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Title: Development of osteoarthritis in patients with degenerative meniscal tears treated with exercise therapy or surgery. A randomized controlled trial

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ABSTRACT

Objective

To evaluate progression of individual radiographic features five years following exercise therapy or arthroscopic partial meniscectomy as treatment for degenerative meniscal tear.

Design

Randomized controlled trial including 140 adults, aged 35-60 years, with a magnetic resonance image verified degenerative meniscal tear, and 96% without definite radiographic knee osteoarthritis. Participants were randomized to either 12-weeks of supervised exercise therapy or arthroscopic partial meniscectomy. The primary outcome was between-group difference in progression of tibiofemoral joint space narrowing and marginal osteophytes at five years, assessed semi-quantitatively by the OARSI atlas. Secondary outcomes included incidence of radiographic knee osteoarthritis and symptomatic knee osteoarthritis, medial tibiofemoral fixed joint space width (quantitatively assessed), and patient-reported outcome measures. Statistical analyses were performed using a full analysis set. Per protocol and as treated analysis were also performed.

Results

The risk ratios (95% CI) for progression of semi-quantitatively assessed joint space narrowing and medial and lateral osteophytes for the surgery group were 0.89 (0.55-1.44), 1.15 (0.79-1.68) and 0.77 (0.42-1.42), respectively, compared to the exercise therapy group. In secondary outcomes (full-set analysis) no statistically significant between-group differences were found.

Conclusion

The study was inconclusive with respect to potential differences in progression of individual radiographic features after surgical and non-surgical treatment for degenerative meniscal tear.

Further, we found no strong evidence in support of differences in development of incident radiographic knee osteoarthritis or patient-reported outcomes between exercise therapy and arthroscopic partial meniscectomy.

Trial registration: www.clinicaltrials.gov (NCT01002794)

Keywords: Degenerative meniscal tears; Knee arthroscopy; Partial meniscectomy; Exercise therapy; Knee osteoarthritis; Rehabilitation

Running title: Exercise or surgery for meniscal tears

Introduction

Degenerative meniscal tears are common in the middle-aged and elderly population[1]. Over the past decades, arthroscopic partial meniscectomy has been the mainstay treatment and it is one of the most performed orthopedic procedures[2]. Several randomized controlled trials including patients with no or mild knee osteoarthritis have found that surgery provides no clinically relevant benefit compared to non-surgical interventions or sham surgery[3-8]. The accumulating evidence questioning the clinical relevant effect of the procedure has led to clinical guidelines refraining to recommend surgery for degenerative meniscal tears[9,10].

Loss of meniscal function increases focal stress across the knee joint, which may lead to cartilage breakdown and subsequent knee osteoarthritis[11]. Both meniscal tears per se and partial meniscectomy are strong risk factors for incident knee osteoarthritis and progression[12-14]. Furthermore, meniscectomy have been found to be associated with a threefold increase in the risk for knee replacement surgery[15]. However, very little is known about the long-term consequences of degenerative meniscal tears following non-surgical interventions. Radiography remains the most used imaging modality for knee osteoarthritis diagnosis, but radiographic classification systems are insensitive to measure progression [16]. Using grades for individual radiographic features and quantitatively measured joint space width may reveal higher progression rates [17]. None of the randomized controlled trials including only patients with no or mild knee osteoarthritis evaluates progression of individual radiographic features of the knee. Hence, there is a need for randomized controlled trials evaluating long-term consequences on both patient-reported and structural outcomes.

In a previous report of the Odense-Oslo Meniscectomy versus Exercise (OMEX) trial no significant difference in patient-reported outcomes was found at two years between exercise therapy and arthroscopic partial meniscectomy[7]. The primary aim of this follow-up study of the OMEX trial was to evaluate progression of individual radiographic features of the knee joint five years following exercise therapy or arthroscopic partial meniscectomy as treatments for degenerative meniscal tears. Secondary objectives were to compare incidence of radiographic and symptomatic knee osteoarthritis and difference in change in patient-reported outcomes.

Method

Trial design

We conducted a randomized controlled trial during the period from October 2009 through September 2012 with two parallel intervention groups (1:1 ratio) comparing exercise therapy with arthroscopic partial meniscectomy. Follow-up assessment at five years was performed during clinic visits and included radiographic assessment and patient-reported questionnaires.

The trial was registered at clinicaltrials.gov (NCT01002794), was conducted according to the Declaration of Helsinki and approved by the regional ethics committee of the Health Region of South-East Norway (ref-no 2009/230). All participants gave written informed consent.

Deviations from trial registration

The primary outcome measure at five years was described as incident and enlarging marginal tibiofemoral osteophytes. However, as the prespecified aim was to describe radiographic changes in knee osteoarthritis development, the primary outcome measure was changed to a radiographic atlas assessing *both* joint space narrowing and osteophytes, separately[18]. This change was made prior to radiographic assessments and analyzing the data.

Participants

Participants were recruited from two orthopedic departments in Norway, Oslo University Hospital (October 2009-April 2011) and Martina Hansens Hospital (May 2011-September 2012). Inclusion criteria were: 35 to 60 years of age, non-traumatic unilateral knee pain (>2 months), MRI-verified medial degenerative meniscal tear, at most grade 2 radiographic changes according to the Kellgren and Lawrence classification[19], able to participate in exercise therapy and be considered eligible for surgery. Degenerative meniscal tear was defined as an intrameniscal linear MRI signal penetrating one or both surfaces of the meniscus[20]. Participants with acute knee trauma, ligament injury, locked knee, and surgery in the index knee during the previous two years were excluded.

Interventions

The exercise therapy intervention was carried out by experienced physical therapists at the Norwegian Sports Medicine Clinic (Nimi) or Gnist Trening og Helse AS. The 12-week exercise therapy program consisted of progressive neuromuscular and strength exercises and has been previously published[21]. Both clinics used the same protocol for a minimum of two and a maximum of three sessions per week, supervised once a week by a physical therapist. The participants wrote exercise diaries and compliance with exercise was defined as the total number of exercise sessions completed out of 24 sessions. Participation in ≤18 sessions was predefined as poor compliance (<80%). Only participants completing at least 19 sessions (>80%) were included in the per protocol analysis (Supplementary Figure S1). For the surgery group, receiving 18 sessions or more of exercise therapy instructed by a physical therapist was defined as not following the protocol.

Standard arthroscopic partial meniscectomy was performed by experienced surgeons (minimum 10 years) at the respective hospital the participants were recruited from. The arthroscopic procedure has been previously described[7]. In short, the procedure involved anteromedial and anterolateral portals, and additional portals and a lavage cannula in the cranial recess were made if required. A diagnostic procedure including systematically probing of both menisci was followed with resection of all unstable meniscal tissue. Postoperative routines included the use of two crutches and simple home exercises, which have been previously published[7] [Supplementary appendix].

Primary outcome

Primary endpoint of the five-year follow-up was progression of osteophytes and joint space narrowing as assessed semi-quantitatively from baseline to the five-year follow-up. Radiographs were acquired utilizing a standardized protocol[22]. The protocol included weight-bearing, posterior-anterior radiographs, 10° caudal x-ray beam angulation and the use of a Synaflexer (Synarc, Newark, CA) positioning frame. Baseline radiographs were acquired at the recruiting hospital, and at a private radiology clinic for the five-year follow-up. Some inconsistencies from the prespecified protocol were identified in the radiographic acquisition methods. Four participants in the exercise therapy group and two in the surgery group had anterior-posterior radiographs at baseline. The anterior-posterior radiographs were included in the analysis. The mean (SD) beam angle was 10.0 (6.3) at baseline and 10.5 (2.8) at five years, with no difference between the groups.

An orthopedic surgeon with more than 20 years of radiographic evaluation experience and a physician graded all radiographs blinded to group allocation and clinical data. Inter-rater reliability for the two readers has been previously evaluated for joint space narrowing and osteophytes assessed by the Osteoarthritis Research Society International (OARSI) atlas and the Kellgren and Lawrence classification (weighted k 0.73, 0.63 and 0.67, respectively)[23]. Images were read paired and unblinded to time sequence with readers working independently. Any discrepancies between the readers were adjudicated in consensus sessions.

The individual radiographic features, joint space narrowing and osteophytes, were scored separately for the medial and lateral tibiofemoral compartments on a 0 (normal) to 3 (severe changes) atlas-based scale from OARSI[18]. Both the involved and uninvolved knee were assessed. When progression had occurred, but without achieving a full grade on the integer scale, half-grades were used[17]. Participants undergoing subsequent tibial osteotomy were given a joint space narrowing score of 3 for the affected compartment. Total knee arthroplasty was considered reflective of end-stage radiographic knee osteoarthritis. The affected compartment was, therefore, given a score of 3 for both joint space narrowing and osteophytes. In addition to assessing progression for each individual radiographic feature, a sum score was calculated to give a total radiographic score for one knee (sum of medial and lateral compartment joint space narrowing and osteophyte score).

Secondary outcomes

Secondary radiographic outcome measures were the Kellgren and Lawrence classification[19] and medial fixed joint space width (fJSW) measured quantitatively[24]. The Kellgren and Lawrence classification classify the severity of knee osteoarthritis in five grades, from 0 (normal) to 4 (severe)[19]. We used the proposed modification by Felson et al, including a grade with definite osteophyte only (grade 2/ost)[25]. Grade 2 (definite osteophyte and possible joint space narrowing) was defined as the cut-off for radiographic knee osteoarthritis, and incidence as emergence of grade ≥2 in knees graded as 0 or 1 at baseline. Participants receiving total knee arthroplasty were also categorize as having incident radiographic knee osteoarthritis. Additionally, we classified participants as having incident symptomatic knee osteoarthritis when reporting knee pain at least weekly in addition to incident radiographic knee osteoarthritis[26]. This information was derived from the Knee Injury and Osteoarthritis Outcome Score (KOOS) pain subscale (question P1)[27].

fJSW was measured in the medial and lateral compartment separately. With the use of a computer software the femoral and tibial margins was automatically delineated. Two readers verified the computer-determined delineations and made corrections where necessary. Based on anatomical landmarks a coordinate system was automatically established to facilitate consistent measurements of fJSW[24]. Medial and lateral fJSW was measured at location x = 0.250 and x = 0.750, respectively[28]. Change in millimeter was calculated by subtracting the fJSW at baseline from the corresponding five-year measurement. Hence, a negative value indicates joint space narrowing. Only the change in medial fJSW was compared between the groups. Participants in which only the lateral compartment exhibited joint space narrowing (indicated by the OARSI score) was excluded from this analysis, since lateral progression may result in widening of the medial joint space width (so-called pseudo-widening)[17]. Lateral fJSW is reported for descriptive purposes only.

Patient-reported outcomes were changes from baseline to five years for the five subscales of the KOOS[27]. The KOOS holds 42 items, covering five dimensions that are scored separately; pain, other symptoms, activities of daily living, sport and recreational function, and knee-related quality of life.

Sample size

The sample size was calculated based on primary end-point at two years in the OMEX trial, the change in $KOOS_4$ from baseline to the two year follow-up[7]. To detect a 10 point difference with a standard deviation of 15, an estimated dropout rate of 15%, and allow for a 20% crossover rate, 140 participants were randomized. For the primary end-point for the five-year follow-up, no power calculations were performed a priori.

Randomization

The participants were randomly allocated into one of the two intervention groups. The computer-generated randomization sequence was determined by an independent statistician at Oslo University Hospital, stratified by sex in blocks of eight. The allocations were placed in sequentially numbered opaque envelopes prepared by the statistician and was concealed from the surgeon who enrolled and assessed the participants.

Statistical methods

Analyses were based on the full analysis set which included all participants as randomized, irrespective of treatment actually received, adherence or crossover, without imputation of missing data. Additionally, as treated and per protocol analyses were performed.

Poisson regression with robust standard errors was used to compare treatment groups with respect to progression of individual radiographic features, with separate models for joint space narrowing and medial and lateral osteophytes. This approach was chosen based on the high prevalence of the outcome, and to avoid convergence problems that may arise from binominal regression[29]. The results are presented as risk ratios with 95% confidence intervals. All models were adjusted for the stratification variable, sex. For ease of interpretation, the adjusted risk difference is also presented. Only a minority of the participants had lateral joint space narrowing, therefore, the medial and lateral compartment were combined and joint space narrowing in either compartment defined as progression. Progression was defined as increase by a compartment sum of 1 or above for osteophytes, and grade 1 or above for joint space narrowing. Due to the small number of participants with more than 1 grade progression, we collapsed grade 1, 2 and 3.

Between-group difference in incident radiographic and symptomatic knee osteoarthritis were analyzed similar to the primary outcome measure. Between-group difference in change in fJSW, in all five KOOS subscales and total radiographic score were tested with the use of analysis of covariance (ANCOVA), with sex and baseline value of the outcome as covariates. Normality of the residuals were visually inspected by histograms and descriptive statistics. Preliminary checks were also conducted to ensure no violation of the assumptions of linearity, homogeneity of variances and homogeneity of regression slopes. For all radiographic outcomes, analyses were repeated for both the involved and uninvolved leg, except for incident symptomatic knee osteoarthritis.

For all analyses, a two-sided p value <0.05 was considered statistically significant. Statistical analyses were conducted using the IBM SPSS Statistics (version 25; IBM, Armonk, NY) (descriptive statistics and ANCOVA) and Stata V.15.0 (StataCorp, College Station, TX, US) (Poisson regression analyses).

Patient involvement

There was no patient involvement in the design of the study or setting of the research question. However, user involvement was included in implementation of the exercise therapy program, discussion of the results, and dissemination of user experiences to health care providers. With respect to the results from this five-year follow-up, information in lay language will be distributed by email to the participants after publication.

Results

One hundred and forty participants were randomized to exercise therapy or arthroscopic partial meniscectomy, each treatment group with 70 participants (Figure 1). At five years 120 participants (86%) underwent radiographic assessment. Participants lost to follow-up differed only with regards to meniscal extrusion (80% vs. 56%, but no significant group differences, Table 1). Participants not receiving the allocated treatment were excluded from the per protocol analysis (Supplementary Figure S1). There were no new crossovers following the two-year follow-up. The 14 participants (20%) who had crossed over to receive surgical treatment were analyzed in the surgery group in the as treated analysis. None in the partial meniscectomy group, including the six participants not receiving surgery, cross over to the exercise group. For the primary outcome, the full analysis set included 58 participants in the exercise therapy group and 62 in the partial meniscectomy group (Figure 1). Per protocol and as treated analyses both included 32 participants in the exercise therapy group, and 57 and 67 participants in the partial meniscectomy group, respectively (Supplementary Figure S1). One participant who crossed over to the surgery group underwent a reoperation six months following the primary procedure. Three participants in the surgical group underwent another partial meniscectomy 12, 15 and 36 months after the index operation. One participant in the surgical group and one who crossed over from the exercise therapy group received an osteotomy four to six months after the index surgery. One participant in the surgical group received a total knee arthroplasty 34 months after the index surgery. No serious harms were recorded in either group.

[Insert Figure 1 here]

Baseline data

Baseline characteristics of the participants are presented in Table 1. Prevalence of radiographic features, Kellgren and Lawrence classification and fJSW at baseline are presented in Supplementary Table S1.

[Insert Table 1 here]

Primary outcome

Participants with progression of joint space narrowing and osteophytes are presented in Table 2. Due to the wide confidence intervals of the risk ratios potential differences between treatment groups cannot be excluded. The results were not different in the per protocol and as treated analyses (Supplementary Table S2). In total radiographic score, the adjusted between-group difference in change between the surgery group and the exercise group was -0.02 (95% CI -0.53 to 0.49; p=0.93) (Supplementary Table S3).

[Insert Table 2 here]

Secondary outcomes

Figure 2 presents the proportions with incident radiographic knee osteoarthritis, incident symptomatic knee osteoarthritis and knee pain at five years. The incidence of radiographic knee osteoarthritis was 15.5% and 16.1% over the follow-up period for the exercise therapy group and surgery group, respectively. The adjusted risk ratio for the surgery group was 1.03 (95% CI 0.46 to 2.30) compared to the exercise therapy group. The corresponding number for symptomatic knee osteoarthritis were 8.8% and 3.3%, (risk ratio 0.37 [95% CI 0.08 to 1.85]). In the per protocol and as treated analysis the proportion with incident radiographic knee osteoarthritis was higher in the surgery group (17.5% and 19.4%, respectively) compared to the exercise group (12.5%). However, differences were not statistically significant, and the confidence intervals of the risk ratios wide (Supplementary Table S4).

[Insert Figure 2 here]

The adjusted change in medial fJSW for the two groups (full-set analysis) are illustrated in Figure 3. Two participants in the exercise therapy group with lateral joint space narrowing only were excluded from this analysis. In the surgery group one participant undergoing total knee replacement was excluded. The adjusted between-group difference for the involved leg was -0.20 mm (95% CI -0.48 to 0.09; p=0.17). In the per protocol and as treated analyses the exercise therapy group had significantly less decrease in medial fJSW. The adjusted between-group difference in change were -0.38 mm (95% CI -0.74 to -0.03; p=0.03) and -0.42 mm (95% CI -0.76 to -0.08; p=0.02), respectively. The absolute values at five years and change from baseline are presented in Supplementary Table S5.

[Insert Figure 3 here]

Figure 4 presents the adjusted between-group difference in change for the five KOOS subscales. No statistically significant or clinically relevant differences were found for any of the subscales. The absolute KOOS scores at five years and change from baseline are presented in Supplementary Table S6. Per protocol and as treated analyses gave similar results (Supplementary Figure S2).

[Insert Figure 4 here]

Discussion

In this five-year follow-up of the OMEX trial involving patients with degenerative meniscal tears, exercise therapy and arthroscopic partial meniscectomy showed comparable results in progression of individual radiographic features and development of incident knee osteoarthritis. Due to the wide confidence intervals we cannot exclude a true difference between the two treatments. However, no statistically significant or clinically relevant differences were found for change in medial fJSW or total radiographic score (OARSI atlas). We also found substantial improvements in patient-reported outcomes in both groups, with no clinically relevant differences between the groups. This supports previous evidence of no added benefit from surgery over exercise therapy as treatment for degenerative meniscal tears[3-5,7,8].

To the best of our knowledge, this is the first study evaluating progression of individual radiographic features of follow-up data from a randomized controlled trial comparing surgical and non-surgical treatment for degenerative meniscal tears in a largely non-osteoarthritic population. In previous studies evaluation of osteoarthritis progression have been limited to crude radiographic grades[3,4]. In one study less than 5% showed slight progression over five years[4]. Their use of the Ahlbäck classification, in which grade 2 requires obliteration of the articular space, makes a direct comparison difficult. Another study reported a two-year incidence of radiographic knee osteoarthritis of 5%, based on the Kellgren and Lawrence classification[3]. Using the same cut-off, we found the incidence to be higher (16%), which may reflect the longer follow-up time. One study evaluates changes in MRI-based features[30], but in contrast to the present study included predominantly patients with established knee osteoarthritis[31]. Over 18 months the surgery group showed greater advancement in cartilage surface area, osteophytes, and effusion-synovitis[30]. The assessment of osteoarthritis markers on MRI is an important distinction to the present study and may explain the difference in the results. Degenerative meniscal tears are regarded as a “preradiographic” sign of osteoarthritis[12] and the manifestation of radiographic changes is also of interest. We further included a quantitative measure of joint space width, which is sensitive to longitudinal changes and offers the ability to measure joint space loss occurring within-grade of the semi-quantitative scales[28,32]. We believe this comprehensive approach gave opportunities to identify potential between-group differences in osteoarthritis progression, however, we cannot rule out that the use of MRI would yield different results.

Focusing on individual radiographic features allowed us to identify more subtle changes as opposed to one grade change in the Kellgren and Lawrence classification. In both groups those who progressed had only modest structural changes. Across all features less than ten percent progressed more than 1 grade. The proportions with progression were comparable between groups, and the change in medial fJSW and total radiographic score indicates no difference in radiographic progression. Structural progression occurred more frequently in the medial compartment, which is in line with previous findings in patients with non-traumatic knee pain[33]. Medial osteophyte progression was present in around 50% of the participants, whereas medial joint space narrowing was somewhat less common and seen in one-third. This is consistent with the change in Kellgren and Lawrence being predominantly from grade 0 to 1, as grade 1 emphasize marginal osteophytes[19]. This is of clinical interest, as grade 1 is an important indicator of longitudinal incident disease. Compared with knees of grade 0 the risk for incident radiographic knee osteoarthritis is found to be 4.5-fold[34].

The prevalence of radiographic knee osteoarthritis at five years was 17% and 19% in the two groups. General population data are scarce, but in a Norwegian population study the prevalence of self-reported knee osteoarthritis (diagnosed by a medical doctor or x-ray) was less than 10 % in the age-group of 54 to 56[35]. Bearing in mind that less than 3% had radiographic knee osteoarthritis at baseline, this strengthen previous reports of degenerative meniscal tears as a “preradiographic” sign and part of the pathological osteoarthritis process[12]. For symptomatic knee osteoarthritis the incidence was 6%, whereas knee pain was reported by over 20% without definitive radiographic knee osteoarthritis. The discordance between structural changes and symptoms may be due to the insensitivity of the Kellgren and Lawrence classification to detect early osteoarthritic changes that cause symptoms.

Medial fJSW decreased in both groups. Meniscal tears are associated with cartilage thickness loss in the adjacent subregion to the tear, hence, a loss of medial joint space was expected[36]. The mean change was greater for the surgery group, which is contrary to the slightly greater proportion in the exercise group with progression of joint space narrowing based on the ordinal OARSI scoring. Combination of the medial and lateral compartment to indicate progression of the ordinal scoring explain some of this discrepancy. Quantitatively measured fJSW also detects changes occurring within the ordinal grades. Additionally, for ordinal scoring of joint space narrowing the focus of the reader is most likely on the minimum joint space width, not the most responsive region of fJSW[32]. In the per protocol and as treated analysis a statistically significant larger decrease in medial fJSW was seen for the partial meniscectomy group. Even though the results from these analyses to a larger extent may reveal the true treatment effect, we do acknowledge the inherent bias of such analyses[37]. In the current study, participants with poor compliance to the exercise therapy program had a change in medial fJSW similar to the surgery group but larger than the compliant participants. The between-group difference was, thus, the result of the exclusion of these participants. We interpret this finding with caution, as compliance is a factor often related to the outcome[37].

In patient-reported outcome measures there were no clinically relevant differences between groups. To put the results at the group level into context, 77% in the exercise group and 82% in the surgery group had improved at least 8 points in KOOS sport/recreational function at 5 years. For KOOS knee-related quality of life the corresponding numbers were 88% and 82%, respectively. The difference between treatment groups was 5 and 6%. We suggest a difference of 5-6% between groups not being clinically meaningful, especially since the direction of the difference between the two treatment groups was inconsistent. The results were identical when a cut-off of 10 points was used. This supports findings from previous randomized controlled trials[3-5,7,8,38]. Compared to age-specific reference data, participants in the current study scored 5-10 points lower on the KOOS subscales knee-related quality of life and sports/recreational function[39]. This may indicate that degenerative changes and not only meniscal damage per se cause knee impairments.

The most important strength of our study is the randomized controlled trial design with long follow-up time and high follow-up rate (86%). Additional strengths are the use of two experienced and blinded radiographic readers, a semi-automatic computer based quantitative measure, and valid and reliable patient-reported outcomes. The present study also has several limitations. First, although the radiographic clinics were to follow a standardized protocol, we identified some deviations. The mean beam angulation was 10° at both time points, however, the variability in the baseline images were large. Importantly, there was no difference between groups in mean beam angle. The number of anterior-posterior radiographs were also balanced between groups, and the images were read in pairs which enabled readers to account for differences in accusation settings between the baseline and follow-up image. Second, MRI has greater sensitivity to change than radiographs. MRI evaluation would have enabled detailed assessment of the knee joint as a whole organ, including direct visualization of the joint cartilage. Third, no radiographic evaluation of the patellofemoral joint was performed. This would have been an important addition, as meniscal tears are associated with increased risk of patellofemoral osteoarthritis[40]. Fourth, the study was not powered to detect differences in individual radiographic features. Fifth, our results can only be generalized to patients without definitive knee osteoarthritis, however, trials including patients with more severe radiographic changes have reported similar results[4,38]. Lastly, when comparing non-surgical and surgical treatments the possibility of one-way crossover is a challenge; patients can cross-over from exercise therapy to surgery, but once a patient has had surgery it cannot be undone[41]. In our trial the crossover rate was 20%, with none after the two-year follow-up. Similar studies have reported crossover rates from 0% to 29%[3-5,8].

In summary, this five-year follow-up of patients with degenerative meniscal tears showed inconclusive results with respect to potential differences in progression of individual radiographic features after surgical and non-surgical treatment. Secondary radiographic outcomes gave stronger evidence for no between-group differences in the extent of radiographic progression. Further, we found no strong evidence in support of differences in development of incident radiographic knee osteoarthritis or patient-reported outcomes between exercise therapy and arthroscopic partial meniscectomy.

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Author contributions

Conceptualization and design of the study: BB, ER, ME, MAR. Collection and assembly of data: NK, LE, MAR. Analysis and interpretation of data: all authors. First draft of manuscript: BB. Critical revision of manuscript for important intellectual content and approval of final version: all authors. Takes responsibility for the integrity of the work as a whole: BB, MAR.

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Conflicts of interest

Bjørnar Berg and May Arna Risberg reports grants from the South-Eastern Norway Regional Health Authority, during the conduct of this study. Ewa Roos is the deputy editor of Osteoarthritis and Cartilage, the developer of Knee injury and Osteoarthritis Outcome Score and several other freely available patient reported outcome measures, and co-founder of Good Life with Osteoarthritis in Denmark (GLA:D), a non-for profit initiative hosted by University of Southern Demark to implement clinical guidelines in primary care. Simo Saarakkala reports grants from the Sigrid Juselius Foundation, during the conduct of this study. Aleksei Tiulpin reports grants from the KAUTE Foundation, during the conduct of this study; and reports board membership, employment, royalties and holds stock/stock options in Ailean Technologies Oy, outside the submitted work. No other disclosures were reported.

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Table 1. Baseline characteristics of participants allocated to exercise therapy (ET) or arthroscopic partial meniscectomy (APM).

Characteristics	ET group		APM group	
	Randomized	**Full analysis set**	**Randomized**	**Full analysis set**
Demographics:	n=70	n=58	n=70	n=62
No (%) men	43 (61)	36 (62.1)	43 (61)	38 (61.3)
Age (years)	50.2 (6.4)	50.3 (6.2)	48.9 (6.3)	48.9 (6.2)
Body mass index (kg/m^2)	26.5 (4.3)	26.2 (4.0)	26.0 (3.7)	25.9 (3.7)
Magnetic resonance imaging†:	n=69	n=57	n=70	n=62
Medial meniscal degradation‡				
No (%) grade 1-2	6 (9)	6 (10.5)	6 (9)	5 (8.1)
No (%) grade 3-4	63 (91)	51 (89.5)	64 (91)	57 (91.9)
Medial meniscal extrusion§				
No (%) no extrusion	23 (33)	22 (38.6)	33 (47)	30 (48.4)
No (%) extrusion	46 (67)	35 (61.4)	37 (53)	32 (51.6)
Lateral meniscal tear, no (%)	3 (4.3)	3 (0.5)	2 (2.9)¶	1 (1.6)
Pain:	n=70	n=58	n=69	n=61
Duration (months)	16.9 (18.7)	16.5 (18.5)	11.7 (15.7)	11.9 (16.6)

Values are numbers (percentages) or means ± standard deviations.

†Data from post hoc reading by one radiologist blinded to group allocation and clinical data.

‡Graded (0-4, best to worst) according to Crues et al.[20]

§Evaluated on coronal sequence images with maximal tibial spine volume, defined as the peripheral border of the meniscus crossing a vertical line on the medial margin of tibia without osteophytes.

¶ One lateral meniscal tear were identified tear identified perioperatively. Three patients had a lateral partial meniscectomy performed.

Table 2. Progression of radiographic features for the exercise therapy (ET) group and the arthroscopic partial meniscectomy (APM) group.

Radiographic feature	**Involved leg**		**Uninvolved leg**	
	ET group	**APM group**	**ET group**	**APM group**
Joint space narrowing†	n=58	n=62	n=58	n=62
No JSN	36 (62.1)	41 (66.1)	39 (67.2)	52 (83.9)
JSN progression	22 (37.9)	21 (33.9)	19 (32.8)	10 (16.1)
Risk ratio (95% CI)‡	Referent	0.89 (0.55, 1.44)	Referent	0.49 (0.25, 0.97)
Risk difference (95% CI)‡	Referent	-0.04 (-0.21, 0.13)	Referent	-0.16 (-0.32, -0.01)
Medial osteophytes				
No OST	32 (55.2)	30 (48.4)	43 (74.1)	44 (71.0)
OST progression	26 (44.8)	32 (51.6)	15 (25.9)	18 (29.0)
RR (95% CI)‡	Referent	1.15 (0.79, 1.68)	Referent	1.12 (0.62, 2.02)
Risk difference (95% CI)‡	Referent	0.07 (-0.11, 0.25)	Referent	0.05 (-0.12, 0.22)
Lateral osteophytes				
No OST	41 (70.7)	48 (77.4)	50 (86.2)	55 (88.7)
OST progression	17 (29.3)	14 (22.6)	8 (13.8)	7 (11.3)
RR (95% CI)‡	Referent	0.77 (0.42, 1.42)	Referent	0.83 (0.32, 2.10)
Risk difference (95% CI)‡	Referent	-0.08 (-0.25, 0.10)	Referent	-0.01 (-0.11, 0.09)

Values are numbers (percentages); Progression= ≥1 grade; RR=risk ratio; 95% CI=95% confidence interval.

ET = Exercise therapy; APM = Arthroscopic partial meniscectomy; JSN=Joint space narrowing; OST=Osteophytes.

† Medial and lateral compartment combined, 1 participant (1.7%) in the ET group and 3 participants (4.8%) in the AMP group had lateral JSN progression in the involved knee.

‡ Adjusted for sex

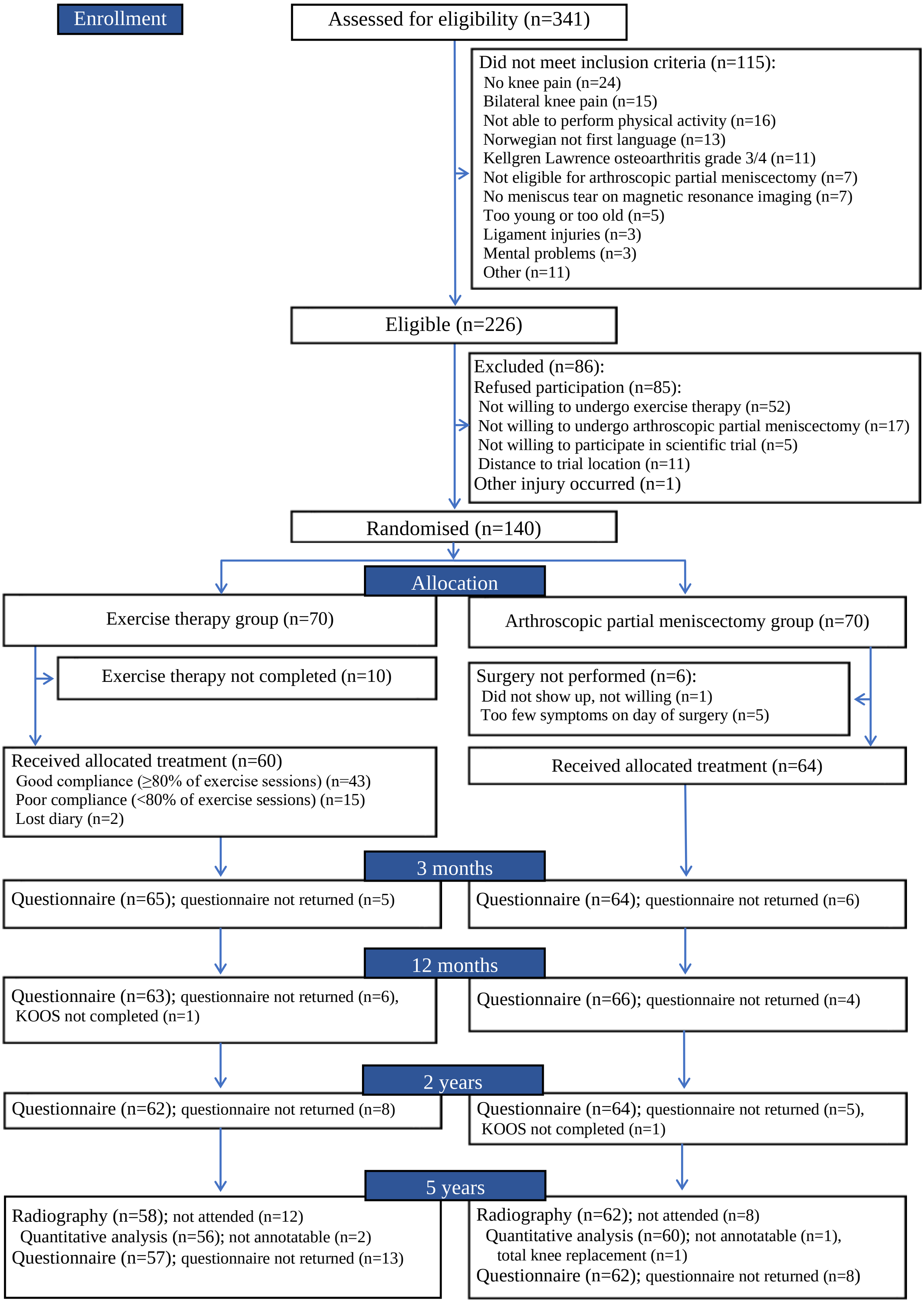

Figure 1. Enrollment and flow of participants through the OMEX trial.

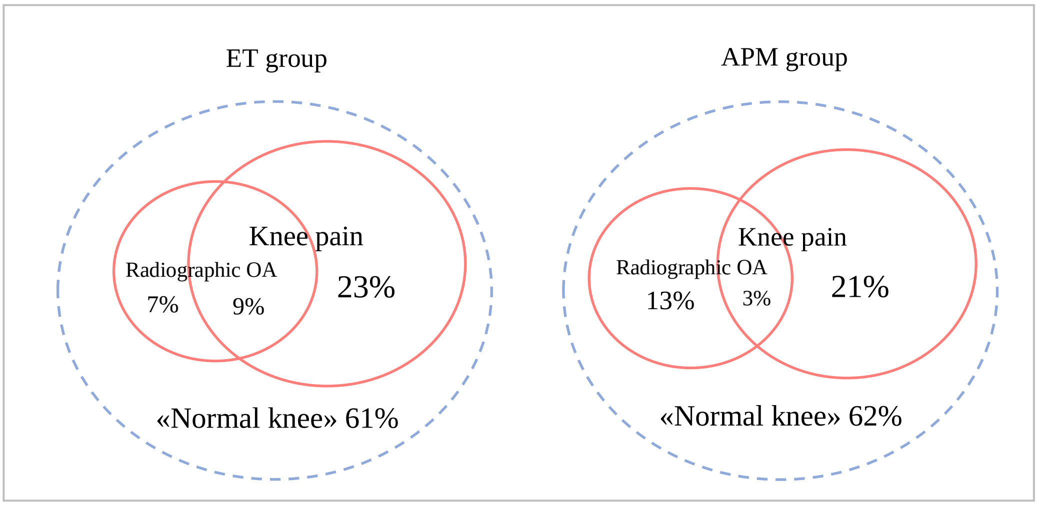

Figure 2. Percentage of participants in the exercise therapy (ET) and arthroscopic partial meniscectomy (APM) group with incident radiographic knee osteoarthritis, knee pain (experiencing knee pain during the last week) or normal knee. Intersection represents participants with incident radiographic knee osteoarthritis and knee pain (incident symptomatic knee osteoarthritis).

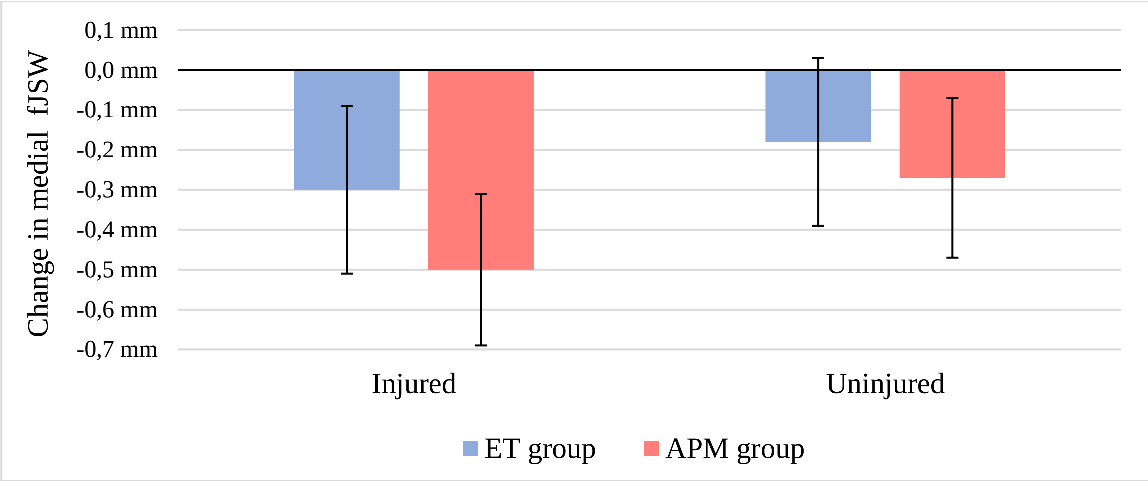

Figure 3. Change from baseline to five years in medial fixed joint space width (full-set analysis), adjusted for sex and baseline value of the outcome. Whiskers represents 95% confidence intervals. ET=exercise therapy (n=54); APM=arthroscopic partial meniscectomy (n=60).

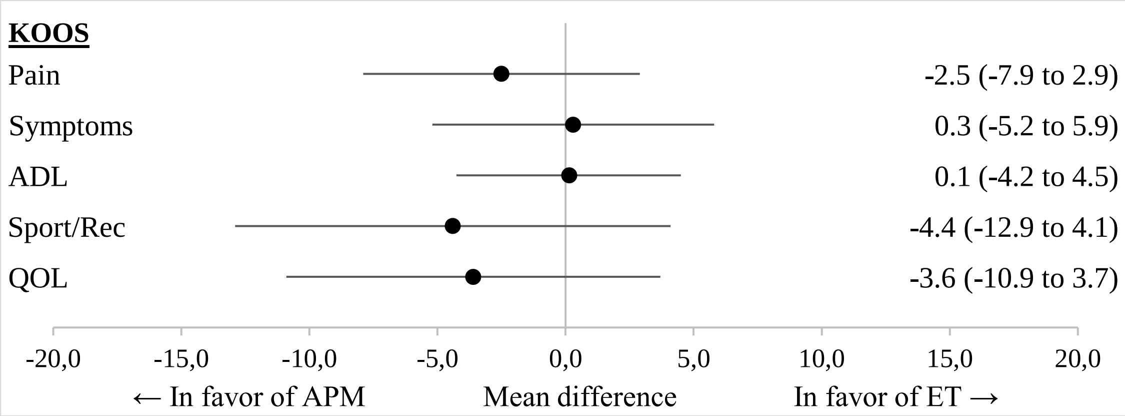

Figure 4. Between-group difference in change from baseline to five years for the five KOOS subscales, adjusted for sex and baseline value of the outcome. APM=Arthroscopic partial meniscectomy; ET=Exercise therapy; KOOS=Knee injury and osteoarthritis outcome score; ADL=Activities of daily living; Sport/Rec=Sports and recreational function; QOL=Knee related quality of life. Whiskers represent 95% confidence intervals.