Systematic Review

Concomitant Treatment of High-Grade Cartilage Lesions Mitigates Risk of Meniscal Allograft Transplant Failure

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Purpose: To identify frequently studied significant preoperative risk factors for meniscal allograft transplantation (MAT) failure. **Methods:** Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines were used to conduct this systematic review. The database analysis was performed in May 2022 and included PubMed, Embrace, and Cochrane. Studies between January 1, 2000, and January 1, 2021, were reviewed with search terms, including "meniscal," "meniscus," "transplantation," "transplant," and "allograft." Twenty-one full-text manuscripts met inclusion criteria of studies assessing preoperative risk factors for MAT failure defined as either clinical failure (Lysholm <65) or surgical failure (revision, removal, or conversion to knee arthroplasty). **Results:** In total, 21 studies were included, comprising 47.6% with Level of Evidence III and 52.4% with Level of Evidence IV. The analysis involved 2,533 patients, and the mean final follow-up ranged from 2.2 to 20.0 years. The presence of high-grade cartilage defects was the only factor found predictive of MAT surgical failure in the majority of studies in which it was analyzed (5/7 studies, 71.4%). Four of the 5 studies that found high-grade cartilage defects to be a predictor of MAT surgical failure did not treat all cartilage lesions, whereas the 2 studies that found high-grade cartilage defects an insignificant predictor of MAT surgical failure treated all defects at the time of MAT. For clinical failure, no risk factors were predictive of MAT failure in the majority of studies, although smoking and concomitant ligamentous or realignment procedures were significant in 1 study. **Conclusions:** The presence of untreated high-grade cartilage appears to elevate the risk of surgical MAT failure; however, concomitant treatment of defects may mitigate their detrimental effect. There is no clear risk factor that consistently predicts clinical failure. Age, sex, body mass index, knee compartment, time from prior meniscectomy, femorotibial alignment (after correction), concomitant cartilage procedure, and laterality do not routinely influence MAT failure. **Level of Evidence:** Level IV, systematic review of Level III and IV studies.

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The meniscus is an essential structure for maintaining joint stability, dissipating force, and providing a chondroprotective effect to the knee joint. In the setting of meniscal injury, depending on the depth and location of the tear, as well as the inherent healing capabilities of the torn region, either repair or meniscectomy is performed. For tears in avascular zones, certain tear morphology, chronic tears, or failed meniscal repairs, meniscectomy becomes the predominant surgical option. Subtotal or complete meniscectomy may leave young, active patients at risk of developing pain, loss of function, and rapid progression of osteoarthritis (OA), due to resultant increased tibiofemoral contact pressures.[1-3]

Meniscal allograft transplantation (MAT) can be a viable intervention to treat symptoms that occur after meniscectomy.[4] Several studies have reported improvements in function, quality of life, and symptoms upward of 10 years postoperatively and no radiographic evidence of further cartilage damage at long-term follow-up.[5,6] Graft survival is an essential factor contributing to long-term postoperative success, with the present literature reporting postoperative graft survival rates ranging from 80% to 90% within 7 years to 15% after 20 years.[1,7-10] A plethora of investigations

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0749-8063/231135/$36.00
https://doi.org/10.1016/j.arthro.2023.11.011

have been performed to elucidate risk factors for failure after MAT. Most commonly, studies report 2 definitions of failure after MAT, clinical failure or surgical failure. Patient-reported outcomes such as the International Knee Documentation Committee (IKDC), Knee Injury and Osteoarthritis Outcome Score (KOOS), Tegner's activity scores, and Lysholm scores have been reported as a proxy for clinical failure across the current literature.[11-13] Meanwhile, the need for revision, graft excision, or conversion to knee arthroplasty have also been defined as surgical failures.[1,14]

Factors such as age, the presence of preexisting chondral defects, sex, affected compartment of the knee, femorotibial alignment, and method of graft processing have all been suggested as potential contributors to failure over time.[11,15] However, significant heterogeneity exists in study design, definition of failure, and risk factors analyzed and controlled for.

The presence of confounding concomitant injuries and treatments, along with differences in study design and variable assessment further hinder the ability to assess which risk factors portend clinical or surgical failure following MAT. As such, the purpose of this systematic review was to identify frequently studied significant preoperative risk factors for meniscal allograft transplantation (MAT) failure. Our hypothesis is that there will be substantial variability in which factors are predictive of surgical and clinical failure, with few factors consistently showing statistical significance across multiple studies.

Methods

Article Identification

Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines were used to conduct a systematic review of scientific literature via Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia, available at www.covidence.org). The database analysis was performed in May 2022 and included PubMed, Embrace, and Cochrane. Studies between January 1, 2000, and January 1, 2021, were reviewed by 2 independent reviewers (Z.W. and M.A.) using search terms, including "meniscal," meniscus," "transplantation," "transplant," and "allograft." Studies with fewer than 10 patients, review articles, systematic reviews, cadaveric studies, animal studies, meta-analyses, letters to editor, or commentaries were excluded. Initial title and abstract screening yielded 2,119 studies, from which 218 full-title studies were assessed for eligibility (Fig 1).

Inclusion Criteria and Risk Factors

Twenty-one, full-text studies met the following inclusion criteria: (1) clinical studies involving lateral or medial meniscal allograft transplantation (MAT), (2) reported clinical outcome data, including failure rates defined by clinical failure (Lysholm Score <65) or surgical failure (revision, graft removal, or conversion to knee arthroplasty), and 3) studies assessing preoperative risk factors for failure. Risk factors that were analyzed include age, sex, compartment, body mass index (BMI), high-grade cartilage lesion (lesions that extend more than 50% cartilage depth), concomitant cartilage procedure, concomitant ligamentous procedures, concomitant high tibial osteotomy, time from prior meniscectomy, femorotibial alignment, limb laterality, smoking status, tibial chondral defects ≥ 3 cm^2, number of past surgeries to index knee, subchondral bone marrow lesions, and time from injury to surgery.

Statistical Analysis

Qualitative comparisons were made between the data, and pooling was avoided due to heterogeneity between included studies.

Risk of Bias Assessment and Study Quality

Two authors (Z.W. and M.A.) employed the MINORS criteria to systematically assess bias and study quality, scrutinizing aspects such as well-defined research objectives, consecutive patient inclusion, prospective data collection, and accurate end-point measurement in nonrandomized studies (see Appendix Table 1). Any disagreements in scores, differing by ≥ 1 points, were resolved by a third author (K.C.).

Results

Failure Rates and Study Characteristics

A total of 16 of the most common risk factors were examined for significance relative to MAT failure. Overall, 2,533 patients were included, and 16 risk factors were evaluated across 21 studies (Level of Evidence III: 10; Level of Evidence IV: 11). Mean final follow-up in included studies ranged from 2.2 to 20 years. The clinical failure rates ranged from 8.56% to 21.74%, and the surgical failure rates had a range of 2.30% to 28.00% (Table 1).

Risk Factors

For surgical failure (Table 2), the presence of high-grade cartilage defects was the only risk factor found predictive of MAT failure in the majority of studies in which it was analyzed (71.4%, 5/7 studies). Further subgroup analysis of cartilage damage as a risk factor for MAT failure was performed (Table 3). Tibial chondral defects ≥ 3 cm^2 were examined in only 1 study and were found to be significant.[16] A higher number of previous surgeries on the same knee was also examined in only 1 study and found to be significant.[17] Age, sex, BMI, concomitant cartilage procedure, ligamentous or realignment osteotomy procedures, time from prior

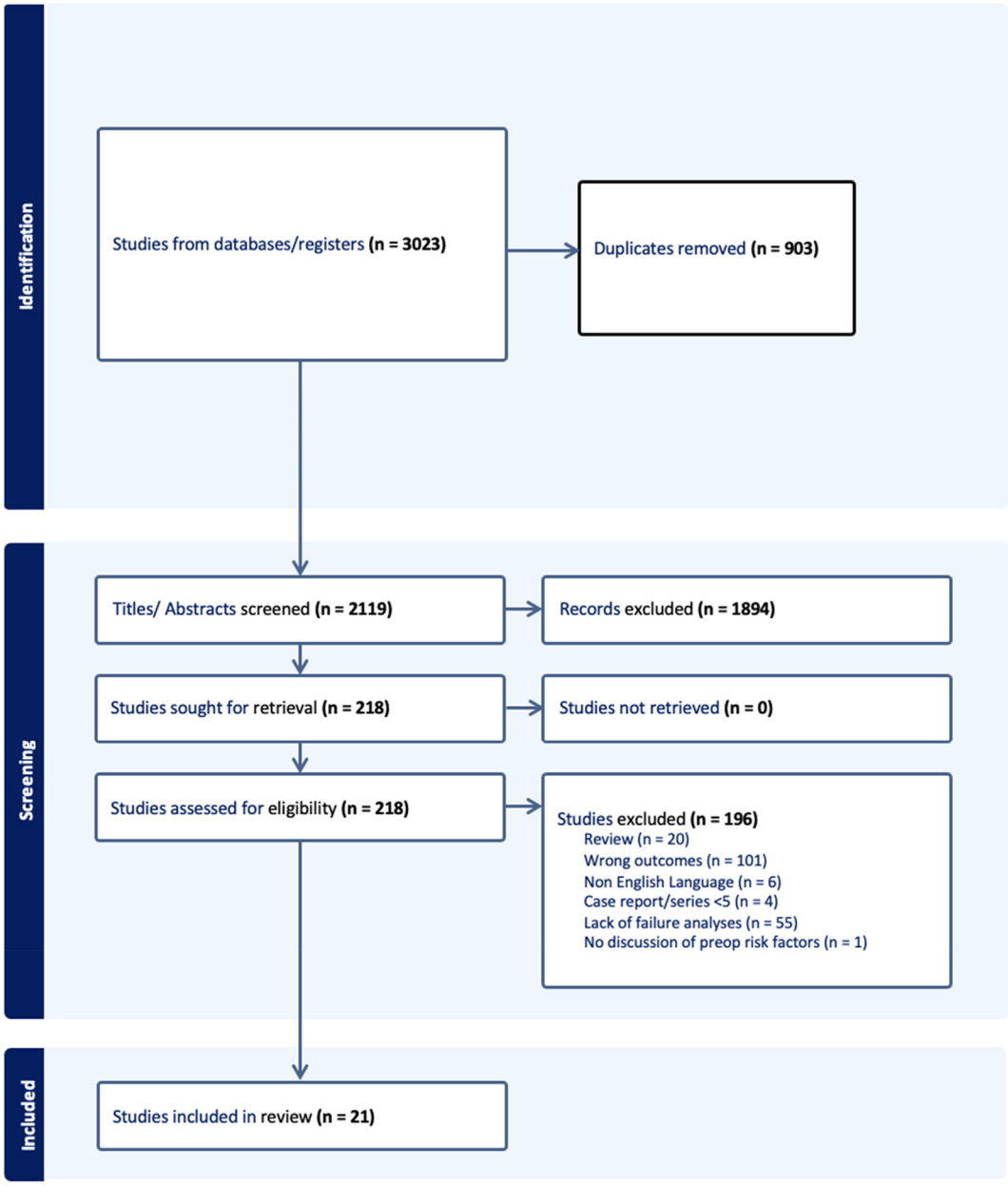

Fig 1. Preferred Reporting Items for Systematic Reviews and Meta-analysis flowchart exhibiting inclusion and exclusion technique for extraction. (Preop, preoperative.)

meniscectomy, femorotibial alignment, and limb laterality were all investigated in at least 3 studies but not found significant.

For studies that examined clinical failure, all studies defined clinical failure as a Lysholm score <65 on patient-reported outcomes, except for 1 study by Waterman et al.,[18] who defined clinical failure as the necessitation of military discharge due to persistent knee limitation (Table 3). There were no risk factors found to be predictive of MAT failure in the majority of included studies. Smoking and concomitant ligamentous and osteotomy procedures were found to be significant but were only investigated in 1 study each. Risk factors studied in at least 3 articles that were not found significant in most studies investigating them include age, sex, BMI, and medial versus lateral compartment.

Cartilage Status Subanalysis

Five of seven (71.4%) studies investigating high-grade cartilage lesions found them to be significantly predictive of surgical MAT failure (Table 4). In 4 of the 5 studies that found high-grade lesions significant,[1,10,13,19] the authors did not treat all high-grade cartilage lesions at the time of MAT. In these 4 studies, we found a range 10% to 70% of high-grade lesions were treated; this includes assuming that all

Table 1. Study Characteristics

First Author (Year)	LOE	N	Final Follow-Up (Range), Years	Mean Time to Failure	Surgical Failure Rate	Surgical Failure Type
Van Der Straeten et al., 2019[10]	III	329	6.8 (0.2-24.3)	Not specified	27.4%	Conversion to knee arthroplasty (n = 63), meniscectomy (n = 27)
Waterman et al., 2016[18]	IV	230	2.1 (NR)	Not specified	5.7%	Meniscectomy (n = 10), revision MAT (n = 1), conversion to knee arthroplasty (n = 2)
Lee et al., 2017[13]	III	222	3.7 (0.3-7.0)	Not specified	2.3%	Graft excisions (n = 5)
Park et al., 2021[16]	IV	28	3.6 (2.0-5.4)	Not specified	25.0%	Revisions MAT, meniscectomy greater than one-third of allograft
Parkinson et al., 2016[19]	III	125	3.0 (1.0-10.0)	Not specified	18.0% (5 years)	Graft excision, revision MAT, conversion to knee arthroplasty
Mahmoud et al., 2018[1]	IV	45	8.6 ± 3.4	6.1 ± 4.4	17.7%	Conversion to knee arthroplasty (n = 4), graft excisions (n = 4)
Van Der Wal et al., 2020[28]	III	109	4.5 (NR)	8.0 (0.8-15.4)	10.1%	Conversion to knee arthroplasty (n = 8), graft excisions (n = 3)
McCormick et al., 2014[24]	IV	172	4.9 (2.0-9.8)	Not specified	4.7%	Conversion to knee arthroplasty (n = 4), revision MAT (n = 4)
Stone et al., 2006[17]	IV	47	5.8 (2.0-7.3)	4.4 ± 1.8	10.6%	Conversion to knee arthroplasty, revision MAT
Searle et al., 2020[20]	III	43	3.4 ± 1.6	1.8 (NR)	9.3%	Graft excision, revision MAT, conversion to knee arthroplasty
Bloch et al., 2019[15]	III	240	3.2 (1.0-10.0)	Not specified	3.3% (1 year), 12.6% (5 years), 17.9% (7 years)	Graft excision, Revision MAT, conversion to knee arthroplasty
Zaffagnini et al., 2016[29]	IV	147	4.0 ± 1.9	Not specified	4.1%	Conversion to knee arthroplasty (n = 1), meniscectomy (n = 5)
Kazi et al., 2015[14]	IV	86	15.0 (2.8-25.1)	12.5 (NR)	28.0%	Conversion to knee arthroplasty (n = 24)
Stone et al., 2015[25]	IV	49	8.6 (2.0-15.0)	5.2 ± 4.4	18.4%	Conversion to knee arthroplasty (n = 4), graft excision (n = 5)
Saltzman et al., 2018 (1)[21]	III	91	3.9 (1.4-7.1)	3.4 (2.3-6.4)	16.5%	Conversion to knee arthroplasty (n = 3), revision MAT (n = 12)
Carter and Brown, 2020[26]	IV	56	20.0 (NR)	12.7 (9.9-19.0)	14.3%	Conversion to knee arthroplasty (n = 8)
Grassi et al., 2020[11]	IV	46	9.0 (2.0-10.0)	2.9 (0.3-7.8)	9.0% (2 years), 9.0% (5 years), 14.0% (10 years)	Meniscectomy (n = 6)
Saltzman et al., 2018 (2)[27]	III	60	4.9 ± 2.30	2.6 ± 1.4	5.0% (2 years), 13.0% (5 years)	Conversion to knee arthroplasty (n = 1), revision MAT (n = 1), Graft excision (n = 2)
Jiménez-Garrido et al., 2019[12]		35	6.3 ± 3.6	Not specified	5.7%	Conversion to knee arthroplasty (n = 1), meniscectomy (n = 1)

LOE, level of evidence; MAT, meniscal allograft transplantation; NR, not reported.

treated lesions in the Van Der Straeten et al.[10] and Mahmoud et al.[1] studies were high-grade lesions, because the authors did not explicitly specify which lesions they treated. Additionally, the 2 studies not finding cartilage status to be significant treated all full-thickness defects at the time of MAT.[20,21] Of the 3 studies that treated 100% of high-grade cartilage lesions,[15,20,21] 2 of 3 (66.7%) found cartilage status did not predict MAT failure.[20,21]

Risk Factor Inclusivity

In studies examining surgery-based failure of MAT, no study controlled for all 16 risk factors. Only Waterman et al.[18] and Van Der Straeten et al.[10] accounted for ≥50% of the risk factors examined. Two studies examined 7 risk factors,[13,16] and 2 other studies examined 5 risk factors.[1,19] The rest of the included studies examined 4 or fewer.

In studies examining clinical failure of MAT, no study controlled for all 13 risk factors. Two studies examined >50% of the risk factors in this study.[13,18] The rest of the included studies examined 4 or fewer.

Discussion

The presence of untreated high-grade chondral defects was the most common significant risk factor

Table 2. Risk Factors Associated With Meniscal Allograft Transplant Surgical Failure

	Age	Sex	Compartment	High-Grade Cartilage Lesions	BMI	Concomitant Cartilage Procedure	Concomitant High Tibial Osteotomy	Concomitant Ligament Procedure	Time From Prior Meniscectomy	Femorotibial Alignment	Laterality (Limb)	Smoking Status	Tibial Chondral Defects ≥3 cm^2	No. of Past Surgeries to Index Knee	Subchondral Bone Marrow Lesion Grade	Time From Injury to Surgery
Van Der Straeten et al., 2019[10]																
Waterman et al., 2016[18]																
Lee et al., 2017[13]																
Park et al., 2021[16]																
Parkinson 2016[19]																
Mahmoud et al., 2018[1]																
Song et al., 2020[23] *																
McCormick et al., 2014[24]																
Van der Wal et al., 2020[28]																
Stone et al., 2015[25]																
Searle et al., 2020[20]																
Bloch et al., 2019[15]																
Zaffagnini et al., 2016[29]																
Kazi et al., 2015[14]																
Stone et al., 2006[17]																
Saltzman et al., 2018 (1)[21]																
Carter and Brown, 2020[26]																
Grassi et al., 2020[11]																
Saltzman et al., 2018 (2)[27]																
Jiménez-Garrido et al., 2019[12]																
	3/13 23.1%	0/12 00.0%	2/9 22.2%	5/7 71.4%	0/7 00.0%	0/6 00.0%	1/5 20.0%	0/5 00.0%	0/4 00.0%	0/3 00.0%	0/3 00.0%	0/2 00.0%	1/1 100.0%	1/1 100.0%	0/1 00.0%	0/1 00.0%

BMI, body mass index.
Red denotes insignificant risk factor.
Green denotes significant risk factor.
*Song et al.[23] was the only study that did not separate surgical and clinical failure and defined failure as any 1 of the following:
1. Meniscectomy of more than half of the allograft
2. Meniscectomy to the zone of meniscocapsular junction
3. Lysholm score <65
4. Conversion to revision meniscal allograft transplant
5. Realignment osteotomy or arthroplasty

Table 3. Risk Factors Associated with Meniscal Allograft Transplant (MAT) Clinical Failure

	Age	BMI	Sex	High-Grade Cartilage Lesions	Compartment	Time From Prior Meniscectomy	Femorotibial Alignment	Laterality (Limb)	Smoking Status	Concomitant Ligament Procedure	Concomitant High Tibial Osteotomy	Concomitant Cartilage Procedure
Waterman et al., 2016[18]*												
Lee et al., 2017[13]												
Song et al., 2020[23]**												
Searle et al., 2020[20]												
Zaffagnini et al., Kazi et al., 2016[29]												
Verdonk et al., 2005[30]												
Jiménez-Garrido et al., 2019[12]												
	1/5 20.0%	1/4 25.0%	0/4 00.0%	0/3 00.0%	0/2 00.0%	0/2 00.0%	0/2 00.0%	0/2 00.0%	1/1 100.0%	1/1 100.0%	1/1 100.0%	0/1 00.0%

BMI, body mass index.

Red denotes insignificant risk factor.

Green denotes significant risk factor.

All studies defined clinical failure as a Lysholm score <65 on patient-reported outcomes except for the following 2 studies:

*1. Waterman et al.[18] defined clinical failure as requiring military discharge due to persistent knee limitation.

**2. Song et al.[23] was the only study that did not separate surgical and clinical failure and defined failure as any one of the following:

1. Meniscectomy of more than half of the allograft
2. Meniscectomy to the zone of meniscocapsular junction
3. Lysholm score <65
4. Conversion to revision MAT
5. Realignment osteotomy or arthroplasty

Table 4. Subanalysis on Concomitant Cartilage Restoration Procedure Treatment Rate With Meniscal Allograft Transplant (MAT)

	Cartilage Status Found as Significant Predictor of MAT Failure	Anatomic Location of Cartilage Lesions	Overall Cartilage Treatment Rate (Including Low-Grade Lesions)	High-Grade/ Full-Thickness Lesion Treatment Rate	Cartilage Restoration Procedure
Bloch et al., 2019[15]	ICRS 3b (full thickness)	Not specified	N/A (unknown/ 240)	100%	Debridement, microfracture, MACI
Parkinson et al., 2016[19]	ICRS 3b (full thickness)	Tibial and femoral surfaces	30.40% (38/125)	70% (38/54)	microfracture (n = 26), MACI (n = 12)
Van Der Straeten et al., 2019[10]	Outerbridge Classification 3-4,	Not specified	18.18% (52/286)	40%* (52/130)	Microfracture (n = 50), OATS (n = 2)
Lee et al., 2017[13]	ICRS 3b (full thickness)	Tibial and femoral surfaces	11.71% (26/222)	19% (26/135)	Microfracture (n = 20), OATS (n = 5), ACI (n = 1)
Mahmoud et al., 2018[1]	Outerbridge Classification 3-4	Not specified	6.67% (3/45)	10%* (3/31)	Not specified
Saltzman et al., 2018 (1)[21]	None	Not specified	75.82% (69/91)	100%	OCA (n = 48), microfracture (n = 9), OATS (n = 3), ACI (n = 13), particulated juvenile allograft cartilage (n = 1)
Searle et al., 2020[20]	None	Not specified	N/A (unknown/43)	100%	Microfracture (n = 5), ACI (n = 10)

ACI, autologous chondrocyte implantation; ICRS, International Cartilage Repair Society; MACI, matrix-induced autologous chondrocyte implantation; N/A, not available; OATS, osteochondral autograft transfer system.

Red denotes that high-grade cartilage lesion is not a significant risk factor for surgical failure.

Green denotes that high-grade cartilage lesion is a significant risk factor for surgical failure.

*Van Der Straeten et al.[10] and Mahmoud et al.[1] did not specify if the cartilage procedures performed were for high-grade versus low-grade lesions. For these studies, the treatment rate of high-grade lesions was calculated assuming all treatments were for higher-grade lesions. Therefore, high-grade cartilage lesion operative treatment rates for these studies are potentially lower than reported in this table.

associated with MAT surgical failure across the majority of the studies included in the analysis. Tibial chondral defects ≥ 3 cm^2, as well as prior surgeries to the index knee, were investigated in 1 study each and found to be significant. For clinical failure, no single risk factor was consistently found to be predictive of clinical failure across multiple studies; however, smoking and concomitant realignment osteotomy or ligamentous procedure were studied in 1 study each and found to be significant. Of the 16 risk factors analyzed, no study focusing on surgical or clinical failure controlled for all risk factors evaluated, and only 2 studies controlled for >50% of the included risk factors.

Factors Predictive of Surgical Failure

Surgical failure following MAT was defined as the need for subsequent procedures, such as graft excision, revision MAT, or conversion to knee arthroplasty. Although reoperation is commonly used as a proxy for failure in current literature, there was heterogeneity, in which an additional procedure was used to determine failure. In terms of risk factors, baseline cartilage status was examined in 7 of the 20 studies examining surgical failure and was reported as a significant predictor in 71.4% of analyzed studies. No other factor was reported as significant in more than 25% of studies in which it was examined.

Less severe cartilage damage (Outerbridge grade less than III) at the time of MAT has been associated with longer average graft survival (17.6 years) compared to more severe defects (Outerbridge III or above) with an average survival of 13.4 years in the cohort examined by Van Der Straeten et al.[10] This represented a nearly 4-fold increased odds of failure in knees with more severe cartilage damage. Regression analyses further found Outerbridge III or above changes to be the most important determinant of MAT failure in the studied cohort.[10] Similarly, Lee et al.[13] stratified their MAT cohort by degree of chondral degeneration. High-grade chondral damage (International Cartilage Regeneration & Joint Preservation Society [ICRS] ≥ 3) on both the femoral and tibial side was associated with a 4-fold increase in failure. For Bloch et al.,[15] a 95% 5-year survival rate was found

for knees without significant chondral damage versus a 77% survival for those with full-thickness chondral wear. Parkinson et al.[19] found a 5-year survival rate of 97%, 82%, and 62% in group 1 (intact or partial-thickness chondral loss), group 2 (full-thickness chondral loss of 1 condyle), and group 3 (full-thickness chondral loss of both condyles), respectively.

These findings are consistent with the fact that patients with severe osteoarthritis (OA) exhibiting diffuse femoral and/or tibial cartilage wear are typically contraindicated for MAT because it may not provide significant benefit due to extensive joint damage.[22] Therefore, many studies in this review excluded patients with severe OA, defined as Kellgren-Lawrence grade 3 or above on radiograph, disappearance of joint space width, or diffuse exposed subchondral bone,[10-13,16,17,19,23-27] whereas others made no comment on preoperative OA status.[1,14,15,18,27-30] However, only 1 study in the review examined preoperative OA status and compared lower OA grades (Kellgren-Lawrence grades 1 and 2), finding no difference in surgical failure rates without comparison to severe arthritis or a healthy control.[27]

In comparison to severe OA, patients with tibiofemoral cartilage defects routinely undergo MAT with or without a concomitant or staged cartilage restoration procedure.[22] In our analysis, 5 studies found that a concomitant cartilage procedure is not a risk factor for MAT surgical failure.[10,16,18,21,25] Furthermore, in the subgroup analysis of studies investigating cartilage status effects of MAT outcomes (Table 4), it was found that the 2 studies that reported cartilage status not to be a significant predictor of outcomes had 100% treatment rate of full-thickness cartilage lesions with techniques, including microfracture, autologous chondrocyte implantation (ACI), particulated juvenile allograft cartilage, or osteochondral auto/allografting.[20,21] In contrast, the studies that found full-thickness cartilage lesions to be significant, either ICRS 3b or Outerbridge III and above, had decreased rates of concomitant cartilage treatment.[1,10,13,15,19] Parkinson et al.[19] treated 70% of full-thickness lesions with either microfracture or ACI, and Lee et al.[13] treated 19% of full-thickness lesions with microfracture, ACI, and osteochondral autograft transfer system (OATS). Van Der Straeten et al.[10] treated ~40% of full-thickness lesions with microfracture or osteochondral autograph, and Mahmoud et al.[1] treated an estimated 10% of lesions. For Van Der Straeten et al.[10] and Mahmoud et al.,[1] the treatment rate of high-grade lesions was calculated, assuming all treatments were for higher-grade lesions. Therefore, operative treatment rates for high-grade cartilage lesions for these studies are potentially lower than reported. Lastly, Bloch et al.[15] found ICRS 3b cartilage status as a significant predictor of surgical MAT despite 100% treatment of all full-thickness cartilage lesions with a combination of debridement, microfracture, or ACI based on size and location. However, the authors did note improvement in patient-reported outcomes was similarly demonstrated irrespective of the grades of cartilage repaired. In aggregate, this subanalysis suggests that full-thickness cartilage defects treated with a concomitant cartilage restoration procedure during MAT may be clinically insignificant in terms of surgical failure. From a broader perspective, it appears that a patient's articular cartilage status postoperatively to MAT is critical to the failure rate of the procedure. Patients with untreated cartilage defects or severe OA are more likely to fare worse after MAT than patients without defects, those with concomitantly treated cartilage lesions, and possibly even patients with lower grades of OA, although this warrants further investigation.

Ten of 13 studies found age insignificant for surgical MAT failure, whereas 3 of 10 found it significant. Van Der Straeten et al.[10] found an odds ratio increase of 2.3 for MAT failure in their ≥35 year age group compared with the <35 age group using Cox regression to reduce confounding. Van Der Wal et al.[28] also found a 5.2 times higher risk of revision surgery after MAT for every 10-year increase in age above 35 years, although they did not control for cartilage damage at the time of index operation. Carter et al.[26] found that of their 8 patients who went on to total knee arthroplasty after MAT, their average age was 45 at the time of initial MAT compared with a cohort average of 33 years and 11 months. A review of preoperative radiographs from these patients found that 4 had moderate degenerative joint changes with <2 mm of joint space and medial femoral condyle spurring, whereas the other 4 had minimal radiographic changes. None of the other 10 studies investigating age as a factor for failure found it statistically significant. It is important to note that many of these studies established cohorts based on degree of cartilage damage because it is known that OA increases with age. In conjunction, these results indicate that age may be confounded by cartilage damage and is likely not an independent risk factor for surgical MAT failure.

Of the 9 studies investigating medial versus lateral compartment as a risk factor for failure, only 2 found significant differences.[11,19] Grassi et al.[11] found lower survival in lateral compartment MAT, whereas Parkinson et al.[19] found lower survival in the medial compartment MAT. The explanations given by the authors include differences in anatomy and biomechanics, including more weight bearing through the medial compartment, as well as increased lateral compartment motion, but it appears that these findings are likely the result of low power and that knee compartment does not significantly influence MAT surgical failure.[11,19]

Only Stone et al.[25] investigated the impact of number of surgeries before undergoing MAT. The authors found 5 failures, as defined by allograft removal in 47 transplants at an average of nearly 11 years. They performed a stepwise discriminant analysis and found increasing number of past surgeries on the same knee as a predictor of failure, which may simply indicate a higher burden of cartilage damage in the knee along with concomitant inflammation and arthrofibrosis.[25]

Other factors included in this review and never found significant for surgical failure included sex, BMI, concomitant cartilage or ligamentous procedure, time from prior meniscectomy, corrected femorotibial alignment, laterality, smoking, bone marrow lesion grade, and time from injury to surgery.

Factors Predictive of Clinical Failure

When identifying preoperative risk factors that portended clinical failure, defined by Lysholm score less than 65, 7 studies met inclusion criteria with no study controlling for all 12 risk factors examined. Of those studies, age, sex, and BMI were most frequently investigated, and the majority of the time, these risk factors were found to have no significant correlation with clinical failure. Of the 5 studies incorporating age as a risk factor for failure, only 1 study found a significant relationship.[13] Lee et al.[13] reported a hazard ratio for clinical failure of 1.095 for each 1-year increase in age ([95% CI, 1.039-1.154]; $P = .001$). On the contrary, Song et al.[23] specifically investigated the effect of advanced age on MAT survivorship and found no significant difference in clinical outcomes between older patients (>43 years of age) compared with a younger cohort matched for cartilage status and time from prior meniscectomy. The investigation of a military population by Waterman et al.[18] also found no significant association between age and clinical failure [OR: 1.03, CI: 0.97-1.08]. Further, neither Searle et al.[20] nor Zaffagnini et al.[29] found a significant relationship between age and clinical failure in their regression modeling of surgical and clinical failure cohorts. These findings are in accordance with recent meniscal repair literature, showing that age itself is not an independent risk factor for clinical or surgical failure after meniscal repair.[31-33] With all other factors being appropriate for MAT, the results of this review indicate that patients should not be excluded solely based on their age.

Prior literature notes patient-related factors such as obesity could influence success after MAT; however, literature on the subject is limited.[34] Only 1 of the 4 studies included here evaluating BMI as a risk factor reported a significant effect on clinical failure.[12] Jiménez-Garrido et al.[12] compared cohorts stratified by BMI and reported a 12-fold increased risk of failure in obese patients (BMI $\geq$30 kg/m^2) compared with nonobese patients when adjusting for age, sex, preoperative degree of arthritis, and affected compartment. This study was limited in its power due to enrolling only 9 patients in the obese cohort and 26 patients in the nonobese cohort. A previous in vivo biomechanical investigation supports this notion, showing individuals with elevated BMI inflicted greater cartilage strain with walking.[35] The 3 remaining studies in this review, involving more than 600 patients, did not observe any significant impact on the risk of clinical failure. This is likely attributed to the narrow range of acceptable BMI among patients undergoing MAT. The literature on the effect of BMI on meniscal repairs and meniscectomy is similarly mixed.[36-38] Together, these results indicate that the association between BMI and MAT failure requires more dedicated prospective investigation, but at this time, has been shown more often not to be associated with clinical failure.

Waterman et al.[18] reported on a cohort of young, active military personnel undergoing MAT. They found current tobacco use was a reported modifiable preoperative risk factor associated with clinical failure, as defined by knee-related military discharge. Although the detrimental effects of tobacco use on postoperative outcomes in orthopedic surgery are well-documented, research specifically focusing on the influence of tobacco use on meniscal procedures has primarily been reported in the context of meniscectomy.[38] In the same study by Waterman et al.,[18] the addition of a concomitant ligamentous procedure or realignment osteotomy at the time of index surgery was also predictive of postoperative clinical failure. It must be noted that although these are mentioned as perioperative risk factors for failure, they were reported after univariate analysis and thus did not control for confounding effects from other collected variables across the cohort. It is likely that the addition of complex concomitant procedures indicates the high complexity of the knee injury and the difficulty in returning to a military level of functionality afterward. No other studies in our review investigated these factors as predictors of clinical failure, and they warrant further investigation.

Other factors included in this review but not found significant for clinical failure include sex, knee compartment, time from prior meniscectomy, concomitantly treated femorotibial alignment, laterality, age, concomitant cartilage procedure, and cartilage defects. Saltzman et al.[21] explore the presence of cartilage defects at the time of MAT on clinical outcomes by determining patients who reached Minimal Clinically Important Difference (MCID) at 2 years and final follow-up. At 2 years postsurgery, patients without cartilage defects at the time of surgery met MCID for 8 patient-reported outcomes measures (PROMs) including Lysholm, IKDC, KOOS pain, symptoms, sport, quality of life (QOL), Western Ontario and McMaster Universities Arthritis Index (WOMAC)

function, and WOMAC total. At final follow-up (4.48 ± 2.63 years) for the same group, MCID was achieved for 5 PROMs: Lysholm, IKDC, KOOS symptoms, QOL, and WOMAC function. In the same study, the cohort of patients with full-thickness cartilage defects met MCID at 2 years postsurgery for 7 PROMs: Lysholm, IKDC, KOOS symptoms, sport, QOL, WOMAC function, and WOMAC total. At final follow-up (3.84 ± 2.47 years), this group met MCID for 8 PROMs: Lysholm, IKDC, KOOS pain, symptoms, sport, QOL, WOMAC function, and WOMAC total. All patients with cartilage defects at time of MAT were treated concomitantly with cartilage restoration procedures, underscoring that healthy cartilage post-MAT may mitigate poor clinical outcomes.

Limitations

There are several limitations of this review to consider. We were unable to register our study protocol prospectively, raising concerns about transparency and external validity. The studies we analyzed showed significant heterogeneity, especially in reporting risk factors and mean final follow-up time (2.2-20.0 years), making it challenging to control for confounding variables. Moreover, our analysis on cartilage defects was hampered by only 7 of 21 studies reporting data on baseline cartilage status. The variability in surgical techniques across the studies, and the differing definitions of failure further complicated our findings. Additionally, the diverse patient populations in the included studies made it challenging to draw broad conclusions. Despite these limitations, our decision to group studies by failure type was a deliberate effort to enhance clarity, even though it resulted in reduced statistical power for individual groups.

Conclusions

The presence of untreated high-grade cartilage appears to elevate the risk of surgical MAT failure; however, concomitant treatment of defects may mitigate their detrimental effect. There is no clear risk factor that consistently predicts clinical failure. Age, sex, BMI, knee compartment, time from prior meniscectomy, femorotibial alignment (after correction), concomitant cartilage procedure, and laterality do not routinely influence MAT failure.

Disclosures

The authors report no conflicts of interest in the authorship and publication of this article. Full ICMJE author disclosure forms are available for this article online, as supplementary material.

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Appendix Table 1. Methodological Index for Non-randomized Studies Criteria of All Included Studies

	Risk Factors Included by Any Statistical Analysis												
	A Clearly Stated Aim	Inclusion of Consecutive Patients	Prospective Collection of Data	End Points Appropriate to the Study Aim	Unbiased Assessment of Study End Point	Follow-Up Period Appropriate to the Study Aim	Loss to Follow-Up <5%	Prospective Calculation of the Study Size	An Adequate Control Group	Contemporary Groups	Baseline Equivalence of Groups	Adequate Statistical Analyses	Total
Van Der Straeten et al., 2019[10]	2	2	0	2	2	2	0	0	0	0	0	2	12
Waterman et al., 2016[18]	2	2	0	2	2	1	0	0	0	0	0	2	11
Lee et al., 2017[13]	2	2	0	2	2	2	0	0	0	0	0	2	12
Park et al., 2019[16]	2	2	0	2	2	2	0	0	0	0	0	2	12
Parkinson et al., 2016[19]	2	2	2	1	2	2	2	0	0	0	0	2	15
Mahmoud et al., 2018[1]	2	2	2	2	2	2	0	0	0	0	0	2	14
Song et al., 2020[23]	2	2	0	2	2	2	0	0	2	2	2	2	18
McCormick et al., 2014[24]	2	2	1	2	2	2	0	0	0	0	0	2	13
Van der Wal 2020[28]	2	2	0	2	2	2	0	0	0	0	0	2	12
Stone et al., 2015[25]	2	2	2	1	2	2	0	0	0	0	0	2	13
Searle et al., 2020[20]	2	2	0	2	2	0	0	0	0	0	0	2	10
Bloch et al., 2019[15]	2	2	2	2	1	2	0	0	0	0	0	1	12
Zaffagnini et al., 2016[29]	2	2	0	2	2	2	0	0	0	0	0	2	12
Kazi et al., 2015[14]	1	2	0	2	2	2	0	0	1	2	0	1	13
Stone et al., 2006[17]	2	2	2	2	2	2	0	0	0	0	0	2	14
Saltzman et al., 2018 (1)[21]	2	2	2	2	2	2	0	0	2	2	2	2	20
Carter and Brown, 2020[26]	2	2	0	1	2	2	0	0	0	0	0	1	10
Grassi et al., 2020[11]	2	2	0	2	2	2	1	0	0	0	0	2	13

(continued)

Appendix Table 1. Continued

	Risk Factors Included by Any Statistical Analysis												
	A Clearly Stated Aim	Inclusion of Consecutive Patients	Prospective Collection of Data	End Points Appropriate to the Study Aim	Unbiased Assessment of Study End Point	Follow-Up Period Appropriate to the Study Aim	Loss to Follow-Up <5%	Prospective Calculation of the Study Size	An Adequate Control Group	Contemporary Groups	Baseline Equivalence of Groups	Adequate Statistical Analyses	Total
Saltzman et al., 2018 (2)[27]	2	1	2	2	2	2	0	0	0	0	0	2	13
Jiménez-Garrido et al., 2019[12]	2	1	0	1	2	2	2	0	2	2	1	2	17
Verdonk et al., 2005[30]	2	2	0	2	2	2	2	0	0	0	0	2	14