DOI: 10.1002/ksa.12065

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Correlation between articular cartilage status on outcomes and survivorship following meniscal allograft transplantation: A systematic review

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Funding information None

Abstract

Purpose: To conduct a systematic review evaluating potential correlations between preoperative articular cartilage integrity on outcomes and survivorship in patients undergoing meniscal allograft transplantation (MAT).

Methods: A literature search was performed by querying SCOPUS, PubMed, Medline, and the Cochrane Central Register for Controlled Trials from database inception through May 2023 according to the 2020 PRISMA statement. Inclusion criteria were limited to studies reporting on outcomes and survivorship following MAT based on preoperative cartilage status.

Results: Sixteen studies, consisting of 1723 patients (*n* = 1758 total menisci), were identified in six level III and 10 level IV evidence studies. There was high heterogeneity in cartilage grading scales, reporting of concomitant cartilage procedures, and indications for MAT based on osteoarthritis. Patients with lower limb malalignment were either excluded or corrected with an osteotomy. MAT failure rate was reported in nine studies, with four studies reporting a greater rate of failure in knees with higher degrees of cartilage damage. Eight studies reported on clinical outcomes based on cartilage grade, with two studies reporting significant differences in clinical outcomes based on cartilage grade. Of the five studies reporting management of full-thickness chondral defects with cartilage surgery, three studies reported no significant difference in survivorship based on preoperative cartilage grade, while one study reported lower survivorship and one study reported unclear results. No studies found significant differences in survivorship and outcomes between medial and lateral MAT.

Conclusions: Conflicting results and high variability in reporting of concomitant cartilage repair and indications for MAT exist in studies evaluating the efficacy of MAT based on articular cartilage status. The

Abbreviations: ACLR, anterior cruciate ligament reconstruction; Cm, centimeters; F, females; ICRS, International Cartilage Repair Society; KOOS, knee injury and osteoarthritis outcome score; LOE, level of evidence; M, males; MACI, matrix-induced autologous chondrocyte implantation; MAT, meniscus allograft transplantation; MFX, microfracture; MINORS, Methodological Index for Non-Randomised Studies; N.s., not significant; NR, not recorded; OCA, osteochondral allograft transplantation; OKS, oxford knee score; OR, odds ratio; PRIMSA, preferred reporting items for systematic reviews and meta-analyses; PRO, patient reported outcome; PROM, patient reported outcome; SD, standard deviation; TKA, total knee arthroplasty; UKA, unicompartmental knee arthroplasty; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

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degree of preoperative chondral damage did not have a strong relationship with clinical outcomes following MAT. Higher degrees of cartilage damage were associated with higher MAT failure rates, with possible improvement in survivorship when treated with an appropriate cartilage procedure.

Level of Evidence: Level IV.

KEYWORDS

cartilage, chondral, meniscus, meniscus allograft transplantation, outcomes

INTRODUCTION

Patients sustaining meniscal injuries, either through traumatic or degenerative processes, often experience pain, effusion, and mechanical symptoms interfering with activities of daily living and effectively decreasing quality of life [45]. While meniscal repair is advocated in young patients and patients with tears in which the potential for meniscal healing is high, certain meniscal tear patterns, namely degenerative tears, are often irreparable and warrant partial, subtotal, or total meniscectomy [4]. In patients undergoing meniscectomy, loss of the meniscus effectively impairs load distribution in the tibiofemoral joint through loss of hoop stresses, altering contact mechanics with increased intracompartmental contact pressures, increasing the risk of early osteoarthritis development and progression [5, 21, 26, 47]. In the setting of functional meniscal deficiency, especially young, active patients experiencing pain and limitations, meniscal allograft transplantation (MAT) has been shown to reduce pain and improve function [24, 40, 44, 48]. Moreover, MAT has been shown to possess long-term survival rates ranging from 73.5% to 81.8% at 10-year follow-up [27].

Isolated cartilage lesions may occur concurrently in patients with meniscal deficiency, requiring concomitant MAT with chondral restoration in order to reduce pain and restore function [12]. While multiple investigations have reported favourable outcomes in patients undergoing MAT with cartilage repair or restoration for >1 cm² full-thickness knee chondral defects, outcomes based on the grade of chondral damage remains largely unknown [12, 19]. Namely, Mahmoud et al. observed that patients with advanced chondral damage (Outerbridge Grades 3-4) experienced increased risk for MAT failure, occurring at an average of 6.1 years postoperatively, when compared to patients with no to low-grade (Outerbridge Grades 0-2) cartilage damage [25]. However, Saltzman et al. reported no difference in patient-reported outcomes (PROs), complications, and MAT failure rates when comparing patients with fullthickness chondral defects at a mean size of 4.43 ± 2.5 cm² (Outerbridge Grade 4) versus those with no or low-grade chondral defects (Outerbridge Grades 0-1) [35]. Additional studies have reported conflicting

results, making it unclear how varying degrees of preoperative cartilage damage effects outcomes following MAT [8, 19, 39].

The purpose of this investigation was to perform an evidence-based systematic review to assess outcomes and survivorship in patients undergoing MAT based on the degree of chondral injury at the time of transplantation. The authors hypothesise that patients with higher degrees of chondral damage would possess inferior clinical outcomes and decreased survivorship when compared to patients with less cartilage damage.

MATERIALS AND METHODS

Search strategy and eligibility criteria

A systematic review was conducted according to the 2020 preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement [31]. A literature search identifying studies reporting clinical outcomes of MAT based on cartilage status was conducted on November 20, 2022 using PubMed, MEDLINE, Scopus, the Cochrane Database for Systematic Review, and the Cochrane Central Register for Controlled Trials. The search included the following terms combined with Boolean operators: "MAT" OR "meniscal allograft" OR "meniscus" OR "cartilage" OR "status" OR "failure" OR "outcomes" OR "survivorship" OR "articular" OR "Outerbridge" OR "extrusion" OR "knee" OR "International Cartilage Repair Society (ICRS)."

Inclusion criteria consisted of level I–IV studies written in English or with English translation, reporting on clinical outcomes and failures following MAT with either comparative groups or subgroup analyses based on articular cartilage status. The exclusion criteria consisted of non-English language studies, review articles, technical notes, case reports, editorial commentaries, biomechanical and animal studies, epidemiological and national database studies, studies reporting outcomes without comparative analyses based on cartilage status, and studies reporting on revision MAT procedures. Studies with patients undergoing concomitant cartilage procedures were included.

Studies with overlapping patient data were selected so that only the most recent study was included. Studies without reported chondral status during MAT were similarly excluded.

Title and abstract screening was performed independently by two authors (Varun Gopinatth and Alec A. Warrier) followed by a full-text screening to determine whether studies met inclusion or exclusion criteria. A third, independent author (Enzo S. Mameri) was designated to consult on any disagreements, during which none were encountered. Reference lists from the included studies were reviewed to ensure that all studies meeting inclusion criteria were identified.

DATA EXTRACTION

Study characteristics from each article were extracted and included: journal of publication, year of publication, level of evidence, intervention (MAT and performance of any concomitant operations), number of patients, patient demographics (age, sex), follow-up time, MAT surgical technique (all-soft tissue, bone plug, bridge-inslot), laterality (medial vs. lateral MAT), size of chondral defect, lower limb alignment, degree of chondral damage at the time of MAT, as well as reported patient outcome measures and MAT graft survivorship, when reported. The definition of MAT failure and incidence of failures was recorded from each study at all reported time points. Both failures and clinical outcomes were collected and stratified based on the reported cartilage grading scales (Outerbridge, ICRS, Cincinnati grading scales) [20, 29, 37] (Table S1).

Risk of bias

All included studies were evaluated by two independent authors (Varun Gopinatth and Alec A. Warrier) using the Methodological Index for Non-Randomised Studies (MINORS) criteria. A third independent author (Enzo S. Mameri) was designated to discuss and resolve any disagreements, if an assigned score of greater than 2 was encountered, which did not occur. The MINORS criteria is a 12-question numerical scale used to evaluate noncomparative, nonrandomised studies. Each question is scored with a 0 if not reported, 1 if reported but inadequate, or 2 if reported and adequate [38]. The ideal score for noncomparative, nonrandomised studies is 24. All studies meeting inclusion criteria were assessed with the MINORS criteria.

Statistical analysis

Study characteristics and patient demographics information were organised and analysed using Microsoft Excel (Version 2206, Microsoft Corporation). Continuous variables, including patient age and mean followup, were calculated and reported as a weighted mean ± standard deviation of the total study population. Discrete variables, including patient sex and meniscus laterality, were reported as proportions of the study population.

RESULTS

The initial literature search identified a total of 982 articles (Figure 1). After duplicates were removed, 370 studies underwent title and abstract screening with 29 studies qualifying for full-text review. A total of 16 studies were found to meet eligibility criteria and were included in this review.

Study characteristics

Of the 16 studies meeting inclusion/exclusion criteria, a total of 1723 patients (n = 1758 total menisci) were identified. There were six Level III studies and 10 Level IV studies (Table 1). Fifteen studies reported patient sex, with males comprising 64.4% (n = 1092/1696) of the patient population. Mean patient age was 35.5 ± 4.9 years (range: 25.7-46.9 years). Mean final follow-up was 66.9 ± 33.4 months (range: 12.9 months-13.1 years). The mean MINORS score was 13.3±4.4 (Figure S1). The mean score for noncomparative studies was 10.5 ± 2.4 and 18.5 ± 1.0 for comparative studies. In eight studies [1, 8, 23, 32-34, 42, 43], a lateral MAT was more commonly performed compared to eight studies [2, 14, 22, 25, 28, 35, 36, 39] in which medial MAT was performed more commonly. Of the 1758 MATs performed, 56% (n = 980/1758 MATs) were lateral and 44% (n = 778/1758) were medial. The most commonly used cartilage grading system was the Outerbridge scale (n = 10 studies [14, 25, 33–36, 39, 42, 43]) followed by the ICRS grading system (n=2)studies [8, 22]), and the Cincinnati scale (n = 1 study)[28]). Reference to a cartilage grading system was not specified in three studies [2, 23, 32]. Cartilage damage was most commonly assessed via arthroscopic visualisation in 14 studies [1, 2, 8, 14, 22, 23, 25, 28, 32, 35, 36, 39, 42, 43], while four studies also evaluated cartilage damage based on preoperative imaging using magnetic resonance imaging [2, 22, 23, 33] and radiographs [2]. Cartilage size was reported in one study at 4.43 ± 2.5 cm² [35]. Lower leg malalignment was reported as a contraindication to MAT in 11 studies [2, 8, 14, 22, 23, 28, 33, 35, 36, 39, 43], with 11 studies also reporting patients undergoing a realignment procedure such as high tibial osteotomy or distal femoral osteotomy to correct malalignment [8, 14, 22, 25, 28, 32, 33, 35, 36, 39, 42]. The threshold of varus or

Identification of studies via databases and registers



FIGURE 1 Preferred reporting items for systematic review and meta-analysis (PRISMA) diagram for study selection.

valgus alignment for patients to be eligible for MAT or require a realignment procedure was most commonly five degrees [14, 22, 36, 43], although Stone et al. used a threshold of seven degrees [39]. Mean axis deviation was reported in two studies, with Lee et al. reporting a mean axis deviation of 1.06 ± 2.38 and Lee et al. reporting a mean axis deviation of 1.00 ± 2.22 [22, 23]. Ahn et al. reported lower leg alignment at 1.1 ± 2.6 and 2.0 ± 2.3 for the minor and major extrusion groups, respectively [1].

Meniscus laterality

Nine studies evaluated the efficacy of medial versus lateral MAT [14, 25, 28, 33, 34, 36, 39, 42, 43]. Seven studies reported no statistical difference in survivorship between medial and lateral MAT [14, 25, 28, 36, 39, 42, 43], while two studies found no difference in clinical outcomes between medial and lateral MAT [33, 34]. The influence of cartilage status on medial versus lateral MAT efficacy was not reported. Three studies utilised exclusively medial or lateral MATs [1, 22, 23]. Of the two studies performing only lateral MATs, one reported that cartilage damage to not be a significant risk for

meniscal extrusion after MAT, while another found that greater cartilage degeneration after meniscectomy and prior to MAT may result in more joint space narrowing [1, 23]. The only study performing exclusively medial MATs found a higher risk of anatomic, but not clinical, failure in knees with ICRS Grade 3/4 cartilage damage [22].

MAT survivorship

MAT survivorship stratified by preoperative cartilage damage was reported in nine studies (Table 2). Across the studies, failure was typically defined as meniscectomy/resection of the meniscal transplant [8, 14, 22, 25, 28, 36, 39, 42], conversion to total knee or unicompartmental knee arthroplasty [8, 14, 22, 25, 28, 35, 36, 39, 42], revision MAT [14, 22, 28, 35, 36], meniscal extrusion >50% of meniscus width [28], or the presence of allograft tearing [22, 28] (Table 2). In four studies, higher degrees of chondral damage were associated with a statistically significant increase in MAT failure rate or lower survivorship [8, 22, 25, 42]. On the other hand, five studies reported no significant difference in MAT survivorship based on articular cartilage damage [14, 28, 35, 36, 39].

Author (year)	Journal	Level of evidence	No of patients	Age, mean±SD (range)	Sey		Laterality
Ahn et al. [1]	Arthroscopy	ო	72	Minor extrusion: 36.3 ± 8.0 (21–5; Major extrusion: 37.7 ± 9.1 (21–5;	3) Mir. 5) Maj	ior extrusion: 26 M/8 F or extrusion: 28 M/10 F	72L
Alentorn-Geli et al. [2]	KSSTA	4	35	27.2 (19–54)	NR		13 L/24 M
Bloch et al. [8]	KSSTA	ю	240	30.79 (13–49)	157	7 M/83 F	173 L/67 M
Grassi et al. [14]	MSLA	4	324	39.5±11.6	246	8 M/76 F	142 L/182 M
Lee et al. [<mark>23</mark>]	MSLA	З	79	33.13 ± 11.66	501	M/29 F	79 L
Lee et al. [<mark>22</mark>]	MSLA	e	78	34.96±9.62	64 1	M/14 F	78 M
Mahmoud et al. [2	25] Arthroscopy	4	45	34.9±10.6	231	M/22 F	15 L/30 M
Noyes et al. [28]	MSLA	4	69	30 (14–49)	331	M/36 F	31 L/41 M
Potter et al. [32]	Radiology	4	24	33.2 (23–43)	16	M/8 F	15 L/14 M
Ren et al. [33]	Journal of Or and Rese	thopaedic Surgery 4 arch	61	32.3	36.	M/25 F	56 L/9 M
Ryu et al. [34]	Arthroscopy	4	25	34.5±8.5 (15–49)	171	M/8 F	16 L/10 M
Saltzman et al. [3	5] Arthroscopy	ო	6	No defect: 26.8 ± 10.7. Full-thickn 30.4 ± 10.3	ness defect: No	defect: 14 M/8 F. Full- thickness defect: 32 M/37 F	35 L/56 M
Searle et al. [36]	BMC Musculo	oskeletal Disorders 4	43	35.6±7.5	311	M/12 F	16 L/27 M
Stone et al. [39]	JBJS British	4	115	46.9 (14.1–73.2)	831	M/32 F	34 L/85 M
Van Der Straeten et al. [42]	Plos One	4	313	33 (15–57)	187	7 M/126 F	210 L/119 M
Van der Wal et al. [43]	KSSTA	ო	109	41 (29–51)	44	M/65 F	73 L/36 M
Author (year) Te	schnique	Mean follow-up		Cartilage status (no of patients)	Concomitant cartilage procedures (no of patients)	Results/conclusions cartilage status affec survival and outcom	related to ting MAT
Ahn et al. [1] Ku	eyhole, inside- out suture only	Minor extrusion: 47.2 ± 18.9 m extrusion: 58.8 ± 22.9 mont	onths (26–97). Major ns (26–102)	Outerbridge Grade 0 (24) Grade 1 (33) Grade 2 (15)	Concomitant cartillage surgery patients excluded	The major graft extrus following lateral $M/$ patients with greate damage than the m group (ρ = 0.004). H cartilage injury was	on group T had more rr cartilage inor extrusion dowever, excluded as

TABLE 1 Overview of included studies.

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(Continues)

Author (year)	Technique	Mean follow-up	Cartilage status (no of patients)	Concomitant cartilage procedures (no of patients)	Results/conclusions related to cartilage status affecting MAT survival and outcomes
					a risk factor for extrusion in the multivariate analysis
Alentorn-Geli et al. [2]	Suture-only	38.6 months	No damage (13) Grades 1–2 (10) Grades 3–4 (12)	None reported	No significant difference in improvement from preoperative to postoperative Lysholm, IKDC, and VAS for pain based on cartilage status
Bloch et al. [8]	Bone bridge with all-inside and inside out suture	3.44 years (1–10)	Group A: ICRS 0–3A Group B: ICRS 0–3A + concomitant osteotomy Group C: ICRS 0–3A + ACLR Group D: ICRS 3b–c, bone on cartilage Group E: ICRS 3b–c, bone on bone	1–4 cm ² lesions treated with MFX, 4 cm ² + lesions treated with MACI	Knees with ICRS Grades 0–3A demonstrated significantly higher survivorship (95%) compared to ICRS Grades 3b–c (77%). Equivalent PROMs were observed between groups.
Grassi et al. [14]	Suture only, double-tunnel technique, all- inside, no bone plug or bridge	5.7 ± 3.0 years (2.0–16.6)	Outerbridge—Grade 0 (130) Grade 1 (12) Grade 2 (63) Grade 3 (61) Grade 4 (58)	MFX for <2 cm ² , scaffold for >2 cm ²	No significant difference in survival rates based on surgical and clinical failure criteria between Outerbridge Grades 0–2 versus Grades 3–4 but lower survival in patients undergoing cartilage surgery
Lee et al. [23]	Keyhole technique, inside-out, suture only	8.49±3.26 years	NR	None recorded	Greater articular cartilage degeneration between meniscectomy and MAT was associated with more joint space narrowing following MAT
Lee et al. [22]	Double bone plug technique	6.9±5.3 years (2–21)	ICRS—Grade 0 (1) Grade 1 (7) Grade 2 (37) Grade 3 (20) Grade 4 (13)	Cartilage procedures (4)	Higher ICRS cartilage Grade (3/4) was associated with a higher risk of anatomic failure, but not clinical failure compared to low- grade cartilage lesions (0–2)
Mahmoud et al. [25]	Medial: Two bone plugs Lateral: keyhole or slot	8.6±3.4 years	Outerbridge— Grades 0–2 (14) Grades 3–4 (31)	Chondral repair (3)	The survival rate for Outerbridge Grades 0–2 knees was 100% compared to 74.2% for Grades 3–4 knees. Significant improvement was seen across

TABLE 1 (Continued)

Results/conclusions related to cartilage status affecting MAT survival and outcomes	most PROs, but Grades 3–4 knees did not see a significant improvement in Tegner while OKS and IKDC score improvements in Grades 0–2 knees were not significant.	There was no difference in survival, symptom, or functional analysis between knees with no cartilage damage and those classified as Cincinnati grade 2B/3.	Moderate to severe cartilage damage was associated with MAT graft fragmentation and degeneration.	No difference in postoperative VAS, IKDC, Tegner, and Lysholm based on preoperative Outerbridge cartilage grade.	Significant difference in postoperative VAS and preoperative VAS and preoperative and postoperative Lysholm scores in Outerbridge Grade 2/3 versus Grade 4 knees. Only 43% of Grade 4 knees were able to achieve a normal or nearly normal IKDC rating compared to 78% of Grade 2/3 knees.	No difference between in knees with Outerbridge Grade 0/1 and Grade 4 in failure rate and improvement in Lysholm, IKDC, KOOS, WOMAC, Overall knee function, Symptom rate, and SF-12.	(Continues)
Concomitant cartilage procedures (no of patients)		Osteochondral autograft transfer (20)	None reported	Microfracture (8)	None reported	Osteochondral allograft (48), ACI (13), MFX (9), Osteochondral autograft (3)	
Cartilage status (no of patients)		No damage (21) Cincinnati 2B/3 (51)	NR	Outerbridge—Grade 0 (8) Grade 1 (17) Grade 2 (23) Grade 3 (7) Grade 4 (6)	Outerbridge—Grade 2 (11) Grade 3 (8) Grade 4 (7)	Outerbridge—Grade 0/1 (22) Grade 4 (69)	
Mean follow-up		13.1 ± 3.1 years	12.9 months (3–41)	31.9 months (18–80)	33 months (12–72)	No defect: 4.48 ± 2.63 years. Full-thickness defect: 3.84 ± 2.47 years	
Technique		Bone-meniscus- bone transplant with inside-out	Bone plug	Bone-plug	Single bone- bridge with inside-out suturing	Lateral: Bridge-in- slot Medial: Keyhole or bridge-in-slot	
Author (year)		Noyes et al. [28]	Potter et al. [32]	Ren et al. [33]	Ryu et al. [34]	Saltzman et al. [35]	

TABLE 1 (Continued)

Author (year)	Technique	Mean follow-up	Cartilage status (no of patients)	Concomitant cartilage procedures (no of patients)	Results/conclusions related to cartilage status affecting MAT survival and outcomes
Searle et al. [36]	Suture-only, trans osseous tibial bone tunnel	3.4±1.7 years	Outerbridge—Grade 0 (2) Grade 1 (3) Grade 2 (21) Grade 3 (1) Grade 4 (16)	MFX (<2 cm ²), chondrotissue grafting for >2 cm ²	Outerbridge grade had no significant effect on surgical failure and clinical failure based on a binomial logistic regression
Stone et al. [39]	Three-tunnel technique, suture	5.8 years (2 months–12.3 years)	Outerbridge—Grade 3 (22) Grade 4 (97)	MFX for defects <2 5 mm ² (69), articular cartilage paste grafting for defects > 25 mm ² (67)	No difference in survival between Outerbridge Grades 3 and 4 knees (n.s.)
Van Der Straeten et al. [42]	R	6.8 years (0.2–24.3)	Outerbridge—Grades 0–2 (156) Grades 3–4 (130)	MFX (5), Osteochondral autograft (2)	Significantly greater survival in Outerbridge Grades 0–2 knees (43.0%) compared to Outerbridge Grades 3–4 knees (6.6%) (<i>p</i> = 0.003)
Van der Wal et al. [43]	Suture-only, no bone block	54 months (27–129) ^a	Outerbridge—Grade 0 (36) Grade 1 (28) Grade 2 (23) Grade 3 (17) Grade 4 (1)	None reported	Outerbridge grade was not associated with significant difference in MAT survival, postoperative KOOS score, patient satisfaction, willingness to have MAT again, and recommendation to other patients.
Abbreviations: AJ KSSTA Knee Sur	SM, The American Jouri	ual of Sports Medicine; F, female; IKDC, Internal Knee Documental ww Arthrosconv 1 Isteral: M male: M madial: NR not recorded	ation Committee; JBJS, journal of bon 1: SF-12 Short Form Survey 12-item	e and joint surgery; KOOS, Kn v. WOMAC_Western Ontario a	ee Injury and Osteoarthritis Outcome Score and McMaster I Iniversities Arthritis Index

TABLE 1 (Continued)

Ъ. KSSTA, Knee Surgery, Sports Trau ^aMedian and IQR.

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Study	Failure definition	Failure rate and survival analyses
Bloch et al. [8]	Removal of MAT or conversion to arthroplasty	Five-year survival rate—(<i>p</i> = 0.001) ^a ICRS Grades 0–3A: 95% ICRS Grades 3b–c: 77%
Grassi et al. [14]	Surgical failure: Requiring TKA, UKA, meniscectomy, or revision MATClinical failure: Lysholm score <65	Surgical failure rate—OR: 2.17 (0.56–8.44), n.s. Outerbridge Grades 0–2: 8.2% (16/196) Outerbridge Grades 3–4: 4.7% (6/128) Clinical failure rate—OR: 2.13 (0.82–5.59), n.s. Outerbridge Grades 0–2: 2.2% (43/196) Outerbridge Grades 3–4: 2.1% (27/128)
Lee et al. [22]	Anatomic failure: allograft tear covering >50% of the allograft or unstable peripheral rim Clinical failure: Lysholm score <65, reoperation—meniscal repair, revision MAT, realignment, arthroplasty, >50% meniscectomy.	Univariate analysis— Anatomic failure rate HR: 3.171 (1.24–8.94), $p = 0.0292^{a}$ Clinical survival rate HR: 0.865 (0.191–3.92), n.s. Multivariate analysis—Anatomic failure rate HR: 3.681 (1.129–12.00), $p = 0.0307^{a}$ Clinical survival rate HR: 0.252 (0.030–2.10), n.s.
Mahmoud et al. [25]	Transplant removal or knee arthroplasty	Survival rate— <i>p</i> = 0.01 ^a Outerbridge Grades 0–2: 100% (14/14) Outerbridge Grades 3–4: 74.2% (23/32)
Noyes et al. [28]	Reoperation, major extrusion (>50% of meniscus width), Grade 3 signal intensity, tear, loss of joint space in PA radiograph	No cartilage damage: 2-year survival: 81% 5-year survival: 75% 7-year survival: 75% 10-year survival: 38% 15-year survival: 22% Cincinnati Grade 2B/3 cartilage damage:2-year survival: 86% 5-year survival: 78% 7-year survival: 66% 10-year survival: 48% 15-year survival: 19%
Saltzman et al. [35]	Revision MAT or conversion to TKA	 Failure rate—rate of revision MAT (n.s.), rate of conversion to TKA (n.s.) Outerbridge Grade 0/1: 13.6% (3/22) Outerbridge Grade 4: 14.4% (10/69)
Searle et al. [36]	Surgical failure: removal of most/all of the graft, revision procedure, conversion to TKA. Clinical failure: Lysholm score <65	Binomial logistic regression based on Outerbridge Grades 0–4 Surgical failure regression coefficient: 0.167 (n.s.) Clinical failure regression coefficient: 0.131 (n.s.)
Stone et al. [39]	Removal of the allograft without revision or conversion to TKA or UKA	Relative odds of allograft failure: Outerbridge 3 versus 4 HR: 5.718 (0.723–45.231), n.s.
Van Der Straeten et al. [42]		Survival rate: <i>p</i> = 0.003 ^a Outerbridge Grades 0–2: 43% (38.4–47.6) Outerbridge Grades 3–4: 6.6% (5.8–7.4) OR for failure: 3.7 Mean survival time: Outerbridge Grades 0–2: 17.6 years Outerbridge Grades 3–4: 13.4 years

TABLE 2 Meniscal allograft transplantation failure definitions and rates.

Abbreviations: HR, hazard ratio; ICRS: International Cartilage Repair Society; MAT: meniscal allograft transplantation; n.s., not significant; OR, odds ratio; PA: posteroanterior; TKA: total knee arthroplasty; UKA: unicompartmental knee arthroplasty. ^aStatistically significant.

Clinical outcomes

Six studies reported no significant difference in outcomes for patients undergoing MAT based on the degree of preoperative cartilage damage [2, 8, 28, 33, 35, 43]. Alentorn-Geli et al. observed no significant difference in improvement from

preoperative to postoperative Lysholm, IKDC, and VAS for pain scores in lower versus higher-grade cartilage-damaged knees [2]. Bloch et al. reported no significant difference in Lysholm, KOOS, Tegner, or IKDC subjective scores between ICRS Grades 0–3A and ICRS Grades 3b–c knees [8]. Noyes et al. found no difference in symptoms or functional analysis in

knees with no cartilage damage versus Cincinnati Grade 2B/3 knees [28]. Ren et al. found no difference in postoperative VAS, IKDC, Tegner, and Lysholm based on preoperative Outerbridge score [33]. Saltzman et al. reported no difference in mean improvement in Lysholm, IKDC, KOOS, WOMAC, SF-12, symptom rate, and overall knee function between Outerbridge Grades 0–1 versus Grade 4 knees [35]. Van der Wal et al. reported no significant difference in postoperative KOOS score, patient satisfaction, willingness to undergo MAT again, and recommendation to other patients based on preoperative Outerbridge score [43].

Two studies reported significant differences in outcomes for patients undergoing MAT based on preoperative cartilage damage [25, 34]. In Mahmoud et al., patients with Outerbridge Grades 3–4 lesions did not report a significant improvement in Tegner score, while patients with Outerbridge Grades 0–2 defects did not report significant improvements in Oxford Knee Score (OKS) and IKDC score [25]. Ryu et al. found significant differences in postoperative VAS and preoperative and postoperative Lysholm scores in Outerbridge Grade 2/3 versus Grade 4 knees, with only 43% of Grade 4 knees able to achieve a normal or nearly normal IKDC rating compared to 78% of Grade 2/3 knees [34].

Concomitant osteoarthritis

The presence of osteoarthritis was either excluded or reported as a contraindication to MAT in five studies, stating that patients required localised wear, no diffuse arthritis changes, or no advanced osteoarthritis [2, 22, 23, 25, 35]. Mahmoud et al. excluded patients with bone-on-bone articulation [25]. Among these five studies, two studies found no difference between cartilage damage and MAT outcomes [2, 35]. Two studies found worse survivorship for ICRS and Outerbridge Grades 3–4 knees versus Grades 0–2 [22, 25]. Lee et al. found that greater cartilage damage between the time of meniscectomy and MAT was associated with more joint space narrowing [23].

Five studies included patients with osteoarthritis, most commonly evaluated based on Kellgren-Lawrence or IKDC grade [1, 14, 28, 39, 42]. Stone et al. included arthritic knees, with 26% having no arthritis, 40% having mild-moderate arthritis, and 34% having severe arthritis [39]. Of these five studies, one study found a greater survival in patients with Outerbridge Grades 0–2 knees versus Grades 3–4 [42]. Four studies did not report any correlation between cartilage status and MAT outcomes, survival, or extrusion [1, 14, 28, 39].

DISCUSSION

The findings from this investigation support the authors' initial hypotheses, which predicted that higher degrees of preoperative chondral damage would correlate with higher rates in MAT failure. The authors found that cartilage damage was not predictive of clinical outcomes following MAT. Although many studies showed a higher failure rate in knees with greater cartilage damage, treatment with concomitant cartilage restoration could improve MAT survivability in knees with highgrade cartilage damage. While this investigation cannot infer causality, it is possible that the presence of any chondral defects may alter the native knee biomechanics and the biologic environment within the knee, leading to increase stress on the allograft in an otherwise less than ideal environment, thereby increasing the risk for MAT failure [9, 16].

While four of nine studies evaluating survivorship found high failure rates in knees with higher degrees of cartilage damage, three of the five studies performing cartilage restoration procedures for full-thickness defects showed comparable survivorship and clinical outcomes when compared to knee with lower degrees of chondral damage. Furthermore, seven of the nine included studies reporting patient outcome scores after MAT found no significant difference when compared to knees based on preoperative cartilage status. These findings suggest that in appropriately selected patients, clinical benefit may be experienced following MAT regardless of the degree of cartilage damage present preoperatively, a conclusion of particular interest considering the lack of consensus in the literature.

It is challenging to discern why such heterogeneity among studies exists. One major factor may be that the definition of survivorship was variable among the included studies in this current review, with the most common definitions of failure being conversion to total knee arthroplasty, revision or removal of the meniscal allograft, and large tears in the allograft. The variable definitions of failure may explain the variable findings in the literature, with some studies reporting clinical failure, surgical failure, or even anatomical failure. Searle et al. attempted to further define outcomes seen in cases considered either "surgical failures" or "clinical failures," observing that up to 60% of patients would still elect to undergo the procedure again, concluding that more specific definitions of "failure" are warranted to better classify outcomes after MAT procedures [36].

Outcomes of MAT with cartilage procedures have shown similar clinical outcomes to each procedure in isolation [15]. However, the efficacy of combined procedures remain unclear due to heterogeneity due to potential confounding variables in defect size and concomitant ligament procedures. In Frank et al., outcomes, reoperations, and failure rates following MAT with or without MAT concomitant OAT were similar –Knee Surgery, Sports Traumatology, Arthroscopy– ${
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across both groups, even with both groups having no significant difference in chondral defect size [12]. Similarly, Getgood et al. reported a failure rate following MAT with OAT that was similar to either procedure alone [13]. The vast majority of literature regarding MAT combined with cartilage restoration is of Level 4 evidence [6, 10, 30], highlighting the need for higher level studies to assess the efficacy of combined procedures to isolated procedures in the setting of high-grade cartilage and meniscus injury.

Historically, relative indications for MAT included patients without full-thickness cartilage damage and those younger than age 50 [18, 46]. These general guidelines, specifically the age criteria, have been challenged prior to the current analysis in the study by Frank et al. [11] revealing no significant difference in outcomes after MAT at a final follow-up of 5.1 years when comparing patients younger than 40 to those older than 40. Those findings are corroborated by another study by Zaffagnini et al. [49] suggesting that even patients over the age of 50 benefit from MAT based on symptomatic and functional improvement. Other previous systematic reviews have revealed positive clinical outcomes with mid- to long-term follow-up after MAT [24, 41]; however, the literature remains limited on correlating outcomes based on the degree of preoperative chondral damage.

This study must be considered within the context of its limitations. All included studies were retrospective in nature with low level of evidence, exclusively of level III or IV. The lack of high-level evidence precluded any clinically meaningful conclusions of causality from being inferred. Studies that examined both medial and lateral MAT were included, despite studies reporting biomechanical and clinical differences in the outcomes between medial versus lateral MAT [7, 17]. There was great variability in the indications for MAT across studies, particularly in patients with concomitant osteoarthritis. All techniques utilised for MAT, namely bone-bridge and all-soft tissue fixation, were included in this review and were not able to be stratified further based on sample size. In addition, a high degree of heterogeneity was appreciated based on mean followup times, grading systems for cartilage damage, definition of failure, reporting of both cartilage defect size and concomitant cartilage procedures, further limiting the authors' ability to perform any meaningful statistical analyses evaluating the predictive capacity of these variables on outcomes. Indications for MAT were consistent among studies, while the reliability of cartilage status grading has been shown to have questionable reliability [3]. Furthermore, there is a relative scarcity of literature on the topic of MAT in patients with increasing degrees of cartilage damage, which could be explained by the fact that increasing grades of osteoarthritis have been a traditional relative contraindication for MAT procedures.

CONCLUSION

Conflicting results and high variability in reporting of concomitant cartilage repair exist in studies evaluating the efficacy of MAT based on articular cartilage status. The degree of preoperative chondral damage did not have a strong relationship with clinical outcomes following MAT. Higher degrees of cartilage damage were associated with higher MAT failure rates, with possible improvement in survivorship when treated with an appropriate cartilage procedure.

AUTHOR CONTRIBUTIONS

Varun Gopinatth: Conception and design of study; acquisition, analysis, and interpretation of data; drafting and revising the manuscript; final approval for publication. Alec A. Warrier: Acquisition, analysis, and interpretation of data; drafting and revising the manuscript; final approval for publication. Harkirat S. Jawanda: Acquisition, analysis, and interpretation of data; drafting and revising the manuscript; final approval for publication. Enzo S. Mameri: Acquisition, analysis, and interpretation of data; drafting and revising the manuscript; final approval for publication. Zeeshan A. Khan: Acquisition, analysis, and interpretation of data; drafting and revising the manuscript; final approval for publication. Sachin Allahabadi: Analysis and interpretation of data; drafting and revising the manuscript; final approval for publication. Derrick M. Knapik: Analysis and interpretation of data; drafting and revising the manuscript; final approval for publication. Brian J. Cole: Analysis and interpretation of data; drafting and revising the manuscript; final approval for publication. Jorge Chahla: Conception and design of the study; interpretation of the data; drafting and revising the manuscript; final approval for publication; supervision.

ACKNOWLEDGEMENTS

Sachin Allahabadi has received support for education from Smith & Nephew and hospitality payments from Stryker, Encore Medical, and Davol. Derrick M. Knapik has received support for education from Smith & Nephew, Elite Orthopaedics, and Medwest Associates; hospitality payments from Arthrex, Encore Medical, Stryker, and Smith & Nephew; honoraria from Encore Medical; and a grant from Arthrex. Brian J. Cole has received consulting and faculty/speaking fees from Arthrex; consulting and faculty/speaking fees from Pacira Pharmaceuticals; consulting and honoraria from Vericel; consulting and hospitality payments from Geistlich Pharma North America; consulting fees from Ossio LTD, Acumed, Bioventus, Anika Therapeutics, Endo Pharmaceuticals, Flexion Therapeutics, Smith and Nephew, and Zimmer Biomet Holdings; hospitality payments from Stryker, Orgenogenesis, LifeNet Health, and GE Healthcare; faculty/speaking fees from

MENISCAL ALLOGRAFT TRANSPLANTATION

Terumo BCT, Aesculap Biologics, and LifeNet Health; investment interest in Cartiva; and royality payments from DJO. Jorge Chahla has received consulting fees from Arthrex, CONMED Linvatec Corporation, Ossur, Smith & Nephew, Vericel, Stryker Corporation, and DePuy Synthes Products; support for education from Arthrex, Medwest Associates, and Smith & Nephew; speaking fees from Linvatec, Arthrex, and Smith & Nephew; hospitality payments from Medical Device Business Services, Medwest Associates, Smith & Nephew, Linvatec, and Stryker; and a grant from Arthrex.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

ETHICS STATEMENT

Not applicable.

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12

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Gopinatth V, Warrier AA, Jawanda HS, Mameri ES, Khan ZA, Allahabadi S, et al. Correlation between articular cartilage status on outcomes and survivorship following meniscal allograft transplantation: a systematic review. Knee Surgery, Sports Traumatology, Arthroscopy. 2024;1–13. https://doi.org/10.1002/ksa.12065