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Higher survivorship following meniscal allograft transplantation in less worn knees justifies earlier referral for symptomatic patients: experience from 240 patients

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Abstract

Purpose To analyse the clinical outcome and survivorship of meniscal allograft transplantation (MAT), performed in a single unit, specifically to assess the impact of concomitant operations and the influence of articular cartilage lesions on outcome.

Method A prospective case series analysis of 240 patients undergoing MAT with follow-up greater than 12 months (range 1–10 years) was performed. Group A represented patients with good chondral surfaces (ICRS 0–3A); Group B had good chondral surfaces with concomitant realignment osteotomy. Group C had good chondral surfaces with ACL reconstruction performed at the same time. Groups D and E had bare bone on one or both surfaces respectively. Kaplan–Meier survivorship and PROMS including Lysholm, KOOS, Tegner, and IKDC subjective scores were analysed.

Results Overall survivorship was 96.7% at 1 year, 87% at 5 years and 82.2% at 7 years. Groups A–C (knees without significant chondral damage) had significantly improved survivorship (95% at 5 years) compared to Groups D, E (full-thickness chondral wear) with 77% survivorship at 5 years. Survivorship and PROMS were equivalent between Groups A–C. Groups D and E had similar PROMS to Group A, but did have a higher failure rate. Overall 27% required further operative intervention.

Conclusions Meniscal transplantation is clinically effective in treating patients with symptomatic meniscal deficiency. Where indicated, the addition of osteotomy or ACL reconstruction achieves results similar to patients undergoing simple meniscal transplantation in stable and normally aligned knees. Survivorship is lower in patients with full-thickness chondral loss and future treatments should, therefore, be directed at improving success in this at-risk group. The results support encouragement for earlier referral of symptomatic patients to a specialist meniscal reconstruction centre before a significant chondral damage is sustained.

Level of evidence III.

Keywords Meniscal · Allograft · Transplant · Survivorship · Outcome · Meniscus transplantation

Introduction

Management of the young patient with symptomatic meniscal loss has traditionally been a challenge. These patients are at risk of early degenerative disease [30] and are highly likely to require arthroplasty in the future. However, they are usually young and active, and are significantly affected by their pain long before they develop osteoarthritis that would be amenable to joint replacement.

Meniscal allograft transplantation (MAT) is now a recognised treatment for the meniscal-deficient knee [16, 28, 41]. It can be combined with other procedures around the knee, including femoral and tibial osteotomy [21, 22], ligament reconstruction [37], and articular cartilage reconstruction [25]. Previous studies have shown good survivorship and clinical results [38].

This paper reports the clinical patient-reported outcomes and survivorship of 240 MATs performed at a single centre with a minimum of 1-year follow-up and relates outcome to the state of the knee at time of implantation as well as the use of concomitant procedures. Our hypothesis was that

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outcome would be better where articular cartilage showed minimal damage and that this, therefore, influences the timing for referral. We also hypothesised that concomitant stabilisation or realignment surgery would not affect outcome.

Materials and methods

Two hundred and forty consecutive patients having a primary MAT were prospectively entered onto a database. The indication for surgery was a young patient with a symptomatic meniscal-deficient compartment of the knee, usually as a result of previous injury and meniscectomy. Patients completed pre- and post-operative outcome scores, including the Knee Injury and Osteoarthritis Outcome Score (KOOS) [32], International Knee Documentation Committee Subjective Knee Evaluation Score (IKDC) [6], and Lysholm and Tegner [43] scores. The patient demographics are shown in Table 1. Patients completed outcome scores at 1, 2, 3, 5, 7, and 10 years following their MAT. Failure was defined as removal of the MAT or conversion to arthroplasty. Outcome data collection and analysis was approved by the Research and Development Department at University Hospital Coventry and Warwickshire NHS Trust.

The meniscal transplant procedure was performed arthroscopically, using a soft-tissue fixation technique [2, 19] and published by the senior author [41]. The remnant of the native meniscus was debrided back to the rim. The donor menisci were sourced from one of three companies: Allosource (JRF Ortho, Centennial, Colorado), NHS tissue bank (NHS Blood & Transplant, Tissue & Eye Services, Liverpool, UK), or RTI (Alachua, Florida). Sizing was performed according to the technique by Pollard [31] or by measurement of total tibial plateau width. The donor meniscus was prepared with a whip stitch at the anterior and posterior horns. Posterior and anterior horn meniscal attachment points were identified anatomically, and an ACL tibial guide or Meniscal Root guide (Smith and Nephew, London, UK) was used to enable drilling of a guide wire from the anteromedial tibia to the attachment position. Bone tunnels were drilled using a 4.5-mm Endobutton reamer (Smith & Nephew, London, UK) to enable passage of passing sutures. The graft was inserted through the arthroscopic portal using a Passport cannula (Arthrex GmbH, Munich, Germany). The anterior and posterior horn stitches were passed down the tunnels and the graft tensioned by hand. The sutures were tied over a bone bridge between the two tunnels on the anteromedial tibia, and the donor meniscus was secured to the meniscal rim using a combination of all-inside sutures (FastFix 360, Smith & Nephew, London, UK) and inside-out sutures using a zone-specific cannula (Conmed, Utica, New York).

Postoperatively patients were non-weight-bearing for 4 weeks before application of an unloading brace (OA Nano brace, DJOrtho, UK) and partial weight-bearing allowed for 2 weeks, before full weight-bearing. Flexion was restricted to 90° for 6 weeks and then cycling was allowed, increasing flexion to full by 3 months. Running was allowed from 6 months and return to sport, if appropriate, was commenced at 12 months. Rehabilitation was slower when multiple procedures were performed, tailored to the surgery.

Principles of biological reconstruction were followed in complex cases [22]. MAT was combined with femoral or tibial osteotomy when alignment was such that the weight-bearing line drawn from centre of hip to centre of talus fell outside the space between medial and lateral tibial spines [5, 9]. Primary or revision ACL stabilisation surgery was performed when indicated using autografts or allografts determined by the lead surgeon [3, 34]. Full-thickness articular cartilage loss was treated with debridement (leaving the surface untreated), microfracture, or autologous chondrocyte implantation (MACI, Genzyme, UK), depending on the lesion size and location [33]. Lesions on the tibia less than 10-mm diameter that were covered by the new graft or were unshouldered lesions, were not treated. Defects from 1 to 4-cm^2 area were generally treated with microfracture, and larger defects on one side of the joint only were treated with the MACI technique. Principles of articular cartilage repair followed the consensus statement from the British Association of Surgeons of the Knee [8].

For the purposes of evaluating the outcome of MAT, patients were divided into several groups, based on chondral surface wear and other concurrent procedures. It was

Table 1 Demographics of patients undergoing MAT, follow-up times, and failures in each group

Group	Total	Age (mean, range)	Male (%)	Lateral meniscus (%)	Failures (*n*, %)	Average follow-up (mean, range)
A	115	29 (13–55)	59	75	4 (4.6)	3.2 year (1–10)
B	19	32 (19–47)	79	74	3 (16)	3.3 year (1–7)
C	20	26 (17–45)	65	40	1 (5)	3.0 year (1–7)
D	48	33 (18–45)	69	77	6 (12.5)	3.3 year (1–7)
E	36	36 (19–49)	78	75	11 (31)	4.8 year (1–10)
N/A	2	23 (19–27)	100	50	0	2.5 year (1–7)

hypothesised that Group A would be the 'ideal' candidate for a MAT, with a well-aligned, stable knee and good chondral surfaces (i.e., no chondral defect greater than ICRS 3a). Group B had good chondral surfaces, but required realignment osteotomy. Group C had good chondral surfaces and a well-aligned knee, but also required an ACL reconstruction. Group D had bare bone (ICRS 3b-c) on either the tibial or femoral surface, and Group E had bare bone on both surfaces. Two patients who required both an ACL reconstruction and an HTO as well as MAT were not covered by these groups and excluded from further analysis. The numbers of patients in each group and follow-up are shown in Table 1.

Statistical analysis

Survivorship was calculated according to Kaplan–Meier analysis and comparison was assessed on Mantel–Cox log-rank testing. Significance was set at $p < 0.05$. Cox regression analysis was used to assess predictive factors affecting survivorship.

Results

In terms of crude survivorship, the whole cohort survivorship was 87.4% at 5 years (Fig. 1). However, when the grade of cartilage damage was taken into consideration, there was a significant difference in survivorship between the cohorts with 'good' chondral surfaces (Groups A, B, and C; 95% at 5 years) and those with 'poor' chondral surfaces (Groups D and E; 77% at 5 years). This was demonstrated in the Kaplan–Meier survivorship analysis shown in Fig. 2, and was statistically significant ($p = 0.001$) on Mantel–Cox log-rank testing. Cox regression analysis revealed that chondral damage was the only statistically significant factor affecting survivorship of the MAT.

We also examined the clinical outcome using patient-reported outcome measures (PROMs). We have included PROMS scores up to 7 years, as only two patients have reached 10-year follow-up, so these scores were not reported. Figure 3a–e shows the KOOS score in each group, with improvement at 1 year that was maintained up to 7 years. Similarly, the IKDC score showed a similar improvement up to 7 years. In Group A, there were four graft failures during the study period.

Groups B and C (good chondral surfaces but combined with concurrent procedures) also exhibited similar improvements in IKDC scores (Fig. 4) to those patients in Group A. Groups D and E (those patients with bare bone) saw similar improvements in IKDC scores to Group A (Fig. 5), but these groups had a much higher rate of concurrent surgery and a higher failure rate – 6 failures in Group D and 11 failures in Group E. It should be noted that the baseline PROMS scores were similar across all groups.

There were adverse events and re-operations in all groups; these are summarised in Table 2. Twenty-four patients (10%) had meniscal tears either of the body or at the root fixation requiring partial resection or repair, salvaging the transplant.

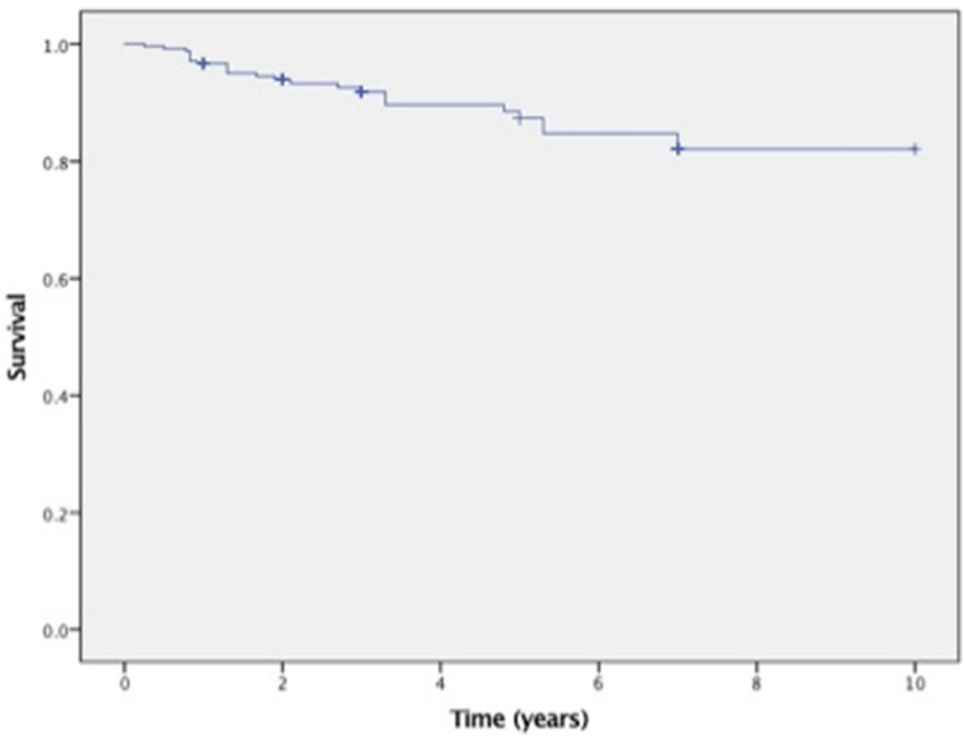

Fig. 1 Kaplan–Meier survivorship analysis of the whole cohort, with failure defined as removal of the graft or conversion to arthroplasty. Survivorship is 96.7% at 1 year, 87.4% at 5 years, and 82.1% at 7–10 years

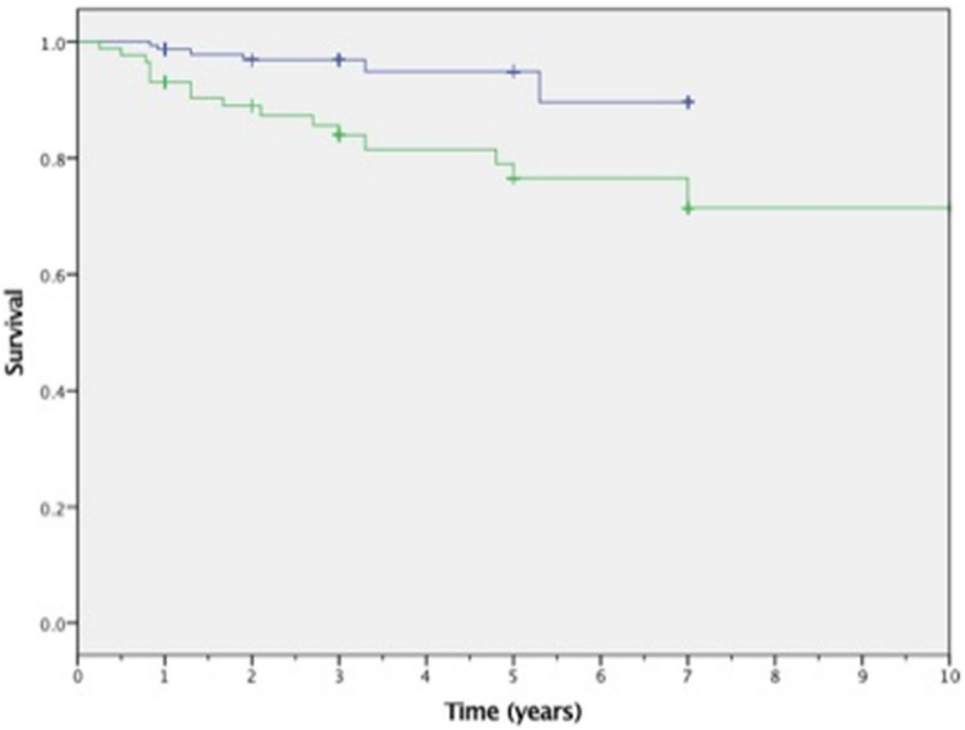

Fig. 2 Kaplan–Meier Survivorship analysis showing improved survivorship in Groups A–C (good chondral surfaces) compared to Groups D, E (bare bone on one or both sides); $p = 0.001$, log-rank (Mantel–Cox) testing

The overall re-operation rate was 27%, including the meniscal tears and procedures for removal of osteotomy plates ($n = 6$), excision of prominent suture knots from fixation ($n = 8$), failed delaminated MACI grafts ($n = 2$), removal of neuromas ($n = 3$), and arthroscopy for assessment of pain without obvious cause ($n = 9$). One patient had non-fatal PE and one patient had a foot drop which spontaneously improved over 6 months.

Discussion

The most important finding of this study of 240 patients with minimum 1-year follow-up and mean 3.2-year follow-up (range 1–10 years) was that MAT performs very well, with an overall survivorship of 96.7%, 87% and 82.2% at 1, 5 and 7 years respectively. We have demonstrated that survivorship was significantly lower in the group of patients who had full-thickness articular cartilage loss at the time of meniscal transplantation. The state of the chondral surface was the only predictive factor for failure which was defined as removal of meniscus or progression to arthroplasty. The surgical technique in this series involved a minimally invasive arthroscopic technique with soft-tissue fixation through bone tunnels. Meniscal allografts were fresh-frozen, non-irradiated and bone-free, sized on pre-operative imaging. 27% required further operative intervention with 10% requiring removal of a torn meniscal transplant and a further 10% undergoing arthroscopy where the transplant could be salvaged either by partial resection and peripheral fixation where hypermobility was found or by reattachment of meniscal root.

Overall, these results are encouraging, but they emphasize the importance of the technical aspects of implantation to reduce the mechanical failure of fixation methods or irritation from prominent fixation sutures. Critical analysis of this information allows for accurate counselling of patients prior to surgery. Patients who had isolated MAT had particularly good results with marked improvement in PROMs, which were maintained over the study period. Failure rate in this group that we have termed 'ideal' was only 3.5% (4 patients) and the re-tear rate where the meniscus could be salvaged was 5%.

Management of the symptomatic meniscal-deficient patient has been difficult. It is well known that meniscal loss is a risk factor for osteoarthritis of the knee [30], with a 134-fold increase in the rate of total knee arthroplasty in this group long term. However, there are a cohort of patients who are more symptomatic than others, and this was reflected in our patients' poor pre-operative PROMs, which were significantly worse than those reported by Pengas et al. on long-term analysis of meniscectomy patients, and at a much younger age [30]. It is likely that the patients that present early are the 'fast progressors' towards symptomatic osteoarthritis. As such, they pose the biggest treatment challenge. Knee replacement in young patients does not give good functional outcomes, especially if return to sport is desired. Second, the risk of revisions is very

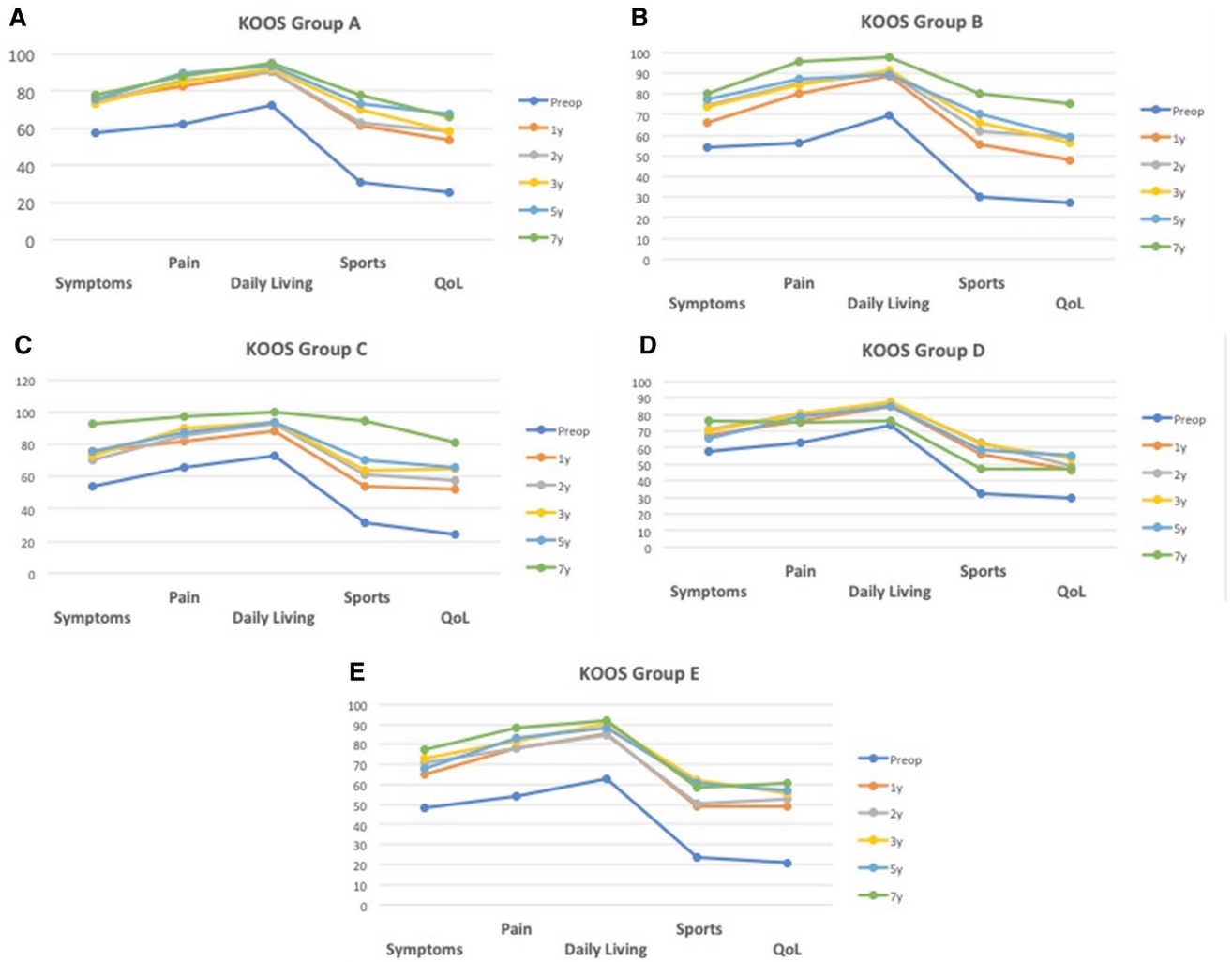

Fig. 3 **a** KOOS scores for Group A (good chondral surfaces, no concomitant procedures). **b** KOOS scores for Group B (good chondral surfaces, concomitant HTO). **c** KOOS scores for Group C (good chondral surfaces, concomitant ACL reconstruction). **d** KOOS scores for Group D (bare bone on one chondral surface). **e** KOOS scores for Group E (bare bone on both chondral surfaces)

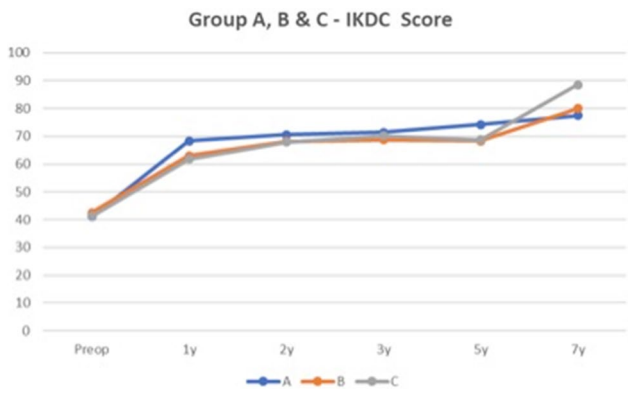

Fig. 4 IKDC scores for Groups A, B, and C. The PROMS outcomes are not significantly affected by the addition of a high tibial osteotomy or an ACL reconstruction, and are maintained up to 7 years

high. In this context, whilst the survivorship of MAT in patients with good chondral surfaces is better (as might be expected), it can be argued the role for MAT is just as important in patients with more degenerate knees. MAT may prevent or delay the need for knee arthroplasty, with its associated problems in this patient cohort.

Isolated MAT was first described in 1984 [27] and was initially an open procedure, with detachment of the femoral epicondyle, laying the donor meniscus into the knee, and open peripheral fixation before reattaching the femoral epicondyle [45]. Since then, this technique has been refined to an arthroscopic-assisted technique [41], with fixation generally being with the aid of sutures within bone tunnels (Fig. 6), bone plugs, or a slot of bone fitting into a trough created in the tibial plateau. A recent systematic review has not shown any one method to be superior to the others [29].

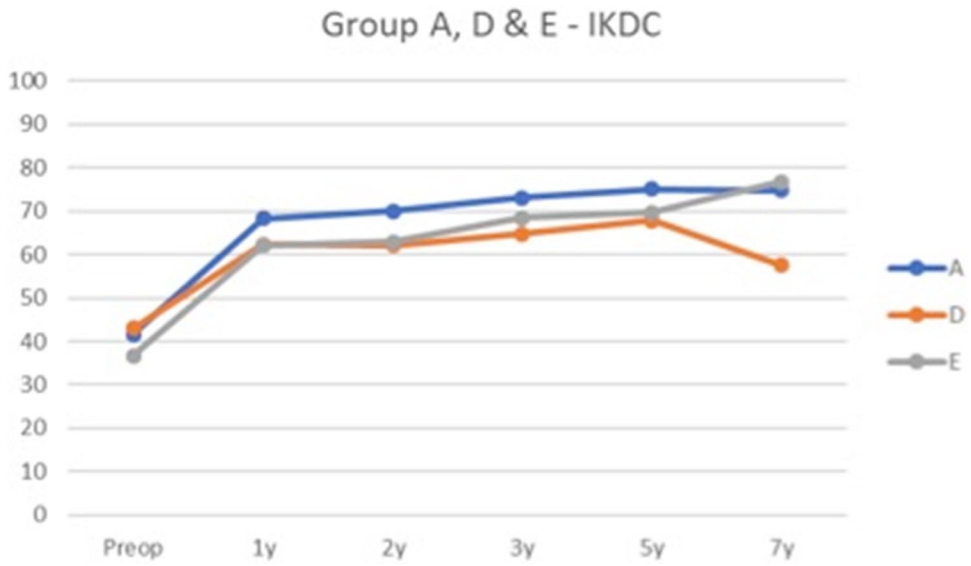

Fig. 5 IKDC scores for Group A (good chondral surfaces) compared with Groups D and E (bare bone on one or both surfaces). The PROMS outcomes are not significantly different between the groups and are maintained up to 7 years

Table 2 Re-operations in each group

Re-operations	Group A	Group B	Group C	Group D	Group E	Total
Root tears re-fixed	4	1	2	1	1	9
Partial tears resected	1	1	0	2	2	6
Meniscal tear repair	1	1	2	4	1	9
Debridement for infection	1	0	0	0	0	1
Arthroscopy for pain	6	0	2	1	0	9
Removal painful suture	8	0	0	0	0	8
Removal of metalware	0	3	1	1	2	7
Excision neuroma	1	1	0	1	0	3
Notchplasty	0	0	0	0	1	1
Peroneal nerve decompression	0	0	0	1	0	1
Patella tendinopathy decompression	0	0	0	1	0	1
ACL rupture	0	0	0	1	0	1
Failed MACI graft	0	0	0	1	1	2

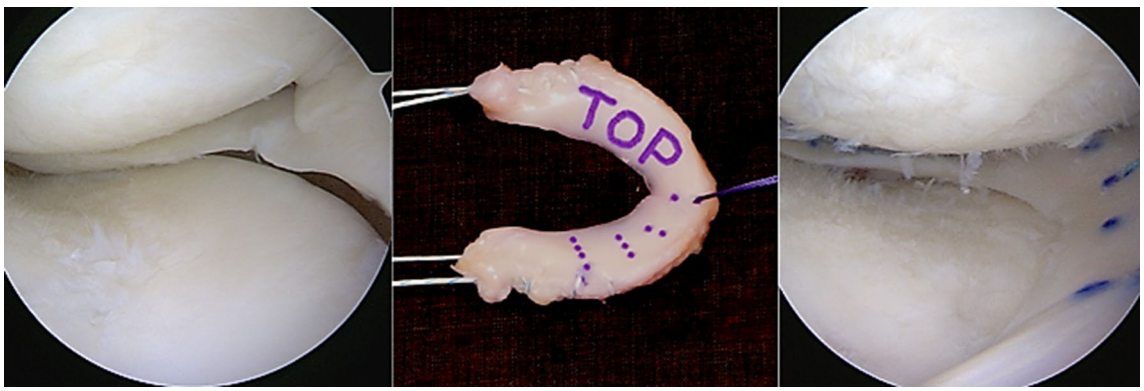

Fig. 6 **a** Left knee lateral meniscal deficiency indicating meniscal extrusion and less than 3 mm residual meniscal rim. **b** Lateral meniscal allograft transplant (MAT) graft prepared using an all suture technique with lead sutures at each root and a further traction suture just anterior to the popliteal hiatus. **c** MAT graft sutured into position

Long-term results of MAT are encouraging [46], although it should be noted that historical series tend to report the outcome of open techniques. It is expected that survivorship will be improved with newer techniques, as the bone tunnels allow for a better anchorage of the anterior and posterior horns and recreation of the hoop stresses of the meniscus. A meta-analysis of 44 trials suggested that if good PROMs could be achieved at 2 years, then they could be maintained for up to 20 years [13].

The ideal patient for a MAT was discussed at the International Meniscus Reconstruction Experts' Forum (IMREF) in 2013 [18] and their consensus statement concluded that the main indications were: unicompartmental pain in the face of a total or subtotal meniscectomy; or as a concomitant procedure to articular cartilage repair; or as a concomitant procedure to revision ACL reconstruction to aid joint stability.

We favoured the approach popularised by Arnold et al. [7], outlining a hierarchy of à la carte strategies to bring the damaged knee into a comfort zone, that is based on the concept of joint homeostasis [12]. This is an orthobiological approach to address limb alignment, stability, meniscal pathology, and articular cartilage damage, in that priority order.

Alignment is critical to a successful MAT. A malaligned meniscal-deficient knee results in more rapid articular cartilage wear than the well-aligned knee [4], with varus malalignment carrying a worse outcome than valgus [11]. Outcomes of high tibial osteotomy (HTO) and MAT have previously been studied and compared with those of MAT alone [35, 46]. Patient-reported outcomes following surgery were improved by the addition of the HTO, compared to those following isolated MAT. When performing the osteotomy, our practice has been to tailor the degree of correction dependent on the compartment that requires protection [1] rather than aiming for the more traditional Fujisawa point [15].

Meniscus reconstruction should only be performed in a stable or stabilised knee to prevent secondary meniscal injury due to altered knee kinematics. MAT has been shown to have a higher failure rate in the ACL-deficient knee [44] and the combination of ACL reconstruction with MAT has been shown to have good medium- and long-term outcomes [20, 47].

Our study showed that chondral damage was a risk factor for failure, but that PROMs did improve following MAT, and that this improvement was similar in all grades of chondral damage. Mahmoud et al. also showed higher failure rates with advanced chondral damage [26]. The authors reported on 45 transplants in 43 knees showing that 8 of 31 with grade 3 or 4 degeneration failed (26%), whereas no failures were seen in the group with normal surfaces. We have also previously reported this [23] in a short-term series, but this current extensive study demonstrates that concomitant ACL reconstruction or osteotomy surgery does not adversely affect outcome. Lee et al. similarly showed good results in all groups, with similar PROMS scores, but again demonstrated worse survivorship in bipolar chondral lesions compared to unipolar lesions [24]. 222 patients were assessed, and survivorship was 62% at 5 years in the salvage indication group compared to 94% in the ideal indication group. Other studies have also shown good results when treating advanced degenerative changes with MAT in conjunction with cartilage repair [42].

Various different chondral treatments have been combined with MAT, including microfracture, autologous chondrocyte implantation (ACI) [14], and osteochondral grafting (OCG) [17, 33]. We used a variety of techniques in our Group D and E patients, and there are as yet not enough patients using each technique to determine whether one has better long-term outcomes than another. It is hoped that future MAT registry studies may provide adequately powered samples to answer these questions.

Whereas this current study and the papers already mentioned detail lower survival in the presence of full-thickness wear, Saltzman et al. [36] have shown equal survivorship and no significant difference in PROMS whether there is a chondral defect or not. This paper reported results from Chicago where articular cartilage defects were treated with ACI or osteochondral allograft. The search, therefore, remains to improve on the results for meniscal transplantation in combination therapy for the joint compromised by full-thickness articular cartilage loss. Such treatments in the future are likely to involve osteochondral grafting, repairing, and effectively re-creating the joint surface with fresh viable articular cartilage on a strong bony base.

This is one of the largest cohorts of MAT with a minimum of 1-year follow-up in the literature. We have demonstrated that MAT is a successful technique for the treatment of symptomatic meniscal deficiency, and that, when the meniscal graft heals and survives, the clinical outcomes are good regardless of concomitant surgery and the degree of chondral damage.

It is not yet known whether MAT has chondroprotective properties. Smith et al. in a review of the animal and clinical data identified indirect evidence for reduced chondral loss after MAT [39], and in the first pilot randomised-controlled trial of MAT against personalised knee therapy [40], Smith et al. showed a clinically significant difference in outcome at 1 year in favour of transplantation. Longer term analysis of this study and definitive RCT's will hopefully help to answer this in the future. It is important to stress, however, that although the evidence points toward a protective effect of the meniscal implant, allograft transplantation in this series was performed in symptomatic patients, not in asymptomatic patients. We have shown a reintervention rate of 27%, partly for persistent meniscal symptoms but also

for pain related to the surgery from prominent sutures, scar tissue, or removal of fixation or osteotomy plates. The possibility of creating symptoms advocates against prophylactic meniscal transplantation. Patients undergoing MAT should be counselled that there may be future interventions, and that the risk of these increases with increased chondral damage. Return to light sport is encouraged, and although we do not recommend return to heavy sport, there are some reports in the literature of athletes returning to their normal activities [10, 48].

Conclusion

We have shown that while good clinical outcomes were obtained with all grades of chondral damage following meniscal allograft transplantation, the best survivorship and re-operation rates were seen in those with minimal chondral wear. We have demonstrated that concomitant stabilisation or realignment surgery did not affect survivorship or clinical outcome of MAT in patients with good chondral surfaces. We, therefore, encourage early referral of patients with symptomatic meniscal loss to a specialist meniscal reconstruction centre.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval Outcome data collection and analysis was approved by the Research and Development Department at University Hospital Coventry and Warwickshire NHS Trust.

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