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EngebretsenTITLE PAGE

Complex tears, extrusion and larger excisions are prognostic factors for worse outcomes 1 and 2 years after arthroscopic partial meniscectomy for degenerative meniscal tears

A secondary, explorative study of the surgically treated group from the Odense-Oslo Meniscectomy versus Exercise (OMEX) trial

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BRIEF SUMMARY

Degenerative meniscal tears: Complex tears, meniscal extrusion and larger excisions are prognostic factors for worse outcomes 1 and 2 years after arthroscopic partial meniscectomy

KEY WORDS

Arthroscopic partial meniscectomy

Arthroscopy

Degenerative meniscal lesions

Degenerative meniscal tears

Knee performance

Lower extremity performance

Middle-aged

Predictors

Prognostic factors

STUDY LOCATION

The study was performed at Oslo University Hospital and Martina Hansen´s Hospital, Norway.

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ABSTRACT

Background: Few studies have examined morphological findings from preoperative Magnetic Resonance Imaging (MRI) and arthroscopic findings as prognostic factors for outcomes 1 and 2 years after arthroscopic partial meniscectomy (APM).

Purpose: To evaluate prognostic factors of preoperative findings on MRI and arthroscopy on lower extremity performance at 1 year and patient-reported outcomes at 1-2 years following APM. The hypothesis was that medial compartment pathology would be prognostic for 1- and 2-year functional outcomes.

Study Design: Prospective cohort.

Methods: This secondary analysis from the OMEX (Odense-Oslo Meniscectomy versus Exercise) trial (www.clinicaltrials.gov NCT01002794) included 40 patients treated surgically. Regression analyses with adjustments for age, gender and BMI explored associations between MRI-findings (tear complexity and extrusion), arthroscopically findings (tear length, cartilage injury and amount of excised meniscal tissue) and the following: Lower extremity performance tests and thigh muscle strength at 1 year and the 5 Knee Injury and Osteoarthritis Outcome Score (KOOS) subscales at 1 and 2 years.

Results: *MRI findings:* Complex meniscal tear was a significant and clinically relevant prognostic factor for worse KOOS Symptoms at 2 years (14.1 points, 95%CI 6.1-22.2). Meniscal extrusion of at least 11%, 25% and 20% were significant and clinically relevant prognostic factors for worse KOOS ADL at 1 year and worse KOOS Sport/Rec at 1 and 2 years, respectively.

Arthroscopy findings: Tear lengths of at least 7.0 mm, 6.7 mm and 6.5 mm were significant and clinically relevant prognostic factors for better KOOS Symptoms at 1 year and better KOOS Sport/Rec at 1 and 2 years, respectively. Presence of cartilage injury in the medial compartment was a significant and clinically relevant prognostic factor for worse KOOS ADL and QoL at 2 years (10.4-19.4 points, 95%CIs 3.4-17.4 and 7.7-31.1). More than 20% meniscal tissue excised was a significant and clinically relevant prognostic factor for worse KOOS Pain, Symptoms, ADL, and Sport/Rec at 1 and 2 years (8.9-41.5 points, 95%CIs ranging from 2.2-15.5 to 21.0-62.0) and worse KOOS QoL at 2 years (25.3 points, 95%CI 13.6-37.0).

Conclusion: Complex meniscal tears, larger extrusions, cartilage injury and larger meniscal excisions were significant and clinically relevant prognostic factors for worse outcomes 1 and 2 years following APM.

What is known about this subject:

MRI-evaluated worse meniscal tear morphology and meniscal extrusion are risk factors for increased osteoarthritis following arthroscopic partial meniscectomy.

Presence of cartilage injuries and excisions of more than 50% of the total meniscal volume is prognostic for worse patient reported outcomes and increased osteoarthritis.

What this study adds to existing knowledge:

MRI- evaluated complex meniscal tears and meniscal extrusion are prognostic factors for inferior 1- and 2-year functional outcomes following arthroscopic partial meniscectomy.

Excisions as small as 20% of the total meniscal volume is prognostic for inferior 1- and 2-year functional outcomes.

INTRODUCTION

Degenerative meniscal tears are common in the general population [7, 17]. As many as 300 people per 100,000 have gone through arthroscopic partial meniscectomies (APMs) annually [1, 34, 40, 45]. However, during the last decade, high quality randomized controlled trials (RCTs) [19, 20, 23, 24, 30, 36, 44, 51, 52, 60, 64] and systematic reviews [10, 25, 33, 39, 43, 56, 57, 61] have shown similar results 1-5 years after treatment with APM or exercise therapy or sham surgery. Following this, declining numbers of APMs has been reported in Japan [31], Sweden and Finland [41] and Norway (Norwegian numbers declined from 14,927 in 2013 to 7,979 in 2016 - data from the Norwegian Patient Registry, data accessed through personal inquiry).

Still, some patients probably benefit from going through APM. RCTs have shown that 7-30% of the patients assigned to non-surgical treatment crossed over to surgery within two years [19, 20, 23, 24, 30, 36, 44, 51, 52, 60, 64] . After surgery, these patients showed results not different from the other patients [36]. The question is whether patients that need surgery could be identified at baseline. Knowledge of prognostic factors for worse and better outcomes available before choice of treatment modality could guide clinicians to better individualized treatment. Likewise, knowledge of prognostic factors available during surgery could guide to better postoperative treatment.

In a systematic review, Eijgenraam et al. identified presence of knee osteoarthritis (OA), long duration of symptoms, larger meniscal resections and smaller meniscal rim width as prognostic factors for worse patient reported outcome measures (PROMs) following APM[16]. Further, MRI-evaluated worse morphologic tear deformity and meniscal extrusion are known risk factors for increasing OA following APM [3, 35]. Known intraoperatively available risk factors for inferior PROMs and increased OA following APM are presence of cartilage injuries [26], osteoarthritis (OA) [26, 46, 53] and excisions of more than 50% of the total meniscal volume [16, 18] . As far as we know, knowledge is lacking about the prognostic value of MRI findings and intraoperative findings on 1- and 2-year postoperative knee function and performance.

MRI is highly accurate in diagnosing the presence of arthroscopically confirmed meniscal tears [12], with a sensitivity of 88% and specificity of 83% [63] and provides information on meniscal tissue degeneration, tear morphology [27] and extrusion grade [21]. Previously, inter-observer reliability of arthroscopic classification of meniscal tears and cartilage injuries has been described with large variations (correlation coefficients ranging from 0.25 to 0.92 [2, 15]), but with higher intra- than inter-observer reliability [15]. Hence, study specific reliability data are beneficial when reporting and interpreting arthroscopic findings.

In this study we hypothesized that medial knee compartment pathology evaluated as complex meniscal tears and meniscal extrusion on preoperative MRI, and arthroscopic findings such as meniscal tear length and cartilage injury, as well as amount of meniscal tissue excised, would be significant prognostic factors for worse 1- and 2-year functional outcomes. The aim was to explore the prognostic value of complex meniscal tears, meniscal extrusion, tear length, cartilage injury, and amount of meniscal tissue excised on lower extremity performance at 1 year and patient-reported outcomes at 1 and 2 years following APM for degenerative meniscal tear.

MATERIALS AND METHODS

The study cohort

The study cohort consisted of 40 patients from the OMEX trial (Odense-Oslo Meniscectomy versus Exercise trial: www.clinicaltrials.gov NCT01002794) [36] treated surgically at one hospital (Martina Hansen's Hospital, Norway) (Figure 1). Inclusion criteria were age 35-60 years, atraumatic unilateral knee pain for more than two months, MRI-verified medial degenerative meniscal tear and osteoarthritis (OA) grade 0-2 according to Kellgren and Lawrence (KL) (grade 0-4, higher is worse) [32]. Exclusion criteria were acute trauma, locked knee, ligament injury, and knee surgery of the index knee the last two years [32]. The posterior-anterior radiographs were taken with the patient standing in a Synaflexer frame (Synark, Newark, CA) [38], and grade 2, defined as presence of an osteophyte and possible joint space narrowing [50], was set as cut-off for diagnosis of radiographic OA.

Demographic data, preoperative function, radiography and MRI were collected at baseline (Table 1).

Figure 1. Flow chart
ET; Exercise Therapy, APM; Arthroscopic Partial Meniscectomy

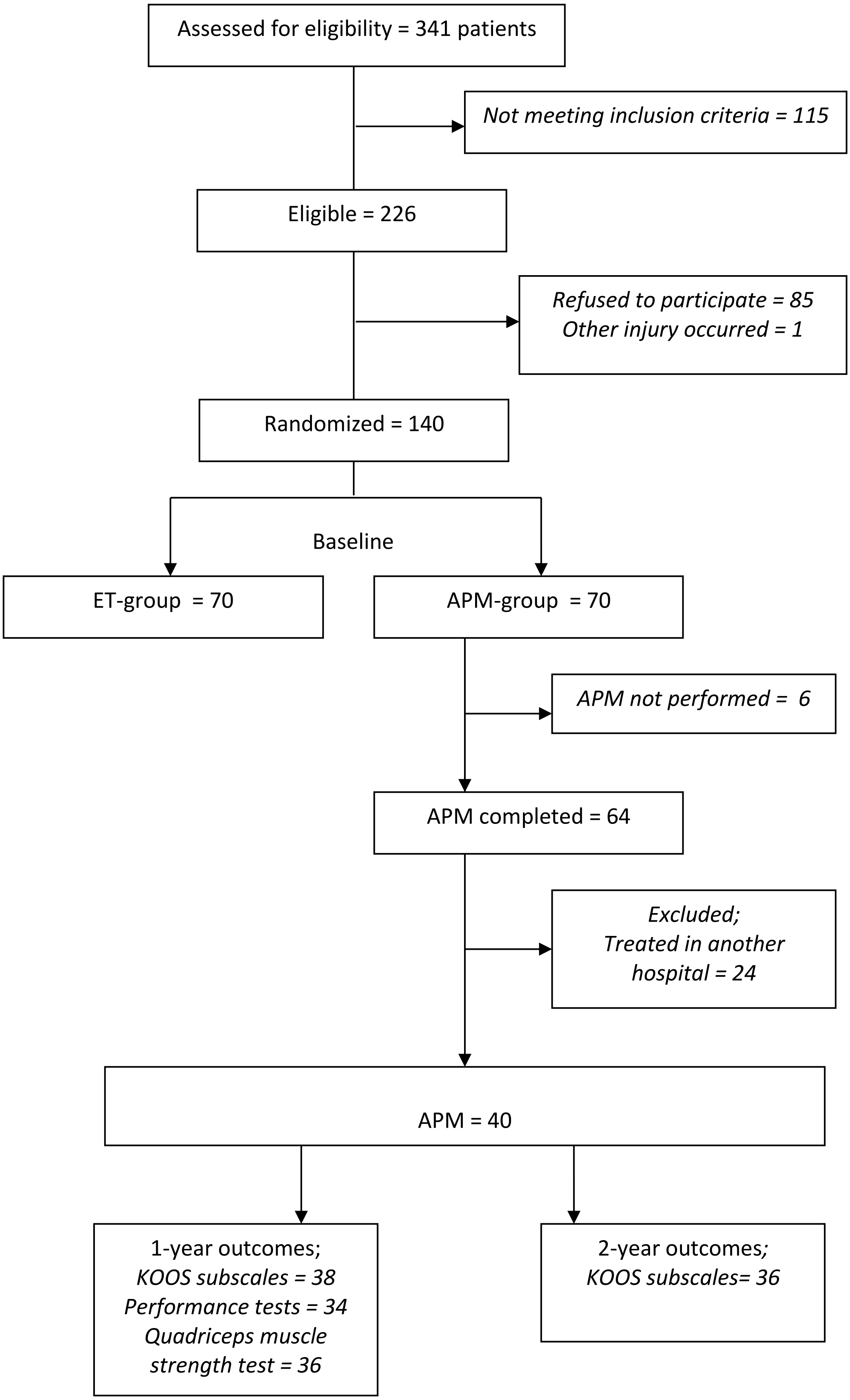

Table 1. Patient characteristics

Demography		N=40
Gender, male, n (%)		25 (63)
Age, years, mean (SD)		48.5 (5.9)
BMI[a], kg/m^2, mean (SD)		25.6 (3.5)
Smokers, n (%)		5 (13)
KL grade[b], n (%)	KL = 0	30 (75)
	KL = 1	8 (20)
	KL = 2	2 (5)
Number of days from MRI[c] to APM[d], n (SD)		112.9 (58.1)
Baseline function		
Performance tests:		
The 1-legged hop test for distance, cm, mean (SD)		89.9 (30.5)
The 6-meter timed hop test, sec, mean (SD)		2.4 (0.8)
The maximum knee bendings in 30 sec test, n, mean (SD)		33.6 (9.0)
Peak torque knee extension, Nm, mean (SD)		172.8 (47.7)
KOOS[e] subscales:		
Pain		69.5 (13.5)
Symptoms		77.7 (14.2)

ADL[f]			81.9 (12.7)
Sport/Recreation			47.3 (20.6)
QoL[g]			45.0 (15.3)
MRI		***Medial meniscus***	***Lateral meniscus***
Meniscal degeneration grade[h], n (%)	Grade 0	0 (0)	0 (0)
	Grade 1	0 (0)	0 (0)
	Grade 2	2 (5)	1 (3)
	Grade 3a	31 (78)	1 (3)
	Grade 3b	7 (18)	0 (0)
Tear localization, n (%)	Corpus only	0 (0)	0 (0)
	Posterior only	29 (73)	0 (0)
	Corpus / posterior	11 (28)	1 (3)
	Ant. /corpus / post.	0(0)	1 (3)
	Tear present	39 (98)	2 (5)
	No tear	1 (3)	38 (95)
Tear pattern, n (%)	Longitudinal-vertical	0 (0)	0 (0)
	Horizontal	13 (33)	2 (5)
	Radial	1 (3)	0 (0)
	Vertical flap	1 (3)	0 (0)
	Horizontal flap	0 (0)	0 (0)
	Root-avulsion	1 (3)	0 (0)
	Complex tears (2 or more patterns), n (%)	23 (58)	0 (0)

Extrusion present, n (%)	Yes	24 (60)		1 (3)
	No	16 (40)		39 (98)
Extrusion grade[i], % mean (SD)		19.3 (19.2)		20.0 (-)
Arthroscopy				
ACL[j] intact, n (%)	Yes		40 (100)	
	No		0 (0)	
		Medial compartment	***Lateral compartment***	***Patellofemoral compartment***
Cartilage injury present, n (%)	Yes	17 (43)	0 (0)	3 (8)
	No	23 (58)	40 (100)	37 (93)
		Medial meniscus		***Lateral meniscus***
Tear present, n (%)	Yes	40 (100)		1 (3)
	No	0 (0)		39 (98)
ISAKOS[k] classification:				
Tear depth, n (%)	Complete	30 (75)		1 (3)
	Partial	10 (25)		0 (0)

Tear length, mm, mean (SD)		15.6 (4.0)	8.0 (-)
Tear localization: Rim width (Circumferential localization), n (%)	Zone 1 (rim width < 3mm)	11 (28)	0 (0)
	Zone 2 (rim width 3-5 mm)	27 (68)	0 (0)
	Zone 3 (rim width > 5mm)	2 (5)	1 (3)
Tear localization, Radial localization, n (%)	Anterior only	0 (0)	0 (0)
	Corpus only	1 (3)	0 (0)
	Posterior only	13 (33)	1 (3)
	Corpus /posterior	26 (65)	0 (0)
	Anterior /corpus / post	0 (0)	0 (0)
Tear pattern, n (%)	Longitudinal-vertical	0 (0)	0 (0)
	Horizontal	5 (13)	0 (0)
	Radial	1 (3)	0 (0)
	Vertical flap	3 (8)	0 (0)
	Horizontal flap	9 (23)	0 (0)
	Root-avulsion	0 (0)	0 (0)
	Complex (2 or more patterns)	22 (55)	1 (3)
Quality of meniscal tissue; Degenerative, n (%)	Yes	40 (100)	1 (3)
	No	0 (0)	39 (98)

Surgery	***Medial meniscus***	***Lateral meniscus***
Amount of tissue excised %, mean (SD)	25.4 (8.9)	10.0 (-)
More than 20%, n (%)	21 (52.5)	0 (0.0)
20% or less, n (%)	19 (47.5)	1 (2.5)

[a]BMI, Body Mass Index; [b]KL grade, Radiographic osteoarthritic changes according to Kellgren and Lawrence (grade 0-4, lower is better); [c]MRI, Magnetic Resonance Imaging), [d]APM, arthroscopic partial meniscectomy; [e]KOOS, Knee Injury and Osteoarthritis Outcome Score; [f]ADL, Activities of Daily Living; [g]QoL, Quality of Life; [h]MRI-evaluated meniscal degeneration grade according to Crues et al. (grade 0-3b, lower is better); [i]MRI-evaluated meniscal extrusion given in percent evaluated on the coronal sequence image with the largest tibial spine volume, defined as meniscal subluxation crossing a vertical line on the medial margin of tibia without osteophytes (lower is better); [j]ACL, anterior cruciate ligament; [k]ISAKOS, The International Society of Arthroscopy, Knee surgery and Orthopaedic Sports medicine

MRI evaluation

MRI scans were read by an experienced radiologist (RT). Sagittal, coronal and transversal images were used to classify medial meniscal tear pattern and grade of meniscal extrusion. For description of baseline characteristics, meniscal degeneration grade and tear localization were recorded. Degeneration grade was evaluated according to Crues et al. [13] (grade 0-3b (better to worse). Grade 0 represents healthy meniscal tissue, grade 1 represents tissue degeneration inside the meniscus, grade 2 a tear not reaching the surface of the meniscus, grade 3 a tear penetrating one (3a) or both (3b) surfaces of the meniscus [13].

Tear localization and tear pattern were evaluated by using parameters comparable to the International Society of Arthroscopy, Knee surgery and Orthopedic Sports medicine (ISAKOS) meniscal tear classification system [2]. Localization was classified as posterior, mid-body (corpus) or anterior, pattern was categorized as longitudinal-vertical, horizontal, radial, vertical flap, horizontal flap or complex (2 or more tear patterns). Suggesting that complex tears with 2 or more tear patterns reflected more severe pathology, the tear pattern was dichotomized into complex tears and tears with only one tear pattern.

Meniscal extrusion was evaluated on the coronal sequence images with the largest volume of the tibia spines. Meniscal tissue crossing a vertical line on the medial margin of the tibia without osteophytes was defined as meniscal subluxation. Extrusion was given in percent (width of subluxated tissue divided by the entire width of the meniscus in the same image, higher is worse) [21] (Figure S1 in the Supplementary appendix).

Treatment strategy

APMs were performed using 30 degrees optics, standard portals and Ringer acetate lavage. A diagnostic procedure (evaluating menisci, joint surface cartilage and cruciate ligaments) was followed by resection of unstable meniscal tissue. The patients were mobilized with crutches for 3-4 days postoperatively and received oral and written instructions for home exercises aimed at reducing symptoms and regaining normal function [36].

Arthroscopic evaluation

Tear length and presence of cartilage injury in the medial knee compartment and amount of meniscal tissue excised were recorded. For description of baseline characteristics, quality of the meniscal tissue (degenerative or not), tear depth and localization, pathology of the lateral meniscus, anterior cruciate ligament and joint line cartilage in the medial, lateral and patella-femoral compartments were recorded.

For grading of the meniscal tears and amount of tissue excised, we used the ISAKOS [2] classification system for meniscal injuries. According to ISAKOS classification[2] tear depth was categorized as partial or total, mirroring the MRI meniscal classification [13] of grade 0-3b [2]. Tear length was evaluated in millimeters (length of the tear penetrating one or both surfaces of the meniscus compared to the known length of the arthroscopic probe). Tear localization was classified circumferentially (rim width; locations included zone 1 (tears of the meniscus-synovial junction or a tear with a rim of <3millimeters), zone 2 (rim of 3 to <5 millimeters) and zone 3 (rim of >5 millimeters)) and radially (posterior horn – corpus of the meniscus – anterior horn) [2]. Tear pattern was classified as longitudinal-vertical, horizontal, radial, vertical flap or horizontal flap or complex (2 or more tear patterns) [2]. Amount of tissue that was excised was estimated relative to the total volume of a healthy meniscus [2]. Since excision of 20% of the total meniscal volume has shown to increase the stress on articular cartilage [59], we dichotomized the amount of tissue excised to less than and equal to 20% or more than 20%. Inter-observer agreement for the ISAKOS classification of meniscal tears has previously been measured with Cohen's kappa (κ) ranging from 0.46 (circumferential localization) to 0.65 (radial localization) and intra-class correlation (ICC) ranging from 0.65 (amount of tissue excised) to 0.83 (tear length) [2].

We included the International Cartilage Repair Society (ICRS) [15] system for classification of cartilage injury. This system classifies the seriousness (depth) of the cartilage injury (graded from 0 to 4, where 0 is normal and is 4 severely abnormal) [15]. Inter-observer reliability for the ICRS classification of cartilage injury has been reported to 0.67 [15].

Inter-rater reliability

To ensure acceptable reliability of the ISAKOS and ICRS classification systems for the rater (NJK) in this study, a small inter-reliability study was performed between NJK and another orthopedic surgeon (CA) (see Supplementary appendix for details). Our inter-observer correlation coefficients (ICCs) for medial meniscus tear depth, length, localization, pattern and amount of tissue that had been excised ranged from 0.46 to 0.83, indicating moderate to high inter-reliability [42]. For the ICRS cartilage injury classification, the ICCs were only 0.27 and 0.15 for medial femur condyle and medial tibia plateau, indicating at most fair inter-reliability [42]. Hence, the ICRS classification was not reported in this study. However, the two surgeons could agree on whether a cartilage injury in the medial compartment was present or absent in 22 out of 23 knees

(95.7%, κ=0.91). Therefore, joint cartilage injuries were evaluated as present (ICRS grade 1-4) or absent (ICRS grade 0).

<u>Outcomes at 1 and 2 years</u>

Lower extremity hop performance, quadriceps muscle strength and a patient-reported measures (the Knee Injury and Osteoarthritis Outcome Score (KOOS) [47]) were recorded at baseline and 1 year. The KOOS was also collected at 2 years.

Lower extremity performance was measured by 3 single-legged tests; the 1-leg hop test for distance, the 6-meter timed hop test and the maximum number of knee-bendings in 30 seconds test [8, 9, 49], and quadriceps muscle strength. Isokinetic knee extension test was measured using a dynamometer at 60^0/second (Biodex 6000 System; Biodex Medical Systems Inc, Shirley, NY, US) [14]. The quadriceps muscle strength was reported in Newton meters (Nm). These test procedures are previously described in detail [54].

The KOOS consists of 42 items, scored from 0 to 4 on a Likert scale, covering 5 subscales; Pain, other Symptoms, ADL (Activity of Daily Living), function in Sport and Recreation (Sport/Rec) and knee related Quality of Life (QoL). The subscales are scored separately and transformed to a 0-100 scale (worse to best). The KOOS is reliable and valid for patients with meniscal tears [47, 48].

The clinically relevant differences between the groups of patients who reported their knee function as "unchanged" compared to those who reported their knee function as "better" for the 5 KOOS subscales have previously been reported for the patients of this study[36, 37]. A five-point global rating of change scale [29] (much worse, worse, unchanged, better, much better) was used and generated the following cut-offs for the 5 KOOS subscales: Pain 8.1, Symptoms 9.2, ADL 5.0, Sport/Rec 11.5 and QoL 15.1 points [36, 37]. These cut-offs for evaluation of clinical relevance of the prognostic factors were included in this study. For the categorical variables (complex meniscal tear, cartilage injury and more than 20% of tissue excised) prognostic factors were considered clinically relevant if they were associated with differences in outcomes larger than the clinically relevant differences given above. For the continuous variables (meniscal extrusion given in percent and meniscal tear length) prognostic factors (measured in percent and millimeters) were considered clinically relevant if they were associated with differences in outcomes larger than the cut-offs given above.

Statistical analysis

No power analysis was performed for this secondary study of a patient subgroup from the OMEX trial [36].

The statistical computation was performed using IBM SPSS Statistics version 25 (IBM Corp. 2017, Armonk, NY, US) (descriptive statistics and correlation analyses) and Stata v15.1 (Stata 2017, College Station, TX, US) (regression analyses). For continuous variables, descriptive statistics were presented in terms of mean, standard deviation (SD) and the number of observations (N), and for categorical variables in terms of frequencies and percent. The uncertainty of parameter estimates was presented in terms of 95% confidence intervals (CIs). The statistical methods' underlying assumptions were fulfilled.

A total of 14 regression models were built. Due to the exploratory nature of this study, no adjustments for multiplicity were done [6]. Multiple linear regression models were applied for the 3 single-legged performance tests [8, 9, 49] and quadriceps muscle strength [14] at 1-year as dependent variables. Longitudinal tobit regression models [58] were applied for the 5 KOOS subscales at 1 and 2 years as dependent variables. All analyses included the following independent variables: MRI-evaluated tear pattern and extrusion grade and arthroscopically evaluated tear length, presence of cartilage injury in the medial knee compartment and amount of meniscal tissue excised. All analyses were adjusted for age, gender, BMI (body mass index) and baseline scores of the dependent variables.

Longitudinal tobit regression analyses [58] were used since ceiling effects of the KOOS subscales are known to be present post-surgery [62]. These analyses censor the data points reaching the minimal and maximal values (which are not normal distributed), and examine the variation between the outer points and minimize the bias of ceiling effects [58]. Additionally, for comparison to the tobit analyses, also conventional regression analyses were performed.

RESULTS

The patients, 25 (62.5%) men and 15 (37.5%) women, were between 35-60 years old (mean 48.5, SD 5.9), had unilateral non-traumatic medial knee pain, a BMI of 25.6 (SD 3.5), a MRI verified medial meniscal tear and only two out of the 40 patients had definite radiographic signs of OA (KL [32] grade 2) . Patient demographics, findings from MRI and surgery are presented in Table 1. Complete results of the regression models are presented in Table 2. Summary of clinically relevant prognostic factors of better and worse outcomes are presented in Table 3. Comparison of longitudinal tobit analyses and conventional linear regression analyses of the KOOS subscales are presented in Table S3.

Table 2. Associations between preoperative MRI[a] -findings, arthroscopic findings and amount of meniscal tissue excised and 1- and 2-year outcomes

	MRI-findings		**Arthroscopic findings**		**Surgery**
	Complex meniscal tear[b]	1% larger meniscal extrusion	1 mm larger meniscal tear	Cartilage injury[c]	More than 20% of meniscal tissue excised
1-year outcomes					
The 1-legged hop test for distance, cm	-6.3 (-18.3 to 5.6)	0.1 (-0.2 to 0.4)	0.7 (-0.7 to 2.0)	-0.1 (-14.1 to 14.0)	1.2 (-14.1 to 16.5)
The 6-meter timed hop test, sec	0.1 (-0.2 to 0.4)	-0.0 (-0.0 to 0.0)	-0.0 (-0.0 to 0.0)	-0.0 (-0.2 to 0.2)	0.0 (-0.3 to 0.3)
The maximum knee bendings in 30 sec. test, n	-4.3 (-9.9 to 1.3)	0.0 (-0.2 to 0.2)	-0.5 (-1.3 to 0.3)	**6.5 (2.3 to 10.7)**	1.5 (-3.0 to 6.0)
Peak torque knee extension, Nm	7.7 (-4.3 to 19.7)	0.2 (-0.3 to 0.7)	-0.1 (-1.8 to 1.6)	-1.6 (-14.8 to 11.6)	-9.1 (-22.4 to 4.2)
KOOS[f] subscales					
Pain	8.5 (-2.5 to 19.4)	-0.2 (-0.5 to 0.1)	0.6 (-0.9 to 2.1)	-0.3 (-9.6 to 9.0)	**-14.4 (-27.3 to -1.4)**
Symptoms	-0.8 (-9.8 to 8.3)	-0.1 (-0.3 to 0.1)	**1.3 (0.1 to 2.6)**	-1.8 (-9.7 to 6.1)	**-12.9 (-23.0 to -2.9)**

ADL[g]	14.9 (-2.0 to 31.8)	**-0.5 (-0.9 to -0.0)**	1.4 (-0.6 to 3.4)	0.3 (-12.4 to 13.1)	**-23.1 (-44.5 to -1.8)**
Sport/Rec	17.8 (2.0 to 33.6)	**-0.5 (-0.8 to -0.1)**	**1.7 (0.1 to 3.4)**	-8.0 (-18.9 to 2.8)	**-17.5 (-33.6 to -1.3)**
QoL[h],	**14.7 (1.9 to 27.4)**	-0.3 (-0.6 to 0.1)	0.2 (-1.3 to 1.8)	-8.1 (-18.6 to 2.4)	-10.4 (-27.2 to 6.4)
Two-year outcomes KOOS[f] subscales					
Pain	-4.1 (-13.8 to 5.7)	-0.2 (-0.4 to 0.1)	0.4 (-0.7 to 1.5)	-7.7 (-15.6 to 0.2)	**-17.8 (-29.1 to -6.4)**
Symptoms	**-14.1(-22.2 to -6.1)**	0.2 (-0.0 to 0.4)	0.7 (-0.2 to 1.6)	**-7.0 (-12.9 to -1.0)**	**-12.0 (-18.9 to -5.1)**
ADL[g]	-7.1 (-14.2 to 0.0)	-0.2 (-0.3 to 0.0)	0.0 (-0.6 to 0.6)	**-10.4 (-17.4 to -3.4)**	**-8.9 (-15.5 to -2.2)**
Sport/Rec	0.9 (-15.9 to 17.8)	**-0.5 (-1.0 to -0.1)**	**1.8 (0.1 to 3.4)**	-10.6 (-28.5 to 7.3)	**-41.5 (-62.0 to -21.0)**
QoL[h]	5.2 (-5.0 to 15.4)	-0.4 (-0.9 to 0.0)	0.9 (-0.6 to 2.5)	**-19.4 (-31.1 to -7.7)**	**-25.3 (-37.0 to -13.6)**

All analyses adjusted for age, gender, BMI and baseline scores of the dependent variable. Data are shown as mean (95% CI). Statistically significant results in **bold**.

[a]MRI, Magnetic Resonance Imaging; [b]Complex meniscal tears, 2 or more tear patterns; [c] Cartilage injury present in medial joint compartment; [f]KOOS, Knee injury and Osteoarthritis Score, higher is better; [g]ADL, Activities of Daily Living; [h]QoL, Quality of Life

Table 3. Prognostic factors for clinically relevant better and worse outcomes for KOOS[a] 1-2 years following APM[b]

	MRI[c] findings		Arthroscopic findings		Surgery
	Complex meniscal tear[d]	Meniscal extrusion larger than the given percent (%)	Meniscal tear larger than the given length millimeters (mm)	Cartilage injury[e]	More than 20% of meniscal tissue excised
1-year outcomes		Worse KOOS ADL[f] (11%), Sport/Rec (25%)	Better KOOS Symptoms (7.0 mm), Sport/Rec (6.7 mm)	Better Maximum knee bendings in 30 sec. test	Worse KOOS Pain, Symptoms, ADL, Sport/Rec
2-years outcomes	Worse KOOS Symptoms	Worse KOOS Sport/Rec (20%)	Better KOOS Sport/Rec (6.5 mm)	Worse KOOS ADL, QoL[g]	Worse KOOS Pain, Symptoms, ADL, Sport/Rec, QoL

Levels of prognostic factors associated with clinically relevant differences (for the KOOS subscales, the following clinically relevant differences were used: Pain 8.1, Symptoms 9.2, ADL 5.0, Sport/rec 11.5, QoL 15.1 points). For the categorical variables (complex meniscal tear, cartilage injury and more than 20% of tissue excised) prognostic factors were considered clinically relevant if they were associated with differences in outcomes larger than the clinically relevant differences. For the continuous variables (meniscal extrusion given in percent and meniscal tear length) exact levels of the prognostic factors associated with the clinically relevant differences were calculated.

[a]KOOS, Knee injury and Osteoarthritis Score; [b]APM, arthroscopic partial meniscectomy; [c]MRI, Magnetic Resonance Imaging; [d]Cpmplex tears, 2 or more tear patterns; [e]Cartilage injury present in medial joint compartment; [e]ADL, Activities of Daily Living; [g]QoL, Quality of Life

MRI-findings

Having a complex meniscal tear was a prognostic factor for clinically relevant worse KOOS Symptoms at 2 years (14.1 points, 95% CI 6.1 to 22.2) (Table 2). Meniscal extrusions of at least 11%, 25% and 20% were prognostic factors for clinically relevant worse KOOS ADL at 1 year and worse KOOS Sport/Rec at 1 and 2 years, respectively (Table 3).

Arthroscopic findings and surgery

Presence of a cartilage injury in the medial compartment was a prognostic factor for clinically relevant worse KOOS ADL and QoL at 2 years (10.4-19.4 points, 95% CIs 3.4 to 17.4 and 7.7 to 31.1) (Table 2). Excision of more than 20% of the meniscal tissue was a prognostic factor for clinically relevant worse KOOS Pain, Symptoms, ADL and Sport/Rec at 1 and 2 years (8.9-41.5 points, 95% CIs ranging from 2.2 to 15.5, to 21.0 to 62.0) and clinically relevant worse QoL at 2 years (25.3 points, 95% CI 13.6 to 37.0) (Table 2).

Counterintuitively, meniscal tear lengths of at least 6.5-7.0 mm were prognostic factors for clinically relevant *better* KOOS Symptoms at 1 and *better* KOOS Sport/Rec at 1 and 2 years, respectively (Table 3). Presence of a cartilage injury in the medial tibiofemoral compartment was associated with performing a *higher* number of knee-bendings in 30 seconds at 1 year (6.5 more bendings, 95% CI 2.3 to 10.7) (Table 2).

DISCUSSION

The main findings of this study were that complex meniscal tears and extrusions of at least 11% evaluated on preoperative MRI scans, cartilage injury diagnosed arthroscopically and meniscal excisions as small as 20% were prognostic factors for clinically relevant inferior outcomes after 1 and 2 years. Identification of these prognostic factors on inferior 1- and 2-year knee function following APMs, is new knowledge.

Arthroscopically, the frequency of complex meniscal tears has been reported to 12%-39% [11, 28]. In our study, 23 out of 40 patients (58%) had MRI-diagnosed complex meniscal tears and only in one out of 40 patients (3%) there was disagreement of presence of complex meniscal tear between the MRI scoring and arthroscopy findings. The prognostic value of the diagnosis of complex tears assessed on preoperative MRI scans might weaken the indication for treatments with APM.

Previously, a cohort study of 718 middle-aged persons without radiographic OA reported a mean medial meniscal extrusion of 2.7 millimeters, and with a concomitant meniscal tear, the extrusion were 0.6-1.0 millimeters larger [55]. Patients who developed OA during the 4-year study period (defined as increase in KL grade from 0-1 to 2-4) had 3.8% larger medial meniscal extrusion at baseline than patients that not developed OA (25.8% versus 22%) [55] . Another study has shown significant correlation between larger meniscal extrusions at baseline and worse patient-reported outcomes 7 years following APMs [35]. Our study of patients with no or minimal radiographic OA and degenerative meniscal tears treated with APMs, have shown that larger extrusions also is prognostic for inferior 1- and 2-year function.

In our study, the frequency of cartilage injuries was 43%. In a study of 497 consecutive knee arthroscopies in somewhat younger patients (mean age 41 years) the frequency was lower, 19% [11] and in a study of 993 consecutive knee arthroscopies, the frequency was 66%, but as many as 13% of this study population had radiographic degenerative changes [4]. Focal cartilage injuries are shown to be associated with more pain and functional impairments [22]. In patients with degenerative meniscal tears and moderate radiographic OA (grade 2-3), cartilage injuries have been found to be predictive of worse patient reported outcomes [26, 46, 53]. Our study showed that an arthroscopically diagnosed cartilage injury also was a significant prognostic factor for inferior outcomes at 2 years in patients with no or minimal radiographic OA (KL grade 0-2 [32]).

Previous studies have shown associations between excisions of more than 50% of the total meniscal volume and inferior outcomes [16, 18]. Our study, with the mean tissue excision of 25.4% (SD 8.9), showed that also excision of smaller amounts of meniscal tissue (20% or more of the total meniscal volume) was a prognostic factor for clinically relevant worse outcomes after 1 and 2 years.

The results of longer meniscal tears and presence of cartilage injury as prognostic for better KOOS outcomes were actually contrary to expectation. However, one theory is that patients with larger meniscal tears, that perhaps were more unstable and gave more symptoms, might have had more symptom relief from meniscal resection than patients with smaller tears. Likewise, patients with cartilage injury might have had symptoms from the incongruency of the surfaces of both the meniscus and the joint cartilage, hence, meniscal resection gave relief. However, these theories are speculative and larger studies should explore this.

This secondary analysis of surgically treated patients from the OMEX trial shows associations between findings on MRI and arthroscopy and inferior 1- and 2-year outcomes. The study is preliminary and by nature hypothesis generating. Therefore, we accepted the following limitations: Firstly, no power analysis was performed. A small sample size might have led to type II errors – increased risk for not discovering associations between meniscal morphology and outcomes. Secondly, the regression models contained five independent variables and adjustments for three variables. Hence, the number of subjects per variable was five. Usually the rule of thumb is to include maximum one variable per ten subjects, but some authors claim that a minimum of approximately two subject per variable give results in estimation of regression coefficients with relative bias less than 10% [5]. Thirdly, no adjustments for multiplicity were included, and the results should definitely be interpreted as exploratory results [6]. Our findings highlight the need for larger prospective cohort studies with the primary aim of examining associations between several morphology variables assessed by arthroscopy and preoperative MRI scans and longer-term outcomes.

In addition to the limitations of this study described above, there are several strengths of this study. Firstly, the study provides new knowledge and is an important hypothesis generating study for evaluation of meniscal morphology as a prognostic factor for patient reported outcomes after 1 and 2 years. Secondly, the MRI scans were evaluated by an experienced senior radiologist. A third strength is the inter-rater reliability testing of the orthopedic surgeon who rated all the arthroscopic findings. Reliability of ISAKOS classification and ICRS classification have in previous studies been shown to be low to moderate. Hence, study specific reliability data are needed. Acceptable correlation values (≥ 0.46) were found for 5 out of 6 parameters, and these variables were therefore considered reliable and included in the analysis. The ICRS classification of cartilage injuries had very low inter-rater reliability and the data was not included in the analysis. Finally, we included longitudinal tobit regression analyses [58] which minimize the bias of ceiling effects [58] of the KOOS subscales, known to be present post-surgery [62]. In this study, large ceiling effects were present for all 5 KOOS subscales at 1 (15.8-55.3%) and 2 years (25.0-61.1%). However, at baseline the ceiling effects were minimal (KOOS Symptoms 7.5% and KOOS ADL 2.5%) and the potential for improvement was definitely present. Comparison of the results of the longitudinal tobit regression analyses to multiple linear regression analyses confirmed the direction of the estimates (Table S5, Supplementary appendix).

CONCLUSION

This study showed that complex meniscal tears and larger meniscal extrusion evaluated on MRI, cartilage injuries diagnosed arthroscopically and excision of amounts of meniscal tissue as small as 20% were statistically significant and clinically important prognostic factors for worse patient-reported outcomes 1 and 2 years after surgery. This study derived important new knowledge and should be a hypothesis generating study for larger cohorts designed to address knee morphology as prognostic factors in patients with degenerative meniscal tear.

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Competing interests

All authors have completed the Author Disclosure Statement (available on request from the corresponding author) and declare that they have no support from any company for the submitted work; no relationships with any company that might have an interest in the submitted work in the previous three years; their spouses, partners, or children have no financial relationships that may be relevant to the submitted work; and they have no non-financial interests that may be relevant to the submitted work.

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Authors' contributions

Ewa M. Roos, May Arna Risberg (MAR) and Silje Stensrud (SS) developed the concept and design for the RCT this study cohort is extracted from. SS, Lars Engebretsen and Nina Jullum Kise (NJK) collected the data. NJK and MAR developed the idea for this secondary study of data from the RCT. Rana Tariq read the MRI images. NJK and Cathrine Aga collected the data for the inter-observer study. NJK wrote the manuscript. NJK and independent statistician Jonas Ranstam did the statistical analyses. All authors had full access to all of the data including statistical reports and tables in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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