Effect of medial meniscus extrusion on arthroscopic surgery outcome in the osteoarthritic knee associated with medial meniscus tear: a minimum 4-year follow-up

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Abstract

Background: The potential benefit of arthroscopic surgery for osteoarthritic knee associated with medial meniscus tear is controversial. This study was conducted to determine the effect of pre-operative medial meniscus extrusion (MME) on arthroscopic surgery outcomes in the osteoarthritic knee associated with medial meniscus tear during a minimum 4-year follow-up.

Methods: This was a retrospective review of a total of 131 patients diagnosed with osteoarthritic knee associated with medial symptomatic degenerative meniscus tear who underwent arthroscopic surgery from January 2012 to December 2014 and were observed for more than 4 years. Patients were classified into two groups: MME ≥3 mm (major MME group, $n = 54$) and MME <3 mm (non-major MME group, $n = 77$). Clinical assessments, including the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score, and radiographic assessments, including the Kellgren-Lawrence (K-L) grade and medial joint space width (JSW), were evaluated pre-operatively and at final follow-up. The longitudinal changes of clinical and radiographic parameters (WOMAC and the medial JSW change, K-L grade progression) were compared between groups unadjusted and adjusted for age, sex, and body mass index. Four-year survival rates (without progression to knee replacement [KR]) were also evaluated using a log-rank test and Cox proportional hazard regression model.

Results: Major MME was present in 41% of patients. After a minimum 4-year follow-up, the mean WOMAC total and pain scores improved significantly in both groups. However, the medial JSW and K-L grade worsened significantly. Patients with pre-operative major MME worsened more in WOMAC total (adjusted mean difference [MD] 3.800, 95% confidence interval [CI]: 0.900, 11.400; $P = 0.037$) and function (adjusted MD 3.100, 95% CI: 0.700, 6.300; $P = 0.038$) scores than patients with pre-operative non-major MME, and no significant difference was observed in WOMAC pain and stiffness score between groups. The group with major MME had significantly higher joint space narrowing (adjusted MD −0.630, 95% CI: −1.250, −0.100; $P = 0.021$) and K-L rate progression (adjusted mean relative risk [RR] 1.310, 95% CI: 1.100, 1.600; $P = 0.038$) than the group with non-major MME. There was a significantly more KR progression in patients with major MME compared with those with non-major MME (adjusted RR 3.100, 95% CI: 1.100, 9.200; $P = 0.042$ and adjusted hazard ratio 3.500, 95% CI 1.100, 9.500; $P = 0.022$).

Conclusions: Osteoarthritic knee patients associated with medial meniscus tear with non-major MME are more responsive to arthroscopic surgery in terms of the clinical and radiologic outcomes and survival for at least 4-year follow-up; however, in terms of pain relief, arthroscopic surgery in patients with major MME is also beneficial as well as in patients with non-major MME.

Keywords: Osteoarthritis; Knee; Meniscus; Arthroscopy; Prognosis; Treatment Outcome

Introduction

Knee osteoarthritis (KOA) with symptomatic knee pain and physical impairment is the most common musculoskeletal disability in the world with a prevalence of approximately 25% of people older than 50 years, and the disease burden of KOA is considerable in the United States and China.[1-3] Arthroscopy is a commonly performed surgery to treat degenerative knee disease and there was a prevalence (53%) of the 4096 arthroscopies that had a diagnosis with derangement of meniscus due to old tear or injury, KOA from Swedish register data.[4] The surgery typically comprises of knee lavage, debridement and most importantly, partial meniscectomy in cases of the torn meniscus. However, the potential benefit of arthroscopy is controversial, and numerous organizations, including the American Academy of Orthopedic Surgeons (AAOS),[5] the Osteoarthritis Research Society International,[6] and the

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British Medical Journal Rapid Recommendation[7] have taken a stand of recommending against performing knee arthroscopy in patients with established KOA, even though AAOS guidelines still leave an option for arthroscopic surgery for patients with a diagnosis of meniscus tear, which is commonly associated with early signs of KOA.[8] Such sub-groups of patients with painful meniscal symptoms were assumed to benefit from arthroscopic surgery, especially patients with so-called "mechanical symptoms" (sensations of the knee giving way, catching, or locking).[9,10] However, Sihvonen's prospective observational data did not show that patients with mechanical symptoms benefit more from arthroscopic partial meniscectomy than those without these symptoms.[11] A recent study showed that no difference in improvement was observed between those with and without mechanical symptoms among older patients (>40 years) after arthroscopic surgery (adjusted mean difference [MD] 0.7, 95% CI: −2.6, 3.9) at 52 weeks follow-up.[12]

Meniscal extrusion typically occurs in medial meniscus,[13] where the outer margin of the meniscal body is markedly located outside the tibial joint margin, and, typically 3 mm or more is considered as major.[14-18] This can result in hoop strain failure under axial loading, leading to a condition biomechanically similar to a total meniscectomy. It can lead to osteoarthritis due to a decreased tibiofemoral contact area and increased contact pressure. Multiple studies affirm that greater meniscus extrusion was a significant predictor of the progression of arthritic changes in knees both with established KOA features and without clinical and radiographic KOA at baseline.[19,20] Kim *et al*[19] showed that pre-operative extrusion of the medial meniscus was negatively correlated with outcomes of surgical partial meniscectomy in the non-osteoarthritic knee. As we know, meniscal extrusion is not only can be seen in non-arthritic knee,[21] it is more often observed in the osteoarthritic knee.[22,23] However, few studies have directly compared outcomes among patients with and without pre-operative major medial meniscus extrusion (MME) in the osteoarthritic knee associated with symptomatic degenerative medial meniscus tears after arthroscopic surgery. So the current study aimed to determine the correlation of MME on the longitudinal (over 4 years) clinical and radiological outcomes and progression to knee replacement (KR) after arthroscopic surgery in the osteoarthritic knee.

Methods

Ethical approval

The study was approved by the Ethics Committee of the Chinese People's Liberation Army General Hospital. Because this was a retrospective study and the data analysis was performed anonymously, this study was exempt from informed consent from patients.

Study population

The consecutive inpatient patients who underwent magnetic resonance imaging (MRI, 3.0T; Siemens, Germany) and subsequent arthroscopic surgery between January 2012 and December 2014 for osteoarthritic pathology associated with medial meniscal tears were retrospectively reviewed. All the patients complained of medial knee joint pain associated with recurrent mechanical dysfunction (sensations of the knee giving way, catching, or locking) or persistent knee swelling without any history of trauma. On physical examination, all patients were found to have medial or posteromedial joint line tenderness, a positive McMurray test for the medial meniscus, and restriction of deep flexion. Patients were included in the current study according to the following criteria: (1) aged ≥45 years at baseline; (2) notable medial knee pain for at least 4 weeks, failed to be managed with conservative therapy (one or more of: medications, activity limitations, or physical treatment); (3) pre-operative MRI showing medial meniscal tear, intra-operative arthroscopic confirmation of meniscus tear; (4) with arthroscopic surgery in osteoarthritic knee with chondral lesion Grade 1 or higher according to the Outerbridge grading system.[24] Since osteoarthritic features can be seen in surgery before changes consistent with osteoarthritis can be detected on X-ray, patients with normal findings on X-ray were also eligible. Patients may have undergone a variety of procedures (eg, lavage, debridement, synovectomy, chondroplasty, or partial meniscectomy); (5) a minimum 4-year follow-up. Exclusion criteria were the following: (1) subjects who had any chronic inflammatory joint disease, including rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis; (2) pre-operatively exhibiting Grade 4 diffuse full-thickness chondral lesion according to the Outerbridge grading system or Kellgren-Lawrence (K-L) Grade 4 in weight-bearing X-ray who would be considered more suitable for arthroplasty surgery (no arthroscopic surgery should be proposed for a patient with late-stage osteoarthritis [OA])[25]; (3) previous trauma or surgical history of lower extremity; (4) severe patellofemoral joint and lateral tibiofemoral joint osteoarthritic cartilage lesions (Outerbridge >Grade 2) or concomitant lateral meniscal surgery; (5) concomitant knee surgery such as ligament reconstruction or meniscal repair or having undergone additional removal of loose bodies and microfracture procedure; (6) severe varus malalignment of the lower extremity (femur-tibia angle <178°); (7) serious medical illness with limited life expectancy or a high intra-operative risk.

Demographic, clinical, imaging characteristics and surgical data

All medical records (including arthroscopic image records) were retrospectively reviewed to extract demographic, surgical, clinical, and radiographic characteristics. Demographic data were noted, including age, sex, body mass index (BMI), and disease duration. All surgeries were performed by the four specialized surgeons. Arthroscopy of the knee was performed under local anesthesia, without tourniquet hemostasis. The information on cartilage and meniscus status was assessed, meniscal tears were classified as longitudinal, radial, horizontal, complex, unclassifiable, and root tear using a modified version of the International Society of Arthroscopy, Knee Surgery and Orthopedic Sports Medicine classification.[26] The severity of associated cartilage damage in the medial compartment at the time

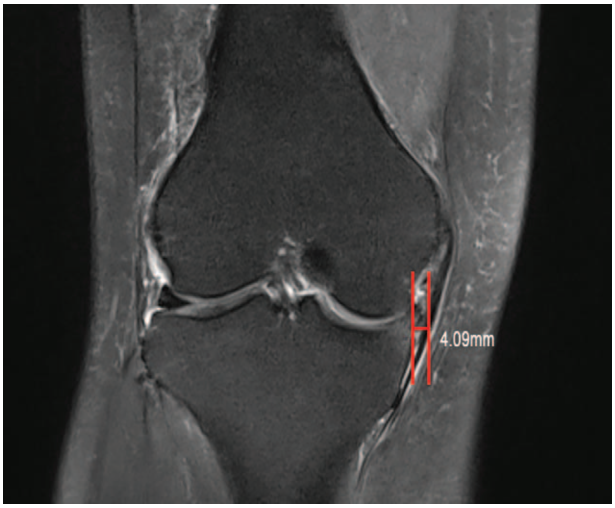

Figure 1: Schematic diagram of the MME. At the apex of the medial tibial spine on the coronal MRI image, the MME was defined as the distance between a vertical line passing by the outer edge of medial tibial plateaus and another vertical line tangential to the outer margin of the medial meniscus. In this patient, the MME was 4.09 mm. MME: Medial meniscus extrusion; MRI: Magnetic resonance imaging.

of surgery was graded according to the Outerbridge classification (Grade 1: cartilage softening and swelling; Grade 2: <50% loss of cartilage thickness; Grade 3: >50% loss of cartilage thickness; Grade 4: exposed sub-chondral bone).[24]

MRI examination was performed in the supine position with a fully extended knee. Measuring meniscal extrusion on the coronal MRI slice corresponding to the apex of the medial tibial spine section was suggested as the most accurate perpendicular extrusion measurement. Vertical lines passing by the outer edge of medial tibial plateaus, excluding osteophytes, were used as the reference to assess extrusion of the body of the meniscus [Figure 1].[27] Extrusion of more than 3 mm was considered major.[15,16] Since not all of the patients with full-limb radiographs were available for lower limb alignment measurement, we used an alternative approach "femur-tibia angle" as McDaniel *et al*[28] suggested with highly reproducible, femur-tibia angle <178° was considered as severe varus. To increase reliability, images were independently evaluated by two investigators who were blinded to patient information, and the mean of the two numerical values was used.

Clinical assessments

The primary outcome was the change in the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) total and its three sub-scales[29]: pain, stiffness, function (each sub-scale, 100 = worst score; total scale, 300 = worst score) from the pre-operative assessment to the final follow-up. If the patients underwent conversion to KR, the final clinical outcomes were assessed just before KR. Since the change in the WOMAC score is a standard outcome in assessing interventions for KOA and is more easily interpreted than the raw score at final follow-up adjusted for the baseline score, as Katz *et al*[30] suggested, we did not render the primary outcome at final follow-up adjusting for the baseline score.

Radiographic assessments

The extension weight-bearing posteroanterior view was used to assess the K-L grade and measure the medial joint space width pre-operatively (JSW) and at final follow-up.[31] The K-L grade was defined as follows: 0 = normal; 1 = possible osteophytes; 2 = definite osteophytes and possible joint space narrowing; 3 = moderate/multiple osteophytes, definite narrowing, some sclerosis, and possible attrition; and 4 = large osteophytes, marked narrowing, severe sclerosis, and definite attrition.[25] The medial joint space was measured from the center of the medial femoral condyle to the center of the medial tibial plateau. Progression of 1 or more K-L grades was defined as K-L grade progression.[31] Radiographic images were assessed by two orthopedic surgeons. The examiners were blinded to the information of the patients.

Survival analysis

We defined failure of the operation as cases with conversion to KR, either total or uni-compartmental, and KR status was confirmed at the final follow-up. It was defined as patient-reported KR, confirmed on a subsequent radiograph. A Kaplan-Meier survivorship analysis was used to visualize and compare the survival analysis.

Statistical analysis

Statistical analysis was performed by SPSS for Windows version 21.0 (SPSS Inc., Chicago, IL, USA), and $P < 0.05$ was considered statistically significant. Descriptive statistics are given as mean ± standard deviations (SD), median (range), or numbers as appropriate. The independent *t*-test or the Mann-Whitney *U* test was used to compare continuous variables between the groups. The Chi-square or Fisher exact tests were used to compare categorical variables including sex and K-L grade. The paired *t*-test and Chi-square test were used to compare the pre-operative results and final results in each group. Unadjusted and adjusted analyses were performed to compare the difference in WOMAC score and JSW change from baseline to the final follow-up between groups; *t*-tests, and Chi-square test were used for unadjusted analyses, and multivariate regression was used for adjusted analyses including age, sex, and BMI. We did not adjust for structural pathology findings at arthroscopy, as these may be part of the causes of the MME. For K-L grades progression and survival rate outcome measures, unadjusted and adjusted logistic regression was used to calculate the relative risk (RR). Kaplan-Meier analysis was used to evaluate the effect of MME on the time-dependent rate of KR. We used the log-rank test and a Cox proportional hazard regression model adjusted for age, sex, and BMI to calculate the hazard ratio (HR) with 95% confidence interval (CI) for survival analysis.

Results

Cohort characteristics

A total of 443 patients were screened for eligibility, of which 143 were eligible. Eight patients who lacked follow-up, two patients who suffered new injury to the knee, and two patients with a post-operative complication were excluded. Thus, 131 patients were included [Figure 2]. The average follow-up time was 67 months and the longest follow-up time was 84 months. Patients were classified into two groups: MME ≥3 mm (major MME group, $n = 54$) and MME <3 mm (non-major MME group, $n = 77$). Baseline demographic and surgical characteristics within the major and non-major MME groups were presented in Table 1. Major MME was present in 41% of patients. The mean ± SD MME in the major MME group was significantly greater than that in the non-major MME group (4.700 ± 2.790 *vs*. 2.070 ± 0.810 mm, $t = 7.840$, $P < 0.001$). No differences were found in age, sex, knee alignment between groups. However, patients in major

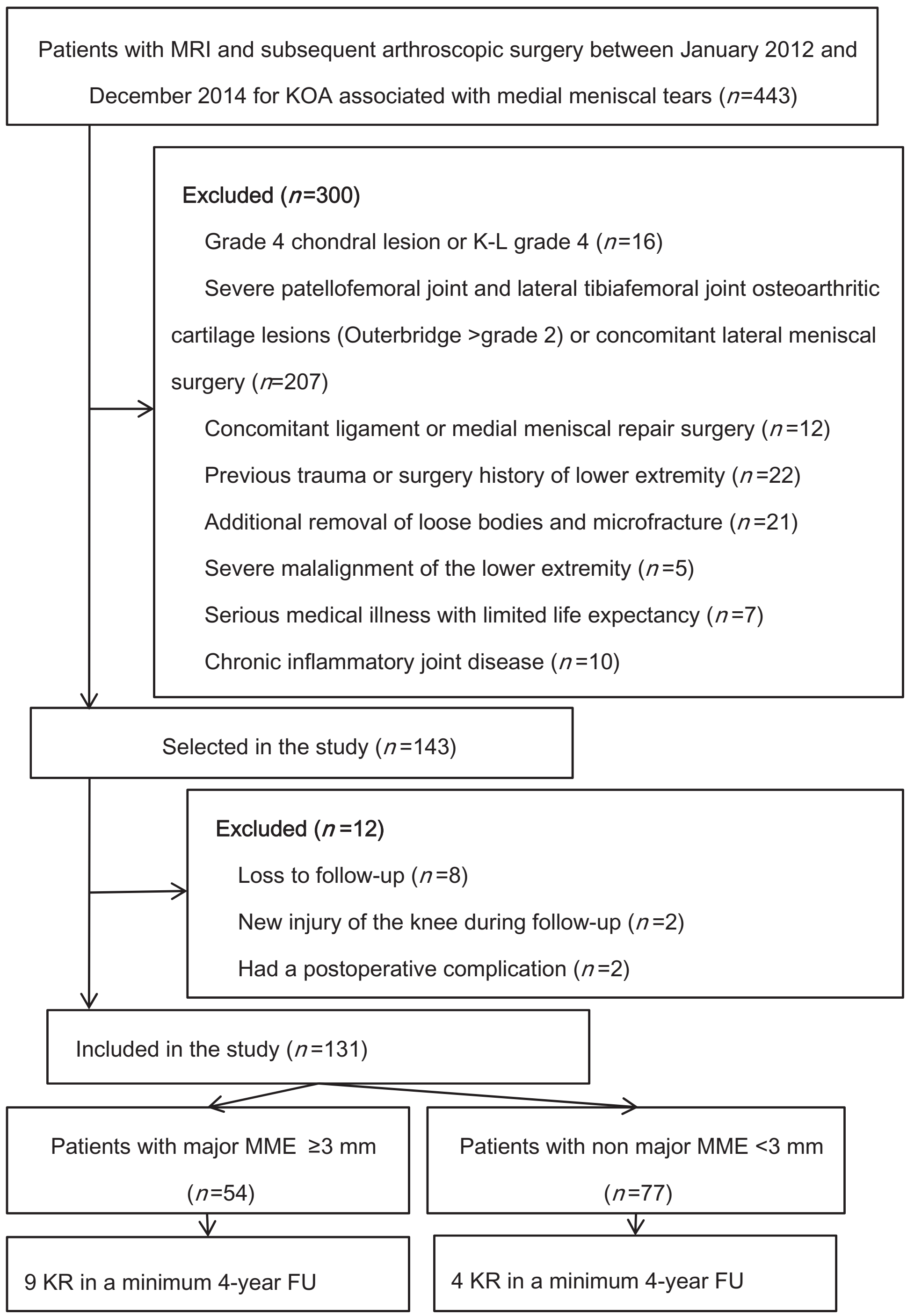

Figure 2: Flow chart of participants in the study. FU: Follow up; K-L: Kellgren-Lawrence; KOA: Knee osteoarthritis; KR: Knee replacement; MME: Medial meniscus extrusion; MRI: Magnetic resonance imaging.

Table 1: Baseline demographic, clinical, and imaging characteristics of the study population.

Characteristics	MME ≥3 mm (major MME group, $n=54$)	MME <3 mm (non-major MME group, $n=77$)	Statistics	P
Age (years)	60 (47–66)	58 (45–73)	$Z=1.200$	0.230*
Sex (male/female)	20/34	25/52	$\chi^2=0.290$	0.588†
BMI (kg/m^2)	26.900 ± 2.900	25.300 ± 2.700	$t=3.230$	0.002‡
Affected side (right/left)	25/29	40/37	$\chi^2=0.400$	0.524†
Symptom duration (months)	12 (1–57)	7 (1–28)	$Z=9.700$	<0.001*
MME (mm)	4.700 ± 2.790	2.070 ± 0.810	$t=7.840$	<0.001‡
Medial JSW (mm)	4.300 ± 0.630	4.620 ± 0.470	$t=3.330$	0.002‡
Femur-tibia angle	181.700 ± 2.900	182.400 ± 2.600	$t=1.450$	0.151‡
Pre-operative K-L grade (0/1/2/3)	2/9/23/20	5/32/33/7	$\chi^2=18.800$	<0.001§
Meniscal tear classification			$\chi^2=13.100$	0.020§
Horizontal tear	14	37		
Complex tear	24	17		
Radial tear	3	4		
Longitudinal tear	2	6		
Root tear	11	10		
Unclassifiable	0	3		
Additional other procedure			$\chi^2=20.600$	<0.001†
None	9	40		
Cartilage surgery	43	34		
Synovectomy	45	37		
WOMAC				
Total (0–300)	122.700 ± 54.700	109.600 ± 64.100	$t=1.220$	0.220‡
Pain (0–100)	46.800 ± 18.100	38.700 ± 21.800	$t=2.240$	0.027‡
Stiffness (0–100)	32.900 ± 17.300	30.300 ± 16.100	$t=0.880$	0.380‡
Function (0–100)	42.900 ± 20.700	40.100 ± 22.400	$t=0.730$	0.469‡

Results are shown as mean ± standard deviation, median (range), or n. * Mann-Whitney U test. † Chi-square test. ‡ Independent t-test. § Fisher exact test. MME: Medial meniscus extrusion; BMI: Body mass index; JSW: Joint space width; K-L grade: Kellgren-Lawrence grade (0 = normal; 1 = possible osteophytes; 2 = definite osteophytes and possible joint space narrowing; 3 = moderate/multiple osteophytes, definite narrowing, some sclerosis, and possible attrition; and 4 = large osteophytes, marked narrowing, severe sclerosis, and definite attrition); WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index (each sub-scale, 100 = worst score; total scale, 300 = worst score).

MME group had a higher BMI (26.900 ± 2.900 *vs.* 25.300 ± 2.700 kg/m^2, $t=3.230$, $P=0.002$), longer symptom duration (12, range from 1 to 57 *vs.* 7, range from 1 to 28 months, $t=9.700$, $P<0.001$), more severe K-L grade ($\chi^2=18.800$, $P<0.001$), narrower JSW (4.300 ± 0.630 *vs.* 4.620 ± 0.470 mm, $t=3.330$, $P=0.002$), and higher pre-operative WOMAC total and pain score than those in the non-major MME group. Major MME was significantly associated with more meniscal complex tear and meniscal root tear.

Clinical outcomes

Both groups showed significant improvement in clinical outcomes, as presented by a decrease in WOMAC total and pain score. The WOMAC function score was significantly decreased in the non-major MME group (MD [95% CI]: −6.500 [−12.800, −3.800], $P<0.001$) while it was not in the major MME group (MD [95% CI]: −3.200 [−8.500, 2.300], $P=0.261$) [Table 2]. Patients with pre-operative major MME worsened more in the WOMAC total and function scores than patients with pre-operative non-major MME (MD [95% CI]: 5.400 [1.200, 13.600], $P=0.028$; 4.600, [0.100, 9.000], $P=0.033$, respectively). However, no difference was observed in the WOMAC pain and stiffness score between groups (MD [95% CI]: −0.200 [−3.600, 3.300], $P=0.894$; 0.900 [−5.000, 7.200], $P=0.789$, respectively) at a minimum 4-year follow-up after surgery. The difference between groups persisted even after adjusting for age, sex, and BMI [Table 3].

Radiological outcomes

Although functional scores improved, the radiological outcomes including medial JSW (MD [95% CI]: −1.090 [−2.300, −0.510], $P<0.001$; −0.470 [−1.080, −0.140], $P<0.001$, respectively) and K-L grade worsened significantly in both groups at a minimum 4 year post-operative follow-up [Table 2]. Patients with major MME had significantly higher joint space narrowing (MD [95% CI: −0.650[−1.330, −0.140], $P=0.013$) and K-L progression rate (RR 1.340, 95% CI: 1.100, 1.650, $P=0.034$) than patients with non-major MME [Table 3]. This result was confirmed in multivariate regression after adjusting for age, sex, and BMI [Table 3].

Survival analysis

Overall, nine patients underwent conversion to KR in the major MME group and only four patients in the non-major MME group. The 4-year survival rate of the major MME group (83.3%) was significantly worse than that of the non-MME group (94.8%). There was a significantly more KR progression in patients with major MME compared to

Table 2: Comparison of pre-operative and post-operative clinical and radiologic outcomes.

Items	Pre-operative	Final follow-up	Mean difference*	P
MME ≥3 mm (*n* = 54)				
Clinical outcomes				
WOMAC				
Total (0–300)	122.700 ± 54.700	110.900 ± 44.200	−12.200 (−28.100, −1.900)	0.033†
Pain (0–100)	46.800 ± 18.100	40.900 ± 20.200	−5.900 (−10.300, −1.300)	0.020†
Stiffness (0–100)	32.900 ± 17.300	29.900 ± 20.100	−2.900 (−10.000, 4.100)	0.404†
Function (0–100)	42.900 ± 20.700	39.600 ± 24.700	−3.200 (−8.500, 2.300)	0.261†
Radiologic outcomes				
Medial JSW (mm)	4.050 ± 0.580	3.030 ± 0.880	−1.090 (−2.300, −0.510)	<0.001†
K-L grade (0/1/2/3/4)	2/9/23/20/0	0/2/15/27/10	$\chi^2 = 19.200$	<0.001‡
MME <3 mm (*n* = 77)				
Clinical outcomes				
WOMAC				
Total (0–300)	109.600 ± 64.100	93.300 ± 59.200	−16.200 (−32.100, −3.700)	0.002†
Pain (0–100)	38.700 ± 21.800	33.100 ± 23.500	−5.600 (−9.700, −0.800)	0.021†
Stiffness (0–100)	30.300 ± 16.100	26.200 ± 18.500	−4.000 (−9.400, 1.600)	0.159†
Function (0–100)	40.100 ± 22.400	33.600 ± 23.100	−6.500 (−12.800, −3.800)	<0.001†
Radiologic outcomes				
Medial JSW (mm)	4.360 ± 0.850	3.890 ± 1.040	−0.470 (−1.080, −0.140)	<0.001†
K-L grade (0/1/2/3/4)	5/32/33/7/0	1/19/32/20/5	$\chi^2 = 17.300$	0.002‡

Data were presented as mean ± standard deviation or mean difference (95% CI) or *n*. * Mean difference is equal to the mean outcome score at the final follow-up minus the mean outcome pre-operatively. † Paired *t*-test. ‡ Chi-square test. MME: Medial meniscus extrusion; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index (each sub-scale, 100 = worst score; total scale, 300 = worst score); JSW: Joint space width; K-L grade: Kellgren-Lawrence grade (0 = normal; 1 = possible osteophytes; 2 = definite osteophytes and possible joint space narrowing; 3 = moderate/multiple osteophytes, definite narrowing, some sclerosis, and possible attrition; and 4 = large osteophytes, marked narrowing, severe sclerosis, and definite attrition); CI: Confidence interval.

Table 3: Comparison of progression of functional and imaging characteristics between groups.

	Mean difference* or relative risk (95% CI)			
Items	Unadjusted	P	Age-, Sex-, BMI-adjusted†	P
WOMAC‡				
Total (0–300)	5.400 (1.200, 13.600)	0.028	3.800 (0.900, 11.400)	0.037
Pain (0–100)	−0.200 (−3.600, 3.300)	0.894	−0.200 (−3.300, 3.000)	0.831
Stiffness (0–100)	0.900 (−5.000, 7.200)	0.789	0.800 (−5.200, 7.300)	0.802
Function (0–100)	4.600 (0.100, 9.000)	0.033	3.100 (0.700, 6.300)	0.038
Medial JSW (mm)‡	−0.650 (−1.330, −0.140)	0.013	−0.630 (−1.250, −0.100)	0.021
Survival rate§	3.200 (1.100, 9.400)	0.031	3.100 (1.100, 9.200)	0.042
K-L progression rate§	1.340 (1.100, 1.650)	0.034	1.310 (1.100, 1.600)	0.038

* The mean difference is equal to the mean progression outcome score in the major MME group minus those in the non-major MME group. † Multivariate regression was used with adjustment for age, sex, and BMI. ‡ Results are shown as mean difference (95% CI) based on independent *t*-tests. § Results are shown as relative risk (95% CI) based on Chi-square test. CI: Confidence interval; BMI: Body mass index; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index (each sub-scale, 100 = worst score; total scale, 300 = worst score); JSW: Joint space width; K-L: Kellgren-Lawrence.

those with non-major MME even after adjusting for age, sex, and BMI (adjusted RR 3.100, 95% CI: 1.100, 9.200, *P* = 0.042) [Table 3]. In terms of survivorship analysis, the Kaplan-Meier survival curve with the percentage of patients free from conversion to KR is shown in Figure 3. In cox regression analyses, major *vs*. non-major MME at baseline was associated with a 3.5-fold increase in the HR of KR progression after adjustment for age, sex, and BMI at a minimum 4-year follow-up post-operatively [Table 4].

Discussion

This study suggests that major MME is associated with significantly worse clinical and radiologic outcomes and survival for at least 4-year follow-up after arthroscopic surgery. Since we demonstrated that major MME is largely related to the arthroscopic surgery outcome of KOA, it is important to know what causes MME. Several studies have reported a significant correlation between MME and severity of chondropathy.[18,23] Costa *et al*[15] also found that major MME was associated with meniscus degeneration, radial, oblique, complex, and root tears, accordingly, longitudinal and horizontal tears were not associated with major MME which is similar to what we observed in our study. However, Lee *et al*[18] reviewed 102 knees with medial meniscus posterior horn degenerative tears that underwent a partial meniscectomy and showed that the incidence and degree of major extrusion were similar in

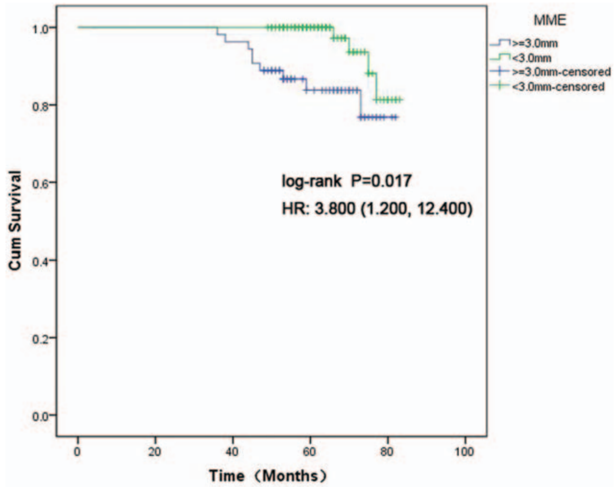

Figure 3: Kaplan-Meier survival analysis of progression to knee replacement between groups. MME: Medial meniscus extrusion.

Table 4: Hazard risk of progression of KR between groups.

Items	Crude HR for KR (95% CI)	*P*	Adjusted HR* for KR (95% CI)	*P*
Non-major MME	1.000		1.000	
Major MME	3.800 (1.200, 12.400)	0.017	3.500 (1.100, 9.500)	0.022

* Cox regression adjusted for age, sex, and body mass index. HR: Hazard ratio; KR: Knee replacement; CI: Confidence interval; MME: Medial meniscus extrusion.

knees with root tears and non-root tears, but a radial component and KOA severity were similarly predictive of absolute and relative extrusion. They suggested that arthroscopic meniscal procedures should be cautiously considered in patients with meniscal extrusion. Intra-articular injuries are associated with pain. Average medial meniscal extrusions of the knees with and without pain were 7.58 mm and 5.88 mm, respectively. Pain was associated with greater medial meniscal extrusions in KOA,[32] which was similar to what we observed.

Although more and more randomized trials including patients with symptomatic KOA and meniscal tears found no greater benefit with arthroscopic surgery followed by physical therapy,[30,33] compared with physical therapy alone, our observational study showed high rates of functional improvement, despite of serious radiologic KOA progression within patients after arthroscopic partial meniscectomy and debridement. We believe that meniscus surgery can promote radiologic KOA progression[34]; however, patient's conscious symptoms and radiological presentations are not completely consistent and even contradictor each other, and some patients were well satisfied with surgical effect while imaging revealed a severe degree of KOA progression. The degree of joint space narrowing does not fully represent the degree of degeneration of the joint. This could also be possibly attributed to the difference in the extent of meniscus resection.

Furthermore, the most important finding of our study was that the presence of major MME could be predictive of clinical and radiologic progression of KOA, even for a long-term increase in progression of KR after arthroscopic surgery. This result was further confirmed after adjustment for age, sex, and BMI, because of the significant baseline BMI differences between the study groups, and a higher age and BMI is related to meniscal extrusion,[35,36] even increased age, female gender, and greater BMI were modestly associated with poorer self-reported outcomes after undergoing arthroscopic meniscal surgery.[37] We did not adjust the results of our analysis for knee structural pathology parameters such as tear meniscus type, cartilage lesions. The above may be part of the causes of the major MME, given that the statistical results showed that those variables were significantly related to meniscal extrusion in our study, combining all those variables prevented us from analyzing the effect of major MME on outcomes, which would have required much larger sample size. Interestingly, there was an unexpected result that patients with major MME treated with surgery had even more benefit in terms of pain relief, although not reaching statistical significance (adjusted MD: −0.200; 95% CI: −3.300, 3.000, $P = 0.831$). The cause of this finding is unknown. One explanation might be that patients with more pre-operative pain are likely to realize more significant pain relief after surgery.

There is more and more investigation into the longitudinal relevance of MME in OA progression, but a lack of data in arthroscopic KOA patients. Choi *et al*[38] measured MME in 56 cases that were associated with cartilage degeneration of ipsilateral medial femoral condyle after 2-year follow-up. Van der Voet *et al*[16] showed that meniscal extrusion was associated with a significantly higher incidence of radiographic KOA (K-L Grade 2 or higher) and medial joint space narrowing of >1.0 mm after 30 months in a high-risk population of overweight and obese women free of clinical and radiological KOA at baseline. Teichtahl *et al*[39] extracted data from osteoarthritis initiative cohort (either with presence or absence of radiographic KOA) during 72 months follow-up, the presence of a baseline meniscal extrusion (independent of bone marrow lesions) was associated with accelerated cartilage volume loss, progressive radiological KOA, and total KR. According to arthroscopic patients, Krych *et al*[40] had concerned meniscus extrusion on the effect of arthroscopic surgery, they recently found that meniscus extrusion was associated with worse outcome, but they only focused on partial meniscectomy patients with symptomatic degenerative medial meniscus posterior root tears and did not adjust for baseline covariates. Kim *et al*[19] recently retrospectively reviewed 208 medial meniscus tear patients who were treated with arthroscopic partial meniscectomy and had a minimum 7-year follow-up. Consistent with our findings, their result showed that the pre-operative extrusion of the medial meniscus was negatively correlated with outcomes of partial meniscectomy, but they just focused on non-osteoarthritic knee.

Our study does suggest that major MME is the important risk factor for radiological OA progression and poor post-operative outcomes after arthroscopic surgery. However, it was impossible to determine whether MME was a cause or consequence of KOA in our present study. Our retrospective information does not prove cause and effect, because the MME may be a marker of other risk factors, such as more severe internal meniscus and cartilage degeneration. The best evidence of a causal relationship between MME and KOA is improved radiological and clinical outcomes after centralization of the extruded medial meniscus. A rat model data support a link between pre-existing MME and OA development and centralization of the extruded medial meniscus by the pull-out suture technique delayed cartilage degeneration.[41] In practice, if we consider that MME is a potential predictive factor of structural progression in OA, pre-operative detection of MME suggests active cartilage breakdown requiring an appropriate treatment such as the medial meniscus centralization procedure and a thorough follow-up. Our study suggests that arthroscopic surgery may have better post-operative outcomes for KOA with symptomatic meniscal tears among those with pre-operative non-major MME; however, in terms of pain relief, arthroscopic surgery in patients with major MME is also beneficial as well as in patients with non-major MME. Thus MME provides an interesting target for patient selection and counseling for arthroscopic surgery in degenerative KOA with a medial meniscus tear.

The present study had some limitations. First, we presented only one outcome score (WOMAC) and did not include knee scores such as the Knee Injury and Osteoarthritis Outcome Score or Lysholm. Also, we had no comparative data between pre- and post-operative MME. Second, the definition for meniscal extrusion used for the present study corresponds to extrusion of 3 mm or more, and we arbitrarily divided the meniscus into two groups which not allow us to account for within-grade progressions of knee OA. Moreover, this semi-quantitative scoring method for the meniscus does not take into account the proportion of the tibial cartilage surface covered by the meniscus. Third, the study involved a retrospective analysis with a relatively small population based on self-reported outcomes and this might have resulted in recall bias which makes comparison less reliable. The missing and unmeasured covariates such as bone marrow lesions,[39,42] and synovitis could also drive the association.[43] Furthermore, pre-operative major MME may involve more arthroscopic meniscus resection, all of which could have affected outcomes, rather than the MME itself, even if our analyses had been adjusted for age sex and BMI to control for the potential confounding. Lastly, we were unable to calculate minimal clinically important differences for our outcome measures; therefore, we cannot evaluate whether our statistically significant findings are clinically meaningful.

In conclusion, this study suggests that osteoarthritis knee patients associated with medial meniscus tear with non-major MME are more responsive to arthroscopic surgery in terms of the clinical and radiologic outcomes and survival for at least 4-year follow-up. However, in terms of pain relief, arthroscopic surgery in patients with major MME is also beneficial as well as in patients with non-major MME.

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Conflicts of interest

None.

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