

MENISCAL ALLOGRAFT TRANSPLANTATION: AN OVERVIEW AND FUTURE DIRECTIONS

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ABSTRACT:

The structure of the menisci allows the effective distribution of load across the knee joint. Even though our first priority goes to meniscus-preserving surgery, but many tears are irreparable, and many repairs are not successful. It is widely accepted that partial meniscectomy leads to early onset of osteoarthritis (OA). Meniscal allograft transplantation (MAT) was developed as a means of treating the symptoms of compartmental overload after meniscectomy and numerous case series have reported a significant improvement in knee function with reasonable rates of complication and survival, but randomized controlled trials have not been undertaken. Meniscal allograft transplantation has been performed for more than 30 years and numerous case series have consistently reported as protective of cartilage. The main goal of this review article is to provide an overview and current status of the role of MAT and also discussed the directions to advance the MAT in the future.

Keyword: *Meniscal allograft transplantation¹, meniscus replacement², meniscus repair³, meniscectomized knee⁴.*

INTRODUCTION:

The menisci are a wedge-shaped semilunar disc of fibrocartilaginous tissue, which is located between the tibia and the condyles of the femur in the medial and lateral compartments of the knee [1]. The ligaments which are attached to the tibia at both the anterior and the posterior horns by insertional ligaments, and to the deep medial collateral ligament, the transverse or intermeniscal ligament and two menisiofemoral ligaments [2]. Normally, menisci are composed of 75% of water and the remaining percentage composed of organic matters like collagen (mostly Type I, with smaller quantities of Types II, III, and V), proteoglycans and elastin [3]. When we go back to history, menisci were used to be considered the vestigial remnants of a muscle within the knee joint, but they have important biomechanical functions within the knee. Having functions as load sharers, shock absorbers, proprioception, joint

lubrication and nutrition of the articular cartilage, they are also functioning secondary stabilizers particularly in the absence of a functioning anterior cruciate ligament [4].

In orthopedic sports medicine, meniscal tears are one of the most common injuries with an incidence of 24 per 100,000 per year and show a bimodal distribution with a first peak in the young and athletic population, and the second peak in middle-aged patients with degenerative joint disease [5]. The most common cause of knee injuries is an injury during sports activity, which is often combined with anterior cruciate ligament (ACL) rupture [6]. Meniscus surgery is the most frequently performed procedure done by orthopedic surgeons (especially sports medicine surgeons) and have quickly advanced from an open procedure to arthroscopic surgery during the previous two decades [7,8]. Though meniscectomy has been promoted as the treatment of choice for many years, the fundamental principle of meniscus surgery is to preserve as much 'normal' meniscus as possible [9]. Therefore, the meniscal tears with a high probability of healing with surgical intervention are repaired (meniscus repair) but most tears are not repairable and partial to total meniscectomy is an alternative [10,11].

To preserve meniscal functions, Meniscal repairs and partial meniscectomies are attempted, but patient-specific factors such as age, concomitant injury, location and size of the tear, degree of injury, recurrent meniscal injury, and tear pattern frequently require subtotal or total meniscectomy, which was the recommended management of meniscal tears since the second half of the 19th century [12,13]. Thus, for central and unstable lesions in the white zone of the meniscus, meniscectomy was indicated to obtain a better short-term outcome [14], but the consequence of the partial or complete loss of the meniscus leads to early development of chondromalacia and osteoarthritis [15]. It has been advocated that the contact area between the tibia and femur is reduced by 50% in a meniscectomized knee [16], and represents a significant risk factor for definite radiological tibiofemoral osteoarthritis (OA) after 21 years with a relative risk of 14.0 (95% confidence intervals) [17].

Thus, to reduce the drawbacks of meniscectomy, to restore the functions of the meniscus, and to reduce pain in a meniscectomized knee, Meniscal allograft transplantation (MAT) has been introduced. The main objective of this review article is to provide an overview and current status of the role of MAT in the management of a case of total meniscectomy and also to improve the understanding of MAT with a recently published data. Additionally, directions to advance the MAT in the future are also discussed.

MENISCAL ALLOGRAFT TRANSPLANTATION:

Meniscal allograft transplants are not better than normal but maybe better than absent. In history, Meniscal replacement began to step forward in the 1980s as a response to the consequences of meniscectomy. In 1989, Milachowski and his team [18] reported a case series of meniscal transplantation in 30 sheep and 22 human patients, where the first human meniscal allograft transplant was performed by this group in May 1984 and concluded that meniscal allograft transplantation was a logical procedure and provide no adverse immunological reactions. The main objective of MAT was to prevent and sometimes even reverse the progressive joint degeneration in a meniscectomized knee. Kazi et al (2015) performed a 15- years follow-up study of eighty-six allograft of mean age 40 years and found that the graft survivorship is good, providing a mean of 12.5 years prior to knee arthroplasty in those requiring conversion with 71 % of allografts still in situ and functioning at a mean of 15 years post-surgery [19].

In 2014, McCormick et al, [20] underwent MAT of 200 patients with mean age of 34.3+/- 10.3 years, Eight of 172 patients (4.7%) went on to require revision MAT or total knee replacement. There was a 32% reoperation rate for MAT, with simple arthroscopic debridement being the most common surgical treatment (59%), and a 95% allograft survival rate at a mean of 5 years. The technique he used was Bridge-in-slot with exception of patients undergoing ACL reconstruction. In addition, Van Der Straeten C et.al. (2016) indicates that meniscal allograft transplantation (MAT) performs well in patients younger than 35 with no-to-mild cartilage damage. These patients may benefit from MAT for the relief of symptoms, but patients and surgeons should be aware of the high number of surgical re-interventions [21].

The major indications for MAT are [22]:

- Total or subtotal knee meniscectomy with early arthritis - to delay the progression of degeneration
- Prophylactic transplantation - to avoid consequences of meniscectomy

- Loss of anterior cruciate ligament (ACL) - to provide additional stabilization and protection of the ACL
- Concomitant osteotomy- to improve the effect of the high tibial osteotomy and to delay recurrent deformity
- Failure of conservative treatment

In addition to the above indications, the patient must have pain in the compartment. This compartment-specific pain in the meniscectomized knee is termed as the “post-meniscectomy syndrome.” Thus, the ideal patient for MAT is young patient, without any ligamentous instability, an appropriate axial alignment has intact cartilage surfaces, and has focal pain in the meniscus deficient compartment [23].

CONTRAINDICATIONS FOR MAT:

Patients with severe degenerative changes in the knee joint and BMI > 35 kg/m² are contraindicated for MAT. Instability, malalignment, open physes, effusion, and history of infection in the knee joint should be also included in the list of contraindications [22,24]. Patients with Noncorrectable grade IV chondromalacia especially those with opposing cartilage surfaces, should not be considered candidates for MAT [25]. In contrast, Kempshall et al. [26] concluded that patients with advanced chondral damage should not be excluded from MAT.

PRE-OPERATIVE EVALUATION:

For meniscal transplantation, the initial assessment of suitable patient starts from a careful history and thorough physical examination because proper patient selection is the key to success with this procedure. Physical examination should include the evaluation of lower extremity alignment, ligament status, and gait, along with the presence of joint line tenderness, positive McMurray's sign, and effusion should also be determined [27]. All the above-mentioned contraindications and indications for MAT should be strictly followed to achieve the better outcome. Rodeo et al. [28] found that standing radiographs including flexion views of the knee joint to examine the flexion weight-bearing zone of the femoral condyle, and standing hip-to-ankle views for assessment of the mechanical axis are required prior to surgery. They also concluded that magnetic resonance imaging (MRI) is possibly the most sensitive tool for the assessment of subchondral bone remodeling, subchondral marrow edema, as well as early softening and fibrillation of hyaline cartilage [28].

GRAFT PROCESSING AND GRAFT SIZING :

Fresh tissue is an ideal meniscal transplant, but due to logistical difficulties and cost issues, fresh frozen and non-irradiated implants give good results. The aggressive preservation and sterilization techniques can reduce the material properties of the meniscus transplant and the risk of disease transmission cannot be omitted completely. Although autogenic tissues are free from infection, always available and inexpensive, but the material properties of autogenic tissues are substandard in comparison to the allograft [29]. Meniscal allografts may be fresh, cryopreserved, fresh frozen, or lyophilized where fresh and cryopreserved allografts contain viable cells at the time of transplantation, while fresh-frozen and lyophilized tissues are acellular [28]. Shukur Ahmad et al. (2017) performed hypothesis that cryopreserved meniscal allograft would maintain the original biomechanical properties compare to fresh frozen allografts and found that cryopreserved menisci showed a higher elastic modulus and higher ultimate tensile strength than fresh frozen. They achieve a significant difference between the two methods of preservations and recommend the use of cryopreserved meniscus as it retains the meniscus biomechanical properties [30].

Careful attention should be paid to obtaining a properly sized graft because a successful meniscal allograft transplantation procedure starts with appropriate size matching. Oversized meniscal allografts increased the forces across the articular cartilage, whereas undersized allografts resulted in normal forces across the articular cartilage, described by Deinst and his coworkers [31]. The most reliable methods of predicting the meniscal size for transplantation is described by Kaleka et al. [32]. According to this study, considering MRI as the gold standard,

Yoon method [33] can be used to assess length for the lateral meniscus and the Pollard method [34] is considered a satisfactory alternative for the medial meniscus. Anthropometric data are an alternative for the width of the graft.

SURGICAL TECHNIQUES:

In the past 2 decades, several techniques have been described for MAT, which has included open and arthroscopically assisted techniques and these techniques are divided into two major groups: fixation with bone plugs or blocks and soft tissue fixation without bone plugs. The International Meniscus Reconstruction Experts Forum (IMREF) believes that there is no superiority of one surgical technique over another technique (bone fixation vs soft tissue). The practice within the IMREF group observed that 74% of surgeons like better to use bone fixation compared with 26% preferring soft tissue. Of those surgeons using bone fixation, the first choice goes for a slot or bone bridge technique on the lateral side and bone plugs for the medial side [35]. The most commonly performed bone fixation methods are double bone plugs and bone bridge techniques (dovetail, trough, and keyhole). Moreover, MAT without bone plugs has shown good and excellent results in terms of pain relief and clinical and functional outcomes [36,37], though the degree of extrusion is higher than the bony fixation [38].

In 2013, Roumazeille et al. [39] performed minimally invasive arthroscopy with fresh-frozen allograft without bone plugs in 22 patients of mean age 37 ± 7.5 years, but the 6-months follow-up were 14 patients, out of which the results show 8/14 (57.1 %) had total graft healing, 2/14 (14.3 %) partial healing and 4/14 (28.6 %) no healing. However, at final follow-up, all functional scores had significantly improved and the average pre- and post-operative joint space thickness was similar. In 2016, Zaffagnini et al. [40] stated that Arthroscopic MAT without bone plugs improved function of knee and pain reduction, allowing return to sports in 74% of patients and return to the pre-injury activity level in 49% of patients at midterm follow-up and also conclude that only age at surgery seemed to affect outcomes. Lee et al. [41] performed arthroscopic medial meniscal transplantation with modified bone plug technique where preparation of anterior bone plug with a long cylindrical shape and the posterior bone plug with a flat bone shell containing a cancellous portion was done which helps to facilitate easy fixation of the posterior bone plug as well as bone-to-bone healing. The bone plug technique also performed by Woodmass et al. [42] but in lateral meniscal transplantation and described the advantages of osseous integration and graft stability through a minimally invasive bone plug technique. The key-hole technique for MAT described by Lee et al. [43] is an effective technique in which an allograft with a bone bridge fixed to accommodate the key-hole –shaped slot which is properly secured with the slot. This technique helps to restore relatively normal anatomy of the meniscus and could be a curative procedure to delay articular cartilage degeneration.

In 2017, Monllau et al. [44] performed a simple, reproducible, and implant-free technique to perform a lateral capsular fixation (capsulodesis) at the time of lateral MAT in an effort to reduce or prevent graft extrusion. Recently, Zhang et al. [45] designed two sets of surgical implements: first set to produce bone plugs of appropriate sizes in the anterior and posterior horns of the allograft meniscus i.e. bone plug implements and a second set to create bone tunnels in the receptor tibial plateau to hold the bone plugs i.e. bone tunnel implements. This study demonstrated that an all-arthroscopic approach to MAT was possible and the specifically designed surgical instruments for consistent preparation of grafts and recipient tissues contribute to a standardized approach to MAT. Overall, it is currently acknowledged that bone attachment of the anterior and posterior horns of the meniscus is the gold standard for MAT [46]. However, the trial of partial replacement of the meniscus by means of meniscal scaffolds mainly collagen or polyethane-based is going on and Tissue Engineering and Regenerative Medicine (TERM), which aim to develop new implants, biomaterials and biological enhancements of surgical approaches like cells, growth factors, proteins, nanotechnology, hydrogels, etc are the other advanced approaches which are under clinical trials and development [61].

REHABILITATION:

Rehabilitation after joint surgery plays an important role to evaluate the outcome of that surgery. The principle behind rehabilitation after MAT is to facilitate the return of knee function while respecting the healing process of the allograft tissue. Zaffagnini et al. [40] in 2016 applied postoperative rehabilitation by immobilization for 2 weeks and

then toe-touch weight bearing but restricted the range of motion (ROM). Then followed by isometric exercises, closed chain strengthening, and ROM from 0 to 90° during 3-4 weeks. Full weight-bearing started at week 6 postoperatively and patients were allowed to fully flex the knee joint. The sport-specific exercises and running were started after 3 months. The low-demand recreational activities like ballet, tennis, skiing, baseball, and boxing were not allowed until the 4th month and before 8 months postoperatively, patients were advised not to involved in competitive sports activities such as soccer, basketball, rugby, and volleyball. Likewise, Kempshall et.al. [26] applied the first 6 weeks of rehabilitation as limited weight bearing to diminish the traction forces on the meniscal root anchor points and followed by early ROM from 0 to 90° and active static quadriceps exercises are commenced with avoidance of open chain quadriceps exercises during this early period. After 6 weeks postoperatively, weight bearing, strengthening, and proprioceptive rehabilitation are steps forward. A functional and sports-specific rehabilitation programme starts from 6 months with a return to normal activities from approximately 9 months.

Marcacci et al (2014) [47] reported a series of 12 professional soccer players who underwent MAT, in which 92% returned to playing soccer professionally. At 36-months follow-up, 9 players (75%) were still playing professionally and 2 were playing semi-professionally. The mean time for returning to competition was 10.5 months and all the clinical scores improved. These facts may allow us to widen the indications to competitive sportsmen, though the high-level clinical data to assess the long-term results of MAT in athletes are still not available. Noyes et.al. estimated the probability of survival for all transplants was 85% at 2 years, 77% at 5 years, 69% at 7 years, 45% at 10 years, and 19% at 15 years [48]. According to International Meniscus Reconstruction Experts Forum (IMREF) 2015, a rehabilitation program and return-to-sport prescriptions are designed to consist of 4 stages [35]:

- Stage 1: Early restorative phase (0-8 weeks)
- Stage 2: Strength and conditioning phase (2-6 months)
- Stage 3: Functional rehabilitation progression phase (6-9 months)
- Stage 4: Sport-specific training and return to sport (>9 months)

FOLLOW-UP EVALUATION/OUTCOME AFTER MAT:

In most studies, the outcomes of MAT have been evaluated using clinical parameters. In addition to detailed physical examination, post-operative evaluation is performed by use of clinical parameters such as the Lysholm score and Tegner activity scale [49], and international knee documentation committee (IKDC) scores [50], as well as Short Form 12 (SF-12), visual analog scale and modified pain scores [51,52]. Although the proven benefits of the procedure are pain relief and functional improvement, these clinical assessments do not accurately reflect the status of meniscal transplants. It is more sensible to carefully assess the graft condition itself and for this diagnostic arthroscopy is the most accurate objective evaluation method, but is an invasive modality. Thus, Radiographic evaluation and MRI scans are more commonly used as a relatively reliable and noninvasive evaluation method [52].

The knee injury and osteoarthritis outcome score (KOOS) is a region-specific score that is widely accepted and presents a measure of the general status of the knee. This is self-administered and evaluates five outcomes: pain, symptoms, activities of daily living, sport and recreation function, and knee-related quality of life. KOOS is particularly important as MAT patients often have significant concomitant knee pathology and has been shown to be responsive to change in patients with knee Osteoarthritis [53]. The western ontario meniscal evaluation tool (WOMET) [54] is a disease-specific score and validates a health-related quality of life (HRQOL) index for patients with meniscal pathology. The other evaluation tool is the marx activity rating scale [55], which is a 4-item activity rating scale. In this tool, patients are asked to rate how often they were able to perform each activity like running, cutting, decelerating, and pivoting in their most healthy and active state. The EQ-5D tool developed by the EuroQol Group [56] is a quality of life and utility tool that is easy to use and becoming more accepted internationally.

FUTURE DIRECTIONS:

Meniscal allograft transplantation appears as a useful alternative for selected patients with a stable knee and appropriate alignment where some long-term studies prove that cartilage protection is achievable [57]. MAT is an

effective biologic reconstruction method for a meniscectomized knee that reduces symptoms in the affected compartment. Although complications including a tear of the allograft, synovitis, effusion, or infection have been reported, when considering only isolated MAT, the acceptable complication rate is 3.6 % [58]. Therefore, the orthopedic surgeons should keep in mind that transplanted menisci could not restore perfectly the normal meniscal function but just improve functions with a possible chondroprotective effect in the meniscectomized knee [59]. Patients should be clearly advised that the procedure is not curative in the long term, and additional surgery will likely be required. Recently, Nordberg et.al. [60] provides a new method for enhanced cellular infiltration in meniscal allografts where human adipose-derived stem cells(hASC) can be easily isolated in large quantities for autologous use and could be an ideal cell source to repopulate an allograft scaffold before transplantation into the patient. This study enhanced successful tissue engineering utilizing hASC, which could improve long-term efficacy of MAT procedures by maintaining the meniscus in vivo. Therefore, High-quality prospective comparative trials and randomized control trials with larger sample sizes are required to further evaluation of the most appropriate technique and selection of the graft. However, more data are necessary to verify the pre-operative evaluation, complication, survivorship, reoperation, and failure rates of MAT. The logistics difficulties and cost issues should be direct properly, and the rehabilitation time after MAT must be idealized to secure the better outcome.

CONCLUSIONS:

The anatomy and microstructure of the meniscus allow the effective distribution of load across the knee joint. Our overview of treatment for meniscectomized knee shows some promising step forward in the understanding of the important role of the meniscus that has led to a move toward meniscal transplantation. The goal of transplantation is to prevent and possibly even reverse the progressive joint degeneration that predictably follows meniscectomy. Careful patient selection and referral to subspecialty-trained, higher-volume surgeons should be considered to optimize clinical outcomes. Therefore, MAT seems to be a reasonable treatment option in correctly selected patients.

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