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Meniscal Allograft Transplantation: Where are we Standing?

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Abstract

Meniscal allograft transplantation (MAT) is becoming a common procedure in Orthopedic departments worldwide. This procedure has demonstrated good and excellent results in terms of pain relief, improvement in clinical and functional outcomes, return to sports, and patient's satisfaction. However, MAT is not a universally accepted procedure due to its questionable chondroprotective effects and the relatively high rate of complications and/or reoperations. The present short review summarizes the principal indications, contraindications, outcomes, and complications. Also, it covers several controversial topics like graft preservation, graft sizing, graft fixation, results in MAT associated with concomitant procedures, and the role of MAT in the prevention of knee osteoarthritis.

Keywords: Meniscal allograft transplantation; Indications; Contraindications; Outcomes; Complications; Graft preparation; Osteoarthritis

Introduction

Meniscal injuries are one of the most common knee injuries in both the athletic and general population [1,2]. The number of meniscectomies for the treatment of meniscal tears has risen dramatically in the last decades, especially with the advancement of arthroscopy. However, the management of meniscal ruptures is currently changing with the better understanding of meniscal function and better knowledge on the short-to-mid-term consequences of meniscectomy on the articular cartilage: osteoarthritis [3-5]. As a consequence, nowadays most orthopaedic surgeons try to preserve as much meniscal tissue as possible or make an attempt for meniscal repair [6]. Unfortunately, many acute and chronic meniscal injuries cannot be fixed with sutures and, if symptomatic enough, the ruptured tissue must be removed [6]. Especially for total or subtotal meniscectomies, the chance of developing post-meniscectomy syndrome is high. Meniscal allograft transplantation (MAT) emerged in mid-80's as a potential solution to restore knee biomechanics, improve post-meniscectomy symptoms and, possibly, prevent or delay the onset of knee osteoarthritis [7]. This article is aimed to report an up-to-date short review of the literature regarding current indications and contraindications, clinical outcomes, complications and controversial issues (allograft preservation and sizing, allograft fixation, MAT in associated procedures, and MAT in the prevention of osteoarthritis).

Indications and Contraindications

The indications and contraindications for MAT have been summarized in (Table 1).

Indications	Contraindications
Tibiofemoral pain and:	Advanced osteoarthritis
Single compartment affected	Uncorrected axial malalignment
Young patient (<50 years old)	Uncorrected knee instability
Total/subtotal meniscectomy	Uncorrected focal high grade chondral/ osteochondral defect
Acceptable axial alignment	Inflammatory arthritis
Knee stability	Synovial disease
	Active knee infection
	Skeletal immaturity

Table 1: Summary of indications and contraindications of meniscal allograft transplantation

Joint replacement procedures cannot be offered to a young patient with post-meniscectomy syndrome who expects to have an active lifestyle or even engage in sports. Essentially, a young patient (<50 years) with unicompartment tibiofemoral pain after total or subtotal meniscectomy would be the indicated case. However, concomitant lesions have to be addressed in order to prevent complications with MAT. Thus, concomitant focal high-grade chodral osteochondral defects in the affected compartment, unacceptable axial malalignment or knee instability have to be corrected before or during MAT. Therefore, concomitant procedures such as cartilage repair, anterior cruciate ligament reconstruction, or tibial/femoral osteotomy can be also performed in the same operation [7-9]. Although some studies have reported acceptable results with MAT in patients with advanced cartilage defects (grades III and IV of the Outerbridge grading system) in terms of graft survival, pain relief, and function improvement [10,11], it is advisable to perform the MAT before these changes occur [9]. Osteophyte formation, femoral condyle flattening, or obesity might be considered relative contraindications to MAT [9,12].

Outcomes

There is an extensive experience with MAT around the world. Overall, clinical and functional outcomes are satisfactory, and MAT is currently considered a safe, reliable and justified procedure in selected patients [6,7,9,12,13]. During the first 5 years after MAT, physicians can expect a mean Lysholm score of 80 points (range 60-100), with still values between 60 and 80 points at a follow-up between 10 and 20 years [7]. Also, several studies have reported a significant improvement in postoperative values of the Lysholm score compared to preoperative values [14-19]. Many studies found significant improvements after MAT in the International Knee Documentation Committee (IKDC) [11,14,15,17,18,20], with percentages between 70 to 90% of nearly normal or normal values [21-23]. MAT has provided most patients with pain relief, adequate return to sports, and excellent satisfaction [6-9,10,11,14,15,17,18,21,24-27]. In general, quality of life has even improved after MAT [28], with physical and mental component summary values above those for the matched U.S. population [22,23]. Most studies report a Tegner score in the first 5 years from 3 to 7, corresponding to return to work and recreational sports [7]. Nonetheless, return to high-level competitive sports has been also reported after MAT [24-26]. Clinical outcomes like knee effusion, range of motion, stability, or dynamic muscular tests have also improved with MAT [9]. Verdonk et al. reported a mean cumulative survival time of 11.6 years, with no differences between medial and lateral allografts [29]. The cumulative survival rates for the medial and lateral meniscal allografts at 10 years were 74% and 70%, respectively [29]. Thus, the surgeon may expect an approximate survival of 70% of allografts at 10 years [30]. Several studies have reported the radiological outcomes of MAT [9]. In general, although some patients have no progression of cartilage degeneration [31], most patients will show worsening of articular cartilage leading to knee osteoarthritis [9]. The relationship of MAT and cartilage protection will be covered later in the article.

Complications

The term “failure” is defined as the need for graft removal with or without conversion to arthroplasty [7]. However, it is important to differentiate if the graft was removed because of progression to osteoarthritis requiring joint replacement, or, instead, because of graft complications itself. El Attar et al., found a mean failure rate of 10.6% and mean complications rate of 21.3% per trial in their systematic review [7]. Failure has been reported to occur at a mean of 2-3 years [32], 5 years [33], and 11.8 years [17]. The failure rate for medial allograft is higher compared to the lateral allograft [29]. Noyes et al. observed a different timing of graft failure in the lateral (mean of 53 months) and medial (mean of 25 months) menisci [34]. The most common complications for MAT are: graft tear, graft shrinkage, graft extrusion, knee stiffness (especially if MAT with associated procedures), infection, immune reaction, suture granulomas, portal pain, synovitis, and intraarticular hematoma [6,7,13,16,35,36]. The rate of graft tear is approximately 8% [6], which may be treated conservatively or operatively with meniscal repair or meniscectomy [18,37]. Regarding graft shrinkage, Milachowski et al. observed that this complication was clearly more common in lyophilized, gamma-irradiated compared to deep frozen grafts (90% and 40%, respectively) [38]. Lee et al. found that graft shrinkage occurred during the first 3 months and stabilized thereafter [39]. They reported that 65% of patients developed minimal shrinkage, 20% mild shrinkage, 16% moderate shrinkage, and 0% severe meniscal shrinkage at 1-year follow-up [39]. The authors reported that preoperative alignment, cartilage status, age, gender, extrusion, and time from previous meniscectomy did not influence the degree of meniscal shrinkage [39]. The average graft shrinkage reported by other authors is 7% (range 0 to 22%), with 32% being at least 10% of meniscal shrinkage [40]. Graft extrusion is a common complication [41-45], with an incidence ranging from 26%-32% [42,45] to 94%-95% [43,44]. The factors potentially related to graft extrusion include, but not limited to, fixation method (bone fixation less extrusion than suture fixation) [45], type of allograft (medial allograft more extrusion than lateral allograft) [41], area of the meniscus (anterior horn and body more extrusion than posterior horn) [31,42], and graft sizing method [42,43]. Despite the high incidence of meniscal allograft extrusion, this complication has not been clearly related to worsening of clinical, functional, and radiographic outcomes [41,43-47].

Controversial Issues

Graft preservation

There are four types of meniscal allografts: fresh, cryopreserved, fresh-frozen, and lyophilized [48]. One of the important differences between these types is the presence of donor cells in the fresh and cryopreserved, as opposed to fresh-frozen or lyophilized. However, it is not clear if presence of viable cells in the graft is an advantage or not. Jackson et al. demonstrated that within 4 weeks, the donor cells of fresh grafts are replaced by host cells in goats [49]. Gelber et al. demonstrated that cryopreservation did not elicit a significant modification in the collagen network by means of degree of disarray and fibril diameter, although the loss of viable cells was unpredictable [50]. In fact, it has been demonstrated that cryopreservation increases cell apoptosis in human menisci [51]. The principal advantage of cryopreserved over fresh allograft is a prolonged storage time in the former, maintaining the theoretical advantage of cell membrane integrity and viability of donor fibrochondrocytes that fresh allograft have [48]. Fresh-frozen grafts have no donor cells or histocompatibility antigens due to the freezing process [48]. Gelber et al. reported that freezing also caused changes in the collagen network in terms of decrease in fibril diameter and increase in fibril degree of disarray [52]. The theoretical advantages of fresh-frozen over cryopreserved allografts are lower immunogenicity, easier process, and lower cost [48]. Lyophilized allografts are not currently recommended because of high percentage of graft shrinkage and greater likelihood of synovitis [19,38,53]. Nowadays, the most commonly used and recommended types of grafts are cryopreserved or fresh-frozen [6,7]. Due to the theoretical risk of disease transmission, several methods of graft sterilization have been used. Use of ethylene oxide may cause synovitis [53], and gamma-irradiation may have detrimental effects on material properties of the allograft, like decreased viscoelasticity [54].

Graft sizing

Adequate graft sizing is important to mimic native menisci function. The most common sizing method is the use of preoperative anterior-posterior and lateral plain radiographs [6,55], although MRI [56,57] and CT scans [58] have also been employed. Plain radiographs take into account bony landmarks, and the most commonly used method has been described by Pollard et al. [55]. On the anterior-posterior plain radiograph, this method uses the landmarks of the peak of the medial tibial eminence and the medial tibial plateau margin, and the same for the lateral side. On the lateral radiograph, each anterior and posterior margins of the tibial plateau are used, but a correction factor is applied so that the medial meniscal length is 80% of the sagittal tibial plateau distance, and the lateral meniscal length is 70% of the sagittal tibial plateau distance [55]. Some studies have found that a reduction of 5% of the meniscal size determined by the Pollard method reduces the percentage of meniscal extrusion with no adverse effect on clinical and radiographic outcomes [43]. Despite plain radiograph are more commonly used for graft sizing [6], some studies have demonstrated that the use of MRI is more accurate than plain radiographs [56,57]. An oversized and undersized graft increases forces across the articular cartilage and allograft, respectively [59]. Dienst et al. suggested that a mismatch up to 10% of the size of the original meniscus would be acceptable [59]. The improvement of graft sizing and the better understanding of tolerance and consequences of size mismatch warrant further research.

Fixation Methods

The fixation of meniscal allograft is crucial to prevent short and mid-term complications due to altered knee kinematics. However, there is a lot of controversy on this topic. Allograft fixation differs when considering meniscal horns or meniscal periphery. While peripheral fixation is achieved by sutures through any of the available techniques (all-inside, outside-in, or inside-out), the fixation of meniscal horns may be achieved through either sutures or bone plugs/bridge (Figure 1).

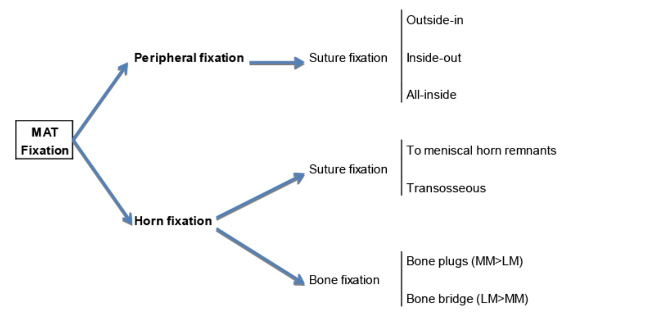

Figure 1: Summary of meniscal allograft transplantation fixation methods MAT, meniscal allograft transplantation; MM, medial meniscus; LM, lateral meniscus

Bone-to-bone healing technique for meniscal horns is different depending on whether dealing with the medial or lateral meniscus. In general, the surgeons preferring bone-to-bone fixation use bone plugs for the medial meniscus, and bone bridge for the lateral meniscus. In the latter, the proximity of both horns makes a bridge more suitable compared to bone plugs. MAT were initially fixed through sutures [38,60], but shortly after bone fixation was described [61]. In bony fixation of the medial meniscus, one tunnel drilled in each horn is performed and the bone plugs (with sutures attached to each one) are inserted in each tunnel, and the sutures attached to each plug are tied together in the anterior cortex of the tibia. Some in vitro studies have demonstrated that fixation with bone plugs is better compared to graft fixation without bone plugs in terms of restoration of normal contact mechanics of the knee [62-64]. Nonetheless, other biomechanical in vitro studies have demonstrated no differences in mean pullout strength of medial meniscus allograft between both fixation methods [65]. Moreover, MAT without bone plugs have demonstrated good and excellent results in terms of pain relief and clinical and functional outcomes with a maximum follow-up between 6 and 14 years [14,16,29], even in the high-level athlete in whom good symptoms relief, knee function and return to sports has been reported [24]. Suture-only fixation has demonstrated higher degree of meniscal extrusion, but this was not related to worst functional outcomes [45]. In addition, clinical studies comparing both fixation methods have demonstrated no differences in clinical, functional, or radiographic outcomes [66]. Although bony fixation is currently more extended than suture fixation [9], some authors still recommend the use of suture fixation to avoid potential cartilage damage on either the tibial or femoral sides [31]. This recommendation is also based on the fact that bone fixation requires a nearly perfect graft sizing to avoid poor results [31,67,68]. It is likely that both bone and suture fixations provide adequate biomechanical and clinical outcomes whenever both are secure and strong enough [6], and allograft size matches the recipient, but this needs further investigation in the coming years. Regarding peripheral fixation, it is important to provide strong vertical sutures tied over the joint capsule, with an adequate meniscal rim not only as a mechanical support to prevent peripheral extrusion [6], but to promote healing and incorporation of the graft whenever a bleeding rim is created.

Associated Procedures

The association of MAT to other surgical procedures (mainly cartilage repair/restoration, anterior cruciate ligament reconstruction, or femoral/tibial osteotomy) is more common than isolated MAT [7]. The most common associated procedure is ligament reconstruction followed by cartilage repair/restoration and then cartilage repair and osteotomy combined [7]. In general, the results of MAT associated with anterior cruciate ligament reconstruction or cartilage repair/restoration are not worst compared to isolated MAT [6-8]. MAT and associated cartilage procedures (autologous chondrocyte implantation, osteochondral allograft, osteochondral autograft or microfractures) essentially provide similar improvement in pain relief, KOOS score, IKDC score (subjective), Noyes score, Tegner score, and sports level compared to isolated MAT [15,32,34,69,70]. Only Lysholm and modified Cincinnati scores were lower in the combined compared to isolated MAT [71,72]. Although MAT associated with cartilage procedures had low complication and failure rates, there was a relatively high rate of subsequent surgery [8]. There are also numerous studies combining MAT and anterior cruciate ligament reconstruction [6,7,9]. In general, the association of this ligament reconstruction to MAT does not worsen pain relief and clinical and functional outcomes when compared to isolated MAT [21,37,73]. Isolated procedures elicit a tendency towards better Lysholm [17], but lower physical-role (SF-36) [33] compared to combined procedures. There are also several studies employing osteotomy as combined procedure to MAT [6,7,9]. Essentially, pain relief, clinical and functional outcomes are not worsened by the addition of femoral/tibial osteotomy to MAT [10,11,34,47,60,74]. The presented evidence suggests that MAT can be associated with any needed additional procedure without high risk of worst results.

Osteoarthritis

MAT attempts to improve knee mechanics by improving the load-distributing properties in the involved compartment and so preventing or slowing the process of cartilage degeneration. However, the role of MAT in the prevention of knee osteoarthritis is strongly questioned. There are several studies reporting on the development or progression of cartilage deterioration after MAT [6,7,9]. In most patients, some degree of joint space narrowing has to be expected but in some cases this narrowing is less than 1 mm [6]. In general, studies have demonstrated a trend of advancing cartilage deterioration overtime that correlates with MAT failure, even when cartilage lesions have been addressed with a cartilage-preserving procedure [10,75]. Although the majority of studies found no protective effect of MAT on knee cartilage [6,7,9], there are also several investigations both in animal models [76-78] and humans [31,33,73,75] reporting on the chondroprotective effects of MAT on knee cartilage. However, many studies have not provided a follow-up long enough to elaborate definitive conclusions on this controversial topic [6,7,9]. Studies with the longest follow-up focus on progression of radiological changes in the affected knee. These studies found a range from progression observed in all treated cases when using lyophilized and deep-frozen grafts [79], to progression evidenced in 59% of the cases with use of cultured viable grafts [47]. Verdonk et al. wrote that surgeons may expect a chondroprotective effect of MAT in about 30% of patients [9], but this has to be further investigated in the coming years. Overall, in the light of the current literature it cannot be stated that a meniscal allograft is able to preserve or even delay the operated knee from osteoarthritis.

Further Directions

Due to the limited availability of meniscal allografts and the concerns related to its use, namely the transmission of infectious diseases, alternative options for meniscal replacement are being developed. Currently two such devices are available in Europe for clinical use: the Collagen Meniscus Implant (CMI. Ivy Sports Medicine, Lochhamer, Germany), a bioresorbable type I highly purified collagen matrix; and the Actifit (Orteq Bioengineering, London, UK), a synthetic, biodegradable, acellular scaffold composed of aliphatic polyurethane. Both of them designed to serve as a template for ingrowths of new meniscal tissue in cases of partial meniscal lose. Meniscal scaffolding implants have been proven to be safe in the last decade and should be considered in the near future.

Recent investigation in this field has been focusing in the use of stem cells for meniscal regeneration. Several recent models have been using mesenchymal stem cells to experimentally replace meniscal tissue [80,81]. In the future, stem cells may provide an alternative, potentially autogenous, source of meniscal tissue to regenerate the resected segment. Therefore, tissue engineered scaffolds and gene therapy, or combinations thereof may either be an alternative to meniscal allografts. Likewise the use of the very same approaches may improve the behavior of meniscal allografts in terms of integration to the surrounding tissue and graft repopulation by new cellularity able to synthesize and maintain a healthy meniscal tissue.

Summary

The principal indication for MAT is tibiofemoral pain in a single compartment in a young or middle-aged individual (usually less than 50 years) with previous total or subtotal meniscectomy with no axial malalignment or knee instability.

The principal contraindications for MAT are: advanced osteoarthritis, uncorrected axial malalignment or knee instability, uncorrected ipsilateral focal high grade chondral or osteochondral defect, inflammatory arthritis or synovial disease, infection, or skeletal immaturity.

In general, MAT has demonstrated significant pain relief and improvements in clinical (knee effusion, range of motion, stability, or dynamic muscular tests) and functional (Lysholm, Tegner, IKDC, or return to sports) outcomes, and patient’s satisfaction.

The cumulative survival of MAT may be around 70% at 10 years.

The most common complications of MAT are: graft tear, graft shrinkage, graft extrusion, knee stiffness, infection, immune reaction, suture granulomas, portal pain, synovitis, and intraarticular hematoma.

The most commonly used and recommended types of grafts are cryopreserved and fresh-frozen.

The most common graft sizing method is the use of preoperative anterior-posterior and lateral plain radiographs, although MRI and CT scans have also been employed.

There are no clear differences between the uses of bone plugs/bridge and suture fixation of the allograft. In general, meniscal periphery is attached through sutures tied on the capsule, whereas horn fixation may be achieved through bone plugs (medial meniscus), bone bridge (lateral meniscus), transosseous sutures, or sutures attaching the graft into the meniscal horn remnants.

The association of anterior cruciate ligament reconstruction, cartilage repair/restoration procedures, or femoral/tibial osteotomy to MAT does not worsen the results compared to isolated MAT.

The role of MAT on the prevention of cartilage degeneration cannot be established with the available literature.

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