INSTRUCTIONAL REVIEW: KNEE

Meniscal allograft transplantation

RATIONALE FOR TREATMENT

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The anatomy and microstructure of the menisci allow the effective distribution of load across the knee. Meniscectomy alters the biomechanical environment and is a potent risk factor for osteoarthritis. Despite a trend towards meniscus-preserving surgery, many tears are irreparable, and many repairs fail.

Meniscal allograft transplantation has principally been carried out for pain in patients who have had a meniscectomy. Numerous case series have reported a significant improvement in patient-reported outcomes after surgery, but randomised controlled trials have not been undertaken.

It is scientifically plausible that meniscal allograft transplantation is protective of cartilage, but this has not been established clinically to date.

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Meniscus structure and function

The menisci are fibrocartilaginous structures located between the two tibiofemoral articulations of the knee. They are crescent-shaped in the axial plane and wedge-shaped in the cross-section. They are attached to the tibia by their insertional ligaments at both the anterior and the posterior horns, as well as by attachments to the deep medial collateral ligament, the transverse (intermeniscal) ligament and two meniscofemoral ligaments.1 They are also attached to the joint capsule along their convex peripheral rim.

The menisci are made up of approximately 75% water, 20% type I collagen and 5% of other substances, including proteoglycans, elastin and type II collagen.2,3 The microstructure of the meniscus is highly complex and varies according to anatomical region. Overall, the collagen fibres form a dense framework, with most running circumferentially and some radially.4 Peterson and Tillmann5 examined menisci under a scanning electron microscope and found three distinct layers: a peripheral fibril network with fibres of no specific direction, a lamellar layer and a central main portion of circumferentially-oriented fibres. Andrews et al6 used optical projection tomography on bovine menisci and found that there was a clear transition from an outer meniscus of highly aligned collagenous fibres in the circumferential direction, to a woven, less aligned structure in the inner meniscus. They described the outer portion as being close to a ligament in structure, whereas the inner portion more closely resembled hyaline cartilage. Two types of fascicle organisation were seen within the meniscus: braided and woven.6 Braiding is commonly seen in ropes and results in increasing stiffness with increasing deformation owing to increasing friction. This organisation is well suited to the circumferential hoop stresses that the meniscus is exposed to during loading.7 The woven structure is commonly used to withstand compressive loads. It converts compressive forces into tensile forces, as occurs in a woven basket.6

Menisci are found in all mammals, although there is variation in their shape and attachments.8 It is generally accepted that their primary role is to distribute load.9-11 The concave upper surface of the meniscus and its flat lower surface increase the congruency of the otherwise incongruent tibiofemoral joint. In the loaded knee the lateral meniscus transmits 70% of the load and the medial meniscus 50% across their respective compartments.12 Biomechanical studies have shown that meniscectomy reduces the area of tibiofemoral contact by 50% to 75% and increases peak contact pressures two to threefold.13-15 The menisci have also been shown to provide secondary constraint to the knee.16-18 Further proposed roles include joint lubrication19 and proprio-
Consequences of meniscectomy

Meniscal tears are a common occurrence. A recent review of knee operations carried out in England under the NHS, found that the yearly incidence of meniscal surgery was 35 per 100,000 population. Throughout the 20th century, treatment shifted from complete excision to meniscus-preserving surgery where possible. Despite this, many tears are irreparable and there is a high rate of failure for repaired tears. The consequences of meniscectomy have been well documented. Roos et al compared 123 patients who had undergone open meniscectomy for an isolated tear with age- and gender-matched controls 21 years after surgery and found a relative risk of 14 (95% confidence intervals 3.5 to 121.2) for definite radiological osteoarthritis (OA). Hunter et al reviewed 257 patients with symptomatic OA of the knee over 30 months and found a strong association between meniscal damage and cartilage loss. The same group also found that loss of meniscal coverage and height was associated with cartilage loss. In a systematic review of studies with a minimum of five years’ follow-up, Papalia et al found that the mean prevalence of knee OA was 53.5% (16.0% to 92.9%) after meniscectomy. They also found that the mean prevalence of radiological evidence of OA in the operated group was 39.5% compared with 6.46% in the opposite knee. Englund et al looked specifically at patients with meniscal damage who had not had surgery, to identify whether meniscal damage was a risk factor for OA independently of meniscectomy. They performed a case-control study over 30 months and found an odds ratio (OR) of 5.7 for developing OA if meniscal damage was present compared with no meniscal damage.

It is thought that damage to the meniscus results in changes to the biomechanical and biochemical environment of the knee which may lead to the progression of OA in susceptible patients. Baratz et al performed a cadaveric study which showed that total meniscectomy reduces the tibiofemoral contact area by 75% but increases peak contact stresses by a factor of 2.35. Similar findings have been reported in other studies. More recent studies have shown that there are local biomechanical changes to the articular cartilage and knee joint after meniscectomy. Song et al reported that meniscectomy accelerates deformation of the articular cartilage during loading and that, compared with the normal knee in a sheep model, the cartilage remains chronically deformed and dehydrated on unloading. Haemer et al found a significant increase in central strain in articular cartilage and subchondral bone, close to the reported failure limits for cartilage. They also found a significant loss of articular fluid pressurisation peripherally, which may allow capillary invasion, subsequent endochondral ossification and osteophyte formation. These changes in articular cartilage have also been seen after partial meniscectomy. Animal studies have also reported articular cartilage softening and fibrillation, swelling, fissures and cytokine-mediated responses following meniscectomy.

Meniscal allograft transplantation

Meniscal substitution and replacement began to emerge in the 1980s as a response to the consequences of meniscectomy. Toyonaga, Uezaki and Chikama reported the results of using a Teflon net as a meniscal substitute in dogs. Three years later, another study reported the successful implantation of medial meniscal allografts in dogs. This showed for the first time that a completely detached meniscus could be successfully implanted. In 1989, Milachowski, Weismeier and Wirth reported a case series of meniscal transplantation in 30 sheep and 22 human patients. The first human meniscal allograft transplant was performed by this group in May 1984. The authors concluded that meniscal
allograft transplantation was a reasonable procedure and produced no adverse immunological reactions.42 Since the first reported human meniscal transplant there have been many case series reported in the literature.43-49 A recent systematic review reported over 1600 cases, although the total number performed is likely to be many more.50 In 2003 it was estimated that more than 4000 transplants had been performed in the United States alone, with a yearly total approaching 800.51 Figure 1 shows arthroscopic images of a meniscal allograft in the lateral compartment of a knee at the time of surgery and two years post-operatively. This operation is primarily performed for relief of compartmental pain in patients who have undergone meniscectomy. These symptoms are thought to result from a biomechanically ‘overloaded’ knee.50 The patient-reported outcomes from case series have been encouraging, but no randomised controlled trials (RCTs) have been performed. A recent systematic review reported that the mean weighted Lysholm score52 (scores 0 to 100, with 100 being the best) improved from 56 pre-operatively to 83 at the final follow-up (weighted mean follow-up 5.1 years; 1 to 20).53 The authors also found that other patient-reported outcome measures had improved by similar degrees at final follow-up, a finding that has been supported by other systematic reviews.50,54,55 Pooled complication rates for isolated meniscal transplantation have ranged from 6% to 11%, although this is likely to be an underestimate.50,54 Graft survival time has been reported to be between ten and 16 years.56-58 Disease transmission and immune rejection are also possible complications, albeit extremely unlikely.59 The meniscal allograft is thought to be immune privileged, and there has only been one reported case of possible rejection.60

**Indications**

The primary indication for meniscal allograft transplantation is to treat a symptomatic compartment of the knee in a patient with a history of a (sub)total meniscectomy. The classic symptom is compartmental pain on activity, although swelling can also be a feature. The upper age limit for meniscal allograft transplantation is usually 50 to 55 years, although most case series usually only define their patients as ‘young’.53

Although there are no RCTs, there is a consensus that malalignment (varus with medial meniscal deficiency or valgus with lateral meniscal deficiency) and ligamentous instability are contraindications to meniscal transplantation, unless addressed at the time of surgery.50,53,61 In a recent systematic review, over half of all patients who had a meniscal allograft transplant had at least one other concomitant procedure, of which approximately 45% were cartilage procedures, 37% were reconstructions of the anterior cruciate ligament and 13% were osteotomies.50

The acceptable degree of chondral loss is controversial. The presence of full-thickness chondral loss may provide a potentially worse mechanical environment for the meniscal transplant. Traditionally, meniscal allograft transplantation was contraindicated in the presence of severe chondral loss (Outerbridge IV/ICRS 3b or worse63). However, some studies have reported undertaking it in this group of patients, mostly with concurrent procedures such as microfracture or matrix-induced autologous chondrocyte implantation, with good results.44,45,64 This may broaden the indications for meniscal transplantation, in the absence of other appropriate interventions.

**Chondroprotection**

It has been stated that the most important question in meniscal allograft transplantation is whether it can help preserve the articular cartilage of the knee.65 This question is also vital to the scientific plausibility that it is an effective treatment. Despite this, there is currently little definitive evidence that this is the case. Sekiya et al66 compared joint space changes after meniscal allograft transplantation with that in the opposite knee, and found no significant difference between the groups. Other studies have found no loss of joint space after meniscal transplantation.67-69 Others still have found a statistically significant loss of joint space.70,71

Biomechanical studies support the hypothesis that meniscal allograft transplantation is chondroprotective, as they have shown that meniscal transplantation improves peak contact stresses and total contact area after meniscectomy.50,72,73 One study found that peak contact stresses were not significantly different in either the native or the transplanted knee.15 Animal model studies have also demonstrated chondroprotective effects of meniscal allograft transplantation when compared with meniscectomy. Szomor et al74 reported significantly better protection of the articular cartilage at four months in the meniscal transplantation group of a sheep model than in the meniscectomy group. Kelly et al75 performed a similar study using MRI and found significantly less articular cartilage degeneration in the transplantation group than in the meniscectomy group.75

**Controversies**

There are various controversial issues surrounding meniscal transplantation. The reported case series are heterogeneous with respect to nearly all aspects of meniscal allograft transplantation. The indications for surgery are routinely reported as a symptomatic meniscus-deficient compartment of the knee, but the severity of symptoms, degree of meniscal loss and amount of cartilage damage are not uniform. The age limit for patients is not agreed, although from the publications it is rare for patients over the age of 55 years to have surgery.55 There are a number of graft preservation techniques, of which fresh-frozen and cryopreserved are most commonly used.53 Cryopreservation is done in the hope of maintaining the integrity of the allograft, but it has not been definitively shown to be better than other techniques.59 It also requires strict thawing protocols, which are difficult to achieve in the clinical environ-
ment. Allograft fixation is also controversial. Studies are divided between bony fixation of the meniscal roots and an all-suture technique. Biomechanical studies may marginally favour the bone fixation technique, but it is more technically demanding and there is no clear clinical benefit. Rehabilitation after surgery also varies in reported studies. Most studies allow return to non-pivoting activities by six months, but some studies report never allowing a return to full activities. The increased risk of damaging the allograft is cited as the reason for this, but at least one study did not find this to be the case.

In summary, the shape and microstructure of the meniscus allow it to distribute load effectively across the knee. Meniscal tears and meniscectomy result in an altered biomechanical and biochemical environment, and are potent risk factors for OA of the knee. Meniscal allograft transplantation has been performed for more than 30 years and is potent to allow it to distribute load effectively across the knee. Mechanical and biochemical environment, and are potent cusc allow it to distribute load effectively across the knee.

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