The Relationship Between Medial Meniscal Extrusion and Outcome Measures for Knee Osteoarthritis

A Systematic Review

David H. Kahat,[*†] MD, MBA, Cyrus M. Nouraee,[‡] BS, Jesse S. Smith,[†] MD, MS, Cassiano C. Santiago,[†] MD, Edward R. Floyd,[§] MD, Stefan Zbyn,[||] PhD, Hasan Abbasguliyev,[||] MD, Abdul Wahed Kajabi,[||] PhD, and Jutta M. Ellermann,[†] MD, PhD
Investigation performed at the Department of Radiology, University of Minnesota, Minneapolis, Minnesota, USA

Background: Medial meniscal extrusion (MME) has been associated with knee osteoarthritis (OA). However, there is no standardized method to measure MME.

Purpose/Hypothesis: The purpose of this study was to investigate the relationship between MME and outcome measures related to knee OA and discuss different magnetic resonance imaging (MRI) methods of measuring MME. It was hypothesized that MME would be associated with outcome measures of OA and that the distance extruded over the tibial plateau would be the most common MRI method to measure MME.

Study Design: Systematic review; Level of evidence, 3.

Methods: The MEDLINE, Embase, Cochrane Library, Scopus, Web of Science Core Collection, Global Index Medicus, and ClinicalTrials.gov databases were systematically searched. The inclusion criteria were studies that (1) measured MME on nonoperated knees using MRI; (2) evaluated knee OA with at least 1 knee OA grading scale, outcome measure, or direct characterization of cartilage or bone; (3) statistically evaluated the association between MME and knee OA outcome measure; (4) were randomized controlled trials, nonrandomized controlled trials, cohort studies, or case series; and (5) reported original results.

Results: A total of 19 studies were included, of which 14 reported MME as the distance extruded over the tibial plateau, 7 reported MME as the volume extruded over the tibial plateau, and 1 reported MME as the percentage of the tibial plateau covered by the meniscus. All studies reported that MME was significantly associated with at least 1 OA outcome measure—including increased Kellgren-Lawrence grade, osteophytes, cartilage damage, varus alignment, knee pain, bone marrow lesions, and progression to arthroplasty. Eight studies found that MME was associated with worse OA outcomes over time (range, 2-10 years).

Conclusion: All 19 reviewed studies reported that MME was associated with at least 1 knee OA outcome measure reflective of worsening arthritis, suggesting a strong association between OA and MME. Future research is needed to investigate this relationship and standardize the methods of measuring MME.

Keywords: cartilage; magnetic resonance imaging; medial meniscal extrusion; osteoarthritis; systematic review

Although once described as an embryonic remnant with no fuction, research has demonstrated that menisci are critically important for the normal function and health of the knee joint.[27] The medial and lateral menisci are wedges of fibrocartilage that absorb shock, transmit loads, act as secondary anterior stabilizers of the knee, play a role in proprioception, and enhance the nutrition of the articular cartilage.[15,32,34] For these reasons, damage to the meniscus is a significant risk factor for developing knee osteoarthritis (OA) later in life.

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Damage to the meniscus in the form of tears or degeneration can cause extrusion, which occurs when the circumferential fibers of the menisci are unable to redistribute compressive axial loads ("hoop stresses") into tensile forces.[9] Inability to dissipate hoop stresses causes extrusion of the menisci either medially or laterally over the tibial plateau, which is thought to lead to biomechanical overloading of the joint articular surface and accelerated cartilage breakdown.[25] As the medial meniscus sustains more weightbearing stress than the lateral meniscus, medial meniscal extrusion (MME) specifically may be implicated in knee OA.[22,31] Causes of MME include root tears, large radial tears, and degeneration.[5] As MME may contribute to knee OA, being able to better understand, quantify, and measure MME is vital to radiologists, orthopaedic surgeons, and other clinicians.

Magnetic resonance imaging (MRI) offers excellent contrast between cartilage and meniscus and is widely used to quantify MME. While MME has been documented in individual studies, no systematic review has investigated (1) the methods of measuring MME and (2) the relationship between MME and OA. Furthermore, no validated reference standards for measuring MME are in the literature. Some studies report the maximum distance of MME over the tibial plateau, some report the volume of the meniscus extruded, and others report the percentage of the tibial plateau that the meniscus covers. In addition, the literature is inconsistent as to what threshold constitutes pathologic extrusion.

The objectives of the present study were as follows: (1) review the literature characterizing the relationship between MME and knee OA; (2) summarize the OA-related sequela of MME; and (3) report and investigate the MRI methods of measuring MME. We hypothesized that MME would be associated with outcome measures of OA and that the distance extruded over the tibial plateau would be the most common MRI method to measure MME.

METHODS

The study protocol was registered a priori with PROSPERO on January 20, 2022, (Central Registration Depository 42022299567) in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. We conducted a comprehensive search utilizing controlled vocabulary and natural language searching in accordance with best practices.[13] The search strategy encompassed the concepts of MME, knee OA, and measurements of OA severity. The search was developed in Ovid MEDLINE and conducted across the following databases in December 2021: MEDLINE via OVID and PubMed; Embase via OVID; Cochrane Library via Wiley; Scopus; Web of Science Core Collection; Global Index Medicus; and ClinicalTrials.gov. No limitations were placed on the language or date of publication, and no search hedges or filters were employed to limit study types. The full search strategy is available separately as supplemental material.

TABLE 1
Inclusion and Exclusion Criteria for Studies[a]

Inclusion Criteria	Exclusion Criteria
• Measured MME with MRI. • Evaluated knee OA with at least 1 validated knee OA scale, outcome measure, or direct characterization or measurement of cartilage or bone quality. • Associated MME and knee OA via statistical analysis with *P* values. • Had to be randomized controlled trials, nonrandomized controlled trials, cohort studies, or case series with measurement of effect. • Reported original results.	• Did not disclose meniscus laterality. • Case reports, studies with nonhuman subjects, basic science studies, anatomic studies, biomechanical studies, or studies that did not report original findings. • Included participants with a history of inflammatory arthropathy or major knee trauma. • Meniscus measurements that were evaluated in knees with an operative history.

[a]MME, medial meniscal extrusion; MRI, magnetic resonance imaging; OA, osteoarthritis.

Selection Criteria

The inclusion and exclusion criteria are listed in Table 1. Studies were required to meet all 5 inclusion criteria for the systematic review. Studies that used preoperative MRI to evaluate MME were included in the review.

Study Identification

The search results from all databases were compiled, and duplicates were removed in Endnote X9 (Clarivate Analytics). A total of 1679 studies were initially identified, and

*Address correspondence to David H. Kahat, MD, MBA, Department of Radiology, University of Minnesota, 420 Delaware Street, SE, MMC 292, Minneapolis, MN 55455, USA (email: Kahat004@umn.edu).
†Department of Radiology, University of Minnesota, Minneapolis, Minnesota, USA.
‡University of Minnesota Medical School, Minneapolis, Minnesota, USA.
§Sanford Orthopedics and Sports Medicine, Sioux Falls, South Dakota, USA.
||Department of Radiology, Center for Magnetic Resonance Research, University of Minnesota, Minneapolis, Minnesota, USA.
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the titles and abstracts were loaded into Rayyan (Rayyan Systems).[26] At least 2 authors independently screened the title and abstract of each study. Any disagreements were discussed between the reviewers; if consensus was not reached, the senior author (J.M.E.), a radiologist with 15 years of musculoskeletal subspecialty experience, decided whether to include or exclude the study. Following the title and abstract screening, the full text of 196 studies was screened using the protocol previously described. Figure 1 displays the PRISMA flow chart of how the final 19 studies were included in the review.[30]

Data Extraction

The study design, objectives, and patient characteristics were extracted from each study. In addition, we collected data on knee OA outcome measures/features, the statistical significance of the association between MME and knee OA, and the methods of quantifying MME.

Statistical and Methodological Analysis

All included studies were assessed for methodological quality utilizing the Joanna Briggs Institute Critical Appraisal Checklist for cohort, case-control, or cross-sectional studies.[3,38] After a comprehensive evaluation, all 19 studies were determined to meet the selection criteria.

All analyses presented in this study are qualitative. A meta-analysis was considered, but after consulting with a statistician, it was decided that a quantitative meta-analysis would not be able to be completed because of the heterogeneity of the data.

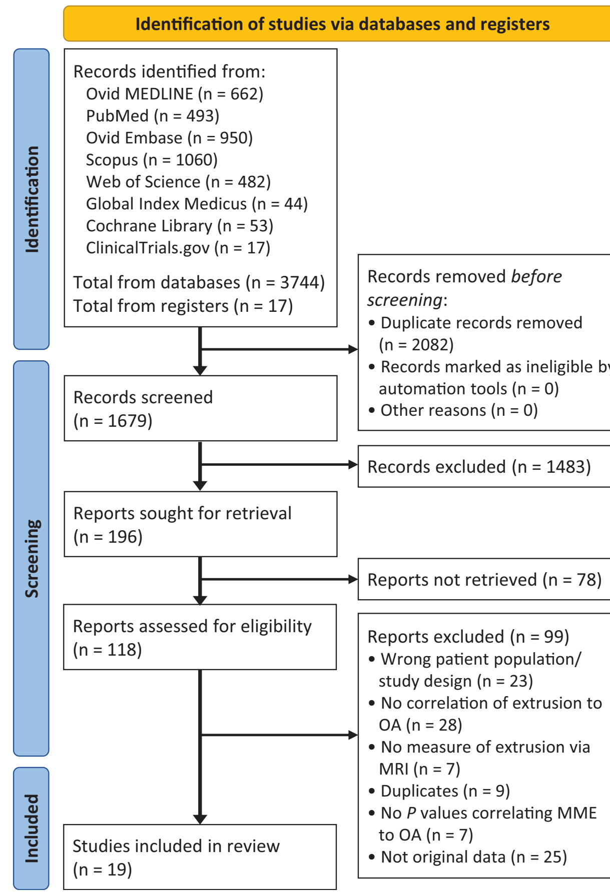

Figure 1. A PRISMA diagram detailing the study inclusion/exclusion process. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses. MME, medial meniscal extrusion; MRI, magnetic resonance imaging; OA, osteoarthritis.

RESULTS

Summary of Studies Based on Study Design

All 19 included studies were published between the years 1999 and 2021. Four articles[4,14,29,35] were prospective cohort studies evaluating patients between 2 and 10 years. Four studies[7,21,27,28] were retrospective cohort studies, 4 studies[1,2,10,36] were case-control studies, and 7 studies[6,11,12,18-20,23] were cross-sectional studies. Table 2 summarizes the study characteristics, OA outcome measures, method of measuring MME, and significant findings. A more detailed overview of the data from each study is in Supplemental Table S1 (available online).

Methods of Measuring MME

Distance Extruded Over the Tibial Plateau. Fourteen studies reported a distance measurement (in mm) to quantify and classify MME via coronal MRI images to measure the absolute distance of the meniscus extruded over the medial tibial plateau, excluding osteophyte.[¶] Most studies did not specify the method of selecting the coronal image on which they measured extrusion; these studies measured extrusion on the coronal slice on which the MME distance was greatest. Only 8 studies[6,7,18,20,21,23,27,36] reported the coronal image or image range where they took measurements. Lerer et al[23] measured MME at the level of the medial collateral ligament. Lee et al[20] used a crosslink tool to measure the distance of MME over the tibial plateau on the coronal plane at 0° with the sagittal plane. Three studies[6,18,21] measured MME at the coronal slice at the level of the midpoint of the femoral condyle. Two studies[2,12] used ranges to classify MME: <2 mm (grade 0), 2 to 2.9 mm (grade 1), 3 to 4.9 mm (grade 2), or >5 mm (grade 3). Six studies[6,19,20,23,27,28] used a cutoff of 3 mm to classify meniscal extrusion as pathologic or severe (Table 2).

Volume Extruded Over the Tibial Plateau. Seven studies[1,4,14,19,20,29,35] reported MME as a measure of volume extruded. Four studies[4,14,29,35] subjectively reported the volume of extrusion as *no extrusion* (grade 0), *partial extrusion* (grade 1), or *complete extrusion with no contact with the joint space* (grade 2). Two studies[19,20] objectively reported the volume of MME as the relative extrusion percentage

[¶]References 2,6,7,10-12,18-21,23,27,28,36.

(RPE), calculated as the percentage of the width of the extruded meniscus compared with the entire meniscus width. Adams et al[1] reported MME as extrusion of less than one-third of the body (grade 1), two-thirds of the body (grade 2), or complete extrusion (grade 3) (Table 2).

Meniscus Coverage Ratio. Wirth et al[36] used segmentation software (Chondrometrics GmbH) to take 3-dimensional meniscus shape and position measures. This approach allowed the MME not only to be measured via distance[36] but also as the percentage of the meniscus that covered the tibial plateau, with greater tibial coverage by the medial meniscus demonstrating an inverse relationship with MME (Table 2).

MME and Kellgren-Lawrence Grade

Eight studies[1,10,11,18-20,35,36] found that MME was associated with radiographic OA findings. Seven of these studies[1,10,11,18,19,35,36] reported that MME was associated with a worse radiographically measured Kellgren-Lawrence (KL) grade. Lee et al[20] reported that MME parameters (MME distance and RPE) were significantly associated with worse KL grade in patients with a root tear. However, when patients were stratified into groups based on MME <3 mm versus >3 mm, no significant differences were found in the KL grade between groups (P = .077).

MME and Joint Space Narrowing

Two studies[14,29] investigated the relationship between MME and radiographically measured joint space narrowing. Ijaz Khan et al[14] investigated the offspring of those who had a knee arthroplasty to see whether patients with a family history of OA were at higher risk of incidental OA than controls. They reported that over a 10 year period, increased volume of MME was associated with increased radiographic joint space narrowing (P < .01) and that increases in MME, but not cartilage defects or volume, were associated with increased joint space narrowing over 10 years (odds ratio, 12.3 [95% CI, 11.1-14.6]; P = .019). On the contrary, Pelletier et al[29] found that neither grade 1 nor grade 2 MME measured via volume extruded was associated with increased joint space narrowing in patients with knee OA (P = .11 and P = .10, respectively).

MME and Mechanical Alignment

Five studies[11,18-20,35] reported an association of MME with various radiographic measures of mechanical alignment. Goto et al[11] reported that an increased MME distance of >3 mm was associated with increased varus alignment as measured by the hip-knee-ankle angle (HKAA), percentage of mechanical axis, medial proximal tibial angle, and joint line convergence angle. However, an MME of <3 mm was not associated with the lateral distal femoral angle or the lateral distal tibial angle. Kim et al[18] found that the severity of MME distance was not associated with alignment via mechanical tibiofemoral angle (mean, 4.3°; range, −2.21° to 14.1°). Lee et al[20] found no significant relationship between the mechanical axis and an MME of >3 mm (3.6° ± 3°) and an MME of <3 mm (3° ± 2.3°) (P = .545). Similarly, Lee et al[19] reported that neither absolute nor relative MME was associated with varus alignment as measured by the HKAA (P = .710 and P = .325, respectively). Wang et al[35] reported no increased knee angle in knees with or without MME measured via volume (180.1° ± 7.4°; 181.2° ± 3.4° [P = .36]) (Table 2).

MME and Cartilage Thinning, Damage, or Loss on MRI

Seven studies[1,4,7,12,23,29,35] investigated the association between MME and cartilage damage, loss, or thinning via MRI. Pelletier et al[29] and Hada et al[12] found MME to be associated with cartilage damage as measured by the Whole-Organ Magnetic Resonance Imaging Score, reporting a significant association between MME and cartilage damage. Two studies used automated segmentation to calculate cartilage volume changes; Berthiaume et al[4] reported that the MME volume of the middle and anterior horns was associated with global and medial tibial plateau cartilage volume loss, while Wang et al[35] reported that although MME was not significantly associated with cartilage loss, there was a significant association between the MME volume and the increased exposed tibial bone. The remaining 3 studies[1,7,23] reported cartilage damage via different methods, all finding a statistically significant relationship between MME and cartilage damage.

MME and Osteophyte Size and Growth on MRI

Four studies[12,14,18,23] investigated the association between MME and osteophyte when measured via MRI. Hada et al[12] reported that MME was significantly associated with the medial tibial osteophyte distance measured via T2-weighted mapping MRI in patients with early-stage knee OA (multivariate β = 0.711; P < .001). However, no significant relationship was reported between MME and medial femoral osteophyte distance (multivariate β = −0.070; P = .648). Kim et al[18] reported statistical significance between the osteophyte size (mean, 1.48 mm [range, 0-4.80 mm]) and the MME severity (P < .001; Pearson r = 0.530) in patients with preoperative imaging who underwent repair for medial meniscus posterior root tear (MMPRT). Lerer et al[23] found a statistically significant association between the presence of pathologic MME (>3 mm) and moderate/large medial compartment marginal osteophytes. Ijaz Khan et al[14] investigated change in MME and radiographically measured osteophyte size over 10 years and did not find a significant relationship after adjusting for age, sex, body mass index, a family history of knee arthroplasty, and baseline MRI and radiographic features (P = .83) (Table 2).

MME and Subchondral Bone Marrow Edema

Kim et al[18] investigated the association between MME and subchondral bone edema in patients with MMPRT and

TABLE 2
Data From the 19 Studies Included in the Review[a]

Lead Author (Year)	Study Design	Sample Size	OA Outcome Measure[e]	Modality for OA Measurement	Method of MME on MRI[b]	OA Measure Associated With MME
Adams[1] (1999)	Case control	S: 32, C: 30	KL grade,[c] CL[d]	Radiograph	Volumetric	JSN, CL ($P < .001$ for both)
Allam[2] (2021)	Case control	S: 219, C: 51	SIFK[d]	MRI	DOTP	SIFK ($P < .01$)
Berthiaume[4] (2005)	Prospective cohort	32	GCVL[d]	MRI	Volumetric	GCVL ($P = .03$)
Choi[6] (2010)	Cross-sectional	248	Chondral lesions[f]	Arthroscopy	DOTP	CL ($P < .001$)
Cohen[7] (2012)	Retrospective cohort	39	Marginal osteophyte, CL[d]	MRI	DOTP	GCVL ($P < .001$), marginal osteophyte ($P = .062$)
Gale[10] (1999)	Case control	S: 234, C: 57	KL grade[c]	Radiograph	DOTP	JSN ($P < .0001$)
Goto[11] (2019)	Cross-sectional	S: 136, C: 54	KL grade[c]	Radiograph	DOTP	JSN ($P < .05$)
Hada[12] (2017)	Cross-sectional	50	Medial tibial osteophyte distance, WORMS[d]	MRI	DOTP	Medial tibial osteophyte distance ($P < .001$), CL ($P = .001$)
Ijaz Khan[14] (2016)	Prospective cohort	211	Chondral lesions,[f] JSN[c]	Radiograph	Volumetric	Chondral lesions ($P < .04$), JSN ($P < .01$)
Kim[18] (2020)	Cross-sectional	99	Chondral lesions,[f] Osteophyte distance, KL grade[c]	Radiograph	DOTP	Chondral lesions (P = .195), Osteophyte distance ($P = .001$), JSN ($P = .001$)
Lee[20] (2018)	Cross-sectional	38	Chondral lesions,[f] KL grade[c]	Radiograph	DOTP	Chondral lesions ($P = .045$), JSN ($P = .077$)
Lee[21] (2021)	Retrospective cohort	640	Progression to arthroplasty	None used	DOTP	Progression to arthroplasty ($P = .018$)
Lee[19] (2011)	Cross-sectional	102	KL grade[c]	Radiograph	DOTP	JSN ($P = .001$)
Lerer[23] (2004)	Cross-sectional	205	Presence of osteophyte, MCCL[d]	MRI	DOTP	Presence of osteophyte ($P < .0001$), MCCL ($P < .0001$)
Pareek[27] (2020)	Retrospective cohort	223	Progression to arthroplasty	None used	DOTP	Progression to arthroplasty ($P = .002$)
Pareek[28] (2020)	Retrospective cohort	S: 66, C: 183	Progression to arthroplasty	None used	DOTP	Progression to arthroplasty ($P < .001$)
Pelletier[29] (2007)	Prospective cohort	107	WORMS[d]	MRI	Volumetric	WORMS ($P = .007$)
Wang[35] (2010)	Prospective cohort	S: 53, C: 47	KL grade,[c] cartilage loss,[d] chondral lesions,[f] bone marrow lesions	MRI	Volumetric	JSN, cartilage loss, chondral lesions, bone marrow lesions ($P < .001$ for all)
Wirth[36] (2010)	Case control	S: 31, C: 11	KL grade[c]	Radiograph	DOTP	JSN ($P = .008$)

[a]C, controls; CL, cartilage loss; DOTP, distance over the tibial plateau; GCVL, global cartilage volume loss; JSN, joint space narrowing; KL, Kellgren-Lawrence; MCCL, medial compartment cartilage loss; MME, medial meniscal extrusion; MRI, magnetic resonance imaging; S, study patients; SIFK, subchondral insufficiency fracture of knee; WORMS, Whole-Organ Magnetic Resonance Imaging Score.

[b]DOTP = MME was measured as the horizontal distance between the medial edge of the tibial plateau and the most medial margin of the meniscus on coronal slices. Volumetric = MME was calculated as a percentage or volume of the medial meniscus extruded over the tibial plateau.

[c]Indirect measurements of cartilage loss were obtained via knee radiography.

[d]Direct measurements of cartilage loss were obtained via MRI.

[e]Indicates methods that quantified OA outcomes via cartilage loss.

[f]Chondral lesions included a variety of cartilage defects, including fissuring, fraying, swelling, and ulceration.

found that knees with subchondral bone edema had a mean MME distance of 4.76 mm compared with 4.35 mm in those without edema. However, this relationship was not statistically significant ($P = .195$) (Table 2).

MME and Arthroscopically Graded Cartilage Lesions

Two studies[6,19] investigated cartilage lesions arthroscopically, reporting conflicting results. Choi et al[6] reported worsening cartilage lesions via Outerbridge scores with increasing MME distance in preoperative MRIs. Lee et al[19] reported no significant relationship between the volume of MME (when measured via RPE) or the MME distance and chondral lesions on the medial tibial plateau or medial femoral condyle via Outerbridge scores. Both studies looked at patients with medial meniscal tears (Table 2).

MME and Subchondral Bone Insufficiency Fracture of the Knee

Allam et al[2] reported that in patients with subchondral bone insufficiency fracture of the knee (SIFK), knees with greater MME distance were more likely to have more severe SIFK lesions based on the surface area of the articular cartilage involved. Also, 90% of high-grade SIFK lesions were either associated with moderate (3-5 mm) or severe (>5 mm) MME distance (Table 2).

MME and Bone Cysts

Two studies[12,35] investigated MME and tibiofemoral bone cysts. Wang et al[35] found that increased MME volume predicted a greater incidence of medial and total tibiofemoral bone cysts but not lateral tibiofemoral bone cysts over 2 years in patients with knee OA. Hada et al[12] reported similar results in a cross-sectional study, finding that the distance of MME was associated with a greater incidence of subchondral bone cysts in patients with early-stage knee OA. However, a multivariate analysis did not demonstrate a significant relationship between MME distance and subchondral bone cysts (Table 2).

MME and Pain and Function Scores

Wang et al[35] reported no association with MME and the Western Ontario and McMaster Universities Osteoarthritis Index scores over 2 years, although a trend was noted for increased patient-reported stiffness in those with MME (Table 2).

MME and Progression to Arthroplasty

Three retrospective cohort studies[21,27,28] used progression to arthroplasty as an indicator of OA, finding that MME at baseline was associated with a higher likelihood of patients having total knee arthroplasty. Lee et al[21] reported that among those with MMPRT, patients with increasing MME distance had a greater likelihood of surgical intervention and progression to arthroplasty. The other 2 studies[27,28] found a significant relationship between MME distance and progression to arthroplasty in patients with SIFK (Table 2).

Relationship Between MME and OA Development/Progression

Eight studies[4,7,14,21,27-29,35] measured the effects of MME on OA changes over time. Four of these studies[4,7,29,35] investigated the relationship between MME and cartilage volume loss over time. Berthiaume et al[4] found that MME volume of the middle and anterior horns was associated with global and medial compartment cartilage volume loss (calculated via MRI) over 2 years in patients with preexisting knee OA. Cohen et al[7] reported that the MME distance was more common in those who experienced progressive cartilage volume loss over a 7 year period compared with those without cartilage loss in populations with a meniscal tear that did not undergo meniscectomy. Pelletier et al[29] reported that both MME and severe MME—defined as extrusion of the entire volume of the medial meniscus—were associated with global and medial compartment cartilage loss over 2 years in patients with knee OA. The study by Wang et al[35] was the only study that did not find an association between MME and medial tibial cartilage loss over time; however, they did report that MME had a significant association with increased exposed medial tibial bone and medial tibial bone marrow lesions over 2 years in patients with knee OA.

In addition, Ijaz Khan et al[14] reported that MME was associated with increased joint space narrowing over 10 years, although no significant relationship was noted between MME and osteophyte progression. Two studies[27,28] reported that MME was significantly associated with an increased risk of progression to arthroplasty for patients with SIFK. Lee et al[21] found that the MME distance was associated with a higher probability of surgical intervention and progression to arthroplasty in patients with MMPRT (Table 2).

DISCUSSION

The most important finding of this systematic review was an associative relationship between MME and OA. Still, additional research is warranted to better establish the associative versus causal relationship between MME and OA and standardize the methods of measuring MME. All 19 studies reported that MME was significantly associated with at least 1 knee OA outcome; 9 of the 19 studies demonstrated MME was significantly associated with higher KL grade[#] or joint space loss analog, namely medial cartilage loss measured by MRI.[1,10,11,14,18-20,35,36] MME was significantly associated with progression to arthroplasty in 3 studies.[21,27,28] Although our findings did not provide sufficient evidence for a causal relationship, the findings highlight the protective function of the meniscus.[9] The inability to dissipate hoop stresses causes extrusion of the menisci, which is thought to lead to biomechanical overloading of the joint articular surface and accelerated cartilage loss.[25] While an association exists between MME and knee OA outcomes, causal links remain unconfirmed and require future studies. This review also highlighted the lack of standardization in measuring MME.

Although all studies included in this review demonstrated a significant association between MME and an assortment of OA sequela, some results reported in the studies demonstrated nonsignificant associations between MME and other OA features. Lee et al[20] reported that MME >3 mm only trended to significance when the KL grade was lower (P = .077). As 95% (36/38) of patients in their study had a KL grade of <2, it is possible that significant findings would have been found in a larger cohort or 1 cohort with more severe OA. Previous research in a larger population has found a significant relationship between MME and KL grade.[8] Kim et al[18] reported that MME was not associated with subchondral edema, a precursor of tibiofemoral cysts. As 2 studies[12,35] in this review reported a significant relationship with tibiofemoral cysts, it is possible that subchondral edema may not have been a severe enough characteristic of OA to demonstrate a significant relationship with MME.

The studies included in this review did not report consistent results investigating the relationship between MME and knee alignment.[11,18-20,35] As none of the studies

[#]References 1,10,11,14,18-20,35,36.

that investigated mechanical alignment in the present review did so over time, further research is needed to examine whether MME precedes varus deformity or whether MME is exacerbated as a result of varus deformity. Conflicting conclusions regarding MME and osteophytes were also reported.[12,14] Ijaz Khan et al[14] found no significant relationship between osteophyte progression and MME over 10 years. However, this may have been because these researchers grouped tibial and femoral osteophytes together. Tibial osteophytes may be more closely associated with MME because of the coronary ligament, which attaches the medial meniscus to the tibia.[9] As tibial osteophytes grow medially, the coronary ligament may pull the meniscus with it centrally, exacerbating extrusion. This premise is supported by Hada et al,[12] who demonstrated significant findings between MME and tibial, but not femoral, osteophyte size. Despite some conflicting results, every study reported that MME was associated with at least 1 feature of knee OA, despite measuring MME with different methods.

The most common method of measuring MME was by assessing the absolute distance of MME over the medial tibial plateau, with 14 studies using this method.** This method is advantageous because it is quick, simple, and does not require segmentation software. An extrusion distance of 3 mm was a commonly used threshold, which either categorized MME as grade 2 (on a scale from 0 to 3)[2,12] or as pathologic or severe.[6,19,20,23,27,28] A threshold of 3 mm of extrusion is commonly cited in the literature. However, Liu et al[24] reported that a threshold of 2.5 mm of extrusion was found to be most useful for predicting knee pain and cartilage damage progression over 4 years in an OA cohort. Contrary to these findings, other research has reported that a threshold of 4 mm instead of 3 mm maximizes the sensitivity (from 54% to 61%) and specificity (from 64% to 79%) with respect to bone marrow lesions, cartilage damage, and radiographic OA.[33]

One limitation of measuring MME as the distance extruded over the tibial plateau is that the absolute value of MME distance may be greater in larger knees due to larger menisci, not necessarily greater MME. Another limitation of this method is that MME values, as measured via distance extruded over the tibial plateau, may not be accurate or comparable between studies, as most studies did not specify the coronal image on which MME distance was measured. Only 8 of the 14 studies reported the method of obtaining the coronal slice on which they measured MME distance.[6,7,18,20,21,23,27,36] The other 6 studies used the coronal image demonstrating the maximal MME distance.[2,10-12,19,28] Previous research has demonstrated that this method of measuring the maximum MME distance (referred to as the "coronal slices" method) can inaccurately report MME, as this method often does not measure MME truly perpendicular to the tibial plateau, which can lead to an overestimation of MME.[16] Because of measurements that are not truly perpendicular to the tibial plateau, Jones et al[16] reported that MME distance measured via the coronal slices method was significantly greater (median, 4.8 mm; mean ± SD, 4.7 ± 1.7 mm) than when it was measured using the tibial spine as a landmark (median, 2.2 mm; mean ± SD, 2.4 ± 1.5 mm) or when segmented manually, which was the reference standard (median, 3.1 mm; mean ± SD, 2.4 ± 1.5 mm). As most studies in this review used the coronal slices method to measure the MME distance, these studies may have overestimated the MME distance. Jones et al[16] suggested that measuring MME at the level of the medial tibial spine is a reasonable proxy for the more labor-intensive method of manual segmentation. It is important to note that none of the included studies in this review used this method.

Seven studies characterized MME via the volume or ratio of the meniscus extruded.[1,4,14,19,20,29,35] One issue in this review was the subjectivity in measuring MME volume. Four of the 7 studies that reported MME via the volume extruded did so via a largely subjective scale, grading extrusion as none, partial, or complete.[4,14,29,35] Among these 4 studies, only Wang et al[35] reported intra- and interobserver intraclass correlation coefficients, which indicated excellent reliability (range, 0.85-0.92). While grouping MME volume into 3 grades is an easy way to classify MME volume, the subjective nature of grading may limit the widespread adoption of classifying MME via this method, as well as the external validity of these findings to be compared with other more objective values of MME distance or MME volume. Two studies reported MME as the RPE, which is calculated as the percentage of the width of the extruded meniscus compared with the entire meniscus width.[19,20] Beyond limiting the subjectivity involved with measuring the MME volume, RPE is beneficial as a measurement method as it provides a standardized measure for knees of different sizes. However, as the RPE includes a measure of extrusion distance, it is subject to the same potential pitfalls as mentioned above if using the coronal slices method.

One study manually segmented the meniscus to report the MME distance and the tibia area that was not covered by the medial meniscus.[36] Manually segmenting the meniscus allowed these researchers to further quantify meniscus thickness, shape, and size. They reported a greater size, increased MME, greater tibial area uncovered by the meniscus, and elevated signal intensity of the medial meniscus in knees with OA.[36] These findings are consistent with previous research reporting greater meniscus volume in knees with OA, suggesting that not all menisci in these knees are macerated or destroyed.[17,37] Although these meniscal characteristics retrieved from manually segmenting the meniscus are insightful, the time and software required to take these measurements may limit the widespread adoption of this method.

Limitations

We acknowledge that our systematic review has limitations, one being that we required studies to analyze original, nonpublicly accessible data. Our criteria were set to

**References 2,6,7,10-12,18-21,23,27,28,36.

use original data to potentially allow for a meta-analysis, which was unable to be completed because of the heterogeneity of the data. We acknowledge that many studies report valid findings investigating MME and OA using publicly accessible data. However, we believe it is a strength to investigate studies that reported original data, as conclusions are drawn from unique populations. Another limitation was the variation of MRI equipment and imaging protocols used. This systematic review included MRIs completed with magnets ranging from 0.25 to 3 T, with slice thickness varying from 1 to 4 mm, and reported interslice gaps ranging from 0 to 1 mm. Different imaging protocols and slice thickness may impact the accuracy of comparisons of MME measurements between studies.

Furthermore, in this study, we focused solely on MRI as the modality to measure MME. We intentionally excluded studies that utilized other modalities to measure MME, such as ultrasound or radiographs. The rationale behind this decision was that making measurements or comparisons from images obtained through different modalities could introduce considerable interstudy variability, leading to incomparable results (eg, comparing MME measured on ultrasound to MME measured on MRI). Further, MRI was selected as the exclusive modality for measuring MME because it is widely recognized as the gold standard for measuring MME. The superior accuracy and detailed soft tissue visualization capabilities make MRI the most reliable method for assessing MME. By employing MRI exclusively, we aimed to ensure consistency throughout our study.

Another limitation is that all the identified studies were observational, meaning strict control was impossible. Overall, major limitations arose from the lack of standardized MME measurement and outcome measures for OA. Last, we did not conduct a meta-analysis of MME and OA outcomes. A statistician was consulted to investigate whether a meta-analysis was possible; nonetheless, a meta-analysis was not completed because of the heterogeneity of the studies included. Studies employed different methods of measuring MME with varying imaging protocols. Studies also evaluated different arthritis outcomes, making the intervariability between studies too large for a valid meta-analysis. Moreover, many studies did not provide exact P values, which interfered with completing a meta-analysis. Despite not completing a meta-analysis, we believe the statistical significance reported from the 19 studies still demonstrates an obvious relationship between MME and OA outcomes. Furthermore, while the heterogeneity of data between studies may have prevented a valid meta-analysis from being completed, we believe that including a broad range of studies with diverse data strengthened our systematic review.

CONCLUSION

The findings of this systematic review indicated that the OA outcome measures associated with MME were as follows: increased KL grade; cartilage damage; varus alignment; progression to arthroplasty; and osteophyte. This review is the first to investigate and summarize the different MRI methods of measuring MME. While there was an association between MME and various knee OA outcome measures, a causal relationship could not be established because of the observational nature of the studies reviewed.

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ORCID iDs

Edward R. Floyd https://orcid.org/0000-0003-2448-9958
Jutta M. Ellermann https://orcid.org/0000-0002-7109-9656

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