Two-year MRI-defined structural damage and patient-reported outcomes following surgery or exercise for meniscal tears in young adults

Stine Haugaard Clausen,1 Søren T Skou,1,2 Mikael Ploug Boesen,3 Dimitar Ivanon Radev,3 Engin Yeter Kurt,3 Camma Damsted,1,2 Per Hölmich,4 Martin Lind,5 Sofus Tørring,6 Christin Isaksen,7 Claus Varnum,8 Martin Englund,9 Jonas Bloch Thorlund1,10

ABSTRACT

Objective To investigate potential differences in structural knee joint damage assessed by MRI and patient-reported outcomes (PROMs) at 2-year follow-up between young adults randomised to early surgery or exercise and education with optional delayed surgery for a meniscal tear.

Methods A secondary analysis of a multicentre randomised controlled trial including 121 patients (18–40 years) with an MRI-verified meniscal tear. For this study, only patients with 2-year follow-up were included. The main outcomes were the difference in worsening of structural knee damage, assessed by MRI using the Anterior Cruciate Ligament OsteoArthritis Score, and the difference in change in the mean score of four Knee Injury and Osteoarthritis Outcome Score (KOOS) subscales covering pain, symptoms, function in sport and recreation, and quality of life, from baseline to 2 years.

Results In total, 82/121 (68%) patients completed the 2-year follow-up (39 from the surgical group and 43 from the exercise group). MRI-defined cartilage damage had developed or progressed in seven (9.1%) patients and osteophytes developed in two (2.6%) patients. The worsening of structural damage from baseline to 2-year follow-up was similar between groups. The mean (95% CI) adjusted differences in change in KOOS4 between intervention groups from baseline to 2 years was −1.4 (−9.1, 6.2) points. The mean improvement in KOOS, was 16.4 (10.4, 22.4) in the surgical group and 21.5 (15.0, 28.0) in the exercise group. No between-group differences in improvement were found in the KOOS subscales.

Conclusions The 2-year worsening of MRI-defined structural damage was similar and limited in young adult patients with a meniscal tear treated with surgery or exercise with optional delayed surgery. Both groups had similar clinically relevant improvements in KOOS, suggesting the choice of treatment strategy does not impact 2-year structural knee damage or PROMs.

Trial registration number NCT02995551.

INTRODUCTION

Meniscal tears in young adults have typically been treated with arthroscopic surgery. Recently, two randomised trials comparing early meniscal surgery to exercise therapy and education with optional delayed surgery (if needed) reported clinically relevant improvements in patient-reported outcomes (PROMs) for both treatment strategies, with negligible between-group differences.1,2 Furthermore, in the two trials, many patients randomised to exercise (84% at 12 months and 59% at 24 months) did not undergo surgery during follow-up.1,2

The risk of developing knee osteoarthritis (OA) is considerably elevated (up to sixfold higher) for knee injury and meniscal tear patients.1,2 However, whether the development of structural knee joint changes and the later onset of knee OA is affected by the initial treatment strategy (surgical or non-surgical) in young patients with meniscal tears is unknown. On the one hand, exercise therapy

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Patients with a meniscal tear are at a higher risk of developing knee osteoarthritis (OA), and surgery to the meniscus might increase the risk of knee OA in patients with degenerative tears. However, the influence of treatment strategy (surgical or non-surgical) on structural knee joint changes and the later risk of knee OA in young patients with meniscal tears is not known.

WHAT THIS STUDY ADDS

⇒ Initial treatment strategy (meniscus surgery or supervised exercise and education) did not influence short-term structural knee joint worsening in young adults with meniscal tears, as worsening of structural knee damage on MRI at the 2-year follow-up was limited and similar between treatment groups. In addition, early meniscal surgery was not superior to exercise therapy and education with optional delayed surgery in improving patient-reported outcomes (PROMs).

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The findings suggest that both surgical and non-surgical treatment strategies yield similar two-year PROMs and structural knee joint changes in young adults with a meniscal tear. Studies on long-term structural damage are needed to investigate long-term knee-joint changes and possible approaches to prevent OA development.
null
No patients or the public were involved in the planning of this secondary analysis.

Outcomes
MRI
Baseline and 2-year follow-up MRIs were performed with a minimum of a 1.5-T scanner using the individual radiology departments’ protocol for suspected meniscal tears. All protocols included sagittal, axial and coronal sequences with and without fat suppression. The main outcomes were the between-group difference in worsening in MRI-defined structural damage (ie, new or progressed cartilage damage, osteochondral damage and osteophytes) from baseline to 24 months, assessed using a slightly modified Anterior Cruciate Ligament OsteoArthritis Score (ACLOAS).13 ACLOAS is a semiquantitative MRI-based scoring system that includes structural features relevant to acute injury, degenerative incident features and longitudinal follow-up of structural OA features. Cartilage damage is scored from 0 to 6 in 14 subregions. Osteochondral damage is scored from 0 to 4 in 14 subregions, and osteophytes are scored from 0 to 7 in 12 locations. The scores for cartilage damage, osteochondral damage and osteophytes were summed on the knee level. Thus, the worsening of individual MRI features includes new or progressed damage in one subregion and progression in the number of subregions affected. We did not include meniscal damage worsening in this study since one of the interventions (APM) specifically altered the meniscus morphology.

We also assessed for any bone marrow lesion (BML), knee joint effusion/synovitis, and anterior cruciate ligament (ACL) and collateral ligament status. A BML was defined as a reticular ill-defined hyperintense lesion on water sensitive fat-suppressed sequences and was scored in 15 subregions (present/absent), and summed on the knee level. Effusion/synovitis or surrogates for this were scored in two locations: capsular distension in the suprapatellar recess (0–3) and signal alterations in Hoffa’s fat pad (0–3). Since effusion is often located in other recesses besides the suprapatellar recess, we added an assessment of overall effusion/synovitis, including all recesses. We used it as the primary effusion/synovitis score. Furthermore, we recorded the presence of Baker’s cysts and any possible change for overall effusion/synovitis and Baker’s cysts (decreased, unchanged, increased). An experienced musculoskeletal (MSK) radiologist (DIR) scored all the MRI scans, blinded to clinical information. The baseline and follow-up MRIs were assessed pairwise and unblinded to the sequence to maximise sensitivity to detect change.14 We assessed inter-rater reliability by another experienced MSK radiologist (EYK) independently reading 20% of the scans. Both MRI assessors were trained and supervised by a third experienced professor in MSK radiology (MPB) to reach a consensus before the scoring. The overall percentage of agreement and prevalence and bias adjusted kappa were calculated, except for the meniscal
damage, where we used weighted kappa due to the high prevalence of lesions (all had lesions). Most scores had an inter-rater agreement of $>95\%$, and the reliability was substantial (range, 0.61–0.8) or almost perfect (range, 0.81–1.0) according to the interpretation by Landis and Koch.\textsuperscript{15}

**Patient-reported outcomes**

We assessed the between-group difference in change in the mean score of the Knee Injury and Osteoarthritis Outcome Scores (KOOS\textsubscript{4}) from baseline to 2 years (ie, primary outcome in the main study). The KOOS\textsubscript{4} is the mean of four of five subscale scores, including pain, symptoms, function in sport and recreation, and quality of life, and ranges from 0 to 100, with lower scores indicating worse symptoms, function and quality of life.\textsuperscript{16,17} Additional PROMs were the between-group difference in change in the individual KOOS subscales and the Western Ontario Meniscal Evaluation Tool (WOMET), a meniscus-specific, valid and reliable PROM measure (converted to scores from 0 to 100, with lower scores indicating a worse quality of life).\textsuperscript{18,19}

**Statistical analysis**

We used descriptive statistics to describe baseline characteristics and frequencies of MRI features.

We conducted all analyses according to the intention-to-treat principle, with patients distributed to the treatment arm they were randomised to (irrespective of the treatment received). In addition, an as-treated analysis was performed. In this analysis, the patients undergoing meniscal surgery up until 2-year follow-up were included in one group. Those undergoing exercise and education (irrespective of their compliance with the exercise), who had not received delayed surgery, were included in the other group. Chi-square or Fisher’s exact test, as appropriate, was used to compare the frequency of participants with MRI-worsening between groups. A detailed analysis of the distribution of ACLOAS grades between the groups was irrelevant since the number and severity of the findings were low.

For the PROMs, we used the same analytical approach as in the primary reporting of the DREAM study\textsuperscript{1}: a linear mixed model with time (baseline, 3, 6, 12 and 24 months as discrete variables), treatment group (surgery or exercise), and the interaction between time and treatment group as fixed effects constraining the difference between the arms to 0 at baseline (ie, adjusting for baseline imbalance). The model was adjusted for the randomisation stratification factors (centre and sex) and age. A patient-specific intercept and slope were added as random effects to accommodate within-person measurement dependence. A common error variance was assumed for all follow-up time points and treatment arms, although error variance can differ at baseline. The assumptions for model validity were checked using scatter plots of the residuals versus time and two-dimensional scatterplots of the best linear unbiased prediction of the random effects. A 95\% CI excluding 10 points or more in KOOS\textsubscript{4}, was interpreted as no clinically meaningful difference. No imputation was performed as the mixed model included all patients.\textsuperscript{20} All statistical analyses were performed using Stata V.17.0 (StataCorp).
RESULTS
Of 121 patients randomised, 82 (68%) consented to participate in the 2-year follow-up (39 from the surgical group and 43 from the exercise group). After several attempts to contact patients or reschedule appointments for MRI scans, 78 provided PROMs, and 77 provided MRI data. Thus, nine patients only had either the MRI or the PROMs data. Baseline characteristics were similar between patients participating in the follow-up and those who did not (online supplemental table S1). The mean time (SD) from baseline to 2-year follow-up was 28 months (4.4). The patients’ mean age (SD) at baseline was 29.5 (6.6).

The primary report of the DREAM study.1 Traumatic or semi-traumatic MRI-defined damage worsening was observed in 9% (n=7) of all patients with MRI and osteophytes in 3% (n=2) of patients. Details of the type of worsening (progression in one subregion or in regions affected are listed in online supplemental table S2). Still, only one patient had MRI-defined OA.21 22 We observed similar worsening of cartilage damage (p=1.000) and osteophytes (p=0.203) between treatment arms, and in the as-treated analyses. BML, knee effusion/synovitis, Hoffa synovitis and Baker’s cysts were unchanged in 73%–90% of the patients and here too we found no essential differences between the groups for these findings (table 2).

Baseline MRI findings
Baseline findings are summarised in table 1. Of the meniscal tears, 65% (n=53) were isolated medial, 30% (n=25) isolated lateral and 4% (n=3) had both medial and lateral tears. For medial meniscal tears, 34% (n=28) were bucket-handle or complex followed by 26% (n=21) horizontal, whereas radial and vertical tears were the most frequent lateral tears, 15% (n=12). There was no essential difference in the type of tears between the groups assessed with ACLOAS. In one participant (1%), the baseline scan was described without a meniscal tear. However, since the patient was included in the study, the clinical MRI report and the including surgeon must have assessed the scan differently, and thus we decided to also include the patient in this secondary analysis. Besides meniscal tears, there were few MRI-defined baseline changes with a similar distribution between groups. One patient fulfilled the suggested criteria for MRI-defined OA.21 22 Seven patients had ACL or medial collateral ligament changes, all related to mild sprains. The most common baseline MRI findings were knee joint effusion/synovitis (n=39), Hoffa synovitis (n=21) and BMLs (oedema) (n=16) (table 1).

Patient-reported outcomes
We observed no essential difference in change between groups from baseline to 2 years in KOOS (table 3). The mean crude and adjusted between-group differences in change were −5.1 (95% CI −13.8, 3.7) and −1.4 (95% CI −9.1, 6.4) points (in favour of the exercise group), respectively. On average, most of the improvement was observed during the first 6 months of the trial. At 2 years the surgical group had improved by 16.4 (95% CI 10.4, 22.0), while the exercise group had improved by 21.5 (95% CI 15.0, 28.0). The individual KOOS subscales yielded similar results (table 3). For the WOMET, these improvements were 20.2 (95% CI 12.9, 27.5) for the surgery group and 26.7 (95% CI 18.6, 34.8) for the exercise and education group, with an adjusted between-group difference in change of −2.4 (95% CI −11.8, 6.9) from baseline to 2 years (table 3). Likewise, the as-treated analyses yielded no essential between-group differences in change (figure 2B; online supplemental table S3).

Table 3  Patient-reported outcomes at 2-year follow-up (main analysis)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Mean improvement from baseline to 2-year follow-up (95% CI)</th>
<th>Between-group difference in mean improvement (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Meniscal surgery group (n=37)</td>
<td>Exercise and education group (n=41)</td>
</tr>
<tr>
<td>Primary</td>
<td>KOOS†,‡</td>
<td>16.4 (10.4, 22.4)</td>
</tr>
<tr>
<td>Secondary</td>
<td>KOOS§ subscale scores</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>16.1 (9.7, 22.6)</td>
<td>19.2 (13.1, 25.2)</td>
</tr>
<tr>
<td>Symptoms</td>
<td>10.5 (4.2, 16.9)</td>
<td>15.3 (10.1, 20.4)</td>
</tr>
<tr>
<td>ADL</td>
<td>10.5 (5.8, 15.3)</td>
<td>14.7 (9.3, 20.2)</td>
</tr>
<tr>
<td>Sport/Rec</td>
<td>22.2 (12.6, 31.7)</td>
<td>30.0 (20.0, 40.0)</td>
</tr>
<tr>
<td>QOL</td>
<td>16.7 (10.3, 23.1)</td>
<td>21.5 (13.5, 29.5)</td>
</tr>
<tr>
<td>WOMET§ score</td>
<td>20.2 (12.9, 27.5)</td>
<td>26.7 (18.6, 34.8)</td>
</tr>
</tbody>
</table>

*Adjusted for the randomisation stratification factors (centre and sex) and age.
†KOOS: Knee injury and Osteoarthritis Outcome Score and its subscales Pain, Symptoms, Function in daily living (ADL), Function in sport and recreation (Sport/Rec) and Quality of life (QOL) have scores ranging from 0 (worst) to 100 (best). KOOS is the mean score of four out of five of the KOOS subscale scores, that is, Pain, Symptoms, Sport/Rec and QOL.
‡Improvements of 10 points or more are considered clinically relevant.
§WOMET: Western Ontario Meniscal Evaluation Tool (converted into 0–100; lower scores indicating worse quality of life). For WOMET we had n=34 in both groups.
MRI—
with radiographic knee OA that reported significantly greater
physical therapy for degenerative meniscal tears in older patients
over, in contrast to an earlier trial comparing APM with phys-

in the APM group compared with the exercise group, 23 we did

ening (short-

indicate an association between the baseline damage and wors-

of young patients with ACL injuries, we find differences that

between age and the worsening of structural damage.

signs of OA (on radiographs) was about 15 years. In contrast,

and 30, the average time until the development of radiological

sustained an isolated meniscus injury between the ages of 17

over age

30 with the same injury, indicating a strong association


due to the low number of patients in each
differences between departments.

Figure 2 Mean unadjusted Knee Injury and Osteoarthritis Outcome Scores (KOOS4). (A) Patients distributed according to the treatment arm they were randomised to (irrespective of the treatment received). (B) In this analysis, the patients undergoing surgery up until 2-year follow-up were included in the surgery group. Those undergoing exercise and education (irrespective of their compliance with the exercise) who had not received delayed surgery constituted the other group. The error bars indicate 95% CIs.

DISCUSSION
We found that the risk of 2-year worsening of structural damage was low and similar in patients undergoing early surgery and patients undergoing exercise and education with optional delayed surgery. Likewise, the as-treated analysis comparing early or delayed surgery to exercise and education did not reveal any essential differences. Moreover, we found that early surgery was not superior to a strategy of exercise and education with optional delayed surgery in improving pain, function and quality of life at 2 years, similar to the 12-month results. 1

Our study, including young patients, found less structural worsening over 2 years than in previous studies, including older patients with degenerative meniscal tears. 6 7 23 Moreover, in contrast to an earlier trial comparing APM with phys-

iotherapy for degenerative meniscal tears in older patients with radiographic knee OA that reported significantly greater MRI-defined worsening of cartilage damage and osteophytes in the APM group compared with the exercise group, 23 we did not detect a difference between groups. Whether the previous finding of more severe structural worsening in knees with OA relates to patients’ age, the degree of structural damage at baseline or other factors, like the type of meniscal repair or resec-

tion, tear/injury or symptom onset, is unknown. Most patients (80%) in our study had traumatic or semi-traumatic symptom onset. However, subgroup differences can exist for those with gradual onset that are most likely degenerative tears. Regarding the influence of age, Roos et al 24 reported that for patients who sustained an isolated meniscus injury between the ages of 17 and 30, the average time until the development of radiological signs of OA (on radiographs) was about 15 years. In contrast, the corresponding time interval was only about 2 years for those over age 30 with the same injury, indicating a strong association between age and the worsening of structural damage.

Comparing the structural worsening in our study to studies of young patients with ACL injuries, we find differences that indicate an association between the baseline damage and wors-

ening (short-term or long-term). The ACL studies 23 26 report

more severe structural baseline knee damage (eg, cartilage and osteochondral lesions) and more structural worsening over time than our study, where the participants had isolated meniscal tears.

Recent systematic reviews report no additional clinically rele-
vant benefit of APM over placebo surgery or exercise therapy in middle-aged and older adults with degenerative meniscal tears. 27–29 Based on this evidence, clinical guidelines generally recommend against arthroscopic surgery and recommend non-
surgical treatment for older patients with degenerative tears. 28 However, young patients with meniscal tears are usually offered surgery. 10 This secondary analysis of the 2-year outcome from the DREAM trial 1 confirms the primary 12-month reporting and yields similar results as the 2-year reporting from the The Study of Traumatic meniscal tears: Arthroscopic Resection vs Rehabilitation (STARR) trial. 2 Early surgery was not superior to exercise and education, with optional delayed surgery for treating isolated meniscal tears in young adults.

Limitations
Thirty-two per cent of patients were lost to follow-up. Although we performed analyses according to the intention-to-treat principle, the assumption of including all patients was violated. The resulting direction of this bias is unknown. Nevertheless, we observed no difference in baseline characteristics between patients participating and those lost to the 2-year follow-up. Also, the as-treated analyses should be interpreted with caution due to the low number of patients in each group in these analyses. The MRI scans were conducted at seven different departments, which may result in a difference in the visualisation of the findings between the departments. Since our primary MRI outcome was worsening structural damage, the scans were assessed pairwise and unblinded to the sequence to maximise sensitivity for change, 15 mitigating some variations caused by differences between departments.
Clinical and research implications
These findings suggest that both treatment strategies are equally effective in relieving symptoms in young patients and highlight the importance of including the patient’s treatment preferences when deciding on a treatment strategy. Specific tear types may benefit more from one treatment than the other, but future studies on effect modification are needed to provide more insight into this important clinical issue. Moreover, studies with longer follow-ups are needed to investigate long-term knee joint changes and possible approaches to prevent OA development.

CONCLUSION
Our results suggest that in young adults treated for isolated meniscal tears the 2-year worsening of MRI-defined structural damage indicative of knee OA is low and similar between treatment strategies (early surgery vs exercise with the option of later surgery). In addition, early meniscal surgery is not superior to exercise and education in improving 2-year PROMs. These findings are important in the decision-making between patients and clinicians on the treatment choice, as both strategies appear viable.

Author affiliations
1 Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, Center for Muscle and Joint Health, Odense, Denmark
2 The Research Unit PROgress, Department of Physiotherapy and Occupational Therapy, Næstved-Slægelse-Ringsted Hospitals, Region Zealand, Slagelse, Denmark
3 Department of Radiology, Copenhagen University Hospital Bispebjerg and Frederiksberg, Copenhagen, Denmark
4 Department of Orthopedic Surgery, Sports Orthopaedic Research Center—Copenhagen (SORM-C), Arthroscopic Center, Copenhagen University Hospital, Amager-Hvidovre Hospital, Copenhagen, Denmark
5 Department of Orthopedics, Aarhus University Hospital Skjæby, Aarhus, Denmark
6 Department of Radiology, Aalborg University Hospital, Aalborg, Denmark
7 Department of Radiology, Diagnostic Centre, University Research Clinic for Innovative Patient Pathways, Silkeborg Regional Hospital, Silkeborg, Denmark
8 Department of Orthopaedic Surgery, Lillebaelt Hospital, Vejle, Denmark
9 Clinical Epidemiology Unit, Orthopedics, Department of Clinical Sciences Lund, Lund University, Lund, Sweden
10 Research Unit for General Practice, Department of Public Health, University of Southern Denmark, Odense, Denmark

Twitter Stine Haugaard Clausen @HaugaardClausen, Søren T Skou @STSkou, Camma Damsted @CammaDamsted, Martin Englund @de_englund and Jonas Bloch Thorlund @jbtthorlund

Acknowledgements The DREAM study group (a complete list of contributors to the DREAM Study Group is provided in online supplemental file).

Contributors Responsible author: SCH is the guarantor and takes full responsibility for the overall content and for the integrity of the data and the accuracy of the data analysis. Concept and design: STH, MFB, PH, ME, JBT. Acquisition, analysis or interpretation of data: all authors. Drafting of the manuscript: STH and JBT. Critical revision of the manuscript for important intellectual content: all authors. Statistical analysis: STH and CHG. Obtained funding: JBT and STS.

Funding The study was funded by the Danish Council for Independent Research (DFF-6110-00045 and Sapere Aude Research Talent Award DFF-6110-00045B). The DREAM study was funded by IMK Almene Fond, Lundbeck Foundation, Spar Nord Foundation, Danish Rheumatism Association, Association of Danish Physiotherapists Research Fund, Research Council at Næstved-Slægelse-Ringsted Hospitals and Region Zealand (Exercise First program grant). The funders had no role in study design, data collection, data analysis, data interpretation or writing of the report.

Competing interests STS has received personal fees from Munksgaard, TrustMed-Ed and Nestlé Health Science, outside the submitted work, and is cofounder of Good Life with osteoArthritis in Denmark (GLA-D), a not-for-profit initiative hosted at University of Southern Denmark aimed at implementing clinical guidelines for osteoarthritis in clinical practice. JBT reports a research grant from Pfizer outside the submitted work (completed in 2022). CV reports no conflict of interest in this study. Outside submitted work CV received travel expenses from Stryker. Other authors: no conflict of interest.

Patient consent for publication Consent obtained directly from patient(s).

Ethics approval This study involves human participants and the study was approved by the Regional Committees on Health Research Ethics for Southern Denmark (S-20160151) and the Danish Data Protection Agency (Agency of Southern Denmark, 16/45314). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

ORCID iDs
Stine Haugaard Clausen http://orcid.org/0000-0002-8632-4596
Søren T Skou http://orcid.org/0000-0003-4386-7059
Camma Damsted http://orcid.org/0000-0002-4627-1338
Jonas Bloch Thorlund http://orcid.org/0000-0001-7789-8224

REFERENCES
15 Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33:159.