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Is meniscal allograft transplantation chondroprotective? A systematic review of radiological outcomes

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Abstract
Purpose The primary aim of this systematic review was to examine the hypothesis that meniscal allograft transplantation is chondroprotective by identifying and appraising studies that have assessed the progression of osteoarthritis following meniscal allograft transplantation. The secondary aim was to identify and appraise radiological measures of meniscal allograft integrity following surgery.
Methods Clinical studies on human participants undergoing meniscal allograft transplantation with a minimum follow-up of 6 months were included. The primary outcome measure was any radiological osteoarthritis progression measure. Secondary outcomes included magnetic resonance measures of meniscal integrity including meniscal size, shape, healing, extrusion and signal intensity.
Results Thirty-eight studies with 1056 allografts were included. The weighted mean joint space loss was 0.032 mm at 4.5 years across 11 studies. Other radiological classification systems were reported in small numbers and with variable progression rates. Meniscal extrusion was present in nearly all cases, but was not associated with clinical or other radiological outcomes. Meniscal healing rates were high, although the size, shape and signal intensity were commonly altered from that of the native meniscus. The quality of the included studies was low, with a high risk of bias.
Conclusion There is some evidence to support the hypothesis that meniscal allograft transplantation reduces the progression of osteoarthritis, although it is unlikely to be as effective as the native meniscus. If this is proven, there may be a role for prophylactic meniscal allograft transplantation in selected patients. Well-designed randomised controlled trials are needed to further test this hypothesis.
Level of evidence Systematic review of studies, Level IV.

Keywords Meniscal allograft transplantation · Osteoarthritis · Chondroprotection · Meniscus

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Introduction

The primary role of the menisci in the knee is load distribution, with meniscectomy decreasing the tibio-femoral contact area by 50–75 % and increasing the contact pressure by 200–300 % [5, 41, 67]. Fairbank, in 1948, was the first person to document radiological knee changes following meniscectomy [18], and a number of subsequent studies have demonstrated a high risk of developing osteoarthritis (OA) following meniscectomy [48, 52]. As recognition of the role the menisci play in knee homoeostasis, there has been a trend towards meniscal preserving surgery. Despite this, only a small number of tears are repairable, and those that are repaired carry a significant failure rate [44].

Meniscal allograft transplantation was first performed in 1984, and there have since been well over 1600 cases reported in the literature [43, 53]. Meniscal allograft transplantation uses a cadaveric human meniscus during an arthroscopically assisted operation [38]. A recent systematic review showed a mean improvement in Lysholm scores from 56 pre-operatively to 81 (out of 100) at final follow-up as well reporting an improvement in all other used patient-reported outcome measures in the medium term [58]. However, it has not been determined whether meniscal allograft transplantation can reduce the risk or delay the progression of OA [55]. If meniscal allograft transplantation reduced the risk of OA, there may be a role for prophylactic surgery in certain patients. It would also be improved the risk–benefit profile of the procedure for patients that are currently deemed suitable for transplantation. The purpose of this systematic review was to examine the hypothesis that meniscal allograft transplantation is chondroprotective by identifying and appraising studies that have assessed the progression of OA following meniscal allograft transplantation.

Materials and methods

Quality of methodology

This study has been reported in accordance with the PRISMA statement for reporting systematic reviews [39]. A protocol for this systematic review has been published and can be viewed at http://www.crd.york.ac.uk/PROSPERO (CRD42014010116).

Eligibility criteria

Study type

- Any clinical study (randomised controlled trial, non-randomised comparative study or case series) written in the English language. Studies that do not contain new patient data, biomechanical studies and case reports were excluded.

Participants

- Any human of any age.

Intervention

- Meniscal allograft transplantation using any allograft preservation method and any grafting technique.
- Any rehabilitation regime post-operatively.

Comparator

- If a comparator group exists, it should be a reasonable alternative treatment, for example a non-operative rehabilitation group. It would also be considered reasonable to use the participants' other knees as a comparator.

Outcome measures

- The primary outcome measure of this systematic review was change in any radiological OA progression measure at a minimum of 1 year post-intervention.
- The secondary outcome measures include magnetic resonance imaging measures of the meniscus at a minimum of 6 months post-intervention, including meniscal appearance, signal intensity, healing and extrusion.

Search strategy

The search strategy was sensitivity maximising in order to reduce the risk of failing to identify eligible studies. The published search strategy was developed using a combination of keywords and subject headings, which were exploded to maximise the inclusion of potentially relevant studies. The search strategy for Medline (Ovid) was adapted for Embase (Ovid) and the Cochrane library (CENTRAL). The references of all included studies were searched for further potentially relevant studies.

Selection and appraisal method

Figure 1 shows a flow diagram of the selection process. Results of the database searches were transferred into EndNote, and duplicates were discarded. Our eligibility criteria were used to assess the remaining studies using the title and abstract. The full papers of any remaining studies were then reviewed. Two reviewers (NS and BP) independently assessed studies for eligibility. Any discrepancies were resolved by discussion and if that failed by the judgement of a senior author (TS).

In order to reduce duplicate publication bias, if two or more eligible studies used some or all of the same

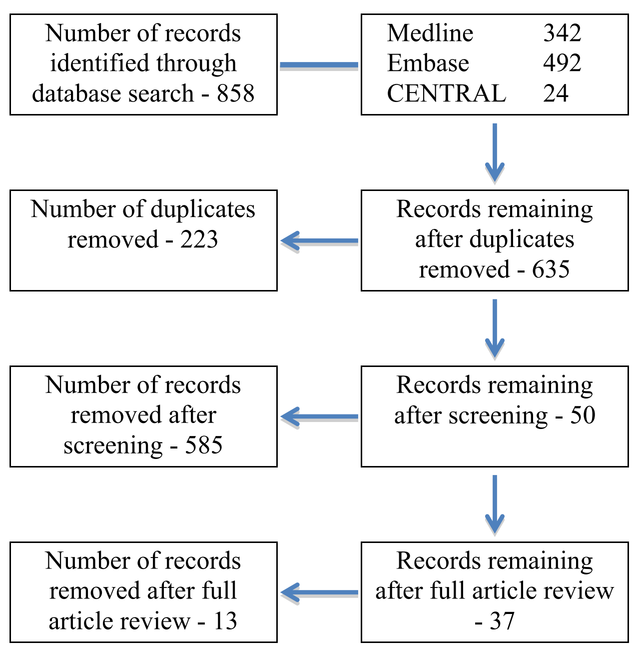

Fig. 1 Flow diagram of the study selection process

participants, both studies were only included if different outcomes measures were used [25]. If multiple studies with the same patient cohort were included on this basis, duplicated outcome measures would only be reported from the study with the longest follow-up.

A weighted mean was calculated for change in joint space width from baseline to final follow-up. Other outcome measures were assessed and summarised descriptively.

Results

There were 1056 meniscal allograft transplantations included across 38 studies that met the eligibility criteria (Tables 1, 2). A number of studies included some or all of the same patients as other included studies, but analysed different outcome measures [1, 2, 16, 21, 27, 30–32, 34–37, 61–63, 66]. There were no randomised controlled studies, with the majority of studies being case series. Two studies used the contralateral knee as a comparator group [51, 56]. The indications for meniscal allograft transplantation in all studies were a symptomatic knee with a history of meniscectomy. Most patients were young, with nearly all patients being between 15 and 50 years of age. The most common graft preservation technique was fresh-frozen, although some studies used cryopreserved and some older studies used irradiation as well. Bone tunnels or bridges were the most common method of fixing the graft, but a number of studies used an all-suture technique.

Osteoarthritis progression measures

Joint space width

Sixteen studies with a total of 428 knees reported the change in joint space between baseline and final follow-up (Table 1). The semi-flexed weight-bearing position was used for joint space width measurement, with Ha et al. [21] also measuring joint space width in full extension. The weighted mean joint space narrowing across all studies was 0.032 millimetres (mm) at a mean follow-up of 4.5 years (Fig. 2). Sekiya et al. [56] used the contralateral knee for comparison of joint space width change, finding no significant differences and very similar mean joint space width changes between the operative and contralateral (comparator) knees. Rath et al. [51] also used the same compartment in the contralateral knee, finding no significant differences, although there were only 11 patients. Two studies looked for a correlation between meniscal extrusion and joint space narrowing, with Ha et al. [21] finding a statistically significant intermediate correlation but Lee et al. [35] finding no correlation. No correlations between joint space width changes and clinical outcomes were made. A number of studies found an increase in joint space width, but none were statistically significant [2, 21, 30, 31]. The majority of studies found a trend towards joint space narrowing, but only two studies reported a statistically significant joint space narrowing [23, 35].

Kellgren and Lawrence classification [28]

Three studies reported KL scores (Table 1). Vunderlinckx et al. [68] had the longest mean follow-up of 8.8 years, finding no change in 19 of 33 patients. The other two studies had a much shorter follow-up, with Ha et al. [21] reporting no change in 28 patients and 1 grade worsening in eight patients at a mean 2.6 years; Chalmers et al. [12] reported five patients with no change and five with progression at a mean of 3.3 years.

Fairbank classification [17]

Three studies reported Fairbank's classification, with varying outcomes (Table 1). Wirth et al. [69] reported that 21 of 23 patients had less than two signs at baseline. Eleven patients reached final follow-up of 14 years, all of which had progression to two or more signs. It should also be noted that 17 of 23 patients had irradiated lyophilised grafts, and the authors reported that only these patients had arthritic changes. Hommen et al. reported a mean preoperative score of 0.5 and a mean score of 1.3 at follow-up of 11.8 years ($p = 0.0001$). They also reported a tendency for lower Lysholm scores if the Fairbank score had worsened, although this was not statistically significant [23]. The study by van Arkel et al. [61] found no change in 18 and an improvement in five patients, although the study had a shorter follow-up of 3 years.

IKDC radiological scores [26]

Two studies used this classification, with Sekiya et al. [56] finding minimal changes at a mean of 2.8 years and Graf et al. [19] finding 1 grade worsening in one of eight patients at a mean of 8.5 years.

Articular cartilage changes on MRI

Three papers have reported a modified Yulish score to grade articular cartilage degeneration on MRI (Table 1) [72]. Ha et al. [21] noted an absence of further articular cartilage degeneration in 78 % of patients at 2.6 years, with the remaining 22 % progressing by 1 or 2 grades. Marcacci et al. [40] reported a significant improvement in the mean articular cartilage degeneration by half a grade on both the femoral and tibial articular surfaces. Verdonk et al. [65]

Table 1 Studies with radiological OA progression measures

Study	Number of patients (allografts)	Follow-up mean—years (range)	Number of allografts with X-ray follow-up	Joint space width—mm pre-op (follow-up)	Other OA progression measures
Abat et al. [2]	88 (88)	5 (2.5–10)	88	S—3.2 (3.2) B—3.1 (3.5)	
Carter and Rabago [11]	40 (41)	10 X-ray follow-up 2 and 10 years	34		OA progression, number of patients: 2 years: 32 no change, 2 mild 10 years: 14 no change, 15 mild, 5 moderate/severe
Chalmers et al. [12]	13 (13)	3.3 (1.9–5.7)	10		KL change: 5—no change 5—1 or more grade change
Graf et al. [19]	8 (8)	9.7 (8.5–10.3)	8	Mean loss medial: 0.38 (range −2.75 to 1.75) Lateral: 0.5 mm (range 0–1.75 mm)	IKDC radiographic scores: Pre-op—1 normal, 5 abnormal, 2 severely abnormal. Follow-up—1 normal, 4 abnormal, 3 severely abnormal
Ha et al. [21]	36 (36)	2.6 (2–3)	36	Extension: 5.07 (5.0) Rosenberg: 4.14 (4.27)	KL change: 28—no change 8—1 grade worse Modified Yulish: 78 % no change 22 % 1 or 2 grades worse
Hommen et al. [23]	20 (20)	11.8 (9.6–13.9)	15	5.15 (4)	12 of 15 patients had a worsening Fairbank score. Mean scores: 0.5 pre-op and 1.3 post-op
Kim et al. [30]	27 (29)	4.5 (2–10.3)	23	3.6 (3.7)	
Lee et al. [35]	43 (43)	5.1 (3.5–8.3)	43	All: 3.65 (3.35) Extruded: 4.14 (3.87) Non-extruded: 3.3 (3.01)	
Marcacci et al. [40]	32 (32)	3.4 (3–5.5)	32 (MRI)		Modified Yulish (median): Femoral pre-op 1.5, follow-up 1 Tibial pre-op 1, follow-up 0.5
Noyes et al. [46]	38 (40)	3.3 (2–5.7)	40	3 knees showed joint space loss.	
Rath et al. [51]	18 (22)	5.4 (2–8)	11	5.2 (4.5). 1 patient lost more than 1 mm	
Ryu et al. (2002)	25 (26)	2.8 (1–6)	8 (min 2-year FU)	5—no change 2—1–2 mm loss 1—>2 mm loss	
Saltzman et al. [54]	22 (22) + 3 failed + 4 not accounted for	8.5 (6.8–11.2)	6 (mean 8.8 years fu)	2—no loss 2—minor loss 1—mild/mod loss 1—loss	
Sekiya et al. [56]	28 (28)	2.8 (1.8–5.6)	26	Mean loss medial: Transplant 0.05 Control 0.1 Lateral: Transplant +0.6 Control +0.4	IKDC radiographic scores: Pre-op: 6 normal, 13 nearly normal, 7 abnormal, 3 severely abnormal Post-op: 4 normal, 12 nearly normal, 10 abnormal, 2 severely abnormal

Table 1 continued

Study	Number of patients (allografts)	Follow-up mean—years (range)	Number of allografts with X-ray follow-up	Joint space width—mm pre-op (follow-up)	Other OA progression measures
Stollsteimer et al. [59]	22 (23)	3.3 (1.1–5.8)	23	Mean loss 0.88 (range 0–3)	
van Arkel and de Boer [61]	23 (23)	3 (2–5)	23		Fairbank's criteria: 18—no change 5—improvement
Verdonk et al. [64, 65]	38 (39)	12.1 (10–14.8)	25 (mean 12-year FU)	13—no loss 12—unspecified loss	Modified Yulish: No change femoral side in 47 %. No change on tibial plateau in 41 %
Vunderlinckx et al. [68]	34 (35) + 5 failures	8.8 (5.2–14.1)	33		KL grade: 19—no change 8—1 grade worse 6—2 grades worse
Wirth et al. [69]	23 (23)	14 (14)	23		Fairbank's criteria: Pre-op: 8 no changes, 13 grade 1, 1 grade 2 3-year Fu: 3 no changes, 9 grade 1, 4 grade 2, 3 grade 3 14-year FU: 6 grade 2, 5 grade 3
Yoldas et al. [70]	31 (34)	2.9 (2–5.5)	34	Medial: 4.9 (5.2) Lateral: 4.1 (4.9)	
Zhang et al. [73]	18 (18)	2.1 (1.5–3.4)	18	Median: 4.5 (4.5)	

Table 2 Studies with MRI measures of meniscal integrity

Study	Number of patients (allografts)	Follow-up mean—years (range)	Number of MRI	MRI Signal Intensity	MRI extrusion—relative percentage extruded (relative percentage extrusion) Minor <3 mm Major >3 mm	MRI—size and shape	MRI—allograft healing
Abat et al. [1]	88 (88)	Min 3 years	88		S: relative percentage extrusion 36.3 % Minor 27 % Major 73 % B: relative percentage extrusion 28.1 % Minor 69 % Major 31 %		
Bhosale et al. [6]	8 (8)	3.2 (2–6)	5	Increased internal 100 %		Wedge 100 % Flattened 40 % Expanded 20 % Irregular surface margin 80 %	Healed 100 %
Carter and Economopoulos [10]	25 (25)	0.5	25			Shrinkage avg. 7 % (0–22 %)	
Choi et al. [14]	23 (23)	0.5	23		Mean 3.2 mm		
Ha et al. [21]	36 (36)	2.6 (2–3)	36				Complete 72 % Partial 28 %
Hardy et al. [22]	22 (22)	4.4 (2.8–6)	14 at 6 m 17 at final	6 m—Heterogeneous 14 % Final—Heterogeneous 74 %	6 m—mean 2.7 mm relative percentage extrusion 36.7 % Final—mean 3.6 mm relative percentage extrusion 46 %		6 m—Complete healing 57 % Partial healing 14 % Not healed 29 %
Hommen et al. [23]	20 (20) + 2 without scores	11.8 (9.6–13.9)	7	Grade 3 71 %		All moderate shrinkage	
Jang et al. [27]	36 (36)	2.6 (2–3)	36		Traditional Pollard: Mean 4.1 mm relative percentage extrusion 46.7 % None 6 % Minor 11 % Major 83 % Modified Pollard: Mean 3.7 mm relative percentage extrusion 35.2 % None 6 % Minor 28 % Major 66 %		
Kim et al. [32]	106 (110)	4.1 (2–13.6)	108	Normal 7 % Variable 93 %	Mean 3.7 mm relative percentage extrusion 42.6 %	Normal volume 69 % Generalised atrophy 3 % Atrophy anterior horn 19 % Atrophy posterior horn 4 % Swollen anterior horn 5 %	

Table 2 continued

Study	Number of patients (allografts)	Follow-up mean—years (range)	Number of MRI	MRI Signal Intensity	MRI extrusion—relative percentage extruded (relative percentage extrusion) Minor <3 mm Major >3 mm	MRI—size and shape	MRI—allograft healing
Lee et al. [34]	31 (31)	1	31			Shrinkage: Minimal 65 % Mild 19 % Moderate 16 % Severe 0 % Width midbody 89 % Thickness midbody 115 %	
Lee et al. [37]	43 (43)	1	43	Higher signal intensity 100 % Anterior horn demonstrated higher signal than posterior horn			
Lee et al. [35]	43 (43)	5.1 (3.5–8.3)	43		Mean 3.0 mm Minor 60 % Major 40 %		Healed 100 %
Lee et al. [36]	21 (21)	1	21		6 w: Mean 2.9 mm relative percentage extrusion 29.2 % 3 m: Mean 2.9 mm relative percentage extrusion 29.4 % 6 m: Mean 3.0 mm relative percentage extrusion 32.4 % 12 m: Mean 2.9 mm relative percentage extrusion 31.9 %		
Koh et al. [33]	99 (99)	2.7 (2–4.9)	99		LM: Mean 4.7 mm relative percentage extrusion 52 % MM: Mean 2.9 mm relative percentage extrusion 31.2 %		
Marcacci et al. [40]	32 (32)	3.4 (3–5.5)	32		% of grafts with extrusion—69% overall MM 50% LM 87%		Healed 100 %
Noyes et al. [46]	38 (40)	3.3 (2–5.7)	29 FWB or PWB conditions	Normal 3 % Grade 1 45 % Grade 2 38 % Grade 3 10 %	Mean 2.2 mm <25 % meniscal width 59 % 26–50 % meniscal width 38 % >50 % meniscal width 3 %		
Potter et al. [49]	24 (29)	1 (0.25–3.4)	29	Increased peripheral signal 100 % Increased signal posterior horn attachment site 63 %	Moderate 24 % Severe 14 %		
Rankin et al. [50]	8 (8)	2 (1.3–2.8)	8 FWB			Mean height and width similar to normal meniscus	
Stollsteimer et al. [59]	22 (23)	3.3 (1.1–5.8)	12	Increased signal 42 %	No extrusion 92 % Minor 8 %	Volume shrinkage to 62 % of normal	
van Arkel et al. [62]	16 (19)	2.6 (1.2 4.6)	19		Subextrusion 65 % Complete extrusion 35 %	Moderate shrinkage 21 % Severe shrinkage 21 %	Complete healing 63 % Partial healing 26 % Failed to heal 11 %

Table 2 continued

Study	Number of patients (allografts)	Follow-up mean—years (range)	Number of MRI	MRI Signal Intensity	MRI extrusion—relative percentage extruded (relative percentage extrusion) Minor <3 mm Major >3 mm	MRI—size and shape	MRI—allograft healing
Verdonk et al. [63]	17 (17)	2 (0.5–9.25)	17		Mean 5.8 mm		
Verdonk et al. [64, 65]	38 (39)	12.1 (10–14.8)	1 year: 25 1 and 10 years: 17	10 years: Normal 41 % Increased signal 59 %	Minor 24 % Major 76 %		
De Coninck et al. [16]	37 (37)	1	37		Open: MM—Mean 4.7 mm relative percentage extrusion 56.7 % LM—Mean 4 mm relative percentage extrusion 50.3 % Arthroscopic: MM—Mean 2.4 mm relative percentage extrusion 40.1 % LM—Mean 3.4 mm relative percentage extrusion 35.1 %		
Wirth et al. [69]	23 (23)	14 (14)	9			Fresh-frozen grafts maintained size. Lyophilised grafts major shrinkage	
Yoon et al. [71]	91 (91)	3.3 (2–10.4)	35		LM Mean 1.7 mm relative percentage extrusion 19.4 % MM Mean 2.6 mm relative percentage extrusion 36.4 %		
Zhang et al. [73]	18 (18)	2.1 (1.5–3.4)	17	Normal 18 % Grade 1 58 % Grade 2 12 % Grade 3 12 %	Minor 35.3 % Major 64.7 %	Atrophy anterior horn 18 % Absent anterior horn 18 %	

FWB full weight bearing, *PWB* partial weight bearing, *w* week, *m* month, *S* suture fixation group, *B* bone fixation group, *MM* medial meniscus group, *LM* lateral meniscus group reported the longer-term articular cartilage changes on 17 patients over an average of 12.1 years. There was no further progression of articular cartilage degeneration on the femoral condyle and tibial plateau in 47 and 41 % of patients, respectively, including 35 % of patients with no progression on both sides of the joint.

Other

One study reported OA progression at 2- and 10-year follow-up with an indeterminate tool [11]. At 2 years there was no change in 32 of 34 patients, but by 10 years nearly half of the patients had a mild change and five had moderate or severe progression of OA.

Magnetic resonance imaging measures

Twenty-six of the 38 studies included in this systematic review reported on MRI findings following meniscal allograft transplantation.

Meniscal extrusion

Eighteen of the 26 studies with MRI outcomes reported meniscal extrusion, with variable techniques (Table 2). The methods used to report meniscal extrusion include the absolute number of millimetres the graft extends beyond the edge of the tibial plateau, the relative percentage extrusion of the meniscus that extends beyond the edge of the tibial plateau, as well as a variety of classification systems. The most commonly reported classification defines extrusion as no extrusion, minor extrusion (less than 3 mm) and major extrusion (more than 3 mm), in relation to the margin of the tibial plateau [1, 15, 27, 35, 65, 73].

All studies reported there was extrusion in the majority of patients, with 11 studies reporting an average extrusion of between 1.7 mm and 5.8 mm. [14, 16, 22, 27, 32, 33, 35, 36, 47, 63, 71] Eight studies quantified extrusion by the relative percentage extrusion of the meniscal allograft and have reported a mean range from 19.4 to 56.7 % [1, 16, 22, 27, 32, 33, 36, 71]. Six studies (eight groups) compared the amount of extrusion between medial and lateral meniscal allografts, with three finding no difference [1, 27], three finding more lateral extrusion [16, 33, 40] and two finding more medial extrusion [16, 71].

The correlation between meniscal extrusion and clinical outcomes had been analysed by 10 studies, with seven finding no significant association [1, 22, 27, 33, 35, 40, 64]. Potter et al. [49] reported poorer clinical outcomes in 11 patients with meniscal extrusion, although these patients represented a subset that all had moderate to severe articular cartilage degeneration at the time of transplantation. Lee et al. [35] and Yoon et al. [71] found an association between meniscal extrusion and Lysholm score, but they did not discuss about the finding further.

Four papers have investigated the effect of surgical technique on the amount of meniscal extrusion. Abat et al. [2] reported a relative percentage extrusion of 36.3 % with root fixation using sutures through bone tunnels, compared with 28.1 % with root fixation using bone plug fixation. There was no association found between the degree of extrusion and functional scores. Choi et al. [14] evaluated the position of the bone bridge in lateral meniscal transplants, finding an association with meniscal extrusion to increased lateral positioning of the bone bridge. Jang et al. [27] compared the traditional Pollard sizing technique to Pollard minus 5 % sizing. The relative percentage extrusion decreased from 46.7 to 35.2 %, but no difference in clinical or other radiographic outcomes was found. De Coninck et al. [16] compared open to arthroscopic surgical technique for meniscal transplantation. In the open technique, the meniscal roots were sutured to the capsule and native meniscal remnants, whilst in the arthroscopic technique the meniscal roots secured by suture fixation through bone tunnels. They found significantly less meniscal extrusion with the arthroscopic technique.

Three papers evaluated the change in meniscal extrusion over time. Lee et al. [36] evaluated meniscal extrusion over the first year post-operatively by serial MRI scans at 6 weeks, 3, 6 and 12 months, finding that average meniscal extrusion did not differ at any time point. Hardy et al. [22] reported 2.7 mm of meniscal extrusion at 6 months post-operatively and 3.6 mm at final follow-up of 4.4 years. The series consisted of 22 patients, and it is not stated if the MRI scans at final follow-up are from the same patients as the 6-month MRI scans. Verdonk et al. [65] evaluated the long-term change in meniscal extrusion from 1 year to an average of 12.1 years, finding progressive meniscal extrusion in 59 % of cases. However, extrusion had no correlation to progressive articular cartilage degeneration or any of the clinical outcome measures.

All except two studies evaluated meniscal extrusion with knees in a non-weight-bearing position. Noyes et al. [46] performed MRI scans on 29 meniscal allografts under weight-bearing conditions and demonstrated a mean of 2.2 mm extrusion. Verdonk et al. [63] evaluated the effect of weight bearing on meniscal extrusion with the use of ultrasound. Ten transplanted lateral meniscal allografts and ten healthy lateral menisci were studied in the supine non-weight-bearing position, bipedal stance and unipedal stance. Mean extrusion was higher in all positions for the transplanted menisci compared with normal menisci. The mean extrusion, however, did not increase during weight-bearing conditions in either group.

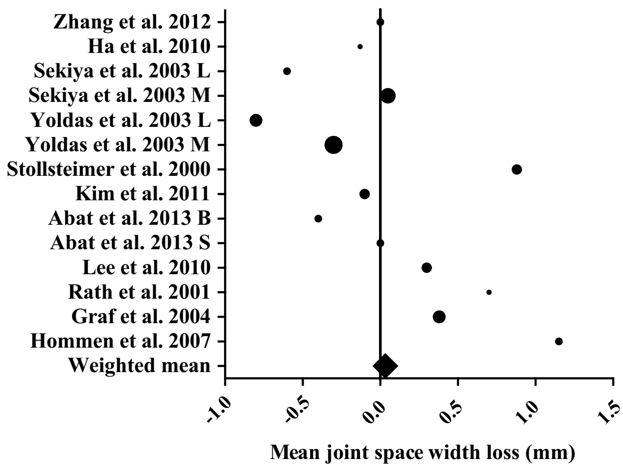

Fig. 2 Forest plot of joint space width loss in each study and a weighted mean. *X*-axis is joint space width loss; therefore, a negative number constitutes a joint space gain. *L* lateral meniscal allograft transplantation group, *M* medial meniscal allograft transplantation group, *B* bone fixation group, *S* suture fixation group

Signal intensity

Ten studies have reported on the signal intensity characteristics of meniscal allografts, with all but one study reporting altered and increased signal changes in the majority of the meniscal allografts (Table 2). Lee et al. [37] evaluated the intrameniscal signal intensity of 43 meniscal allografts with serial MRI scans over the first year (6 weeks, 3, 6 and 12 months). They standardised the signal intensity within the meniscal allograft to the normal ipsilateral meniscus. The intrameniscal signal intensity was higher within all the allograft menisci at all time points, with significantly increased signal starting at 3 and 6 months for the anterior and posterior horns, respectively. They found no correlation between intrameniscal signal intensity and clinical outcomes. Hardy et al. [22] also reported on the meniscal allograft appearance at 6 months and 4.4 years. At 6 months they found 86 % of menisci returned a normal homogenous appearance, compared with only 26 % at 4.4 years. Verdonk et al. [65] found the majority of meniscal grafts had increased signal intensity at 12.1 years, with 82 % having no progression of their signal intensity from 1 year to final follow-up.

Meniscal size and shape

Ten studies have reported the size and shape changes in meniscal allografts after implantation (Table 2). Meniscal shrinkage was reported by multiple studies, with Carter et al. [10] demonstrating an average of 7 % volume loss over the first 6 months. Kim et al. [32] and Zhang et al. [73] found shrinkage to predominantly affect the anterior horn of the meniscus. Zhang et al. also performed a second-look arthroscopy, which confirmed atrophy and fraying of the anterior meniscus horn that corresponded to the MRI changes in the same region.

Meniscal healing

MRI assessment of allograft healing to the capsule was reported by six studies (Table 2). Three studies reported a healing rate of 100 % [6, 35, 40], whilst the others reported some partial and non-healing menisci. The study by van Arkel et al. correlated MRI healing to arthroscopic healing at a mean of 3 years post-operatively on 19 patients. On MRI, they found complete healing in 63 %, partial healing in 26 % and no healing in 11 % of cases. However, MRI was found to underestimate healing rates; the cases with partial healing on MRI were found to be completely healed at arthroscopy, and the cases with no healing on MRI were found to be partially healed at arthroscopy.

Risk of bias

Missing studies

Only published studies were searched for, which may exacerbate publication bias. Secondly, studies written in languages other than English were not included, which may cause some important studies to be lost.

Missing outcomes

Most studies had patients that were lost to follow-up. Whilst this is inevitable, especially in studies with long-term follow-up, it can introduce bias. It was common for studies to exclude failures from follow-up assessment. This is highly likely to bias results towards outcome scores. It was also common for some patients to not have imaging at follow-up. It was not always clear why some patients did and others did not have follow-up imaging, but this is a potential source of bias.

Discussion

There has been substantial research interest in assessing whether interventions can modify the long-term disease process of OA. Radiological markers for joint damage, especially joint space narrowing, have become widely accepted as appropriate surrogate measures of OA progression and have been recommended as the outcome measure of choice by regulatory agencies in the USA and Europe [7]. It has been shown that joint space narrowing is highly predictive of the need for future OA-related surgery, usually total knee replacement [9]. Bruyere et al. [9] found that the relative risk for future OA-related surgery with a joint space narrowing of 0.7 mm or more over 3 years was 5.15 (95 % confidence interval 1.7–15.6). A recent systematic review assessing the imaging options for OA progression concluded that joint space narrowing was the only imaging tool that should be recommended for the assessment of OA progression in clinical trials [20]. In this context, the negligible (0.032 mm) joint space narrowing at 4.5 years in this systematic review provides some support for the hypothesis that meniscal allograft transplantation may have a chondroprotective effect. As well as this, the two studies that used the contralateral normal knee as a comparator of joint space changes found no significant differences between the groups at final follow-up.

It is possible that joint space width on plain radiography is not an accurate measure of cartilage loss in patients undergoing meniscus transplant as joint space width is affected by meniscal volume and position [24]. Other limitations of plain radiography are that it is insensitive to early changes or focal disease and joint space can be affected by changes in the other compartment [13]. High-resolution MRI with volume analysis and T2 mapping is increasingly being used to measure cartilage changes, as it is sensitive and precise [8].

The underlying aim of meniscal allograft transplantation is to restore normal meniscal coverage of the tibial plateau. Meniscal extrusion is a surrogate marker to assess the extent to which this has been achieved; minimal extrusion implies good tibial plateau coverage and vice versa. Studies on native menisci have shown that extrusion is associated with accelerated chondral loss and osteoarthritis [24, 29, 57, 60]. This systematic review found no clear association between extrusion and other adverse outcomes. This may be because it is possible for an oversized meniscal graft to restore adequate tibial plateau coverage, whilst exhibiting a large amount of extrusion and an undersized or shrunken graft does not restore plateau coverage, whilst having no extrusion [42]. An additional limitation is technique of measuring extrusion in the coronal plane at a single point, the midbody position. Marcacci et al. [40] and Noyes et al. [46] demonstrated minimal extrusion in the sagittal plane, suggesting that the assumption that extrusion is uniform may be incorrect for meniscal allograft transplantation. Therefore, measuring extrusion at a single point on a single plane may not be an accurate measure of either total extrusion or tibial plateau coverage [45]. High-resolution MRI may be able to provide a better measure by 3D modelling the meniscus and tibial plateau.

MRI has become the investigation of choice to assess meniscal allograft integrity and healing, as it is cost-effective and non-invasive. This systematic review found high rates of meniscal healing to the capsule, whilst signal intensity and meniscal shape were predominantly altered. Studies have shown that the meniscus is repopulated by cells resembling fibrochondrocytes in the first 6 months, but the normal meniscal collagen architecture, orientation and histological appearance are changed [3, 4]. A correlation between MRI and histological appearance has been shown, with biopsies from areas of homogenous low signal demonstrating near normal collagen appearance and biopsies from areas of high signal showing a disorganised collagen appearance [49]. Concerns remain over the consequences of this altered tissue structure and the ability of a meniscal allograft to provide chondroprotection, but no association with clinical outcomes has been found [37, 46, 65].

There are a number of limitations that reduce the strength of the conclusions: the quality of included studies was low, with a high risk of selection and measurement bias. The limited number of studies using control groups also limits the value of results, especially when interpreting OA progression. The studies included in this systematic review are also heterogeneous, with different inclusion criteria, techniques, graft type, associated procedures, rehabilitation and follow-up.

Conclusion

Given the lack of high-quality controlled trials, it is difficult to draw definitive conclusions. It appears that meniscal allograft transplantation cannot universally reverse or prevent OA changes in patients with a symptomatic meniscal-deficient knee. Some studies showed minimal progression of OA in the long-term and the weighted mean joint space narrowing was also negligible. These results support the hypothesis that meniscal allograft transplantation may delay or reduce the progression of OA. Given the high risk of early OA in these patients, there may be a role for prophylactic transplantation in selected young patients if this hypothesis is proven. Secondly, it would improve the risk–benefit profile of meniscal transplantation for patients that are currently indicated for the procedure. The gold standard study design needed to definitively test this hypothesis is an RCT. Quantitative MRI may provide the most sensitive measure of early OA progression and may be a useful future outcome tool for a definitive trial.

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

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