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Factors Associated with Meniscal Extrusion in Knees with or at Risk for Osteoarthritis: The Multicenter Osteoarthritis Study[1]

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Purpose: To assess the associations of meniscal tears, knee malalignment, cartilage damage, knee effusion, and body mass index with meniscal extrusion.

Materials and Methods: The Multicenter Osteoarthritis study is an observational study of individuals who have or are at risk for knee osteoarthritis (OA). The HIPAA-compliant protocol was approved by the institutional review boards of all participating centers, and written informed consent was obtained from all patients. All subjects with available baseline knee radiographs and magnetic resonance (MR) images were included. MR imaging assessment of meniscal morphologic characteristics, meniscal position, and cartilage morphologic characteristics with use of the Whole-Organ Magnetic Resonance Imaging Score system was performed by two musculoskeletal radiologists. Cross-sectional associations of severity of meniscal tears, knee malalignment, tibiofemoral cartilage damage, knee effusion, and body mass index with meniscal extrusion were assessed by using logistic regression, with multiadjustments when testing each predictor.

Results: A total of 1527 subjects (2131 knees; 2116 medial and 2106 lateral menisci) were included. Medially, meniscal tears, varus malalignment, and cartilage damage were associated with meniscal extrusion, with odds ratios (ORs) of 6.3 (95% confidence interval [CI]: 5.0, 8.0), 1.3 (95% CI: 1.1, 1.7), and 1.8 (95% CI: 1.4, 2.2), respectively. Laterally, meniscal tears, valgus malalignment, and cartilage damage were associated with meniscal extrusion, with ORs of 10.3 (95% CI: 7.1, 14.9), 2.2 (95% CI: 1.5, 3.2), and 2.0 (95% CI: 1.3, 2.9), respectively.

Conclusion: Meniscal tears are not the only factors associated with meniscal extrusion; other factors include knee malalignment and cartilage damage. Meniscal extrusion is probably an effect of the complex interactions among joint tissues and mechanical stresses involved in the OA process.

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The role of meniscal pathologic findings in knee osteoarthritis (OA) has been extensively explored, including prediction of incident knee OA on radiographs and structural deterioration of the surrounding articular tissues (1–16). Meniscal pathologic findings are common among persons with and without knee OA (17–19). In the knee joint, the role of the menisci includes important functions, such as load bearing, shock absorption, lubrication, and joint stability (20,21). Thus, mechanical impairment of the meniscus caused by tearing or extrusion may alter the weight-bearing capacities of the tibiofemoral compartments, leading to damage in the articular cartilage, as well as in the subchondral bone, ultimately contributing to progression of knee OA (1,2,5,16). It has been demonstrated that meniscal extrusion is an independent predictor of tibiofemoral cartilage loss (2,4,8,9,13,15) and degenerative subchondral bone marrow lesions (10,16). Thus, the knowledge of potential factors associated with meniscal extrusion is of utmost importance, as it may help prevent extrusion and further deterioration of the adjacent articular cartilage and subchondral bone.

Tearing of the meniscus is a known factor related to meniscal extrusion (22–26). Although root tears are considered by many authors as the most relevant factor associated with extrusion of the meniscus (25,27–29), it has been demonstrated that several types of meniscal tears, including nonroot tears, are also related to meniscal extrusion (23,24,30). Magnetic resonance (MR) imaging has become established as the most important imaging modality in the assessment of knee pathologic findings, exhibiting excellent diagnostic performance in the detection of meniscal pathologic abnormalities (31,32). Also, MR imaging has proved to be a useful tool in the assessment of meniscal extrusion (2,9,22).

Other factors may also be related to meniscal extrusion, even when no other meniscal pathologic findings are detected (25,26,33). Factors such as knee malalignment, tibiofemoral cartilage loss, and body mass index (BMI) might increase the load transmitted to the tibiofemoral compartments, and thus to the menisci, which may lead to meniscal extrusion. Also, it has been demonstrated that knee effusion may be responsible for meniscal extrusion in the medial compartment, since displacement of the joint capsule by fluid might pull the tightly attached medial meniscus with it (34).

In the present study, we aimed to assess the cross-sectional association of meniscal tears with meniscal extrusion in subjects who have or are at risk for knee OA. Also, we aimed to assess the cross-sectional associations of factors other than meniscal tears, such as tibiofemoral cartilage damage, knee malalignment, knee effusion, and BMI, with meniscal extrusion in the same tibiofemoral compartment.

Advances in Knowledge

- All Whole-Organ Magnetic Resonance Imaging Score grades of severity of meniscal pathologic findings are independently associated with meniscal extrusion, with higher grades of meniscal tears having stronger associations with meniscal extrusion in both compartments; root tears are strongly and independently associated with meniscal extrusion in the medial compartment.
- Factors other than meniscal tears, such as tibiofemoral cartilage damage and knee malalignment, are independently associated with meniscal extrusion in the same tibiofemoral compartment.

Implication for Patient Care

- Several factors are associated with meniscal extrusion; targeting such factors during management might help prevent meniscal extrusion and further deterioration of the tibiofemoral joint in subjects who have or are at risk for knee osteoarthritis (OA); further exploration of the longitudinal effect of management of these factors on meniscal extrusion and on progression of knee OA is needed.

Materials and Methods

Two authors (M.D.C. and M.D.M.) are shareholders in and one author (F.W.R.) is vice president of and partner in Boston Imaging Core Lab (Boston, Mass), a company that provides radiologic image assessment services. One author (A.G.) is president of Boston Imaging Core Lab. Four authors (D.T.F., M.C.N., J.C.T., and C.E.L.) had control of the data.

Study Design and Subjects

Subjects were participants in the Multicenter Osteoarthritis (MOST) study, a prospective epidemiologic study of 3026 people aged 50–79 years (overall mean age, 62.5 years) with a goal of identifying risk factors for incident and progressive knee OA in a population either with or at high risk of developing

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Abbreviations:
BMI = body mass index
CI = confidence interval
MOST = Multicenter Osteoarthritis
OA = osteoarthritis
OR = odds ratio
STIR = short-tau inversion recovery
WORMS = Whole-Organ Magnetic Resonance Imaging Score

Author contributions:
Guarantors of integrity of entire study, M.D.C., M.C.N., J.C.T., A.G.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; literature research, M.D.C., F.W.R., M.E., M.D.M., A.G.; clinical studies, F.W.R., D.T.F., M.J., J.T., A.G.; statistical analysis, K.W.; and manuscript editing, M.D.C., F.W.R., D.T.F., M.E., M.D.M., J.C.T., A.G.

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Potential conflicts of interest are listed at the end of this article.

OA. Included were 1820 female (mean age, 62.7 years; range, 50–79 years) and 1206 male (mean age, 62.2 years; range, 50–79 years) patients. They were recruited from two U.S. communities (Birmingham, Ala, and Iowa City, Iowa) through mass mailing of letters and study brochures, supplemented by media and community outreach campaigns. The Health Insurance Portability and Accountability Act–compliant study protocol was approved by the institutional review boards at the University of Iowa, University of Alabama at Birmingham, University of California at San Francisco, and Boston University School of Medicine. We obtained written informed consent from all patients. Participants at high risk of developing OA considered in the MOST study *(a)* were overweight or obese subjects; *(b)* were subjects with knee pain, aching, or stiffness on most of the past 30 days; *(c)* had a history of knee injury that made it difficult to walk for at least 1 week; and *(d)* had a history of knee surgery. Subjects were not eligible to participate in the MOST study if they had positive results of screening for rheumatoid arthritis (35); had ankylosing spondylitis, psoriatic arthritis, reactive arthritis, renal insufficiency that required hemodialysis or peritoneal dialysis, or a history of cancer (except for nonmelanoma types of skin cancer); underwent or planned to undergo bilateral knee replacement surgery; were unable to walk without assistance; or were planning to move out of the area in the next 3 years.

In the present study, we included all participants with available baseline radiographs and MR images of the knee. These knees were previously selected for one or more of three substudies in the MOST study: *(a)* a cohort study of risk factors for radiographically depicted OA progression that included randomly selected knees with either patellofemoral or tibiofemoral OA; *(b)* a case-control study of risk factors for incident OA on radiographs; and *(c)* a case-control study of risk factors for onset of consistent, frequent knee pain (36). Of all subjects eligible to participate in the MOST study, 2131 knees from 1527 subjects were examined with both long-limb radiography and MR imaging of the knee at baseline and were included in the analysis.

Radiographs

At baseline, all subjects underwent weight-bearing posteroanterior fixed-flexion knee radiography by using the protocol of Peterfy et al (37) and a Plexiglas positioning frame (SynaFlexer; Synarc, San Francisco, Calif). Long-limb radiographs were acquired with a 14 × 51-inch cassette. Mechanical alignment was measured as the angle formed by the intersection of the femoral and tibial mechanical axes. The femoral mechanical axis is the line from the center of the femoral head through the center of the knee, and the tibial mechanical axis is drawn as a line from the center of the ankle to the center of the knee. Neutral alignment was defined as 179°–181°, varus malalignment as 178° or less, and valgus malalignment as 182° or greater. A musculoskeletal radiologist and a rheumatologist, who are not authors of this work, who both had more than 10 years of experience in reading study radiographs and were blinded to clinical data, independently graded the radiographs according to the Kellgren-Lawrence scale (38). Radiographs were presented sequentially, with readers blinded to all clinical data and to MR imaging findings. Radiographic tibiofemoral OA was considered present if the Kellgren-Lawrence grade was two or higher. If readers disagreed on the presence of radiographically depicted OA, readings were adjudicated by a panel of three readers (two nonauthors and D.T.F.).

MR Image Acquisition

MR images were obtained in both knees at baseline with a 1.0-T dedicated extremity unit (ONI MSK Extreme; GE Healthcare, Waukesha, Wis) with a circumferential extremity coil using fat-suppressed fast spin-echo proton density–weighted sequences in two planes, sagittal (repetition time msec/echo time msec, 4800/35; section thickness, 3 mm; intersection gap, 0 mm; number of sections, 32; matrix, 288 × 192; number of signals acquired, two; field of view, 140 × 140 mm; echo train length, eight) and axial (4680/13; section thickness, 3 mm; intersection gap, 0 mm; number of sections, 20; matrix, 288 × 192; number of signals acquired, two; field of view, 140 × 140 mm; echo train length, eight), and a short-tau inversion-recovery (STIR) sequence in the coronal plane (repetition time msec/echo time msec/inversion time msec, 6650/15/100; section thickness, 3 mm; intersection gap, 0 mm; number of sections, 28; matrix, 256 × 192; number of signals acquired, two; field of view, 140 × 140 mm; echo train length, eight). Examinations were performed at the University of Alabama at Birmingham and at the University of Iowa at Iowa City by using the same MR unit.

MR Image Interpretation

Two musculoskeletal radiologists (F.W.R. and A.G., with 7 and 9 years of experience, respectively, in standardized semiquantitative MR imaging assessment of knee OA), who were blinded to radiographically determined OA grade and clinical data, independently graded meniscal and tibiofemoral cartilage status according to the Whole-Organ Magnetic Resonance Imaging Score (WORMS) system (39). A recent study showed that WORMS assessment with use of a 1.0-T dedicated extremity MR system is possible with a moderate to high degree of agreement and accuracy compared with WORMS assessment performed with a 1.5-T large-bore MR unit (40). The presence of motion artifacts or field inhomogeneity on MR images in some knees did not allow the assessment of features such as meniscal morphologic characteristics and extrusion in one of the tibiofemoral compartments of the knee, and those menisci were excluded. The anterior horn, body, and posterior horn of the medial and lateral menisci were evaluated separately, and findings were assigned grades (grade 0, intact; grade 1, minor radial tear or parrot-beak tear; grade 2, nondisplaced tears including horizontal and vertical tears or prior surgical repair; grade 3,

displaced tears including displaced flap tears and bucket-handle tears, or partial resection or maceration; and grade 4, complete maceration or destruction or complete resection). A meniscal tear was designated only when an abnormal meniscal signal intensity touched the articular surface of the meniscus on at least two consecutive sections (31). The presence of meniscal root tears, which is not evaluated in the WORMS system, was assessed in both menisci of all knees included in our study sample by a trained musculoskeletal radiology fellow (M.J.), by using the coronal STIR images. Meniscal root tears were assessed as present or absent.

Cartilage morphologic characteristics and signal were scored semiquantitatively from zero to six in each of the five subregions in the medial and lateral tibiofemoral compartments (grade 0, normal thickness and signal; grade 1, normal thickness but increased signal on proton density–weighted or STIR images; grade 2.0, partial-thickness focal defect < 1 cm in greatest width; grade 2.5, full-thickness focal defect < 1 cm in greatest width; grade 3, multiple areas of partial-thickness defects intermixed with areas of normal thickness, or a grade 2.0 defect wider than 1 cm but $< 75\%$ of the region; grade 4, diffuse [$\geq 75\%$ of the region] partial-thickness loss; grade 5, multiple areas of full-thickness loss or a grade 2.5 lesion wider than 1 cm but $< 75\%$ of the region; and grade 6, diffuse [$\geq 75\%$ of the region] full-thickness loss). Knee effusion was scored semiquantitatively from zero to three in terms of maximal distention of the synovial cavity: score 0, absence of effusion; score 1, less than 33% of maximal potential distention; score 2, 33%–66% of maximum potential distention; and score 3, greater than 66% of maximal potential distention.

Extrusion of the medial and lateral meniscal body was assessed by using coronal STIR images. The reference section for extrusion assessment in all knees is the one where the medial tibial spine has the greatest volume (2,9). The edge of the tibial plateaus (excluding osteophytes) was used as the reference for measuring extrusion of the body of both menisci (Fig 1). Medial and lateral meniscal extrusion was assigned grade 0–2 (grade 0, no extrusion; grade 1, extrusion $\leq 50\%$ of the body; grade 2, extrusion $> 50\%$ of the body [Fig 2]).

The weighted κ coefficients of interobserver reliability (30 knees randomly selected and images obtained in those knees read by both readers) were 0.80 for meniscal morphologic characteristics, 0.65 for meniscal extrusion, and 0.78 for cartilage morphologic characteristics.

Figure 1

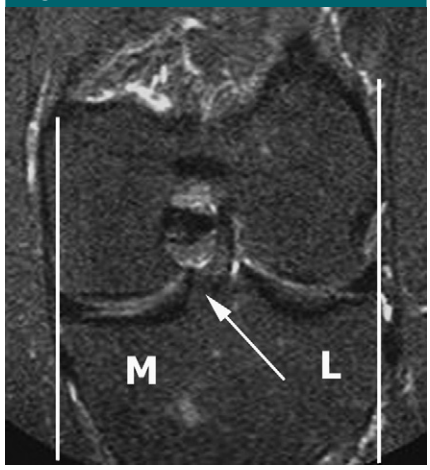

Figure 1: Coronal STIR image used for the assessment of medial and lateral meniscal extrusion. The section of reference is the one where the medial tibial spine (arrow) is seen with its greatest volume. Vertical lines passing by the outer edge of medial *(M)* and lateral *(L)* tibial plateaus, excluding osteophytes, are used as reference to assess extrusion of the body of the meniscus. No extrusion is seen on this image (grade 0).

Figure 2

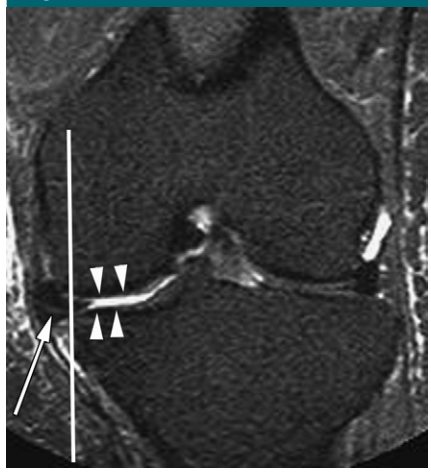

Figure 2: Coronal STIR image shows a grade 2 extrusion of the body of the medial meniscus. A single horizontally oriented oblique tear is depicted in the body of the medial meniscus (arrow). Note areas of cartilage damage in the medial tibiofemoral compartment (arrowheads).Vertical line = reference line for measuring extrusion in the coronal plane.

Statistical Analysis

Prevalent meniscal extrusion was defined as grade 1 or higher. Prevalent meniscal damage was defined as grade 1 or higher. To evaluate whether meniscal pathologic findings as classified with the WORMS (grades 1–3) is associated with meniscal extrusion, only the maximum of the meniscal regions (anterior, body, and posterior) was considered for the analysis (eg, anterior, grade 1; body, grade 2; posterior, grade 1; overall score for the whole meniscus, grade 2). Grade 4 menisci were excluded from the analysis, as they represent complete maceration or complete resection of the meniscus, and measurement of extrusion is not possible. Tibiofemoral cartilage damage was defined as grade 2 or higher in any of its five medial or lateral subregions. Abnormal intrasubstance cartilage signal with normal cartilaginous morphologic characteristics (grade 1) was not considered cartilage damage, as it demonstrates limited sensitivity for cartilaginous pathologic findings in the knee, by using arthroscopy as the reference standard (41,42). To evaluate whether tibiofemoral cartilage status is associated with meniscal extrusion, only the maximum of each medial or lateral tibiofemoral subregion was considered for the analysis. The presence of knee effusion was defined as grade 1 or higher.

Medial and lateral meniscal extrusion was considered the outcome. Factors considered for association with medial meniscal extrusion were medial meniscal damage (including both WORMS and meniscal root tears),

Table 1

Associations between Medial Meniscal Tears and Medial Meniscal Extrusion

Meniscal Tear	Prevalent Extrusion*: Absence at Baseline, Score 0	Prevalent Extrusion*: Presence at Baseline, Score ≥ 1	Adjusted OR†
Absence of meniscal tear at baseline, score 0	1004 (47.4)	395 (18.6)	1.0 (reference)
Presence of any meniscal tear at baseline, score ≥ 1‡	176 (8.3)	541 (25.6)	6.3 (5.0, 8.0)§
Extent of meniscal tear‡			
Grade 1	41 (1.9)	59 (2.8)	3.6 (2.3, 5.7)§
Grade 2	90 (4.2)	195 (9.2)	4.6 (3.5, 6.2)§
Grade 3	45 (2.1)	287 (13.6)	12.7 (8.8, 18.3)§
Root tear	3 (0.1)	51 (2.4)	10.2 (3.0, 34.1)§

* Numbers in parentheses are percentages.

† All main effects (meniscal damage including root tears, tibiofemoral cartilage damage, knee malalignment, knee effusion, BMI) and covariates (age and sex) were simultaneously entered into the model.

‡ Three missing values.

§ A significant difference was defined as one with $P < .05$. Numbers in parentheses are 95% CIs.

medial tibiofemoral cartilage damage, knee effusion, and varus alignment. Factors considered for association with lateral meniscal extrusion were lateral meniscal damage (WORMS only), lateral tibiofemoral cartilage damage, knee effusion, and valgus alignment. Because only three root tears were found in the lateral meniscus, we were not able to test their association with meniscal extrusion, nor could we include them in models for adjustment. Reference groups for analyses were: normal meniscus (grade 0); absence of compartmental cartilage defect (grades 0 and 1); absence of knee effusion, neutral and valgus alignment (medial meniscus); and neutral and varus alignment (lateral meniscus).

Cross-sectional associations were performed by using logistic regression with generalized estimating equations to account for correlations among the subregions within a knee (using one knee per person) with multiadjustments performed when testing each predictor. The effect of baseline BMI on meniscal extrusion was also tested by using logistic regression, with baseline BMI used as a continuous variable (odds ratios [ORs] were based on one unit increase in baseline BMI). All main effects (meniscal damage, tibiofemoral cartilage damage, knee malalignment, BMI) and covariates (age and sex) were simultaneously entered into the model. All statistical calculations were performed by using software (SAS, version 9.1 for Windows; SAS Institute; Cary, NC).

Results

Participants' Characteristics

A total of 2131 knees (2116 medial and 2106 lateral menisci) were included. The subjects' mean age was 62.3 years ± 8.0 (standard deviation), with a mean BMI of 30.1 kg/m^2 ± 5.0 and a range of 18.0–55.8 kg/m^2. Also, of the subjects (n = 1527), 61.5% (n = 939) were women, and 38.5% (n = 588) were men. In addition, 36.5% had tibiofemoral radiographic OA (Kellgren-Lawrence grade ≥ 2) at baseline (n = 557). Further, in 1326 (62.2%) knees, effusion was detected at baseline, and of this number of knees, the Kellgren-Lawrence grade was as follows: 926 (69.8%) knees, grade 1; 337 (25.4%) knees, grade 2; and 63 (4.8%) knees, grade 3.

Medial Compartment

Medially, 16 menisci were excluded, as they were not assessable, mainly because of motion artifacts or field inhomogeneity at baseline that did not allow scoring of the features evaluated (meniscal tears and extrusion). Also, two medial menisci were excluded, as they were grade 4 (complete maceration or resection).

Prevalent extrusion was found in 936 (44.2%) medial menisci, prevalent tears (WORMS grades 1–3) were found in 717 (33.9%) medial menisci, prevalent root tears were found in 54 (2.6%) medial menisci, prevalent cartilage damage was found in 1334 (63.0%) medial compartments, and prevalent varus alignment was found in 961 (45.1%) knees. Among the 936 medial menisci that exhibited extrusion, 541 (57.8%) had concomitant tears (WORMS grade ≥ 1); of these tears, 51 (5.4%) were root tears. Prevalent medial meniscal tears showed a strong association with prevalent medial meniscal extrusion, with an OR of 6.3 (95% confidence interval [CI]: 5.0, 8.0; $P < .0001$). Higher WORMS grades of medial meniscal tears had stronger associations with extrusion in the medial meniscus (P value for trend, < .0001) (Table 1). Root tears were strongly associated with prevalent medial meniscal extrusion, with an OR of 10.2 (95% CI: 3.0, 31.4; P = .0002) (Table 1).

The associations of prevalent medial tibiofemoral cartilage, prevalent varus malalignment, and prevalent effusion with medial meniscal extrusion are shown in Table 2. Prevalent medial tibiofemoral cartilage damage showed a significant association with medial meniscal extrusion, with an OR of 1.8 (95% CI: 1.4, 2.2; P = .0001). Considering different extents of medial cartilage damage, we found that focal cartilage defects (WORMS grades 2 and 2.5 combined) were not significantly associated with medial meniscal extrusion. Medial compartments with areas of partial-thickness cartilage loss (WORMS grades 3 and 4 combined), as well as compartments with areas of full-thickness cartilage loss (WORMS grades 5 and 6 combined), were significantly associated with medial meniscal extrusion (ORs of 1.7 [95% CI: 1.3, 2.1; P = .0002] and 3.2 [95% CI: 2.4, 4.4; $P < .0001$]), respectively.

Prevalent varus alignment demonstrated a significant association with prevalent medial meniscal extrusion, with an OR of 1.3 (95% CI: 1.1, 1.7; P = .005). No significant association was found between BMI and meniscal extrusion, nor between knee effusion and meniscal extrusion in the medial compartment.

Lateral Compartment

Laterally, 15 menisci were excluded, as they were not assessable, mainly because of motion artifacts or field inhomogeneity at baseline that did not allow scoring of the features evaluated (meniscal tears and extrusion). Also, 14 lateral menisci were excluded, as they were grade 4 (complete maceration or resection).

Prevalent extrusion was found in 199 (9.4%) lateral menisci, prevalent tears (WORMS grades 1–3) were found in 214 (10.2%) lateral menisci, prevalent root tears were found in three (0.1%) lateral menisci, prevalent cartilage damage was found in 932 (44.3%) lateral compartments, and prevalent valgus alignment was found in 319 (15.0%) knees. Among the 199 lateral menisci that exhibited extrusion, 102 (51.3%) had concomitant tears (WORMS grade ≥ 1); of these tears, two (2.0%) were root tears. Prevalent lateral meniscal tears showed a strong association with prevalent lateral meniscal extrusion, with an OR of 10.3 (95% CI: 7.1, 14.9; P < .0001). Higher WORMS grades of lateral meniscal tears had stronger associations with extrusion in the lateral meniscus (P value for trend, < .0001) (Table 3).

The associations of prevalent lateral tibiofemoral cartilage, prevalent valgus malalignment, and prevalent effusion with lateral meniscal extrusion are shown in Table 4. Prevalent lateral tibiofemoral cartilage damage showed a significant association with lateral meniscal extrusion, with an OR of 2.0 (95% CI: 1.3, 2.9; P = .0005). Considering different extents of lateral cartilage damage, we found that focal cartilage defects (WORMS grades 2 and 2.5 combined) were not significantly associated with lateral meniscal extrusion. Lateral compartments with areas of partial-thickness cartilage loss (WORMS grades 3 and 4 combined), as well as compartments with areas of full-thickness cartilage loss (WORMS grades 5 and 6 combined), were significantly associated with lateral meniscal extrusion (ORs of 1.7 [95% CI: 1.1, 2.7; P = .02] and 3.9 [95% CI: 2.4, 6.5; P < .0001], respectively).

Prevalent valgus alignment demonstrated a significant association with prevalent lateral meniscal extrusion, with an OR of 2.2 (95% CI: 1.5, 3.2; P < .0001). No significant association was found between BMI and meniscal

Table 2

Associations of Varus Malalignment, Medial Tibiofemoral Cartilage Damage, and Knee Effusion with Medial Meniscal Extrusion

Factors	Prevalent Extrusion*: Absence at Baseline, Score 0	Prevalent Extrusion*: Presence at Baseline, Score ≥ 1	Adjusted OR†
Alignment‡			
Neutral and valgus malalignment	722 (34.1)	415 (19.6)	1.0 (reference)
Varus malalignment	452 (21.3)	511 (24.1)	1.3 (1.1, 1.7)§
Medial tibiofemoral cartilage damage‖			
Absence at baseline, grades 0 and 1	576 (27.2)	204 (9.6)	1.0 (reference)
Presence at baseline, grade ≥ 2	604 (28.5)	730 (34.5)	1.8 (1.4, 2.2)§
Knee effusion#			
Absence at baseline, grade 0	492 (23.3)	311 (14.7)	1.0 (reference)
Presence at baseline, grade ≥ 1	687 (32.5)	625 (29.5)	1.0 (0.8, 1.2)

* Numbers in parentheses are percentages.

† All main effects (meniscal damage including root tears, tibiofemoral cartilage damage, knee malalignment, knee effusion, BMI) and covariates (age and sex) were simultaneously entered into the model. Numbers in parentheses are 95% CIs.

‡ Nineteen missing values.

§ A significant difference was defined as one with P < .05. Numbers in parentheses are 95% CIs.

‖ Five missing values.

One missing value.

Table 3

Associations between Lateral Meniscal Tears and Lateral Meniscal Extrusion

Meniscal Tear	Prevalent Lateral Extrusion*: Absence at Baseline, Score 0	Prevalent Lateral Extrusion*: Presence at Baseline, Score ≥ 1	Adjusted OR†
Absence of meniscal tear at baseline, score 0	1795 (85.2)	97 (4.6)	1.0 (reference)
Presence of any meniscal tear at baseline, score ≥ 1‡	112 (5.3)	102 (4.8)	10.3 (7.1, 14.9)§
Extent of meniscal tear‡			
Grade 1	29 (1.4)	7 (0.3)	3.1 (1.3, 7.4)§
Grade 2	55 (2.6)	34 (1.6)	8.2 (4.9, 13.6)§
Grade 3	28 (1.3)	61 (2.9)	22.1 (12.8, 38.1)§

* Numbers in parentheses are percentages.

† All main effects (meniscal damage, tibiofemoral cartilage damage, knee malalignment, knee effusion, BMI) and covariates (age and sex) were simultaneously entered into the model.

‡ Two missing values.

§ A significant difference was defined as one with P < .05. Numbers in parentheses are 95% CIs.

Table 4

Associations of Valgus Malalignment, Lateral Tibiofemoral Cartilage Damage, and Knee Effusion with Lateral Meniscal Extrusion

Factors	Prevalent Extrusion*		
	Absence at Baseline, Score 0	Presence at Baseline, Score ≥ 1	Adjusted OR†
Alignment‡			
Neutral and varus malalignment	1584 (75.1)	114 (5.4)	1.0 (reference)
Valgus malalignment	308 (14.6)	83 (3.9)	2.2 (1.5, 3.2)§
Lateral tibiofemoral cartilage damage‖			
Absence at baseline, grades 0 and 1	1123 (53.3)	50 (2.4)	1.0 (reference)
Presence at baseline, grade ≥ 2	783 (37.1)	149 (7.1)	2.0 (1.3, 2.9)§
Knee effusion#			
Absence at baseline, grade 0	755 (35.8)	48 (2.3)	1.0 (reference)
Presence at baseline, grade ≥ 1	1151 (54.7)	151 (7.2)	1.2 (0.9, 1.8)

* Numbers in parentheses are percentages.

† All main effects (meniscal damage, tibiofemoral cartilage damage, knee malalignment, knee effusion, BMI) and covariates (age and sex) were simultaneously entered into the model. Numbers in parentheses are 95% CIs.

‡ Nineteen missing values.

§ A significant difference was defined as one with $P < .05$. Numbers in parentheses are 95% CIs.

‖ Five missing values.

One missing value.

extrusion, nor between knee effusion and meniscal extrusion in the lateral compartment.

Discussion

We assessed the association of several factors, such as meniscal tears, tibiofemoral cartilage damage, knee malalignment, knee effusion, and BMI, with meniscal extrusion in the same tibiofemoral compartment. We demonstrated that meniscal tears are not the only factors associated with meniscal extrusion; other factors, such as tibiofemoral cartilage damage and knee malalignment, are independently associated with meniscal extrusion.

The relationship between meniscal tears and meniscal extrusion has been explored previously (22–26,30). The intricately woven pattern of collagen fibrils is responsible for the strength of the meniscus, which maintains its shape and structure when axially loaded (43). Different types of meniscal tears may alter the circumferential extension of the meniscus that resists radial displacement (also known as hoop strain) when the meniscus is axially loaded (44), which leads to extrusion. In the literature, this effect has been evaluated in relation to each type separately (eg, horizontal, vertical, radial, complex, degeneration), as well as in various groups (eg, root tears vs nonroot tears). However, many of these studies did not adjust for other factors that might be associated with meniscal extrusion (22,23,30).

Our results showed strong and significant associations between meniscal damage of any degree of severity (as classified with the WORMS) and meniscal extrusion in both compartments. Also, we showed that all grades of severity of meniscal pathologic findings were independently associated with meniscal extrusion, with higher grades of meniscal tears having stronger associations with meniscal extrusion in both compartments. Also, we demonstrated that root tears were strongly associated with meniscal extrusion in the medial compartment, even after adjusting for all the other covariates, including other grades of meniscal damage. However, grade 3 meniscal lesions, representing displaced tears and partial meniscal resection or maceration, demonstrated the higher ORs for meniscal extrusion compared with all factors evaluated in this study.

Investigators in previous work have attempted to demonstrate a relationship between tibiofemoral chondral lesions and meniscal extrusion. Lee et al (24) assessed the association of arthroscopy-depicted chondral lesions and preoperative radiographic Kellgren-Lawrence grade with meniscal extrusion and found that only the Kellgren-Lawrence grade was significantly related to extrusion. However, a cross-sectional MR imaging study conducted by Lerer et al (25) showed a significant association between moderate to severe MR imaging–depicted medial compartment articular cartilage damage and medial meniscal extrusion. Further, Puig et al (33) demonstrated that MR imaging–depicted medial meniscal extrusion was significantly correlated with chondral lesions detected at arthroscopy in the medial compartment. The researchers in none of these studies attempted to adjust results for other factors, especially concomitant meniscal tears (25,33). In our study, tibiofemoral cartilage damage was independently associated with meniscal extrusion in both tibiofemoral compartments. Furthermore, the severity of cartilage damage is independently associated with meniscal extrusion, with higher grades of cartilage damage having stronger associations with meniscal extrusion in both compartments. Only compartments exhibiting focal cartilage defects (WORMS grades 2 and 2.5 combined) were not associated with meniscal extrusion. We hypothesize that loss of cartilage could narrow the tibiofemoral space, squeezing the meniscus and leading to extrusion. Also, cartilage loss as part of OA might lead to a loss of tissue that protects the tibiofemoral compartment, increasing loading to the adjacent meniscus and perhaps leading to meniscal extrusion. However, the cross-sectional nature of our study does not allow the assumption that cartilage damage is predictive of meniscal extrusion. Previous longitudinal works have

demonstrated that meniscal extrusion is an independent predictor of cartilage loss in the tibiofemoral compartment (2,4,8,9,13,15). Further longitudinal studies would be necessary to test the hypothesis that cartilage damage leads to meniscal extrusion.

Knee malalignment is a known risk factor for progression of knee OA (45). In our study, we hypothesized that knee malalignment could be an independent factor associated with meniscal extrusion, as the malalignment could increase the load transmitted to the meniscus, which could lead to extrusion. We demonstrated that varus and valgus alignment are independent factors associated with, respectively, medial and lateral meniscal extrusion. This finding supports the idea that malalignment may have consequences beyond its direct effects on articular cartilage (46) and subchondral bone (47). However, we cannot affirm that knee malalignment precedes meniscal extrusion, as alignment may also change as OA progresses and may itself be influenced by structural changes in the knee, such as meniscal extrusion (45).

We found no evidence of an independent association between the presence of knee effusion and meniscal extrusion in our study sample. In a previous study, Miller et al (34) demonstrated that knee effusion is associated with medial meniscal extrusion. The authors hypothesized that distention of the joint capsule, which is firmly attached to the medial meniscus, medially would be responsible for meniscal displacement. This would also explain why they did not find a significant association between knee effusion and meniscal extrusion in the lateral compartment, because joint fluid tends to collect in the lax and yielding meniscal-capsular attachments. However, the relationships demonstrated in their study did not take into account all potential factors that might lead to extrusion (no adjustments were performed), so we do not know whether knee effusion is independently associated with medial meniscal extrusion. In our study sample, after adjusting for all covariates considered, knee effusion was not independently associated with meniscal extrusion in either compartment. Of all knees exhibiting effusion at baseline, only 4.8% had grade 3 effusion (> 66% of maximal potential distension), which might help explain why effusion was not associated with meniscal extrusion in our study.

In our study, we found no evidence of an independent association between increasing BMI and meniscal extrusion. We originally hypothesized that increased BMI would be an independent factor related to meniscal extrusion. On the basis of our negative finding, we now speculate that an increased BMI modulates the effect of other concomitant risk factors, and without the presence of other factors (eg, meniscal tears, cartilage damage, and knee malalignment), BMI itself would have no effect on meniscal position.

There were some limitations to this study. First, MR images were acquired with the subjects in a supine, nonweight-bearing position, and the measurements of meniscal extrusion are likely to be an underestimation of what would be expected in axially loaded knees. It has been demonstrated that meniscal position may vary under loading conditions in both asymptomatic volunteers (48) and subjects with knee OA (49). Ideally, the presence and degree of meniscal extrusion should be assessed with the knee bearing a full load. However, in very large samples, such as that in the MOST study with more than 3000 subjects, it would be difficult indeed to implement loading conditions while performing MR imaging of the knee. Further, we assessed extrusion only in the body of the meniscus, and not at the anterior and posterior horns. Second, the assessment of associations was performed in persons aged 50–79 years who had or were at risk for knee OA, and it is possible that our results may not be accurately extrapolated to young, athletic individuals who do not have or are not at risk for knee OA. Third, the cross-sectional nature of our study does not allow us to affirm that the factors associated with meniscal extrusion in this study actually precede meniscal extrusion. However, this study could show that meniscal damage is independently associated with cartilage damage and malalignment, stressing the close interrelation of all joint tissues involved in the OA disease process. Further longitudinal studies will have to show whether risk factors for incident and progressive meniscal extrusion can be identified. Fourth, the WORMS system used in this study allows evaluation of meniscal pathologic findings according to severity and extension, but not type. However, to minimize this limitation, we performed an additional assessment to evaluate the presence of root tears in our study sample, because this feature is not evaluated separately in WORMS. Finally, no additional method of assessment, such as arthroscopy, was performed to evaluate meniscal tears and cartilage damage.

In conclusion, our results demonstrated that, in persons who have or are at risk for knee OA, meniscal tears are not the only factors associated with meniscal extrusion; other independent factors include tibiofemoral cartilage damage and knee malalignment. Also, our results showed that the severity of meniscal damage and the presence of root tears are independently associated with meniscal extrusion. Meniscal extrusion seems to be a result of the complex interaction of the different joint tissues and biomechanical loading involved in the OA process.

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