



The Bone & Joint Journal

Journal club: 18 August 2013

Chairman: Mr A Ajuied & Mr A Davies

Convener: Mr I Findlay

Guy's and St. Thomas' Hospitals NHS Trust

Theme: Meniscal Allograft

1. **Verdonk PCM, Verstraete KL, Almqvist KF, De Cuyper K, Veys EM, Verbruggen G, Verdonk R.** Meniscal allograft transplantation: long-term clinical results with radiological and magnetic resonance imaging correlations. *Knee Surg Sports Traumatol Arthrosc* 2006;14:694-706.

Reviewer: Mr M Tahir

Background

The fibrocartilaginous menisci improve joint stability, load distribution, shock absorption and articular cartilage lubrication. The now obsolete approach in managing meniscal pathology was traditionally surgical excision, resulting in degenerative changes. For patients with complete meniscal loss, the authors claim MAT will result in a decreased contact pressure on the cartilage surface. At the time of publication, only medium-term reports had been published, demonstrating significant improvement in function and symptoms.

Aims

The purpose of this study was to report on long-term clinical results of MAT, hypothesizing this would significantly reduce pain and increase function of the involved joint in the long term. A secondary goal of this study was to document possible graft failure or progressive degenerative changes using plain radiology and magnetic resonance imaging (MRI) as objective outcome measuring tools.

Methods

42 MATs were performed in 41 patients between 1989 and 1993 (35 M: 6 F). This included a total of 27 medial and 15 lateral meniscal allografts. 11 medial MATs were associated with a high tibial osteotomy (HTO). 3 medial and 1 lateral MAT were associated with an ACL reconstruction. Inclusion criteria for MAT were young and middle-aged patients (22-50years) with moderate to severe pain post-total meniscectomy.

All patients underwent viable MAT, performed solely by the senior surgeon (RV) through a parapatellar arthrotomy and fixed with PDS sutures only. All grafts were harvested from young donors (<45 years) within 24 h of death following an acute disease who had not received corticosteroids or cytostatic drugs.

Clinical evaluation at the time of transplantation and at the final follow-up was performed using the modified Hospital for Special Surgery (MHSS) scoring system. The knee injury and osteoarthritis outcome score (KOOS) was used as an evaluation tool for patient-related outcome at the FFU. Radiological evaluation was performed using the International Knee Documentation Committee system and Fairbank changes for standing plain radiographs, and the Yulish system on MR imaging.

Subgroup statistical analysis was performed. Pre and postoperative clinical and radiological parameters was performed using the Wilcoxon signed rank test, and subgroup analysis was performed using the Mann–Whitney test. Correlation studies between modified HSS and KOOS subscales and between specific radiological parameters and clinical outcomes were performed using the Spearman's ρ two-sided test. The level of evidence was 2B.

Results

Patients were divided into 3 groups; medial MAT (MMT), MMT+HTO, and lateral MAT (LMT). At FFU the mean post-operative MHSS pain, walking and stair climbing ability scores improved significantly for all groups. The MMT+HTO had a significantly more favourable outcome than the MMT group. On the KOOS scores, the MMT+HTO subgroup complained of significantly less of swelling, stiffness and frequency of pain.

X-Ray follow-up was available for 25/41 (61%), with 12 (48%) demonstrating progressive joint space narrowing, mostly by 1 grade (n=8, 32%). MRI follow-up was available for 17/41 (41%). Degeneration of the femoral and tibial cartilage occurred in 7/17 (53%) and 8/17 (47%), respectively. 3 (18%) grafts showed a change in signal intensity (all LMT). Extrusion occurred in 10 (59%). 2 allografts developed tears diagnosed on MRI. No comment was made on how they were treated.

Failure was considered conversion to arthroplasty, which occurred in 7 cases (18%). These patients outcome scores were not included in the FFU data. Overall, >90% of patients were satisfied with the outcome at FFU.

There were significant correlations between the MHSS pain, walking and stair-climbing subscales (Spearman ρ test, $P<0.007$), and also between the different KOOS subscales (Spearman ρ test, $P<0.001$). No significant correlations were found between any of the X-Ray or MRI parameters and the clinical subscales at the time of transplantation or at the FFU. Axial alignment did not correlate with progression of femoral/tibial cartilage degeneration and signal intensity of the graft. The statistical tests used were appropriate.

Paper's Conclusions

At the time of publication, MAT was considered an investigational procedure, with scarce long-term follow-up data. Much of the published results were questionable due to numerous confounding factors, including concomitant procedures, graft preservation and fixation techniques, clinical scoring systems, and duration of follow-up.

This study demonstrated MAT was associated with significant long term improvements in function and pain, with comparable clinical outcomes for MMT and LMT. Others studies demonstrated increased MMT failure in unstable knees, but this was addressed by concomitant ACL reconstruction. Overall, some patients however did have substantial disability at FFU, but despite this there was a high patient satisfaction rate at FFU.

With regard to predictors of MAT failure, there was no correlation between initial cartilage damage and clinical or radiological outcome parameters suggesting favourable outcomes with viable allografts, there was no difference in patients with focal cartilage lesions compared to those who did not, and those undergoing axial alignment had significantly better clinical outcomes. Additionally, extrusion did not demonstrate a significant risk of cartilage degeneration.

In this series cartilage degeneration was prevented in a number of patients based on radiological criteria, indicating potential chondro-protective effect. The MRI outcome did not correlate with the

clinical outcome, which has already been published by several authors, and therefore the primary and outcome measure should be clinical. Nonetheless, MRI is a valuable objective tool.

Appraisal

Long-term results are encouraging in terms of pain relief and improvement of function for patients undergoing MAT. Initial concomitant axial alignment and stabilising procedures are important in long term success, though there were no true comparative groups in this study. Some patients had substantial disability and symptoms, but despite this there were high satisfaction rates.

The study design is prospective, but understandably there are no real control groups. Positives aspects of the study include standardisation of the type of allograft and the consistent surgical technique solely by the senior author. Additionally, although the modified HSS scoring system used (initially designed to evaluate the outcome of knee arthroplasties), due to a lack of validated meniscal pathology scores when the study commenced, at FFU, KOOS scores were integrated. However, more commonly used indicators such as Lysholm and Tegner scores could have been considered to allow this study to be more comparable to most medium-long term outcome studies.

It should also be noted that patients with focal osteochondral defects were left untreated as this was the approach when the study was commenced. Other authors may have considered intervention based on ethical grounds, though this would have introduced a confounding factor into the study.

The main limiting factor in this study is the small numbers, particularly those followed up with plain radiography and MRI. This could have influenced the statistical analysis. Subsequent meta-analyses on MAT have been performed, but these are still based on relatively poor study designs.

Recommendations for our Practice

MAT is no longer considered experimental surgery, and there are excellent long term clinical outcomes. It is, however, a very difficult option in the UK due to numerous ethical restrictions, such as the human tissue act, donor shortages and the necessary infrastructure required. Increasing satisfactory long term outcome of arthroplasties and meniscal repairs are a viable alternative when applicable, but in the young patient with devastating meniscal pathology this may be the best option. It should certainly only be undertaken by experienced knee surgeons with the skill set to perform ACL reconstructions and HTO.

2. Lee D-H, Kim S-B, Kim T-H, Cha E-J, Bin S-I. Midterm Outcomes after Meniscal Allograft Transplantation: Comparison of Cases with Extrusion versus without Extrusion. *Am J Sports Med* 2010;38:245-253.

Reviewer: Miss Z Beech

Background

Although graft extrusion is of concern after meniscal allograft transplantation (MAT), the correlation between extrusion and clinical and radiological outcomes remains unclear. Meniscal allograft transplantation is becoming more common

Aims

The paper examines whether graft extrusion post meniscal allograft transplantation is associated with poorer clinical or radiological outcomes in the mid-term. The Lysholm score was used to assess clinical outcome. Joint space width was used as a marker of chondral damage and progression of osteoarthritis.

Methods

Study Design: Retrospective cohort study; Level of evidence, 3.

Methods: Forty-three patients underwent MAT between 1999 and 2004. Selection criteria for operation included a symptomatic knee with Outerbridge grade I-II degenerative changes. Grafts were screened fresh-frozen allograft. Medial meniscal grafts were secured using the double-bone-plug technique; lateral grafts by a keyhole technique.

Grafts were classified as either non-extruded (<3 mm) or extruded (>3 mm) according to the 1 year post op MRI scan findings. The mean patient age at the time of surgery was 33.5 years (range, 17-43 years), and the mean follow-up period was 5.1 years (range, 3.5-8.3 years). The Lysholm score was used to evaluate knee function. In addition, preoperative and postoperative (final follow-up) measurements were taken to determine the absolute and relative (affected side/normal side) joint space width (JSW) on a standing 45° flexion posteroanterior view.

Results

They state their hypothesis, although not their null hypothesis, and their assumptions about the clinically relevant difference in joint space width. They perform a power calculation and have the required number of cases. They also test to determine both inter- and intra-observer reliability.

They used the Student t test to compare clinical and radiological outcomes between the two groups. They do not include any results demonstrating that the data follows a normal distribution but imply that the data was parametric. To look at correlation between extrusion and outcome they use Pearson's correlation coefficient and multiple linear regression analysis.

26 knees had non-extruded grafts and 17 extruded grafts. Maximum extrusion was 6 mm. Preoperative characteristics were similar between the two groups. There was non-association between extrusion and either Lysholm score or Joint space width. There was an association between pre and post op Lysholm score and between pre and post op joint space width.

Paper's Conclusions

The discussion covers the normal alteration in joint space width and changes found in animal models. There is no formal systemic review of previously published results.

They discuss the phenomenon of meniscal extrusion in the osteoarthritis knee and conclude that following a meniscal transplant the reasons for extrusion may vary. They emphasise the importance of good surgical technique and stable fixation.

Limitations are considered.

Appraisal

The paper is clearly written with enough details given about methods to enable the study to be replicated. The authors identify some weaknesses including small group size and the retrospective nature of the study.

The patient group does not fit with current practice as it excludes those with moderate - severe arthritic changes (Grade III or above wear at arthroscopy) limiting applicability.

At present meniscal allograft transplantation is an operation that is performed to alleviate symptoms. It is a weakness of this study that only a single measure, the Lysholm scoring system - validated for use in ligamentous injuries- is used to determine clinical outcome. Repeated MRI scans may have been useful to further assess extrusion and chondral damage.

Recommendations for our Practice

Based on this data meniscal extrusion does not affect the outcome from meniscal allograft transplantation. Extrusion alone should not be used as criteria to define failure of a meniscal transplant.

3. Stone KR, Adelson WS, Pelsis JR, Walgenbach AW, TurekTJ. Long-term survival of concurrent meniscus allograft transplantation and repair of the articular cartilage. A prospective 2 to 12 year follow-up report. *J Bone Joint Surg [Br]* 2010;92-B: 941-8.

Reviewer: Mr S Singh

Background

Longest follow up of meniscal allograft transplantation.

Aims

To assess the longevity of meniscal allograft transplantation (with concurrent articular cartilage repair) and its benefits to the patients

Methods

Prospective case series of a single surgeon. Level of evidence IV

Results

Kaplan-Meier estimated mean survival time for the whole series was 9.9 years. Significant improvement in patient pain, activity and function

Paper's Conclusions

Good long-term survival

Significant patient benefit

Age of patient at surgery and number of previous procedures statistically significant predictors of good result

Axial mal-alignment, gender, degree of chondral damage or joint space narrowing does not affect survival of allograft

Appraisal

Contemporary topic, all results valid and relevant.

Heterogeneous population

Revision was considered additional procedure rather than failure

More robust studies needed as only level IV evidence

Recommendations for our Practice

To consider referral to tertiary centre for meniscal allograft transplantation in a young (up to 50 year old patient), active patient.

4. ElAttar M, Dhollander A, Verdonk R, Almqvist KF, Verdonk P. 26 years of meniscal allograft transplantation: is it still experimental? A meta-analysis of 44 trials. *Knee Surg Sports Traumatol Arthrosc* 2011;19:147-157

Reviewer: Mr C Smith

Background

The management of meniscal tears has changed dramatically following improved understanding of their function in force transmission across the femoro-tibial joint, and its role in the pathogenesis of osteoarthritis. Originally the menisci were thought to be functionless remnants of intra-articular knee muscles, and as a result were frequently excised en bloc. In the 1970s menisci preserving surgery was adopted as their purpose become more apparent. In 1984 meniscal allograft

transplantation (MAT) was introduced, but after almost 30 years it is still perceived as experimental surgery.

Aims

The paper's aim was to test the hypothesis that MAT is safe and reliable for the treatment of post-meniscectomy symptoms in select patients. Continuous satisfactory outcomes coupled with acceptable failure rates should make it the 'gold standard' for treating such patients.

Methods

The paper is a systematic review and attempted meta-analysis performed from a database search conducted on January 2010. Multiple databases were searched with the term 'meniscal AND allograft'. Exclusion criteria stipulated that only English-language articles, on human subjects, with a minimum of 6 months follow up were to be analysed. From this search, 44 papers were included, which represented 1136 grafts in 1068 patients. The Coleman methodological score was used to qualitatively assess the methods of the trials.

Results

40 prospective cohort or case series and 4 retrospective case series were included.

- The mean patient age range in the trials was 25-48, with an overall mean patient age of 34.8 year (total range 14-69 years).
- Sex distribution: 613 males: 265 females: 190 undisclosed
- 678 medial grafts: 458 lateral grafts
- Average 2.5 previous operations for the problem (max = 30)
- Indications for MAT: joint line pain, swelling and crepitation following (sub)total meniscectomy
- Contraindications: asymptomatic, diffuse joint pain/degeneration, arthrofibrosis, muscular atrophy, previous septic arthritis, certain general medical condition (eg diabetes).

Grafts used in the studies

- Lyophilized 1.5%
- Cryopreserved 40%
- Deep frozen 36.2%
- Viable 11.2%
- No preference 7.7%
- Not specified 3.5%

Sterilisation and immune matching was only performed in early studies

Size and laterality matching was only considered in later trials.

Technique

- 17 trials performed open procedures, progressing to arthroscopic transplantation in the 15 later trials. 3 trials used a combination of open and arthroscopic procedures.
- Soft tissue fixation became superseded by bony fixation, however there was a huge variety of techniques between trials.
- Average time from injury to transplantation was 10.7 years.
- Rehabilitation protocols varied massively, with no consistent agreement between studies regarding immobilisation or brace use, acceptable early range of movement and weight bearing status.

Outcome

- Clinical outcome was evaluated at an average follow up of 4.6 years (range 8 months – 20 years)
- Large variation in measuring clinical outcome, with 12 different outcome tools used between studies. A time dependent decrease in outcome score was noted.
- Radiological outcome varied as well, with studies utilising radiographs (16 studies) MRI (19 studies) ultrasound scans (1 study), arthrogram (1 study) or routine 2nd look arthroscopy (3 studies).

Failure and complications

- Different definitions between studies with some deciding rejection of the graft representing failure; poor relief of symptoms in other studies; partial meniscectomy or subsequent procedure (egg, osteotomy) in other studies.
- Graft destruction/removal rate was 10.6%
- 128 complications were reported (21.3%)
- Graft tears requiring subsequent repair or partial meniscectomy 43
- Adhesions requiring MUA 27

Paper's Conclusions

The authors conclude that MAT is safe and reliable and should no longer be considered an experimental procedure. Medial and lateral grafts were performed in almost a 1:1 ratio in the later trials, with alleged significant improvements in pain and function. The complication rate was 21.3%, which the authors consider to be comparable to arthroscopic meniscal repair (a view not held by this author or our group). Coleman Methodology Score was on average around 50%, a fairly poor result for the quality of the trials. MAT does not prevent further procedures occurring, such as arthroplasty in the future.

Appraisal

The aim was to prove meniscal allograft transplantation is safe and reliable for post-meniscectomy symptoms in select patients and that the continuously satisfactory outcome and acceptable failure rates should make it 'gold standard'.

The paper was a meta-analysis with high levels of heterogeneity between trials included. As a result level of evidence is quite hard to determine and at best is 2a, but is more likely to represent 3a evidence. There was a huge variation between operative technique, rehabilitation, outcome measures, complications and even the definition of failure between studies; as a result no viable conclusions can be made for the success of MAT. A large number of concurrent procedures were performed at the same time as the MAT, making the benefits of the procedure even less apparent.

MAT may represent a possible last-ditch procedure for people with post-meniscectomy symptoms prior to arthroplasty, however we feel it has a high failure and complication rate (10% and 20% respectively) and no homogeneity in practice between surgeons, so are unable to draw significant conclusions as to its appropriateness.

Recommendations for our Practice

We cannot agree with the authors' conclusions, and as a result cannot advocate the procedure as safe and reliable in alleviating symptoms. Further large randomised-control trials, ideally multi-centred with agreed protocols of technique, rehabilitation and outcome scoring are needed to further assess the validity of MAT.