, showing its superiority comparing to X-rays, by demonstrating less errors in measurements. [1,4,22,54] Using an MRI to size the allograft seems to underestimate the real size of the meniscus by as much as 44%, however this can be improved by scanning the contralateral meniscus as well. [4,22,54]

Surgical approaches and fixation techniques

Surgical approaches

Meniscal transplantation was originally performed by open surgery of the knee, especially when dealing with open multiligament repair after a trauma. [8,11] Initially, a femoral condyle osteotomy including the detachment or splitting of collateral ligaments was performed, and then joint distractors started to be implemented to preserve the collateral ligaments. [9–11] Surgical techniques kept evolving over time, and currently most meniscal transplantations are performed through an arthroscopic-assisted procedure, meaning most of the surgery is arthroscopic, although a small arthrotomy is required to insert the graft. [4,7,9–11]

Fixation techniques

Once the graft is inserted into place, the meniscus needs a firm attachment and a good peripheral fixation of the meniscal horns. [4,9,11,23] This presents as one of the main controversies around meniscal transplantation, as there are two main techniques to achieve fixation of the graft,

suture-only fixation and bone fixation. [1,4,9,10,22,23,55] The choice of which fixation technique to perform relies on the surgeon preference and familiarity to the method, as well as on possible concomitant procedures performed at the same time as the transplant, as there is no clear superiority between them. [7–10,22,23,55,56] Nevertheless, numerous studies show a clear preference from surgeons in using bone fixation. [10,22,23,56]

In regard to bone fixation, it can be accomplished through two bone plugs attached to the anterior and posterior horns, securing a bone-to-bone fixation, or with a bone bridge linking them. [1,4,22] Both techniques require the preparation of osseous beds in the receptor of the graft, so the bridge or the plugs can be inserted. [22,23] The bone plug technique allows the surgeon to adjust the attachment site of the roots, while the bone bridge facilitates the insertion of the graft, avoids detaching the collateral ligament and allows the relationship between the anterior and posterior horns to be left intact. [7] With a slight superiority to the bone plug technique, both options proved to restore the contact biomechanics of the meniscus, although, depending on which meniscus is going to be addressed surgically, there can be a preference on which technique to use. [1,57] Currently, there is a clear tendency favouring bone plugs for the medial meniscus and bone bridge for the lateral one. [4,7,10,23] Most professionals prefer to use a more aggressive procedure such as bone bridge for the lateral meniscus as it is more efficient in preserving the native space between the horns and these structures are physically closer on this side. The bone plugs technique is less invasive, which is why it is chosen for the medial meniscus, preserving the tibial eminence, as the tunnels are drilled through the horns of the residual native meniscus. [4,7,9,22]

The suture-only fixation consists in fixating a soft tissue graft by suturing the meniscal body and horns, as well as using a transtibial suture technique to attach the meniscal roots. [9,22] Numerous trials report a high rate of graft survival using a suture-only fixation method, although it is not able to provide enough stability to prevent mid-body extrusion, leading to a great proportion of reinterventions. [1,4,9,10,23,56,58] Many studies comparing different fixation techniques show that the bone fixation method is superior regarding the strength of the graft attachment and its resemblance to the native meniscus stress forces, whereas the suture-only technique seems to allow a higher contact pressure on the tibial cartilage. Additionally, the latter allows a more accurate and easier placement of the graft, meaning it is a less time consuming and less technically challenging procedure. [1,4,9–11,56] This technique is mostly used on the medial meniscus as this side is not as biomechanical demanding and it makes the procedure much easier, with promising long-term function and clinical results. [9,22]

Postoperative management and rehabilitation

Several rehabilitation protocols have been tested for this purpose, following meniscal-suturing protocols when there was a lack of scientific data on meniscal transplantation and its ideal postoperative management. [4,9–11] Nowadays, whenever the transplantation is uncomplicated and without any concurrent procedure, most experts seem to follow a three phases protocol. For the first two months the patient is advised to do non-weight-bearing and static strengthening, with a range of motion between 0 and 90 degrees, limiting this range to 60 degrees in the first two-three weeks after surgery. Followed by a four-months conditioning phase, in which the patient is allowed to do exercises with full weight-bearing and full range of motion, starting with a precautionary limit of 80 degrees for squats and strengthening exercises. [4,9–11,22,23,59–61] Half a year after the transplant, the patient enters the functional rehabilitation phase for three months that consists of a more sport-specific training or even a full return to their previous sport activities depending on the individual achievements regarding muscle strength, control, endurance, and graft healing. [4,9,11,22,23]

The consequences of returning to sports after a meniscal transplant are still being debated by professionals, as it has been shown to cause a high rate of meniscal tears and shorten the longevity of the meniscus, especially when high-impact motions, like cutting and pivoting, are involved. [2,4,9,62–64] Many recent studies have been focusing on the post-operative sporting level after the transplantation, so far reporting promising rates, between 61 and 92%, of patients able to return to competitive play. [1,2,4,12,59,62–66]

Short and long-term outcomes

The ultimate goal of submitting a patient to a meniscal transplant is the chondroprotection of the remaining articular interface, slowing the progression to osteoarthritis, as well as pain relief from the previous meniscectomy. [1,7–9,29,55,64,67,68] The most recent studies show positive results on short and long-term outcomes regarding pain relief and functional improvement of the articular joint, revealing percentages of asymptomatic patients at a 15-year follow-up of 40-60% and excellent results in terms of pain, function and activity levels of 85% at an 8-year follow-up, which shows a tendency for the clinical improvement to decline over time. [4,7–11,18,24,29,67,69–71] Considering the overall survival of the graft, trials reach slightly different results, finding a cumulative survival rate of 95-96% at 1 year, 87-88% at 5 years, 78-82% at 7 years and a range from 40% to 85% at 10 years or more. [1,7,9,18,72,73] Analysing the survival time of a meniscus allograft, researchers reached the interval of 14.8 to 17.5 years, with a mean of 16.1 years, with no significant difference between

the lateral and the medial meniscus. However, the lateral side showed higher pain scores in comparison to the medial meniscus. [10,18,22,74]

The chondroprotective effect of a meniscal transplant was established in an animal model, but it has been difficult to replicate these results in humans. Some studies report that, by using consecutive radiographs, it is clear the progression to osteoarthritis with the narrowing of the joint space, while others claim no statistically significant changes when comparing both knees of the patient. [1,8–11,20,22,28,70,75]

The definition of transplant failure is not consensual among specialists, some consider the graft revision or the conversion to total knee arthroplasty, while others refer to it as poor clinical results, poor MRI findings or a subsequent meniscectomy. [7,10,72] It is difficult to discern which factors negatively affect the outcome, however it has been proven that transplant failure is strongly connected to the age of the patient, with trials showing increasing revision and overall failure rates at an age higher than 35, especially in patients older than 50 years. For every decade older than 35 years at the time of the transplant, the risk of resection, with or without conversion to total knee arthroplasty, increases five times, which might be explained by a worst graft ingrowth, consequence of a lower biological vitality of the knee, and by the decision to reoperate, which is age-dependent with few acceptable alternatives for those patients. [10,18,25,26] Regarding the failure rate of each side of the knee, no clear consensus was found, although most studies report a higher rate of graft failure in the medial side when compared to the lateral meniscus. [2,10,22,27,74]

Comparisons between the survival of the graft when the meniscal transplantation is performed alone or with a concomitant ACL reconstruction or malalignment procedure found that there was no significant difference between the two groups of patients, suggesting that this lack of disparity may be due to the fact that the concomitant procedures improve the weight-bearing chondral properties, joint stabilization and overall function of the knee. [2,7–9,18,36,64,68,74,76–79] On the other hand, the number of previous knee surgeries has a negative impact on the postoperative outcome, particularly when the patient has been submitted to more than two procedures. [2,18,26]

When the patient has some evidence of chondral lesion, even though it is not a contraindication for the transplant, this will greatly influence its outcome, especially in long-term, as studies found that patients with a significant cartilage defect, Outerbridge grade 2 or higher, have a higher rate of graft failure, estimating graft-survival at five years to be inferior to 65%, as opposed to around 90% in ideal candidates. [2,22,31,72,80,81] If an articular cartilage repair procedure is done at the time of the transplant, no difference has been found in complications or failure rates. [9,30,31]

Most common complications

Recent studies estimate a complication rate after a meniscal transplantation between 10.6% and 15,6%, whether acute or chronic, frequently requiring a revision when the symptoms are disabling. [1,10,11,82] The most common complication is meniscal tear, most often in the capsular junction or in the posterior horn, possibly due to the high contact stress of the graft and from the suture material, followed by debris removal in the joint space, all accurately detected by a follow-up MRI. [1,8–11,82,83] Apart from these, other common complications have been described, such as arthrofibrosis, aseptic synovitis, extrusion, cellulitis, infection, hematoma, limited range of motion and bone plug loosening. [11,84] Some authors refer to the need of further reintervention as the greatest complication of all, some reporting a reoperation rate between 32% and 36%, where debridement was the most performed procedure. [1,7,29,83]

Extrusion

Extrusion is an increasingly reported complication that has been drawing much attention in the last years, consisting of the radial displacement or subluxation of the allograft that appears shortly after the surgery, usually not progressing overtime, leaving the articular cartilage exposed and possibly altering the biomechanics of the knee. [1,4,7,85–87] It is common to find some degree of extrusion on an MRI after a meniscal transplant, being considered acceptable and normal when it is less than 3 mm. [1,4,11,22,56,67] When the extrusion surpasses this value, it has the potential to increase cartilage wear, ultimately leading to osteoarthritis, by rising the peak contact stress and decreasing the tibiofemoral contact area, despite most trials claim that it is asymptomatic in most patients. [1,4,22,23,73,75,87,88] This complication occurs with greater frequency in the anterior horn, when the sizing of the graft is not carefully performed, and when soft tissue fixation is used, which is why the bone plug technique is now becoming the fixation technique of choice, as it clearly shows the lowest rate of extrusion. [1,4,9,56,89] Several anatomic factors were found to play a role in meniscal extrusion, such as joint laxity, cartilage wear and the presence of osteophytes. The excision of peripheral osteophytes of the tibial plateau and the fixation of the graft to the tibial surfaces are proposed techniques to limit and minimize this complication. [1,4] Additionally, there is some evidence supporting that a delayed rehabilitation protocol where the patient uses unloading braces for 9 weeks causes less coronal graft extrusion. [90]

Conclusion and future trends

Meniscal transplantation has evolved greatly in the last years, now being considered a safe and viable solution for young and active patients that suffer from chronic pain and functional disability, consequence of a previous meniscectomy. [4,8,9,23]

Not every patient is an ideal candidate for this procedure, as there are certain criteria that should to be filled to guarantee the safest and most predictable outcomes. The most agreeable criteria among specialists are young and active patients under fifty years old, that suffer from chronic pain in the knee compartment after a partial or total meniscectomy, refractory to conservative management. Degenerative cartilage damage and instability in the knee joint are no longer contraindications for this procedure, as long as they are amenable through surgical intervention during the transplant. Currently, the list of contraindications is growing shorter as new techniques are developed, allowing for the decision to perform the transplant to be addressed between the patient and the surgeon, discussing if the risk of failure is acceptable. It is important that every candidate is warned that there is a possibility that, even though the transplant is successful, they may never return to their previous sports activities and there is a likelihood that a re-operation is needed to amend a meniscal tear. [2,22]

Lately, there has been a lot of debate whether the transplant should be performed soon after the meniscectomy, with some experts even pondering if a prophylactic transplant would be advisable. It has been proven that an increase of the degeneration of the cartilage comes with a higher the graft failure, so delaying this procedure may negatively affect the outcome of the transplant. Meniscal transplantation is currently approved for symptomatic patients only, however this indication might change in the future. [91,92]

When choosing what graft to use for the transplant, there are three options available, even though only one is currently used for this end, the allograft. The autograft has an historical use, as it was abandoned many years ago, mainly due to its lack of resemblance to the native meniscus. Acellular and prosthetic scaffolds or implants seem to be the future of meniscal transplantation as they were proven to promote tissue regrowth, however a lot of research in this area needs to be made as the biomechanics of the meniscus are complicated and still not fully understood. [4,44,46,60,92,93]

The allograft is widely studied and the most predictable graft, turning it into the safest choice at the moment for meniscal transplantation. However, there are still some areas that lack consensus among surgeons, especially regarding the fixation and sizing methods, as there is no clear superiority between the different approaches. There is a need to optimize the meniscal allograft transplant protocol in order to enable comparative studies to reach more accurate outcomes of

this procedure. Additionally, these techniques still have a lot to evolve as complications, such as extrusion, continue to occur, mostly due to the difficult and singular biomechanics the meniscus entails. Several studies focusing on this particular complication have been making progresses, suggesting different techniques to minimize extrusion cases in transplanted patients, such as combining the suture-only technique, which has a higher rate of extrusion associated, with capsulodesis in the lateral meniscus. [94,95]

After the surgery, there is a three phases standard rehabilitation protocol that is followed in most centers. However, studies that compare this protocol to a delayed one state that the latter shows less coronal graft extrusion and reduces the progression to osteoarthritis, meaning that the standard protocol may be abandoned soon, reducing complications rate. [90]

Most outcomes studies seem promising and reach encouraging results, nevertheless it is important to keep in mind that these results may not be accurate, as there are still a lot of variability between them, regarding not only the pre-operation and surgical protocols, but also the lack of a clear and unanimous definition of transplant failure. This has a clear influence on the conclusions of long-term trials, as those who define failure as structural damage, imaging alterations, pain or reoperation not related to the graft will naturally report higher failure rates than the ones that only consider failure when the patient becomes symptomatic, there is a need for a graft repair or for an arthroplasty. If a clear definition cannot be accomplished, there could be two different concepts, symptomatic failure and mechanical failure, enabling future studies to compare these two variables, reaching more accurate outcomes results. [8,9]

The main goal of a meniscal transplant is, apart from improving knee pain, to slow down the progression to osteoarthritis, as it is a known and unfortunate result of a meniscectomy. To prove the effectiveness of the transplant has been the main focus of many scientists, however this has been a difficult challenge, barely reaching any agreeable results. In the future, it is essential to clarify if the meniscal transplant is purely a symptomatic treatment or if it has curative potential to stop the accelerated joint degeneration.

Tables

Table I - Indications and current limitations of meniscal transplantation

Indications	Limitations
Patients under 50 years of age	Patients older than 50 years of age
Active patients	Patients with a BMI higher than 35 kg/m^2
Patients suffering from chronic and debilitating knee pain due to a meniscectomy	Patients with radiographic evidence of osteophytes or other high-grade chondral lesions
Failure of conservative management	Inflammatory arthritis, synovial disease, or prior joint infection
Appropriate or correctable knee alignment	Non-operative joint malalignment or instability
Appropriate or correctable ligament stability	Skeletal immaturity
No significant degenerative cartilage damage if the patient cannot be submitted to a cartilage restoration procedure	Degenerative cartilage damage not amenable through a restoration procedure
Patients able to comply with rehabilitation protocols and follow-up instructions	Non-compliant patients

Table II - Advantages and disadvantages of different preservation methods

	Advantages	Disadvantages
Fresh grafts	No need for any preservation procedure	Short viability
	Alive cells that improve mechanical properties	Limited availability
		Increased risk of infectious diseases transmission
		Unlikely to find a perfect match in size
Lyophilized grafts	Opportunity for the establishment of donor banks	Extremely low temperatures that may cause deleterious effects on the mechanical properties
	Longer viability	Higher risk of transplant failure
		Higher cost
		Excessive tissue deformation
Cryopreserved grafts	Opportunity for the establishment of donor banks	Extremely low temperatures that may cause deleterious effects on the mechanical properties
	Longer viability	Higher cost
	Collagen network remains intact	Logistical issues, regarding the necessary temperature, the usage of cryoprotectant and strict thawing protocols
	Cell viability between 4 and 54%	
Fresh-frozen grafts	Opportunity for the establishment of donor banks	Prevents any cell viability
	Immediately available	Cause an abnormal collagen network in the graft
	Viability of the graft up until 5 years	

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