

# Risk Factors for Graft Failure After Meniscal Allograft Transplantation

## A Systematic Review and Meta-analysis

Kyle N. Kunze,<sup>\*†</sup> MD, Ryann A. Davie,<sup>†</sup> MD, Prem Narayan Ramkumar,<sup>‡§</sup> MD, MBA, Jorge Chahla,<sup>||</sup> MD, PhD, Benedict U. Nwachukwu,<sup>‡§</sup> MD, MBA, and Riley J. Williams III,<sup>‡§</sup> MD

**Background:** Graft failure after meniscal allograft transplantation (MAT) may necessitate revision surgery or conversion to arthroplasty. A comprehensive understanding of the risk factors for failure after MAT of the knee may facilitate more informed shared decision-making discussions before surgery and help determine whether MAT should be performed based on patient risk.

**Purpose:** To perform a systematic review and meta-analysis of risk factors associated with graft failure after MAT of the knee.

**Study Design:** Systematic review; Level of evidence, 4.

**Methods:** The PubMed, OVID/Medline, and Cochrane databases were queried in October 2021. Data pertaining to study characteristics and risk factors associated with failure after MAT were recorded. DerSimonian-Laird binary random-effects models were constructed to quantitatively evaluate the association between risk factors and MAT graft failure by generating effect estimates in the form of odds ratios (ORs) with 95% CIs. Qualitative analysis was performed to describe risk factors that were variably reported.

**Results:** In total, 17 studies including 2184 patients were included. The overall pooled prevalence of failure at the latest follow-up was 17.8% (range, 3.3%-81.0%). In 10 studies reporting 5-year failure rates, the pooled prevalence of failure was 10.9% (range, 4.7%-23%). In 4 studies reporting 10-year failure rates, the pooled prevalence was 22.7% (range, 8.1%-55.0%). A total of 39 risk factors were identified, although raw data presented in a manner amenable to meta-analysis only allowed for 3 to be explored quantitatively. There was strong evidence to support that an International Cartilage Regeneration & Joint Preservation Society grade >3a (OR, 5.32; 95% CI, 2.75-10.31;  $P < .001$ ) was a significant risk factor for failure after MAT. There was no statistically significant evidence to incontrovertibly support that patient sex (OR, 2.16; 95% CI, 0.83-5.64;  $P = .12$ ) or MAT laterality (OR, 1.11; 95% CI, 0.38-3.28;  $P = .85$ ) was associated with increased risk of failure after MAT.

**Conclusion:** Based on the studies reviewed, there was strong evidence to suggest that degree of cartilage damage at the time of MAT is associated with graft failure; however, the evidence was inconclusive on whether laterality or patient sex is associated with graft failure.

**Keywords:** meniscal allograft transplantation; failure; graft; meta-analysis; knee

Meniscal allograft transplantation (MAT) of the knee is performed in young, active patients with meniscal deficiency. Initial studies report improvement in clinical and functional outcomes in appropriately selected patients, from patient satisfaction to delay in the need for conversion to arthroplasty. However, several studies have also demonstrated that there exists a failure rate after these procedures,<sup>7,15,19,25</sup> with rates approaching 55% at the 10-year follow-up.<sup>24</sup>

A better understanding of the risk factors for failure after MAT is important, as it may allow for more informed patient selection. Prior factors investigated for their potential association with graft failure include graft mismatch, articular cartilage damage, patient sex, method of graft fixation, and

graft laterality.<sup>7,8,18,19,30,34</sup> Despite a substantial increase in the volume of literature reporting on factors associated with graft failure after MAT, these associations are conflicting in many circumstances and therefore remain unclear.

The purpose of the current study was to perform a systematic review and meta-analysis of risk factors associated with graft failure after MAT of the knee. We hypothesized that cartilage status and graft compartment laterality would be associated with an increased risk of graft failure.

## METHODS

### Article Search Process

Articles were extracted in accordance with the 2009 PRISMA (Preferred Reporting Items for Systematic

The Orthopaedic Journal of Sports Medicine, 11(6), 23259671231160296  
DOI: 10.1177/23259671231160296  
© The Author(s) 2023

This open-access article is published and distributed under the Creative Commons Attribution - NonCommercial - No Derivatives License (<https://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits the noncommercial use, distribution, and reproduction of the article in any medium, provided the original author and source are credited. You may not alter, transform, or build upon this article without the permission of the Author(s). For article reuse guidelines, please visit SAGE's website at <http://www.sagepub.com/journals-permissions>.

Reviews and Meta-Analyses) statement.<sup>21</sup> The query was performed in October 2021 for literature pertaining to graft failure after MAT utilizing the Boolean search phrase “(meniscal allograft transplantation AND (failure) AND ((knee)))”. The query was performed using the Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, PubMed (2008-2019), and OVID/Medline (2008-2019) databases. The protocol for this systematic review and meta-analysis was registered on PROSPERO (ID: 293726).

## Article Eligibility

Eligible articles included those written in the English language that reported on clinical outcomes after MAT at any postoperative follow-up period. No minimum follow-up was used to restrict the search, as the primary outcome was all-cause failure after MAT. Included were studies with evidence levels 1 to 3 that directly compared cases and controls or level 4 studies that performed a subanalysis allowing for information necessary to generate odds ratios (ORs). Articles were excluded if failure rates were not evaluated; data were not readily analyzable; populations included pediatric patients; or studies included conference abstracts, narrative or systematic reviews, case reports, technical notes, biomechanical studies, and letters to the editor. Additionally, the references of included articles were cross-referenced for additional investigations that may have been missed in the systematic search.

## Quality Assessment

The methodological index for non-randomized studies (MINORS) checklist<sup>13</sup> was used to evaluate the quality of all included studies. The checklist involves 12 items to assess quality, of which 4 are applicable only to comparative studies. The 4 additional criteria specific to comparative groups were used to assess the bias present in articles when selecting cohorts. Each item is scored on a scale of 0 to 2; thus, the maximum MINORS score is 16 for noncomparative studies and 24 for comparative studies. Two reviewers (K.N.K. and R.A.D.) scored each study, and any discrepancies were mitigated by consensus agreement or excluded altogether.

## Statistical Analysis

All statistical analyses and related figures were produced via OpenMetaAnalyst, using metafor R console code.<sup>32</sup> A 2-tailed  $P$  value  $<.05$  was considered to indicate statistical significance. Risk factors were recorded from each included study, and ORs were calculated from 2-by-2 tables for each study. If risk factors were used to match cohorts 1:1 by exact values, they were not included in the quantitative meta-analysis. Risk factors not amenable to calculation of ORs because of the method of reporting were quantified using mean differences when appropriate. Furthermore, risk factors without sufficient data to perform a meta-analysis were described narratively and excluded from being analyzed quantitatively. DerSimonian-Laird random-effects models were used to determine pooled effect sizes<sup>4-6</sup> because study heterogeneity was expected given that patient populations were not identical, study designs differed, surgical indications may vary, and surgeon experience has inherent variability.

In accordance with previous recommendations and guidelines for performing meta-analyses from statistical methods literature, a minimum of 2 studies were incorporated into each meta-analysis, as this number is efficient in drawing conclusions from resultant data.<sup>9,11</sup> The pooled effect size was calculated as a weighted average of the effects estimated in the individual studies, with weights representing the amount of information from each study. The 95% CI was used to report all pooled statistics. Heterogeneity was assessed by the  $P$  value of chi-square statistics and the  $I^2$  statistic using random-effects models. We regarded heterogeneity as possibly unimportant at an  $I^2$  value  $<40\%$  and considerable at an  $I^2 >75\%$ .<sup>14</sup> Risk factors were classified as having strong evidence, moderate evidence, minimal evidence, or marginal to no evidence, according to previously established criteria (Table 1).<sup>28</sup>

## RESULTS

### Study Characteristics

After consensus was reached between the 2 reviewers, 17 studies<sup>#</sup> investigating the outcomes of 2184 patients were included in the final quantitative and qualitative analysis

<sup>#</sup>References 1, 2, 7, 8, 15–20, 24–26, 29–31, 34.

\*Address correspondence to Kyle N. Kunze, MD, Hospital for Special Surgery, 535 E 70th Street, New York, NY 10021, USA (email: kylekunze7@gmail.com) (Twitter: @kylekunzemd).

<sup>†</sup>Department of Orthopedic Surgery, Hospital for Special Surgery, New York, New York, USA.

<sup>‡</sup>Long Beach Orthopaedic Institute, Long Beach, California, USA.

<sup>§</sup>Sports Medicine and Shoulder Institute, Hospital for Special Surgery, New York, New York, USA.

<sup>||</sup>Department of Orthopaedic Surgery, Rush University Medical Center, Chicago, Illinois, USA..

Final revision submitted December 2, 2022; accepted January 17, 2023.

One or more of the authors has declared the following potential conflict of interest or source of funding: P.N.R. has received consulting fees from Pacira Pharmaceuticals. J.C. has received education payments from Arthrex and Smith & Nephew; consulting fees from Arthrex, DePuy, ConMed Linvatec, Ossur, Smith & Nephew, and Vericel; speaking fees from Linvatec; and hospitality payments from Stryker. B.U.N. has received grant support from Arthrex; education payments from Arthrex and Smith & Nephew; and consulting fees from Stryker, Wright Medical, and Zimmer Biomet; and has stock/stock options in BICMD. R.J.W. has received research support from Histogenics; consulting fees from Arthrex, JRF Ortho, and Lipogems; royalties from Arthrex; and hospitality payments from Stryker; and has stock/stock options in MICMD, Cymedia, Engage Surgical, Gramercy Extremity Orthopedics, Pristine Surgical, and RecoverX. AOSSM checks author disclosures against the Open Payments Database (OPD). AOSSM has not conducted an independent investigation on the OPD and disclaims any liability or responsibility relating thereto.

TABLE 1  
Risk Factor Strength of Evidence Classifications<sup>a</sup>

Evidence Classification	Description
Strong	Increased risk for failure after MAT compared with baseline risk (OR, >2.0) or had a strong protective effect (OR, <0.8), and statistically significant
Moderate	OR between 1.5 and 2.0 or between 0.8 and 0.9 if protective, and statistically significant
Minimal	OR between 1.0 and 1.5 or 0.9 and 1.0 if protective, and statistically significant
Marginal to none	Nonsignificant OR ( $P > .05$ ) or presented no plausible explanation for being a risk factor

<sup>a</sup>MAT, meniscal allograft transplantation; OR, odds ratio.

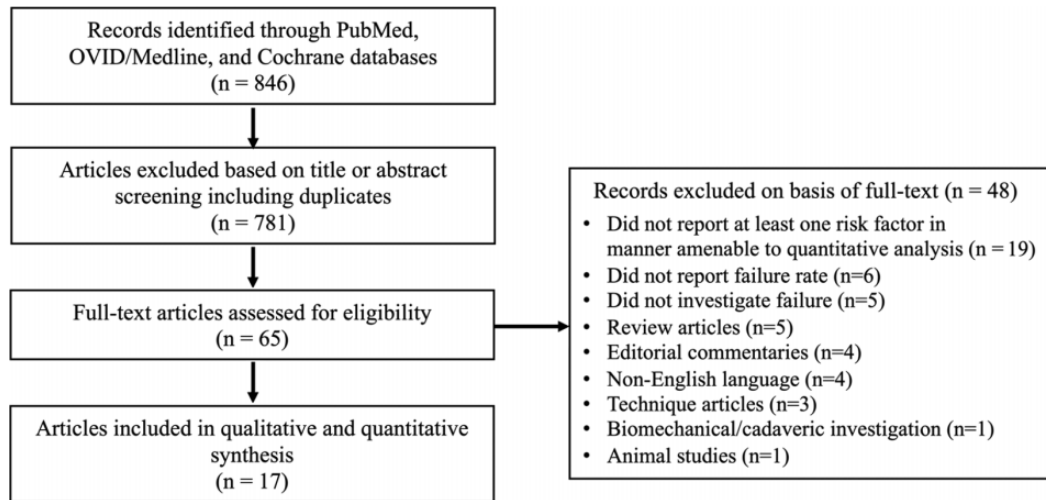


Figure 1. Study selection flowchart.

(Figure 1). Eleven (64.7%) studies<sup>1,2,7,8,15-18,26,29,30</sup> were retrospective cohort studies, while the remaining 6 (35.3%) articles<sup>19,20,24,25,31,34</sup> were case series. The overall pooled prevalence of failure at latest follow-up was 17.8% (range, 3.3%-81.0%). In 10 studies<sup>\*\*</sup> reporting 5-year failure rates, the pooled prevalence of failure was 10.9% (range, 4.7%-23%). In 4 studies<sup>17,24,30,34</sup> reporting 10-year failure rates, the pooled prevalence was 22.7% (range, 8.1%-55.0%).

The overall pooled age and body mass index (BMI) of included patients were  $35.1 \pm 5.2$  years and  $25.1 \pm 3.9$ , respectively. The definitions of failure were largely consistent across studies (Table 2) but were generally defined as need for revision MAT or graft removal, meniscectomy, conversion to arthroplasty, or gross appearance of graft failure at second-look arthroscopy.

### Methodological Quality

The mean ( $\pm$  SD) MINORS score was  $16.7 \pm 3.9$  among all studies (Table 3). For the comparative studies, the mean MINORS score was  $20.6 \pm 0.7$  out of 24. For the noncomparative studies, the mean MINORS score was  $12.7 \pm 0.7$  out of 16.

\*\*References 1, 2, 7, 8, 15, 17-20, 24, 26, 29, 30.

### Risk Factors

A total of 39 risk factors were studied among the 17 included articles. Qualitative analysis was performed when heterogeneity was present or when the risk factor was investigated in <3 studies. A quantitative random-effects meta-analysis was performed in the absence of these conditions. The following associated potential risk factors for graft failure after MAT of the knee were pooled in a meta-analysis as follows: International Cartilage Regeneration & Joint Preservation Society (ICRS) grade, MAT laterality, and sex (Table 4). The remaining risk factors were described narratively (Appendix Table A1). Notably, of the 8 studies<sup>8,17-19,24,25,29,34</sup> that analyzed age as an independent risk factor, 5 studies<sup>8,17,24,25,34</sup> identified it as non-contributory to graft failure after MAT, whereas 3 studies<sup>18,19,29</sup> implicated age as a risk factor for failure. Of the 3 studies<sup>15,25,34</sup> that analyzed BMI as an independent risk factor, 2 studies<sup>25,34</sup> identified BMI as non-contributory to graft failure after MAT, whereas 1 study<sup>15</sup> implicated it as a risk factor for failure.

### ICRS Grade as a Risk Factor for Failure After MAT

Four studies<sup>2,16,18,26</sup> investigated the association between ICRS grade and failure after MAT (Figure 2). The pooled analysis revealed that ICRS grade >3a conferred

TABLE 2  
Characteristics of the Included Studies<sup>a</sup>

Lead Author (Year)	Design (LOE)	N	Failure Definition	Failure Prevalence	Risk Factors <sup>b</sup>
Stone (2006) <sup>31</sup>	Case series (4)	45	Allograft removal, conversion to UKA or TKA	10.6% at 4.4 y	MAT laterality, sex, fresh-frozen vs cryopreserved allograft, OCS, number of concomitant procedures, type of concomitant procedure, number of prior surgeries on ipsilateral knee
Abat (2013) <sup>1</sup>	Retrospective cohort (3)	88	Allograft removal	5.7% at 5 y	Suture only vs osseous MAT graft fixation
Faivre (2014) <sup>7</sup>	Retrospective cohort (3)	23	Partial or complete allograft removal	17.4% at 5.5 y	Open vs arthroscopic MAT
McCormick (2014) <sup>20</sup>	Case series (4)	172	Allograft removal, revision MAT, or conversion to UKA or TKA	4.7% at 5 y	Need for secondary procedure, MAT laterality
Kempshall (2015) <sup>16</sup>	Retrospective cohort (3)	99	Allograft removal, conversion to UKA or TKA	9% at 2 y	ICRS grade, concomitant procedures, age, MAT laterality, graft type
Noyes (2016) <sup>24</sup>	Case series (4)	69	Allograft removal, revision MAT, or conversion to UKA or TKA	15% at 2 y; 23% at 5 y; 55% at 10 y; 81% at 15 y	MAT laterality, presence of cartilage defect in ipsilateral tibiofemoral compartment, concurrent OAT, age <30 vs ≥30 y
Parkinson (2016) <sup>26</sup>	Retrospective cohort (3)	125	Allograft removal, revision MAT, or conversion to UKA or TKA	18% at 5 y	ICRS grade, MAT laterality, baseline IKDC score, sex, concomitant procedures
Zaffagnini (2016) <sup>34</sup>	Case series (4)	147	Allograft removal, revision MAT, or conversion to UKA or TKA	4% at 2 y; 17% at 10 y	MAT laterality, single vs double tunnel, sex, age <50 vs ≥50 y, BMI <25 vs ≥25, concomitant procedures, smoking, time from meniscectomy to MAT
Lee (2017) <sup>18</sup>	Retrospective cohort (3)	222	Graft tear or meniscectomy of greater than one-third of the allograft observed on MRI or second-look arthroscopy	15% at 5 y	ICRS grade, sex, MAT laterality, time from meniscectomy to MAT, mechanical alignment, concomitant procedures
Mahmoud (2018) <sup>19</sup>	Case series (4)	45	Allograft removal, conversion to UKA or TKA	17.7% at 6.1 y	MAT laterality, sex, knee laterality, age <35 vs ≥35 y, OCS ≤2 vs >2
Bloch (2019) <sup>2</sup>	Retrospective cohort (3)	240	Allograft removal, conversion to UKA or TKA	3.3% at 1 y; 12.6% at 5 y	ICRS grade
Stevenson (2019) <sup>30</sup>	Retrospective cohort (3)	73	Allograft removal, conversion to UKA or TKA	4% at 5 y; 10.6% at 10 y	Graft under- or oversizing, age, concomitant procedures
Kim (2020) <sup>17</sup>	Retrospective cohort (3)	299	Tears involving >50% of the graft or unstable peripheral rim on MRI	5.1% at 5 y; 8.1% at 10 y	MAT laterality, age, sex, cartilage status (ideal/relative/salvage), type of concomitant procedures, mechanical axis deviation, preoperative JSW, postoperative JSW
Song (2020) <sup>29</sup>	Retrospective cohort (3)	264	Tears involving more than half of the graft, unstable allograft peripheral rim on MRI	8.5% at 5 y	Age <43 vs ≥43 y
Frank (2022) <sup>8</sup>	Retrospective cohort (3)	212	Revision MAT, conversion to UKA or TKA, macroscopic graft failure on second-look arthroscopy	12.3% at 5 y	Sex, age <40 vs ≥40 y, BMI, traumatic origin, MAT laterality, type of concomitant procedures
Jimenez-Garrido (2021) <sup>15</sup>	Retrospective cohort (3)	35	Allograft removal, conversion to UKA or TKA	22.9% at 6.3 y	BMI <30 vs ≥30
Park (2021) <sup>25</sup>	Case series (4)	26	Revision MAT, meniscal tear or meniscectomy greater than one-third of the allograft on MRI	30.7% at 3.6 y	Concomitant cartilage procedures, chondral defect size in LTP, chondral defect size in LFC, LTP defect size <3 vs ≥3 cm <sup>2</sup> , age, sex, BMI, time from meniscectomy to MAT, mechanical axis deviation, allograft coverage

<sup>a</sup>In all studies, the study population consisted of patients who underwent primary meniscal allograft transplantation (MAT). BMI, body mass index; ICRS, International Cartilage Regeneration & Joint Preservation Society; IKDC, International Knee Documentation Committee; JSW, joint-space width; LFC, lateral femoral condyle; LOE, level of evidence; LTP, lateral tibial plateau; MRI, magnetic resonance imaging; N, number of patients; OAT, osteochondral autograft transplantation; OCS, Outerbridge cartilage score; TKA, total knee arthroplasty; UKA, unicompartmental knee arthroplasty.

<sup>b</sup>Risk factors reported in format with data amenable to quantitative analysis. For full list of risk factors, see Appendix Table A1.

TABLE 3  
Methodological Quality of Included Studies as Determined by the MINORS Checklist<sup>13a</sup>

Lead Author (Year)	MINORS Item <sup>b</sup>												MINORS Score
	1	2	3	4	5	6	7	8	9	10	11	12	
Stone (2006) <sup>31</sup>	2	2	2	2	2	2	2	0	—	—	—	—	14
Abat (2013) <sup>1</sup>	2	2	2	2	2	2	2	0	2	1	2	2	21
Faivre (2014) <sup>7</sup>	2	2	2	2	2	2	1	0	1	2	2	2	20
McCormick (2014) <sup>20</sup>	2	2	2	2	2	2	1	0	—	—	—	—	13
Kempshall (2015) <sup>16</sup>	2	2	2	2	2	2	2	0	2	2	1	2	21
Noyes (2016) <sup>24</sup>	2	2	2	2	2	2	2	0	—	—	—	—	14
Parkinson (2016) <sup>26</sup>	2	2	2	2	2	2	1	0	1	2	2	2	20
Zaffagnini (2016) <sup>34</sup>	2	2	2	2	2	2	1	0	—	—	—	—	13
Lee (2017) <sup>18</sup>	2	2	2	2	2	2	1	0	2	2	2	2	21
Mahmoud (2018) <sup>19</sup>	2	2	2	2	2	2	2	0	—	—	—	—	14
Bloch (2019) <sup>2</sup>	2	2	2	2	2	2	2	0	2	2	2	2	22
Stevenson (2019) <sup>30</sup>	2	2	2	2	2	2	1	0	2	1	2	2	20
Kim (2020) <sup>17</sup>	2	2	2	2	2	2	1	0	2	2	2	1	20
Song (2020) <sup>29</sup>	2	2	2	2	2	2	0	0	—	—	—	—	12
Frank (2022) <sup>8</sup>	2	2	2	2	2	2	1	0	—	—	—	—	13
Jimenez-Garrido (2021) <sup>15</sup>	2	2	2	2	2	2	1	0	—	—	—	—	13
Park (2021) <sup>25</sup>	2	2	2	2	2	2	1	0	—	—	—	—	13

<sup>a</sup>Dashes indicate areas not applicable (noncomparative studies). MINORS, methodological index for non-randomized studies.

<sup>b</sup>Items: 1 = a clearly stated aim; 2 = inclusion of consecutive patients; 3 = prospective collection of data; 4 = endpoints appropriate to the aim of the study; 5 = unbiased assessment of the study endpoint; 6 = follow-up period appropriate to the aim of the study; 7 = loss to follow-up <5%; 8 = prospective calculation of the study size; 9 = an adequate control group; 10 = contemporary groups; 11 = baseline equivalence of groups; 12 = adequate statistical analyses.

TABLE 4

Summary Table for Odds Ratios for Failure in Decreasing Order of Strength of Association Derived From Meta-analyses<sup>a</sup>

Risk Factor	OR (95% CI)
ICRS grade >3a	5.32 (2.75-10.31)
Female sex	2.16 (0.83-5.64)
Medial MAT vs lateral MAT	1.11 (0.38-3.28)

<sup>a</sup>ICRS, International Cartilage Regeneration & Joint Preservation Society; MAT, meniscal allograft transplant; OR, odds ratio.

a significantly higher odds of failure after MAT than ICRS grade ≤3a (OR, 5.32; 95% CI, 2.75-10.31; *P* < .001). Heterogeneity was considered unimportant (*I*<sup>2</sup> = 14.3%; *P* = .32). Based on the results, there was strong evidence to suggest that ICRS grade >3a is an important risk factor for failure after MAT.

Patient Sex as a Risk Factor for Failure After MAT

Three studies<sup>8,19,31</sup> investigated the association between sex and failure after MAT (Figure 3). The pooled analysis revealed that female sex was not significantly associated with failure after MAT compared with male sex (OR, 2.16; 95% CI, 0.83-5.64; *P* = .12). Heterogeneity was considered unimportant (*I*<sup>2</sup> = 0.52%; *P* = .37). Based on the results, there was marginal to no evidence to suggest that female sex is an important risk factor for failure after MAT.

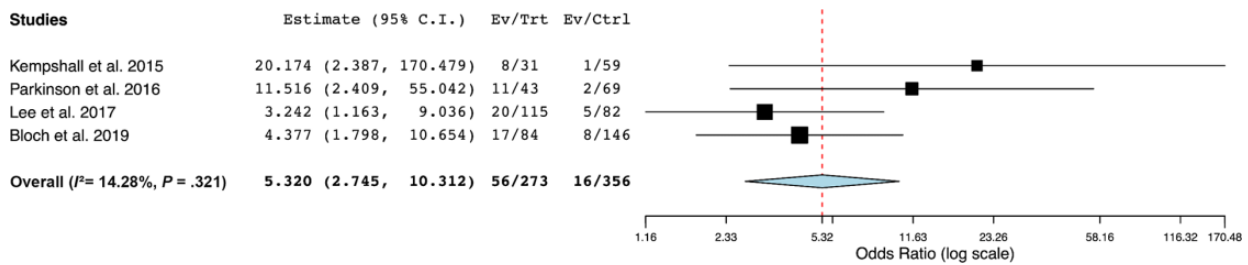
Graft Laterality as a Risk Factor for Failure After MAT

Six studies<sup>17,19,24,26,31,34</sup> investigated the association between medial versus lateral MAT and failure after MAT (Figure 4). The pooled analysis revealed that medial MAT was not significantly associated with failure after MAT compared with lateral MAT (OR, 1.11; 95% CI, 0.38-3.28; *P* = .85). Heterogeneity was considered moderate (*I*<sup>2</sup> = 65.8%; *P* = .012). Based on the results, there was marginal to no evidence to suggest that graft laterality is an important risk factor for failure after MAT.

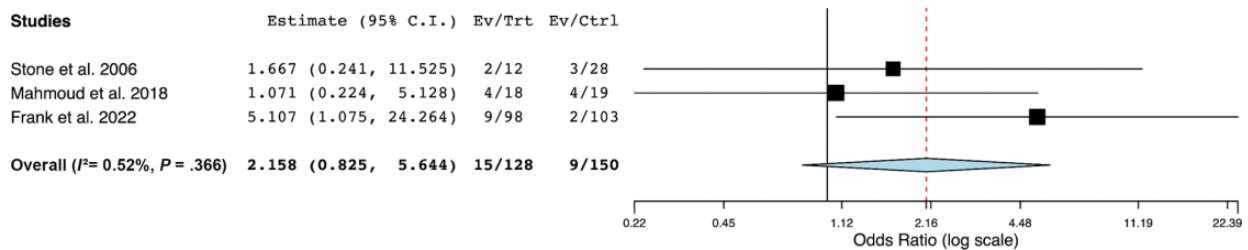
DISCUSSION

The main findings of the current systematic review and meta-analysis are as follows: (1) strong evidence was found to support that ICRS cartilage grade >3a at the time of primary MAT is an important risk factor for graft failure after MAT; (2) little to no evidence was found to support that MAT laterality and patient sex were important risk factors for failure after MAT; and (3) numerous risk factors have been investigated in isolation as they pertain to graft failure after MAT for which association and importance remain unknown. Importantly, this is the largest combined cohort studied for patients undergoing MAT, representing increased statistical power derived from more than 2000 primary patients who underwent MAT.

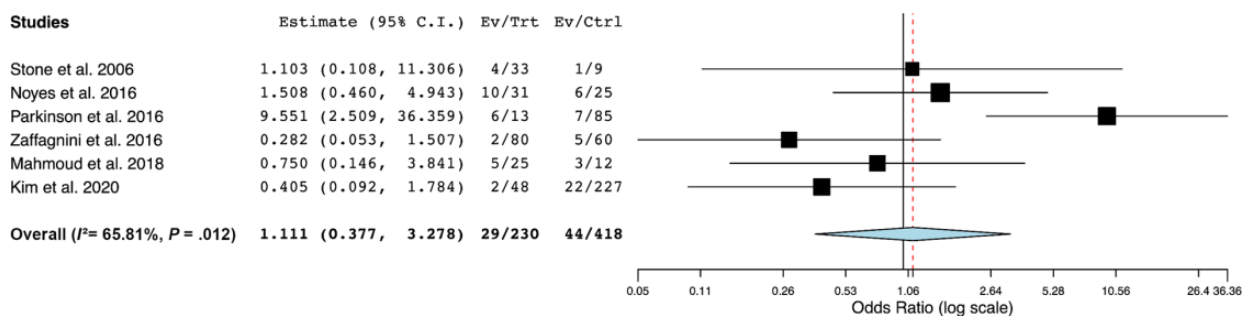
The current study quantitatively analyzed 3 reported risk factors investigated in the literature, ultimately concluding that the presence of ICRS grade >3a increases the



**Figure 2.** Forest plot demonstrating random-effects meta-analysis for risk factor of International Cartilage Regeneration & Joint Preservation Society grade. Ctrl, control; Ev, event; Trt, treatment.



**Figure 3.** Forest plot demonstrating random-effects meta-analysis for risk factor of sex. Ctrl, control; Ev, event; Trt, treatment.



**Figure 4.** Forest plot demonstrating random-effects meta-analysis for risk factor of meniscal allograft transplant laterality. Ctrl, control; Ev, event; Trt, treatment.

risk for graft failure by 532% in certain patients. However, it should be noted that the presence of chondral damage does not necessarily imply impending failure but only that there exists a higher likelihood that the MAT will fail. The ICRS scale defines a grade 3a cartilage defect as when the lesion extends beyond 50% of the cartilage depth, whereas a grade 3b defect is a more abnormal lesion that extends into the calcified layer.<sup>3</sup> This suggests that proposed chondroprotective effects associated with MAT cannot compensate for high-grade cartilage lesions identified at the time of surgery. Furthermore, this suggests that the transition to full-thickness cartilage loss may be associated with MAT failure. Interestingly, we did not identify any studies that compared lower ICRS cartilage grades with ICRS grades  $\geq 3$ , precluding the analysis of a wider spectrum of cartilage pathology on MAT failure. Parkinson et al<sup>26</sup> reported the outcomes of 125 consecutive patients treated with MAT, reporting that patients with ICRS articular cartilage grades  $\leq 3a$  had an 85% reduction in the probability of failure compared with patients with severe cartilage damage.

Although purely speculation given the current data, it is plausible that since cartilage status is a time-dependent prognostic factor where damage may accumulate over time in the presence of meniscal deficiency,<sup>29</sup> the influence of time from meniscectomy or irreparable meniscal injury to MAT should be considered since expeditious surgery may positively influence graft survivorship. Based on the rates of MAT failure identified in this review, additional procedures may eventually be necessary in select patients, especially in those with high-grade cartilage damage at the time of MAT, as evidenced by ICRS grades  $>3a$ .

No significant association was found between patients receiving either a medial or lateral MAT with respect to the risk of graft failure, suggesting that MAT may successfully provide relief regardless of the compartment and their differential congruencies. In the neutrally aligned knee, a greater proportion of force is transmitted through the medial compartment, and therefore one may hypothesize that this could negatively influence graft survivorship.<sup>27,33</sup> On the contrary, 1 study<sup>10</sup> reported that the survival of



medial MAT is actually 6 months longer than that of lateral MAT. While this statistical difference does not likely translate to clinical significance, prior literature<sup>12</sup> supports the findings of this meta-analysis that laterality is not associated with graft failure. Therefore, it appears that MAT laterality is a less important consideration in determining optimal surgical candidates for MAT.

In our analysis, patient sex did not demonstrate an association with MAT graft failure, but the literature surrounding the effect of sex on MAT survival is conflicting, with any statistical relationships likely because of poorly powered reports. Frank et al<sup>8</sup> reported that female patients were more likely to undergo revision MAT (1.9% vs 8.4%); however, there were no significant differences in complications or time to reoperation. Interestingly, female patients were more likely to have undergone prior meniscectomy before meniscal transplant compared with male patients, while male patients <40 years of age were more likely to undergo concomitant high tibial osteotomy than female patients of the same age. However, female patients demonstrated greater postoperative patient-reported outcome scores compared with male patients. Parkinson et al<sup>26</sup> reported on the outcomes of 124 patients (one was lost to follow-up), noting that there was no significant difference in rates of graft failure or need for revision surgery between male and female patients. Mahmoud et al<sup>19</sup> also demonstrated in their series of 45 consecutive MAT procedures that sex was not associated with graft survivorship. Despite conflicting results in the literature, the increased statistical power associated with pooling data in the current meta-analysis provides greater clarity into this association and suggests that MAT graft survivorship is not associated with patient sex.

### Limitations

The current study is not without limitations. First, the quality of the meta-analysis is a product of the evaluated studies. While standard pooling and analytic techniques were applied to mitigate this risk, the conclusions are limited by the quantity and methodology of the included studies. As an example, only 3 studies were included in the analysis that found patient sex was not a statistically significant risk factor for MAT graft failure. It is important to note that not a single analyzed study included a prospective cohort or randomized controlled trial. Second, several risk factors were not amenable to meta-analysis because of heterogeneity in reporting, and therefore additional risk factors may or may not exist whose effect could not be quantitatively estimated given the current data. Future studies, especially those of higher levels of evidence, are warranted to both establish causation between risk factors and failure and provide more insight into potential risk factors for failure not captured in the current study. Third, publication bias is always a risk with systematic reviews, although all risk factors identified in the current review were reported regardless of whether the association with failure was positive, negative, or neutral.

Several risk factors were noted in the literature although not amenable to formal analysis because of (1) variability in

reporting (such as age), (2) infrequent reporting (such as graft under- or oversizing), or (3) reporting associations or lack thereof without presenting data (underreporting). Importantly, this does not indicate that these factors are unimportant but rather that further studies are warranted to clarify these potential associations. Several variably and underreported factors, including age, BMI, and sex, are strongly believed to affect the survivorship of MAT grafts. Furthermore, graft-specific factors, such as fixation method and storage method (ie, fresh-frozen vs cryopreserved), may be important factors associated with graft failure. However, causation is limited in the setting of low-power, retrospective series. Data transparency and reporting therefore become essential because methods that may clarify these relationships, such as meta-analyses and machine learning-based processes, depend on these practices. The finding that only 3 variables among the 39 identified in the MAT literature could be explored quantitatively underscores the need for an improved quality and clarity in reporting the clinical outcomes of MAT.<sup>22,23</sup> This is particularly important when considering the narrow patient selection criteria and high functional expectations accompanying this procedure. This study suggests that emphasis must be placed on reducing the methodological heterogeneity present in MAT research to optimize insight and better guide surgeons and the patients they serve.

### CONCLUSION

There is strong evidence to suggest that degree of cartilage damage at the time of MAT is associated with graft failure; however, based on the current data, there is inconclusive evidence that laterality or patient sex is associated with graft failure.

### REFERENCES

1. Abat F, Gelber PE, Erquicia JI, et al. Prospective comparative study between two different fixation techniques in meniscal allograft transplantation. *Knee Surg Sports Traumatol Arthrosc.* 2013;21(7):1516-1522.
2. Bloch B, Asplin L, Smith N, Thompson P, Spalding T. Higher survivorship following meniscal allograft transplantation in less worn knees justifies earlier referral for symptomatic patients: experience from 240 patients. *Knee Surg Sports Traumatol Arthrosc.* 2019;27(6):1891-1899.
3. Brittberg M, Peterson L. Introduction of an articular cartilage classification. *ICRS NewsL.* 1998;1(1):5-8.
4. DerSimonian R. Meta-analysis in the design and monitoring of clinical trials. *Stat Med.* 1996;15(12):1237-1248.
5. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials.* 1986;7(3):177-188.
6. DerSimonian R, Laird N. Meta-analysis in clinical trials revisited. *Contemp Clin Trials.* 2015;45(pt A):139-145.
7. Faivre B, Boisrenoult P, Lonjon G, Pujol N, Beaufile P. Lateral meniscus allograft transplantation: clinical and anatomic outcomes after arthroscopic implantation with tibial tunnels versus open implantation without tunnels. *Orthop Traumatol Surg Res.* 2014;100(3):297-302.
8. Frank R, Gilat R, Haunschild ED, et al. Do outcomes of meniscal allograft transplantation differ based on age and sex? A comparative group analysis. *Arthroscopy.* 2022;38(2):452-465.e3.

9. Friede T, Rover C, Wandel S, Neuenschwander B. Meta-analysis of two studies in the presence of heterogeneity with applications in rare diseases. *Biom J*. 2017;59(4):658-671.
10. Gilat R, Cole BJ. Meniscal allograft transplantation: indications, techniques, outcomes. *Arthroscopy*. 2020;36(4):938-939.
11. Gonnermann A, Framke T, Grosshennig A, Koch A. No solution yet for combining two independent studies in the presence of heterogeneity. *Stat Med*. 2015;34(16):2476-2480.
12. Hergan D, Thut D, Sherman O, Day MS. Meniscal allograft transplantation. *Arthroscopy*. 2011;27(1):101-112.
13. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327(7414):557-560.
14. Higgins JPT, Thomas J, Chandler J, et al, eds. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 6.0. Updated July 2019. Cochrane; 2019.
15. Jimenez-Garrido C, Gomez-Caceres A, Espejo-Reina MJ, et al. Obesity and meniscal transplant failure: a retrospective cohort study. *J Knee Surg*. 2021;34(3):267-272.
16. Kempshall PJ, Parkinson B, Thomas M, et al. Outcome of meniscal allograft transplantation related to articular cartilage status: advanced chondral damage should not be a contraindication. *Knee Surg Sports Traumatol Arthrosc*. 2015;23(1):280-289.
17. Kim C, Bin SI, Kim JM, et al. Medial and lateral meniscus allograft transplantation showed no difference with respect to graft survivorship and clinical outcomes: a comparative analysis with a minimum 2-year follow-up. *Arthroscopy*. 2020;36(12):3061-3068.
18. Lee BS, Bin SI, Kim JM, Kim WK, Choi JW. Survivorship after meniscal allograft transplantation according to articular cartilage status. *Am J Sports Med*. 2017;45(5):1095-1101.
19. Mahmoud A, Young J, Bullock-Saxton J, Myers P. Meniscal allograft transplantation: the effect of cartilage status on survivorship and clinical outcome. *Arthroscopy*. 2018;34(6):1871-1876.e1871.
20. McCormick F, Harris JD, Abrams GD, et al. Survival and reoperation rates after meniscal allograft transplantation: analysis of failures for 172 consecutive transplants at a minimum 2-year follow-up. *Am J Sports Med*. 2014;42(4):892-897.
21. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA statement. *BMJ*. 2009;339:B2535.
22. Moore N, Juillet Y, Bertoye PH; Round Table No. 4, Giens XXII. Integrity of scientific data: transparency of clinical trial data. *Therapie*. 2007;62(3):203-209, 211-206.
23. Nguyen VT, Engleton M, Davison M, et al. Risk of bias in observational studies using routinely collected data of comparative effectiveness research: a meta-research study. *BMC Med*. 2021;19(1):279.
24. Noyes FR, Barber-Westin SD. Long-term survivorship and function of meniscus transplantation. *Am J Sports Med*. 2016;44(9):2330-2338.
25. Park JG, Bin SI, Kim JM, et al. Large chondral defect not covered by meniscal allograft is associated with inferior graft survivorship after lateral meniscal allograft transplantation. *Knee Surg Sports Traumatol Arthrosc*. 2021;29(1):82-89.
26. Parkinson B, Smith N, Asplin L, Thompson P, Spalding T. Factors predicting meniscal allograft transplantation failure. *Orthop J Sports Med*. 2016;4(8):2325967116663185.
27. Saxby DJ, Modenese L, Bryant AL, et al. Tibiofemoral contact forces during walking, running and sidestepping. *Gait Posture*. 2016;49:78-85.
28. Snoeker BA, Bakker EW, Kegel CA, Lucas C. Risk factors for meniscal tears: a systematic review including meta-analysis. *J Orthop Sports Phys Ther*. 2013;43(6):352-367.
29. Song JH, Bin SI, Kim JM, Lee BS, Son DW. Does age itself have an adverse effect on survivorship of meniscal allograft transplantation? A cartilage status and time from previous meniscectomy-matched cohort study. *Am J Sports Med*. 2020;48(7):1696-1701.
30. Stevenson C, Mahmoud A, Tudor F, Myers P. Meniscal allograft transplantation: undersizing grafts can lead to increased rates of clinical and mechanical failure. *Knee Surg Sports Traumatol Arthrosc*. 2019;27(6):1900-1907.
31. Stone KR, Walgenbach AW, Turek TJ, Freyer A, Hill MD. Meniscus allograft survival in patients with moderate to severe unicompartmental arthritis: a 2- to 7-year follow-up. *Arthroscopy*. 2006;22(5):469-478.
32. Viechtbauer W. Conducting meta-analyses in R with the metafor package. *J Stat Softw*. 2010;36(3):48.
33. Walter JP, D'Lima DD, Colwell CW Jr, Fregly BJ. Decreased knee adduction moment does not guarantee decreased medial contact force during gait. *J Orthop Res*. 2010;28(10):1348-1354.
34. Zaffagnini S, Grassi A, Marcheggiani Muccioli GM, et al. Survivorship and clinical outcomes of 147 consecutive isolated or combined arthroscopic bone plug free meniscal allograft transplantation. *Knee Surg Sports Traumatol Arthrosc*. 2016;24(5):1432-1439.

## APPENDIX

TABLE A1  
Qualitative Analysis of Risk Factors With Data Not Amenable to Meta-analysis<sup>a</sup>

Lead Author (Year)	Risk Factor	Findings
		Descriptive/Clinical
Park (2021) <sup>25</sup>	Age	Not associated with graft failure (OR, 1.0; 95% CI, 0.9-1.1; $P > .05$ )
Kim (2020) <sup>17</sup>	Age	Not associated with graft failure ( $P = .77$ )
Lee (2017) <sup>18</sup>	Age	Significantly associated with graft failure (HR, 1.095; 95% CI, 1.039-1.154; $P = .001$ ; 9.5% increase in graft failure per each additional year of age)
Noyes (2016) <sup>24</sup>	Age	Age >30 y not associated with graft failure ( $P > .05$ )
Mahmoud (2018) <sup>19</sup>	Age	Age >35 y significantly associated with increased risk of graft failure ( $P < .05$ )
Frank (2022) <sup>8</sup>	Age	Age ≥40 y not associated with graft failure ( $P > .05$ )
Song (2020) <sup>29</sup>	Age	Age ≥43 y significantly associated with increased risk of graft failure ( $P = .01$ ), which became insignificant after controlling for cartilage status and time from previous meniscectomy
Zaffagnini (2016) <sup>34</sup>	Age	Age >50 y not associated with graft failure ( $P > .05$ )
Park (2021) <sup>25</sup>	Sex	Not associated with graft failure (OR, 1.2; 95% CI, 0.2-8.7; $P > .05$ )
Kim (2020) <sup>17</sup>	Sex	Not associated with graft failure ( $P = .22$ )

(continued)



Table A1 (continued)

Lead Author (Year)	Risk Factor	Findings
Park (2021) <sup>25</sup>	BMI	Not associated with graft failure (OR, 0.7; 95% CI, 0.5-81.1; $P > .05$ )
Jimenez-Garrido (2021) <sup>15</sup>	BMI	BMI $\geq 30$ significantly increased risk of graft failure (HR, 11.8; 95% CI, 1.5-91.4; $P < .05$ )
Zaffagnini (2016) <sup>34</sup>	BMI	BMI $\geq 25$ not associated with graft failure ( $P > .05$ )
Park (2021) <sup>25</sup>	Time from meniscectomy	Not associated with graft failure (OR, 1.0; 95% CI, 0.9-1.1; $P > .05$ )
Stone (2006) <sup>31</sup>	No. of prior surgeries	Greater number of surgeries significantly associated with increased risk of graft failure ( $P = .012$ )
McCormick (2014) <sup>20</sup>	Subsequent procedures	Significantly associated with increased risk of graft failure (OR, 8.4; 95% CI, 1.6-43.4; $P = .007$ )
Procedural/Intraoperative		
Park (2021) <sup>25</sup>	Concomitant cartilage procedures	Not associated with graft failure ( $P > .05$ )
Noyes (2016) <sup>24</sup>	Concomitant cartilage procedures	Significantly associated with increased risk of graft failure at 7 y ( $P < .05$ )
Kim (2020) <sup>17</sup>	Concomitant cartilage procedures	Not associated with graft failure ( $P = .72$ )
Kim (2020) <sup>17</sup>	Concomitant ligamentous procedures	Not associated with graft failure ( $P = .30$ )
Kim (2020) <sup>17</sup>	Concomitant osteotomy procedures	Not associated with graft failure ( $P = .30$ )
Stone (2006) <sup>31</sup>	Any concomitant procedure	Not associated with graft failure ( $P = .20$ )
Zaffagnini (2016) <sup>34</sup>	Any concomitant procedure	Not associated with graft failure ( $P > .05$ )
Park (2021) <sup>25</sup>	Allograft coverage of chondral defect	Significantly associated with increased risk of graft failure (OR, 20.5; 95% CI, 1.8-2872.4; $P = .011$ )
Stevenson (2019) <sup>30</sup>	MAT sizing	MATs undersized by $>5$ mm had an increased risk of mechanical failure (OR, 5.66; $P = .046$ )
Lee (2017) <sup>18</sup>	High-grade bipolar cartilage damage	Significantly associated with increased risk of graft failure (OR, 3.56; 95% CI, 1.272-9.967; $P = .016$ ) compared with low-grade chondral degeneration
McCormick (2014) <sup>20</sup>	MAT laterality	No significant differences in failure between medial, lateral, or bicompartamental MAT ( $P = .61$ )
Stone (2006) <sup>31</sup>	Allograft material (fresh-frozen vs cryopreserved)	Not associated with graft failure ( $P > .05$ )
Faivre (2014) <sup>7</sup>	Open vs arthroscopic MAT	Open vs arthroscopic MAT not associated with graft failure ( $P > .99$ )
Abat (2013) <sup>1</sup>	Suture-only vs osseous-only fixation	Suture-only vs osseous-only fixation not associated with graft failure ( $P > .05$ )
Imaging		
Park (2021) <sup>25</sup>	LTP chondral defect size $>3$ cm <sup>2</sup> on MRI	Significantly associated with increased risk of graft failure (OR, 28.3; 95% CI, 2.5-4006.7; $P = .004$ )
Park (2021) <sup>25</sup>	LFC defect size	Significantly associated with increased risk of graft failure (OR, 3.3; 95% CI, 1.4-11.6; $P = .005$ )
Park (2021) <sup>25</sup>	LTP defect size	Significantly associated with increased risk of graft failure (OR, 2.3; 95% CI, 1.1-7.5; $P = .026$ )
Park (2021) <sup>25</sup>	Mechanical axis deviation on radiograph	Not associated with graft failure (OR, 1.2; 95% CI, 0.9-2.0; $P > .05$ )
Kim (2020) <sup>17</sup>	Mechanical axis deviation on radiograph	Not associated with graft failure ( $P = .31$ )

<sup>a</sup>BMI, body mass index; HR, hazard ratio; LFC, lateral femoral condyle; LTP, lateral tibial plateau; MAT, meniscal allograft transplantation; MRI, magnetic resonance imaging; OR, odds ratio.