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a secondary analysis of the DREAM trial

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Title

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Contributorship
STS and JBT conceived the DREAM trial. The analysis plan for this study was developed by CD, STS and JBT, with critical feedback and input from PH, ML, CV, MSH and MDV. CD and MDV performed the statistical analyses and interpreted the data with input from STS and JBT. CD drafted the first version of the manuscript with assistance from STS and JBT. PH, ML, CV, MSH and MDV provided critical intellectual input to the manuscript and all authors approved the final version of the manuscript.

Competing interests
None declared.

ABSTRACT

Objective

To compare the effect of early surgery versus exercise and education on mechanical symptoms and other patient-reported outcomes in patients aged 18-40 years with a meniscal tear and self-reported mechanical knee symptoms.

Methods

In a randomized controlled trial, 121 patients aged 18-40 years with a MRI-verified meniscal tear were randomized to surgery or 12-weeks supervised exercise and education. For this study, 63 patients (33 and 30 patients in surgery and exercise groups, respectively) reporting baseline mechanical symptoms were included. Main outcome was self-reported mechanical symptoms (yes/no) at 3, 6, and 12 months assessed using a single item from the Knee Injury and Osteoarthritis Outcome Score (KOOS). Secondary outcomes were $KOOS_4$ and the 5 KOOS-subscales and the Western Ontario Meniscal Evaluation Tool (WOMET).

Results

In total, 55/63 patients completed the 12-month follow-up. At 12 months, 9/26 (35%) in the surgery group and 20/29 (69%) in the exercise group reported mechanical symptoms. The risk difference and relative risk at any time point was 28.7% (95% CI 8.6 to 48.8) and 1.83 (95% CI, 0.98 to 2.70) of reporting mechanical symptoms in the exercise group compared with the surgery group. We did not detect any between-group differences in the secondary outcomes.

Conclusion

The results from this secondary analysis suggest that early surgery is more effective than exercise and education for relieving self-reported mechanical knee symptoms, but not for improving pain, function and quality of life in young patients with a meniscal tear and mechanical symptoms.

Trial registration

ClinicalTrials.gov number, NCTO2995551

Data Availability Statement

Data are available upon reasonable request

Key messages

- What is already known on this topic

  Surgery is typically considered the best treatment to alleviate mechanical symptoms in young patients with a meniscal tear. However, there is no evidence for a better effect of meniscal surgery over non-surgical alternatives in alleviating mechanical symptoms.

- What this study adds

  Surgery seemed more effective in alleviating patient reported mechanical symptoms compared with a treatment strategy of exercise therapy and patient education in patients aged 40 years or younger. No relevant between-group treatment difference was observed for other patient reported outcomes including pain, function and quality of life.

- How this study might affect research, practice or policy

  The findings of this study highlight the importance of including the patient's perception of the importance of different symptoms as well as treatment preferences and needs when deciding an individual treatment strategy.

INTRODUCTION

Knee arthroscopy is among the most common orthopaedic procedures. [1][2] A large proportion of these procedures are carried out to treat meniscal tears, [2-4] especially in patients reporting concomitant mechanical knee symptoms. [1][3][5][6] This tenet is based on the assumption that the knee joint is mechanically blocked by a trapped piece of damaged meniscal tissue causing episodes of restricted knee joint motion, leading to a patient-reported sensation of catching or locking of the knee. [7-9] Although surgery is often considered the treatment of choice to relieve mechanical symptoms (i.e. caching/locking or inability to extent the knee fully), evidence supporting that surgery is superior to non-surgical alternatives in alleviating mechanical symptoms is lacking. In middle-aged and older patients with a meniscal tear and mechanical symptoms, a secondary analysis of a randomized trial found no difference in alleviation of mechanical symptoms between patients randomized to arthroscopic partial meniscectomy (APM) versus placebo (sham surgery). [8] In middle-aged and older patients, other factors than the meniscus such as degenerative changes or osteoarthritis are also likely reasons for mechanical symptoms [10] whereas the entrapped meniscal tissue following trauma may be a cause of mechanical symptoms in younger patients. [3][5][11-14] Consequently, it is important to compare the effect of meniscal surgery with a non-surgical treatment alternative on self-reported mechanical symptoms also among patients 40 years or younger.

The aim of this study was to compare the effect of early meniscal surgery versus exercise therapy and patient education (with the option of later surgery) in alleviating patient-reported mechanical symptoms in patients aged 18-40 years with a meniscal tear, using the data from a recently reported RCT. [15] In addition, we compared the 12-month effect of the two treatment strategies on patient-reported outcomes among patients with mechanical symptoms.

METHODS

Equity, diversity, and inclusion statement

The author group consists of one woman and seven men from five different locations spread nation-wide in Denmark with different background disciplines including; physiotherapy, sport and health, biostatistics and medical doctors. Our study population included both male and female young patients with a meniscal tear and mechanical symptoms consulting one of seven different public hospitals located across Denmark, which increases diversity and generalizability of the results. However, we acknowledge that inequity in care-seeking behaviour might exist in this population, which could have excluded some individuals with knee injury from participating.

Study design and study population

This study is a secondary analysis of the "Danish RCT on Exercise versus Arthroscopic Meniscal surgery for young adults (DREAM) trial". [15] A detailed description of the study design and conduct has previously been described and reported. [15 16] In short, the DREAM-trial was a pragmatic, comparative effectiveness, multicenter, parallel-group RCT (1:1 treatment allocation) including 121 patients aged 18-40 with a magnetic resonance imaging (MRI)-verified meniscal tear randomized to a strategy of early surgery (APM or meniscal repair) or 12-weeks of supervised exercise therapy and patient education, with the option of later surgery if needed.

The DREAM-trial was approved by the Regional Committees on Health Research Ethics for Southern Denmark (S-20160151) and the Danish Data Protection Agency (University of Southern Denmark, 16/45314) and registered at ClinicalTrials.gov (NCT02995551).

Patients

In the DREAM trial we included adults 18 to 40 years of age with knee pain, a clinical history and symptoms consistent with a meniscal tear, verified on magnetic resonance imaging (MRI), deemed eligible for meniscal surgery (arthroscopic partial meniscectomy or repair) by an orthopedic surgeon in one of seven orthopedic departments that were willing to be randomized and provided oral and written informed consent.

Exclusion criteria were:

- Previous knee surgery on the affected knee.

- Clinical suspicion (acute locking of knee and/or extension deficit) of displaced bucket-handle tear confirmed by MRI.

- Fracture of the affected extremity within the previous 12 months.

- Complete rupture of one or more knee ligaments.

- Participation in supervised systematic exercise therapy for knee problem within the last 3 months prior to recruitment.

- Other reasons for exclusion (unable to understand Danish, mentally unable to participate, etc.).

In this study we only included patients self-reporting mechanical symptoms at baseline. Self-reported mechanical symptoms (i.e. the sensation of knee catching or locking) were assessed using the single item question 'Does your knee catch or hang up when moving?' (time frame: last week) from the Knee Injury and Osteoarthritis Outcome Score (KOOS) [9] with response options ranging from 'never' to 'always'. Patients were categorized as having mechanical symptoms unless replying 'never' to this question. [17]

Patients and public involvement

Yes, patients and clinicians were involved in the development of the design of the intervention as described in the pilot paper. [18]

Interventions

Patients were randomized to either meniscal surgery or supervised exercise therapy and patient education (with the option of later surgery). An in-depth description of the two interventions has previously been reported. [15 16 18]

Patients randomly assigned to receive meniscal surgery underwent APM or meniscal repair following standard procedures. [19] The type of surgery was determined by the operating surgeon during surgery as in routine clinical practice. After surgery, patients undergoing APM received a standard brochure with exercises to facilitate at least a minimum level of postoperative rehabilitation. Patients undergoing meniscal repair received postoperative rehabilitation, ranging from control of range of motion and instructions in standard postoperative exercises to a supervised, knee-related exercise program based on patient needs and local procedures.

The supervised exercise therapy and patient education program lasted for 12 weeks, in which the patients received 60 to 90-minute sessions of supervised group-based neuromuscular and strengthening exercise therapy twice a week, and two patient education lessons placed at the beginning and end of the exercise program. The exercise program was developed based on evidence from other types of knee injuries and osteoarthritis [20-24] and feasibility tested before the RCT in collaboration with patients and experienced physical therapists. [18]

Outcomes

Main outcome:

The main outcome was presence/absence of self-reported mechanical symptoms (i.e. the sensation of knee catching or locking) assessed at baseline and at 3, 6 and 12 months of follow-up from the single KOOS item described above. The psychometric properties of this item were evaluated together with the rest of the KOOS questionnaire as described below and has in this dichotomized version previously been used to assess presence/absence of mechanical symptoms. [6,7]

Secondary outcomes:

Secondary outcomes were the between-group difference in change in patient reported outcomes assessed with the KOOS ($KOOS_4$ and the 5 KOOS subscales) [9] and the Western Ontario Meniscal Evaluation Tool (WOMET) [24,25] from baseline to 12 months.

The KOOS is a knee-specific, valid, and reliable patient-reported outcome measure for individuals on the continuum from knee injury to osteoarthritis, [9][26][27] and is assessed using five subscales (pain, symptoms, activity of daily living, function in sport and recreation and quality of life) all ranging from 0 to 100, with lower scores indicating worse pain, symptoms, function, and quality of life. The $KOOS_4$ is the average score of four of the five subscale scales, including pain, symptoms, function in sport and recreation, and quality of life. [9] In the $KOOS_4$ we excluded the activities of daily living (ADL), as this construct is not sensitive in the young population [26] This definition of the $KOOS_4$ is the same as used in a trial comparing surgery to supervised exercise as treatment for ACL tears in patients of similar age as in the present trial and thus, allows for comparability across studies. We applied a cut-off value on 10 KOOS units as this value typically is considered as the MCID for all the KOOS scales in general [28], although acknowledging that the MCID for the KOOS score has been suggested to be different for the different subscales of KOOS and may vary by population and context. [29]

WOMET is a disease-specific tool designed to evaluate Health-Related Quality of Life (HRQoL) in patients with meniscal pathology, and has been found to be a valid, reliable and responsive patient-reported outcome measure. [25][30] WOMET consist of 16 items addressing three different subdomains; physical symptoms, disabilities due to sports, recreation, work and lifestyle, and emotions which are measured on three different subscales. The scores from each subscale, and a total overall score from all 3 subscales, are converted and reported as a percentage ranging from 0 to 100 for which 0 corresponds to the least symptomatic situation and 100 to the most symptomatic. The MCID for the WOMET total overall score scale has been reported to be 15.5 units. [31]

Statistics

In this secondary analysis of the DREAM-trial only patients with mechanical symptoms at baseline were included.

Descriptive data are presented as means with SD, medians and Interquartile Range (IQR) or as numbers with percentages as appropriate. Results are presented with 95% confidence interval (CI). The reporting of the statistical analysis and interpretation of the results followed the CHAMP statement. [32]

Main outcome

To estimate the effects of the two treatments on alleviating mechanical symptoms, the subgroup of patients with mechanical symptoms at baseline (n=63) were considered. The prevalence of patients with presence/absence of mechanical symptoms were counted at all follow-up timepoints (3-, 6-, and 12-months follow-up). The longitudinal binary observations of patients with mechanical symptoms (present/absent) were modeled as different linear combinations of treatment arm (surgery or exercise therapy); sex and age; the time from baseline; and the interaction between treatment arm and time (full model) using mixed effects logistic regression for estimating the between subject variation. The different and nested models were compared via likelihood ratio tests, which resulted in a final model including only treatment arm and sex, since when modelling the model including other variables made no contribution to the effect. To quantify the difference in terms of risk difference and relative risk across treatment arm, a prediction of the average marginal effects were computed using the estimated odds ratio (OR = 8.77 (95% CI, 1.62–47.6)) and the interclass correlation coefficient (ICC = 0.6) derived from the fitted logistic regression model.

Secondary outcomes

The secondary outcomes were the between-group difference in change in the $KOOS_4$, the 5 KOOS-subscales, and the Western Ontario Meniscal Evaluation Tool (WOMET) evaluated in the subgroup of patients with mechanical symptoms at baseline. For that purpose we applied the same model as in the primary analysis of the DREAM-trial [15], where the primary outcome was $KOOS_4$ and

treatment effect estimation was based on a linear mixed model. To assess the assumptions for model validity, the two types of outcomes were checked as below:

In case of continuous outcomes, we created scatter plots of the residuals versus time and two-dimensional scatterplots of the BLUPs (Best Linear Unbiased Prediction) of the random effects. In case of binary outcomes, only the latter was used. All scatterplots were stratified by treatment. These plots indicated distributions compatible with the assumption of normality and did not indicate the existence of outliers.

The detailed description of the statistical analysis can be found in the supplemental material. This approach ensures consistency and allows for comparing the results with the primary analysis of the DREAM-trial.

Sensitivity analysis

A sensitivity analysis was performed to check if a different interpretation appeared when analysing data in accordance to the per protocol principle, which in this case excluded patients who were randomly assigned to exercise therapy but participated in fewer than 18 of the 24 exercise sessions or crossed over to surgery and patients not having surgery in the surgery group.

All statistical analyses were conducted using STATA/BE version 17.0 (StataCorp LLC, College Station, TX, USA).

RESULTS

In the DREAM-trial, a total of 121 patients were randomly assigned to either exercise therapy and education (n=61) or to surgery (n=60). Of these, 33 and 30 patients reported mechanical symptoms at baseline in the surgery and exercise therapy group, respectively (Figure 1). An overview of the baseline characteristics for the whole study population grouped in subgroups of patients without and with mechanical symptoms at baseline (n=58 and n=63 respectively) is shown in Table 1.

Figure 1 around here…

Table 1 around here…

Alleviation of mechanical symptoms

At the 12-month follow-up, 9/26 (35%) in the surgery group and 20/29 (69%) in the exercise therapy group reported having mechanical symptoms (Table 2). During follow-up, 22/33 patients in the surgery group and 26/30 patients in the exercise therapy group reported having mechanical symptoms at least once, while 7/33 and 3/30 in the surgery group and exercise therapy group respectively reported having no mechanical symptoms at any timepoint during follow-up. Five patients (four patients in the surgery group and one in the exercise therapy group) had missing data at all follow-up timepoints. During follow-up eight patients crossed over from the exercise therapy group to the surgery group of which the reason for seven of the patients for crossing over was increased pain, no improvements of the mechanical symptoms or other symptoms still persisting (reason missing for one patient).

Table 2 around here

The results from the likelihood ratio tests of the different models showed no difference across the three follow-up time points, as the final model was not inferior to the more complex models, also including age, time, and the interaction between time and treatment group (p = 0.10). Thus the final model included only treatment arms and sex. The results from the fitted logistic regression model showed an odds ratio (OR) of 8.77 (95% CI, 1.62–47.62) of having mechanical symptoms for a subject in the exercise therapy group compared to if the subject was in the surgery group, and showed that 60% of the variance (interclass correlation class: ICC = 0.6) was due to variation between subjects. Based on the prediction of the average marginal effects, we found a risk difference of 28.7% (95% CI 8.6 to 48.8) and a relative risk of 1.83 (95% CI, 0.98 to 2.70) for having mechanical symptoms in the exercise therapy group as compared to the surgery group at any of the time points.

Comparison of patient reported outcomes

We did not detect a change between groups from baseline to 12 months in the $KOOS_4$ scores (16.9 vs. 18.4 in the surgery vs. exercise therapy groups; adjusted mean difference, 0.3 [95% confidence interval, -8.7 to 9.3]). Similarly, we did not detect a change in WOMET total scores (24.7 vs. 24.5 in the surgery vs. exercise therapy groups; adjusted mean difference, 4.4 [95% confidence interval, -6.9 to 15.7]), (Figure 2 and Table S1 in supplemental material).

The between group change on the 5 KOOS-subscales and on the WOMET subscales showed similar results (Supplementary Table 1).

Figure 2 around here

Sensitivity analysis

In the sensitivity analysis, excluding patients randomized to exercise therapy but participating in fewer than 18 of the 24 exercise sessions (n=11) or crossing over to surgery (n=8) and patients not having surgery in the surgery group (n=6), results supported the main analysis as 8 out of 24 (33%) in the surgery group and 9 out of 10 (90%) in the exercise therapy group reported mechanical symptoms at the 12-month follow-up (Table 3). This corresponded to a risk difference at 12 months of follow-up of 44.2% (95% CI 19.4 to 69.0) and the corresponding relative risk was 2.45 (95%CI, 1.1 to 3.8).

DISCUSSION

In this secondary analysis of a randomized trial comparing a strategy of early surgery with a strategy of exercise therapy and patients education (with the option of later surgery) for young adults with a meniscal tear, we observed that surgery seemed to be more effective in alleviating mechanical symptoms in the subgroup of patients with mechanical knee symptoms at baseline. In contrast to the results from the analyses of the main outcome, we did not detect a difference between groups in improvements in patient-reported pain, function and quality of life at 12-months.

Previous studies in middle-aged and older patients found no difference in effect between different treatments strategies for alleviating mechanical symptoms [8 33 34], while our study is the first in young adults. An explanation for the contrasting results could be the different population in the present study, in which all patients were 40 years or younger, which supports the rationale that different age-related etiologies lies behind the origin of mechanical tears with mechanical symptoms. [5 11-14] The results from the sensitivity analysis of the main outcome, excluding 25 patients, supported the finding that more patients had their mechanical symptoms relieved in the surgery group compared with the exercise and education group, even when exercise was performed at an appropriate dose.

We did not detect a difference in change from baseline to 12 months for the secondary outcomes between the two treatment strategies. It is worth noting that baseline patient reported outcome scores were generally slightly lower among patients with mechanical symptoms as compared to those without, and for the patients in the exercise group compared to those in the surgery group. This may signal larger room for improvements and/or regression to the mean for the patients with mechanical symptoms at baseline. However, as all analyses were adjusted for baseline imbalance, this was likely to have minimal influence on the results.

Fluctuation of mechanical symptoms over time

There was some variability in the presence/absence of mechanical symptoms over time. Such fluctuation in mechanical knee symptoms over time aligns with the findings in the study by Sihvonen et al. [33] in which they observed considerable intra-individual fluctuation of mechanical symptoms between the following four time points; preoperatively and at 2, 6, and 12 months postoperatively. A closer look into the presence of this pattern in our study showed that the proportion of these fluctuations were lower for the surgery group at all time points compared with the exercise group.

Knowledge about the fluctuating nature of self-reported mechanical symptoms associated with a meniscal tear is important in clinical practice as the variability in mechanical symptoms may lead to confusion in the decision-making about which treatment strategy to choose. One solution to this would be to monitor such symptoms over a period of time before considering this as an indication to surgery.

Limitations

Given that only patients with mechanical symptoms at baseline were included in this study, the sample size can be considered a limitation. Restricting the sample to a subgroup of patients could also lead to larger differences between groups in baseline characteristics, since the original

randomization is not fully retained. Nevertheless, excluded patients without mechanical symptoms were similar in baseline characteristics compared with the patients included in this study. Another challenge related to the reduced sample size is the possibility to adjust for multiple confounders. Tear pattern may influence presence/absence of mechanical symptoms. However, given the limited sample size we did not adjust for this in our analysis. Importantly, tear patterns were relatively similar between groups.

Some patients had missing data on mechanical symptoms at several timepoints – especially in the surgery group at the 6-month follow-up, which increases the risk of bias owing to the sparse data phenomenon. [35] The risk of introducing selection bias when analyzing the data as per-protocol should also be mentioned as a limitation. Finally, as this study was a secondary analysis from the DREAM-trial, and therefore the results should be interpreted with caution.

Clinical implications

Surgery may be more effective than exercise therapy and patient education in alleviating mechanical symptoms in patients aged 40 years or younger. In a previous study, [36] we found that patient-reported mechanical symptoms were one of the most common clinical symptoms experienced by young patients about to undergo surgery for a meniscal tear. However, other clinical symptoms like general knee pain and knee pain during activities such as going up and down stairs, bending the knee fully and when twisting the knee were similarly frequent, highlighting the importance of including the patients' preferences, symptoms and needs in the shared decision making on which treatment strategy to choose.

CONCLUSION

Our results suggest that early surgery is a more effective treatment strategy for relieving self-reported mechanical knee symptoms in young patients with a meniscal tear and mechanical

symptoms compared with a strategy of exercise therapy and patient education. However, both treatment strategies resulted in similar clinically relevant improvements in pain, function and quality of life, suggesting that both strategies are viable in clinical practice and should be included in the shared decision making on treatment.

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TABLES

Table 1:
Baseline characteristics for the whole study population grouped in subgroups of patients without and with mechanical symptoms at baseline (n=58 and n=63 respectively).

	Subgroup *without* baseline mechanical symptoms (n=58)		Subgroup *with* baseline mechanical symptoms (n=63)	
	Meniscal surgery (n=27)	Exercise therapy (n=31)	Meniscal surgery (n=33)	Exercise therapy (n=30)
Age, mean (SD)	30.1 (6.5)	32.0 (6.3)	26.6 (6.1)	30.2 (6.7)
Gender, no. (%)				
Female	10 (37.0)	7 (22.6)	8 (24.2)	9 (30.0)
BMI; kg/m^2, mean (SD)	24.6 (4.5)	26.4 (4.8)	26.2 (4.0)	27.1 (4.8)
Mechanical symptoms (yes/no)**, no. (%)**	0	0	33 (100)	30 (100)
Sport participation prior to injury (Tegner score) median (IQR) ¶	5 (4-7)	6 (4-7)	5 (2-6)	5 (4-7)
Symptom onset, no. (%)				
Slowly evolved over time	7 (25.9)	6 (19.4)	6 (18.2)	13 (43.4)
Semi-traumatic	11 (40.7)	15 (48.4)	14 (42.4)	9 (30.0)
Traumatic	9 (33.3)	10 (32.3)	13 (39.4)	8 (26.7)
Duration of symptoms, no. (%)				
0-3 months	5 (18.5)	6 (19.4)	4 (12.1)	9 (30.0)
4-6 months	12 (44.4)	11 (35.5)	13 (39.4)	9 (30.0)
7-12 months	4 (14.8)	9 (29.0)	7 (21.2)	4 (13.3)
13-24 months	2 (7.4)	1 (3.2)	5 (15.2)	3 (10.0)
>24 months	4 (14.8)	4 (12.9)	4 (12.1)	5 (16.7)
KOOS scores, mean (SD) ‡				
KOOS$_4$	63.8 (12.2)	58.7 (16.6)	54.5 (16.1)	47.2 (14.9)
Pain	70.1 (14.7)	68.1 (17.2)	68.2 (16.1)	59.3 (18.2)
Symptoms	77.7 (14.4)	77.8 (14.2)	62.8 (15.2)	58.2 (14.7)
ADL	81.5 (14.9)	77.9 (20.9)	75.7 (17.0)	71.4 (17.9)
Sport/Rec	53.0 (19.9)	42.9 (24.9)	41.2 (26.5)	33.5 (21.8)

QOL	54.4 (13.1)	46.2 (19.1)	45.7 (18.7)	37.9 (16.9)
WOMET total scores, mean (SD) §	53.5 (17.2)	47.6 (19.0)	45.3 (22.4)	35.9 (15.6)
Tear pattern, no. (%)				
Lateral meniscus				
Horizontal tear	1 (3.7)	4 (12.9)	2 (6.1)	2 (6.7)
Radial and vertical tear	4 (14.8)	6 (19.4)	3 (9.1)	2 (6.7)
Bucket-handle or complex tear	3 (11.1)	4 (12.9)	6 (18.2)	2 (6.7)
Medial meniscus				
Horizontal tear	9 (33.3)	9 (29.0)	8 (24.2)	10 (33.3)
Radial and vertical tear	1 (3.7)	2 (6.5)	2 (6.1)	4 (13.3)
Bucket-handle or complex tear	10 (37.0)	8 (25.8)	13 (39.4)	10 (33.3)

Table 1: All numbers are presented as means with SD (or medians and IQR) and as percentages as appropriate.

n: Number, SD: Standard Deviation, kg: Kilogram, cm: Centimeter, BMI: Body Mass Index (kg/m^2).

¶ The Tegner Activity Scale ranges from 0 to 10, with 0 representing sick leave or disability pension because of knee problems to 10 representing competitive sports such as European football (national and international elite level).

‡ The Knee Injury and Osteoarthritis Outcome Score (KOOS) includes subscales for pain, symptoms, function in daily living, function in sport and recreation, and quality of life, with scores ranging from 0 (worst) to 100 (best). $KOOS_4$ is the mean score of four of five of the KOOS subscale scores (i.e., pain, symptoms, function in sport and recreation, and quality of life). Improvements of 10 points or more are considered clinically relevant.

§ Western Ontario Meniscal Evaluation Tool (WOMET) results were converted to scores from 0 to 100, with lower scores indicating worse quality of life. Improvements of 15.5 points or more are considered clinically relevant.

Table 2:
Presence and absence of mechanical symptoms at follow-ups for the subgroup of patients with mechanical symptoms at baseline (n=63)

	3 month follow-up		6 month follow-up		12 month follow-up	
	Exercise therapy	Meniscal surgery	Exercise therapy	Meniscal surgery	Exercise therapy	Meniscal surgery
	n=23	n=25	n=23	n=16	n=29	n=26
Presence of mechanical symptoms, no.(%)	15 (65)	9 (36)	14 (61)	3 (19)	20 (69)	9 (35)
Absence of mechanical symptoms, no.(%)	8 (35)	16 (64)	9 (39)	13 (81)	9 (31)	17 (65)
Relative risk (95% CI)					1.83 (0.98-2.70)*	
Risk difference (95% CI)					28.7 (8.60-48.8)*	

Table 2: Results are expressed as numbers (no.) and percentage (%) of patients with and without mechanical symptoms at 3, 6, and 12 months of follow-up. At baseline, there were 33 and 30 patients with mechanical symptoms for the meniscal surgery group and the supervised exercise therapy group, respectively.
Further, the relative risk and the risk difference with 95% CI for having mechanical symptoms after 12 months of follow-up are giving in the table. The surgery group was considered the reference and thus a risk difference greater than 0 or a risk ratio greater than 1 denote an increased risk for mechanical symptoms in the supervised exercise therapy group.
* Adjusted for sex.

Table 3:
Presence and absence of mechanical symptoms at follow-up for the subgroup of patients included in the sensitivity analysis (n=38)

	3 month follow-up		6 month follow-up		12 month follow-up	
	Exercise therapy	Meniscal surgery	Exercise therapy	Meniscal surgery	Exercise therapy	Meniscal surgery
	n=10	n=24	n=10	n=15	n=10	n=24
Presence of mechanical symptoms, no.(%)	6 (60)	8 (33)	7 (70)	3 (20)	9 (90)	8 (33)
Absence of mechanical symptoms, no.(%)	4 (40)	16 (67)	3 (30)	12 (80)	1 (10)	16 (67)
Relative risk (95% CI)					2.45 (1.1-3.8)*	
Risk difference (95% CI)					44.2 (19.4-69.0)*	

Table 3: Results are expressed as numbers (no.) and percentage (%) of patients with and without mechanical symptoms at 3, 6, and 12 months of follow-up after excluding the 25 patients who participated in fewer than 18 of the 24 exercise sessions or crossed over to surgery during follow-up (in total 19) and patients not having surgery in the surgery (n=6). The number of

patients with mechanical symptoms at baseline were then 27 and 11 for the meniscal surgery group and the supervised exercise therapy group respectively.

Further, the relative risk and the risk difference with 95% CI for having mechanical symptoms after 12 months of follow-up are giving in the table. The surgery group was considered the reference and thus a risk difference greater than 0 or a risk ratio greater than 1 denote an increased risk for mechanical symptoms in the supervised exercise therapy group.

* Adjusted for sex.

LEGENDS TO TABLES AND FIGURES

Table 1:
All numbers are presented as means with SD (or medians and IQR) and as percentages as appropriate.
n: Number, SD: Standard Deviation, kg: Kilogram, cm: Centimeter, BMI: Body Mass Index (kg/m^2).
¶ The Tegner Activity Scale ranges from 0 to 10, with 0 representing sick leave or disability pension because of knee problems to 10 representing competitive sports such as European football (national and international elite level).
‡ The Knee Injury and Osteoarthritis Outcome Score (KOOS) includes subscales for pain, symptoms, function in daily living, function in sport and recreation, and quality of life, with scores ranging from 0 (worst) to 100 (best). $KOOS_4$ is the mean score of four of five of the KOOS subscale scores (i.e., pain, symptoms, function in sport and recreation, and quality of life). Improvements of 10 points or more are considered clinically relevant.
§ Western Ontario Meniscal Evaluation Tool (WOMET) results were converted to scores from 0 to 100, with lower scores indicating worse quality of life. Improvements of 15.5 points or more are considered clinically relevant.

Table 2:
Results are expressed as numbers (no.) and percentage (%) of patients with and without mechanical symptoms at 3, 6, and 12 months of follow-up. At baseline, there were 33 and 30 patients with mechanical symptoms for the meniscal surgery group and the supervised exercise therapy group, respectively.
Further, the relative risk and the risk difference with 95% CI for having mechanical symptoms after 12 months of follow-up are giving in the table. The surgery group was considered the reference and thus a risk difference greater than 0 or a risk ratio greater than 1 denote an increased risk for mechanical symptoms in the supervised exercise therapy group.
* Adjusted for sex.

Figure 2: Patient-reported outcomes in patients with a meniscal tear and mechanical symptoms
Error bars indicate 95% confidence intervals.
The Knee Injury and Osteoarthritis Outcome Score (KOOS) includes subscales for pain, symptoms, function in daily living, function in sport and recreation, and quality of life, with scores ranging from 0 (worst) to 100 (best). $KOOS_4$ (Fig. 2A) is the mean score of four of five of the KOOS subscale scores (i.e., pain, symptoms, function in sport and recreation, and quality of life). Improvements of 10 points or more are considered clinically relevant.
Western Ontario Meniscal Evaluation Tool (WOMET; Fig. 2B) results were converted to scores from 0 to 100, with lower scores indicating worse quality of life. Improvements of 15.5 points or more are considered clinically relevant.
n = number of participants with available data at the specific time points.

Table 3: Results are expressed as numbers (no.) and percentage (%) of patients with and without mechanical symptoms at 3, 6, and 12 months of follow-up after excluding the 25 patients who participated in fewer than 18 of the 24 exercise sessions or crossed over to surgery during follow-up (in total 19) and patients not having surgery in the surgery (n=6). The number of patients with mechanical symptoms at baseline were then 27 and 11 for the meniscal surgery group and the supervised exercise therapy group respectively.
Further, the relative risk and the risk difference with 95% CI for having mechanical symptoms after 12 months of follow-up are giving in the table. The surgery group was considered the reference and thus a risk difference greater than 0 or a risk ratio greater than 1 denote an increased risk for mechanical symptoms in the supervised exercise therapy group.
* Adjusted for sex.