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Arthroscopic surgery for degenerative knee: systematic review and meta-analysis of benefits and harms

J B Thorlund,¹ C B Juhl,^{1,2} E M Roos,¹ LS Lohmander^{1,3,4}

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¹University of Southern Denmark, Department of Sports Science and Clinical Biomechanics, Campusvej 55, 5230 Odense M, Denmark

²Department of Orthopedics, Copenhagen University Hospital, Gentofte, Denmark

³Department of Orthopedics and Traumatology, Odense University Hospital, Odense, Denmark

⁴Department of Orthopedics, Clinical Sciences Lund, University of Lund, Sweden

Correspondence to

J B Thorlund;
jthorlund@health.sdu.dk

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ABSTRACT

Objective To determine benefits and harms of arthroscopic knee surgery involving partial meniscectomy, debridement, or both for middle aged or older patients with knee pain and degenerative knee disease.

Design Systematic review and meta-analysis.

Main outcome measures Pain and physical function.

Data sources Systematic searches for benefits and harms were carried out in Medline, Embase, CINAHL, Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL) up to August 2014. Only studies published in 2000 or later were included for harms.

Eligibility criteria for selecting studies

Randomised controlled trials assessing benefit of arthroscopic surgery involving partial meniscectomy, debridement, or both for patients with or without radiographic signs of osteoarthritis were included. For harms, cohort studies, register based studies, and case series were also allowed.

Results The search identified nine trials assessing the benefits of knee arthroscopic surgery in middle aged and older patients with knee pain and degenerative knee disease. The main analysis, combining the primary endpoints of the individual trials from three to 24 months postoperatively, showed a small difference in favour of interventions including arthroscopic surgery compared with control treatments for pain (effect size 0.14, 95% confidence interval 0.03 to 0.26). This difference corresponds to a benefit of 2.4 (95% confidence interval 0.4 to 4.3) mm on a 0–100 mm visual analogue scale. When analysed over time of follow-up, interventions including arthroscopy showed a small benefit of 3–5 mm for pain at three and six months but not later up to 24 months. No significant benefit on physical function was found (effect size 0.09, –0.05 to 0.24). Nine studies reporting on harms were identified. Harms included symptomatic deep venous thrombosis (4.13 (95% confidence interval 1.78 to 9.60) events per 1000 procedures), pulmonary embolism, infection, and death.

Conclusions The small inconsequential benefit seen from interventions that include arthroscopy for the degenerative knee is limited in time and absent at one to two years after surgery. Knee arthroscopy is associated with harms. Taken together, these findings do not support the practise of arthroscopic surgery for middle aged or older patients with knee pain with or without signs of osteoarthritis.

Systematic review registration PROSPERO CRD42014009145.

INTRODUCTION

Arthroscopic knee surgery with meniscus resection is common for middle aged or older people with persistent knee pain.^{1–3} The knees of these patients often show “degenerative” lesions of cartilage, meniscus, and other tissues, suggestive of osteoarthritis. However, population based studies using magnetic resonance imaging show that incidental findings of such lesions are also very common among people without knee symptoms and among those without plain radiographic signs of osteoarthritis, suggesting that the clinical significance of such findings is unclear.^{4–6} All but one of the nine randomised clinical trials to date of arthroscopic surgery in middle aged or older people with persistent knee pain failed to show an added benefit of interventions including arthroscopic surgery over a variety of control treatments.^{7–15} Uncertainty thus exists about the benefit of arthroscopic surgery including meniscus resection for these patients. However, many specialists are convinced of the benefits of the procedure from their own experience,^{16–19} and several recent reports show an increase, or no decrease, in the incidence of arthroscopic knee surgery with meniscus resection during the past decade.^{3 20–23} The arthroscopic procedures discussed here are reported to be associated with adverse events, including deep venous thrombosis, infections, cardiovascular events, pulmonary embolism, and death.^{24–26}

The balance of benefits and harms weighs importantly in the choice of treatment. To inform the choice of treatment for these patients, we did a comprehensive, up to date systematic review and meta-analysis of the benefits and harms of arthroscopic surgery compared with control treatments for middle aged and older people with persistent knee pain. We extend existing knowledge by including more patients and by presenting outcomes on pain, function, and harms in patients ranging from those with degenerative meniscal tears and no radiographic signs of osteoarthritis to those with degenerative meniscal tears and more severe signs of osteoarthritis. We also accounted for the study designs used and, when appropriate, did a priori defined subgroup analyses.

METHODS

We used the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement as a guideline for this study.²⁷

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Eligibility criteria

We included randomised controlled trials assessing the benefits (pain and physical function) of arthroscopic surgery involving partial meniscectomy, debridement, or both for patients with or without osteoarthritis compared with non-surgical treatments such as sham surgery (including lavage), exercise, and medical treatment. Our aim was to include studies on middle aged and older patients, but we applied no restriction on age in the search as degenerative knee disease is rare before middle age. We excluded studies on patients with concomitant cruciate ligament injuries. For the search on harms, we also allowed cohort studies, register based studies, and case series, again excluding studies on patients with concomitant cruciate ligament injuries.

Literature search and study selection

We did systematic searches for benefits and harms in Medline, Embase, CINAHL, Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL) in April 2014 and updated them in August 2014. Owing to advances in surgical and anaesthetic procedures over time, we included only studies published in 2000 or later for harms. We adjusted the search strategies according to the specifications of the individual database (see web appendix). We set no search restrictions for follow-up time, patients' age, study size, or language. Two members of the study team independently assessed all titles and abstracts of identified reports for eligibility (benefits: JBT and CBJ; harms: JBT and LSL). We obtained the full text if at least one of the reviewers judged a study to be eligible. We reviewed reference lists of included studies to identify additional studies. Disagreements on inclusion were resolved by consensus.

Data extraction

The pre-specified outcomes for benefits were patient reported pain and physical function. When a report provided data on more than one pain or physical function scale, we used a published hierarchy for selection of patient reported outcomes (please refer to the PROSPERO protocol).²⁸ We extracted outcomes for all reported follow-up assessments in the included studies.

For the primary analysis on pain and physical function, we used data from the primary follow-up time as defined in the individual studies, varying from three to 24 months. If a study did not explicitly state a primary follow-up time, we included the longest follow-up time from the initial trial report in the primary analysis. We extracted the standard deviation or estimated it from the confidence interval, the P value, or the interquartile range or used other methods recommended by the Cochrane Handbook for Systematic Reviews.²⁹ If necessary, we approximated means and measures of dispersion from figures in the included studies.

In addition to the outcomes specified above, we extracted the number of participants allocated to intervention and control groups, distribution of sex, mean age at baseline, body mass index at baseline, baseline pain (transformed into a visual analogue pain scale from 0 to 100 mm), and interventions performed in the intervention and control groups. We also extracted data on the presence or absence of radiographic knee osteoarthritis in the study populations. As some studies included patients both with and without radiographic knee osteoarthritis, we divided the studies into three subgroups on the basis of the population included: no radiographic knee osteoarthritis population (that is, all patients had Kellgren and Lawrence grade 0 or 1³); radiographic knee osteoarthritis population (that is, all

patients had Kellgren and Lawrence grade 2 or higher); and mixed population (some patients with and some without radiographic knee osteoarthritis). For studies using the Ahlback scale for defining radiographic knee osteoarthritis,³¹ we considered a grade of 0 as no radiographic knee osteoarthritis and grade 1 or higher as radiographic knee osteoarthritis.

We extracted all adverse events reported. However, we had decided a priori to do meta-analysis only on the following adverse events: deep venous thrombosis, pulmonary thromboembolism, venous thromboembolism, infection, and death (all cause mortality). We chose these adverse events on the basis of a preliminary search and their seriousness and frequency. If a study did not report the rate of venous thromboembolism but reported both deep venous thrombosis and pulmonary thromboembolism, we combined the last two to generate a venous thromboembolism variable for meta-analysis.

In addition to adverse events, we registered the study design, mode of reporting (that is, per patient or per procedure), sample size, period of adverse events collection, types of adverse events, and number of adverse events. We used customised forms to independently extract all data for benefits (JBT, CBJ) and harms (JBT, CBJ, LSL).

Synthesis of results

For the analysis on benefits, we calculated the effect sizes in the individual studies as standardised mean differences, allowing pooling and comparison of the various outcomes assessed in the individual trials. We estimated the standardised mean difference as the difference between the mean score of the intervention and control groups divided by the pooled standard deviation of the final score. This estimate of the effect size using standardised mean difference has a slight bias overestimating the effect size, and we applied a correction factor to convert the effect size to Hedges' g.³²

We used meta-analysis to combine the individual study results by using the Stata software package (version 13.0). We applied the REstricted Maximum Likelihood (REML) method to estimate the combined effect size and the between study variance. We examined heterogeneity between trials with Q tests and calculated the I² statistic,³³ measuring the proportion of variation (that is, inconsistency) in the combined estimates due to between study heterogeneity.³⁴ We transformed the effect size measured as standardised mean difference into a visual analogue scale ranging from 0 to 100 mm by multiplying it by a standard deviation equal to 16.9 mm for pain and 16.6 mm for physical function.³⁵ The standard deviations used for conversion of standardised mean difference to millimetres were based on a cohort of 914 patients with knee osteoarthritis.³⁶ Furthermore, we used the formula proposed by Chinn in the Cochrane Handbook to estimate the odds ratio and number needed to treat.^{35–38}

We analysed the effect of arthroscopic surgery involving partial meniscectomy, debridement, or both for patient reported pain and physical function. We did subgroup analyses to explore the effect of severity of degenerative knee disease defined by presence of radiographic knee osteoarthritis in the respective study populations (no patients with radiographic knee osteoarthritis, patients with or without radiographic knee osteoarthritis, or all patients with radiographic knee osteoarthritis), the effect of partial meniscectomy with or without concomitant debridement, risk of bias, and type of study design. To investigate whether the results were dependent on follow-up time, we also did meta-analysis on all available follow-up time points with at least two studies available.

In the analysis on harms, we transformed the numbers of adverse events into log odds of events, allowing pooling of data from the individual studies. Results are reported as number of adverse events per 1000 procedures with 95% confidence intervals. We applied a REML method to estimate the combined odds of events and the between study variance. We assessed study heterogeneity by calculating the I^2 statistic.

Risk of bias assessment

Two reviewers (JBT and CBJ) independently assessed risk of bias by using the Cochrane Handbook for Systematic Reviews of Interventions.²⁹ For studies on benefits, the two reviewers independently assessed sequence generation, allocation concealment, blinding, handling of incomplete outcome data, selective outcome reporting, and other bias. For harms, they assessed each of the included studies for description of intervention, type of adverse events reported, and loss to follow-up. Each of the domains was scored as “adequate,” “inadequate,” or “unclear.” Disagreements were resolved by consensus. For a full elaboration on the criteria for each of the bias assessment domains, please refer to the study protocol (PROSPERO registration number CRD42014009145).

Patient involvement

There was no patient involvement in this study.

RESULTS

Benefits

The literature search yielded 1789 reports after exclusion of duplicates. Of these, 18 were considered for inclusion after review of title and abstract. After full text review, six reports were excluded because of no or insufficient data on patient reported pain or physical function,^{39–44} and two were excluded because they were not clinical trial reports.^{45 46} We included 10 reports on nine different trials in the systematic review (supplementary figure A).^{7 8–14 47} One report was not included in the final meta-analysis as it was a secondary trial report and the only one providing five year follow-up data.⁴⁷

Study characteristics

The nine included trials had randomly allocated 1270 patients to interventions including arthroscopic surgery with partial meniscectomy, debridement, or both or a variety of control treatments ranging from placebo surgery to exercise (supplementary table A). Mean age of patients in the individual trials ranged from 49.7 to 62.8 years. Mean baseline pain in the

included studies ranged from 36 to 63 mm on a 0–100 mm visual analogue scale. In two trials,^{8 10} all patients had radiographic knee osteoarthritis (Kellgren and Lawrence grade 2 or more); in five trials,^{7 9 11 12 15 47} some of the patients had radiographic knee osteoarthritis; and in two trials,^{13 14} no patients had radiographic knee osteoarthritis. The follow-up time for the primary endpoint in the trials varied between three and 24 months.

Synthesis of results

Our primary analysis for pain, combining the individual trials' primary endpoints ranging from three to 24 months, showed a small but statistically significant benefit for interventions including knee arthroscopy compared with control treatments (effect size 0.14, 95% confidence interval 0.03 to 0.26; $I^2=0.0\%$) (figure 1 and supplementary table B). This effect size corresponds to a difference of 2.4 (95% confidence interval 0.4 to 4.3) mm between treatment groups on a 0–100 mm visual analogue scale. Evaluation of between group differences at different postoperative time points showed a statistically significant benefit in favour of interventions including knee arthroscopy at three months (effect size 0.27, 0.14 to 0.41; $I^2=20.6\%$) and six months (0.18, 0.05 to 0.30; $I^2=0.0\%$) but not at later postoperative times (figure 2 and supplementary table B).

For physical function, we found no significant difference between interventions including knee arthroscopy and control treatments (effect size 0.09, –0.05 to 0.24; $I^2=11.9\%$) (figure 3). When evaluating physical function over time, we found no between group differences at any of the analysed time points (figure 4).

Risk of bias

Agreement between assessors on risk of bias ranged from 78% to 100% (that is, κ values ranging from 0.53 to 1.00). Only one included report was assessed as “adequate” on all domains (supplementary table C),¹⁴ and only two reports were assessed as “adequate” for blinding.^{8 14} The remaining studies were not blinded.^{7 9–13 15 47}

Subgroup analysis

Analysis of the effect of risk of bias showed no differences between studies scored as adequate, unclear, or inadequate on any of the domains investigated (figure 5 and supplementary figure B). We also did subgroup analyses on the primary endpoint analysis of pain and physical function for the osteoarthritis status of the study population (ranging from no

Figure 1 Results of primary analysis on benefit on patient reported pain of interventions including arthroscopic knee surgery compared with control interventions (follow-up time range: 3–24 months).

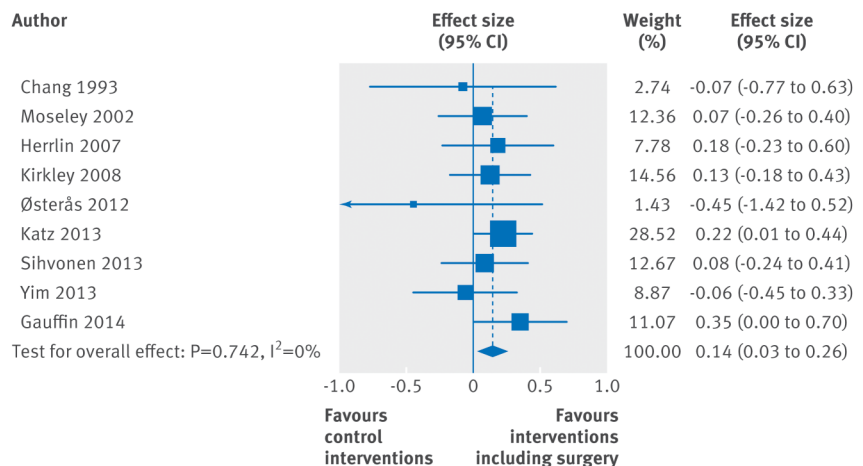
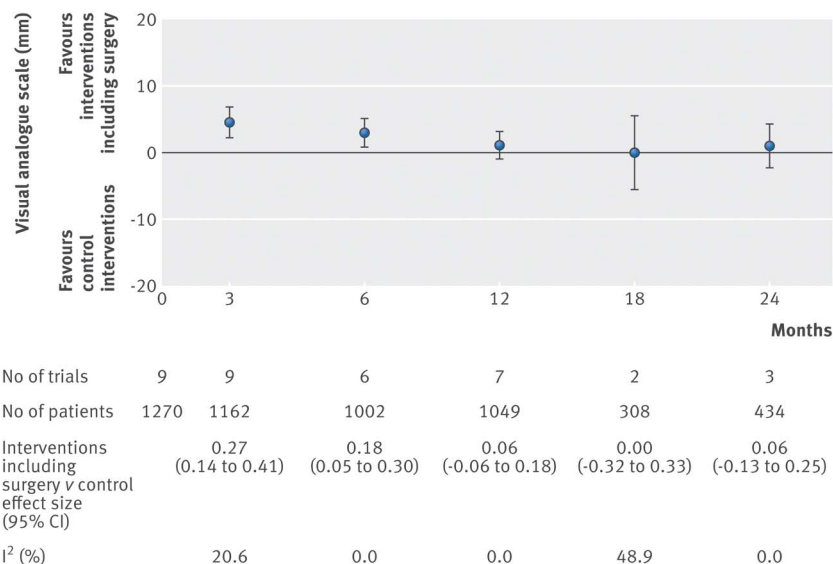


Figure 2 Effect of interventions including arthroscopic knee surgery compared with control interventions on patient reported pain presented as difference in mm on 0-100 mm visual analogue scale, with 95% confidence interval error bars. Table below shows number of studies and patients included in analyses at different follow-up time points, with estimated difference between interventions calculated as effect size and estimates of heterogeneity (I^2). Data from 2 months' follow-up from Osteraas *et al* and Sihvonen *et al* are included in 3 month estimate.



radiographic osteoarthritis at all via a mixed population to all having radiographic osteoarthritis) and for type of surgery (partial meniscectomy with or without concomitant debridement) (figure 6 and supplementary figure C). These analyses did not change the interpretation of the results from the primary analyses. Subgroup analysis stratified for presence/absence of mechanical symptoms was not possible owing to lack of data. In a further subgroup analysis to evaluate the influence of study design, we found no differences between studies with different control interventions (figure 6 and supplementary figure C).

Harms

We screened titles and abstracts of 2330 reports after exclusion of duplicates; of these, 37 were reviewed as full text. This resulted in exclusion of 28 reports,⁴⁸⁻⁷⁵ leaving nine reports for meta-analysis (supplementary figure A).^{12 14 24-26 76-79}

Study characteristics

Two randomised trials and seven observational/registry studies reported on adverse events (supplementary table D).^{12 14 24-26 76-79} Quality of reporting of adverse events was frequently low in both observational studies and randomised clinical trials, and only two of nine arthroscopy trials provided useful information on adverse events.

Synthesis of results

Deep venous thrombosis was the most frequently reported symptomatic adverse event associated with arthroscopic

meniscectomy, with 4.13 (95% confidence interval 1.78 to 9.60) events per 1000 procedures, followed by infection, pulmonary embolism, and death (table 1 and supplementary table B). Heterogeneity of all the estimates was high (table 1).

Risk of bias

Only one study was assessed as “adequate” on all three domains (supplementary table E).¹² All reports sufficiently described the surgical intervention, but seven of nine studies reported only a few types of adverse events in the same report (supplementary table D).

DISCUSSION

In this meta-analysis, in which the primary endpoint of each of the nine included randomised trials ranged from three to 24 months after surgery, we found a small but statistically significant effect on pain relief from interventions including arthroscopic surgery compared with control treatments, corresponding to a 2.4 mm between group difference on a 0-100 mm visual analogue scale. When we analysed pain for different postoperative time points, the benefit favouring arthroscopic surgery was present only at three and six months, but not at later time points. We found no between group differences for self reported physical function in any of the analyses. Deep venous thrombosis was the most frequently reported symptomatic adverse event, followed by infection, pulmonary embolism, and death.

Figure 3 Results of main analysis on benefit on patient reported physical function of interventions including arthroscopic knee surgery compared with control interventions (follow-up time range: 3-24 months).

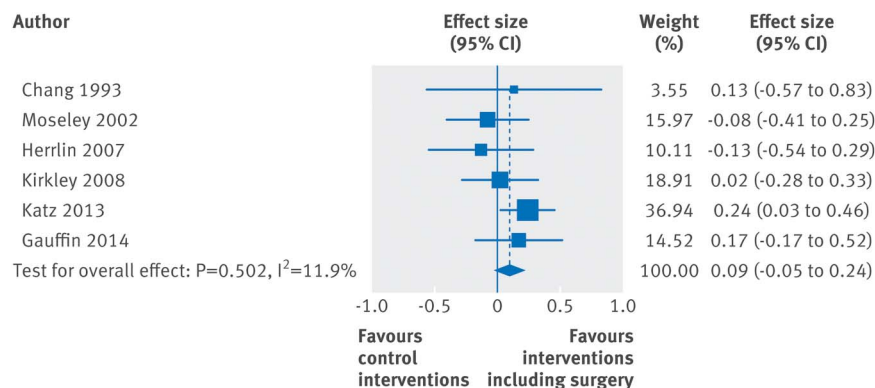
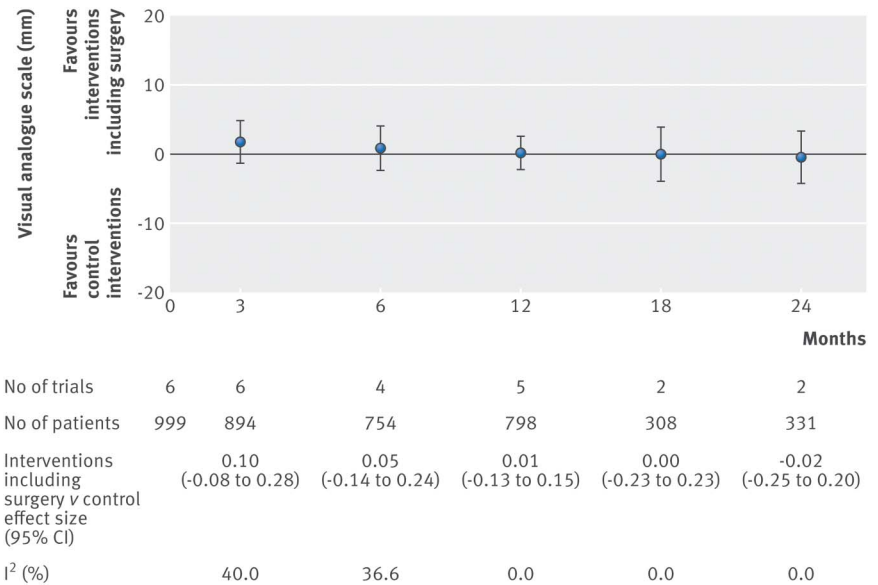


Figure 4 Effect of interventions including arthroscopic knee surgery compared with control interventions on patient reported physical function presented as difference in mm on 0–100 mm visual analogue scale, with 95% confidence interval error bars. Table below shows number of studies and patients included in analyses at the different follow-up time points, with estimated difference between interventions calculated as effect size and estimates of heterogeneity (I^2).



Strengths and weaknesses

Previous systematic reviews have investigated the benefits of knee arthroscopy in patients with established knee osteoarthritis or no/mild knee osteoarthritis.^{80 81} To the best of our knowledge, ours is the first systematic review and meta-analysis to include both benefits and harms of arthroscopic surgery and to include the whole continuum of degenerative knee disease, ranging from patients with degenerative meniscal tears without radiographic changes to those with meniscal tears and other joint changes combined with more severe radiographic changes. We included all identified randomised controlled trials of arthroscopic surgery for the degenerative knee comparing interventions including arthroscopic surgery with control treatments. To facilitate interpretation of pain and function results, we based our analysis on patient reported pain and function. Composite measures of “knee function,” aggregating arbitrarily weighted more or less correlated items into one score, are notoriously difficult to interpret and were therefore not

included. We also searched the literature for information on harms associated with this intervention, and we included observational studies published from 2000 onwards. The individual trials from different countries and populations showed consistent results, with low heterogeneity for benefit, whereas heterogeneity for harms was large.

Only two of the nine arthroscopy trials were adequate for blinding, and these trials included a control group with sham surgery. Many of the other trials, being inadequately blinded and using control groups with various non-invasive treatments, were assessed according to the Cochrane Collaboration criteria as having a high risk of bias.²⁹ Given that invasive procedures have a stronger placebo effect than do non-invasive ones, the resulting bias from inadequate or absent blinding would be expected to favour the treatment arm including arthroscopic surgery.^{82,85}

The focus of five of the nine trials was, by study design, on the additional benefit from arthroscopic surgery when the same

Figure 5 Evaluation of risk of bias in primary analysis of pain. P value indicates difference between studies dependent on risk of bias scoring (that is, adequate, inadequate, and unclear).

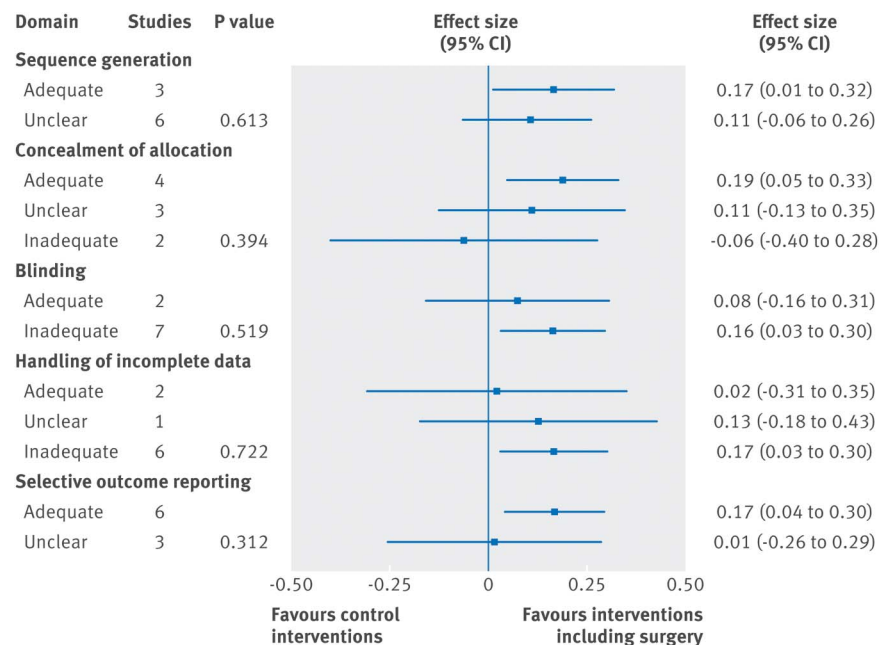
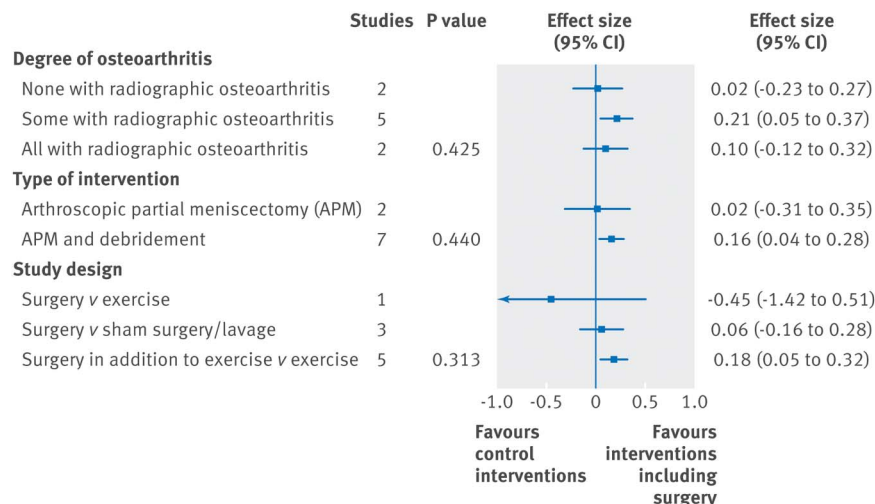


Figure 6 Subgroup analysis on primary analysis of pain stratified by study population knee osteoarthritis status, surgery type, and study design. P value indicates difference between different subgroups.



non-surgical intervention was provided to both the intervention and comparator group. The exercise therapy component, applied both in the intervention and in the comparator arms, was in many cases of inadequate dose for an optimal efficacy or poorly described.⁸⁶ In light of our incomplete understanding of the possible interaction between exercise therapy and a surgical intervention and their resulting combined efficacy, compared with the efficacy of exercise therapy in isolation, the resulting direction of bias is uncertain.

The randomised controlled trials of arthroscopic surgery were small, limiting their usefulness in assessing harms, and most of them provided no useful information on adverse events. We therefore included observational studies to obtain information on harms associated with arthroscopic surgery involving meniscectomy, debridement, or both.⁸⁷ The heterogeneity for assessing harms was high, reflecting differences in study size and design and quality of reporting of adverse events. Generally, the terminology and consistency in reporting of adverse events was poor. We did not systematically search the literature for harms associated with the control treatments, notably exercise. However, serious adverse events seem to be rare whereas minor events related to joint pain and muscle soreness are commonly reported from resistance training, including from patients with knee osteoarthritis.⁸⁸

Meaning of study

The overall additional benefit on pain from arthroscopic surgery, using the primary endpoint of each trial, was small (effect size 0.14) and limited in time. This benefit is comparable to the small pain relieving effect on knee pain seen from

paracetamol (effect size 0.14), less than that of non-steroidal anti-inflammatory drugs (0.29),⁸⁹ and markedly smaller than the moderate to large pain relieving effect seen from exercise therapy as treatment for knee osteoarthritis (overall standardised mean difference 0.50 regardless of type or dose, or 0.68 for exercise performed three times a week).⁸⁶ A previous systematic review and meta-analysis of benefits of arthroscopy suggested that a clinically relevant improvement for arthroscopic surgery in this patient group would correspond to a standardised mean difference of 0.45.⁸¹ Effect sizes can be difficult to interpret, so we converted them to mm on a 0–100 visual analogue scale. The effect size of 0.14 corresponds to difference of 2.4 mm. This is a negligible difference on a 0–100 scale and much smaller than the 15–20 mm commonly suggested as representing a clinically relevant difference for pain.⁹⁰ Claims of benefit in subgroups of patients are not supported by published evidence.

We observed a substantial improvement in the intervention group receiving surgery, corresponding to the clinical impression of many surgeons.^{16–19} Accordingly, recent reports show an increase, or no decrease, in the incidence of arthroscopic knee surgery in middle aged or older people with persistent knee pain.^{3 20–23} However, the improvements in the control groups were similarly impressive, with no clinically relevant between group differences at any time point. This is in line with a recent systematic review of the use of placebo controls in the evaluation of surgery, with considerable improvement in placebo arms of randomised trials and similar or only marginally superior benefit from surgery in half of the included studies.^{91 92}

Arthroscopic meniscectomy is associated with short term risk of harms, of which the most common was deep venous thrombosis, and in rare cases death. Arthroscopic meniscus resection may also be associated with long term harms. Resection of the meniscus increases local contact pressures in the knee, increasing the risk for development of osteoarthritis.^{93–95} In support, patients with previous knee surgery undergo total knee arthroplasty at a significantly younger age than do patients without previous knee surgery.⁹⁶

Arthroscopic surgery in the middle aged and older population with knee pain represents most arthroscopies and is routinely performed on the basis of a suspected meniscal tear by clinical examination or as diagnosed by magnetic resonance imaging, the reasoning being that the pain is associated with the meniscal tear. However, meniscal tears and other structural abnormalities (such as osteophytes, cartilage damage, and bone marrow lesions) are characteristics of knee osteoarthritis, often coexist,

Table 1 Summary of meta-analysis on harms of arthroscopic meniscectomy

Adverse event	No of studies (No of patients/ procedures)	No of adverse events per 1000* (95% CI)	I ² (%)
Deep venous thrombosis	5 (432 663)	4.13 (1.78 to 9.60)	98.3
Pulmonary embolism	6 (736 823)	1.45 (0.59 to 3.54)	98.6
Venous thromboembolism	6 (571 793)	5.68 (2.96 to 10.9)	99.3
Infection	4 (946 230)	2.11 (0.80 to 5.56)	99.6
Death	2 (106 967)	0.96 (0.04 to 23.9)	90.3

*Mix of studies reporting per patient and per procedure.

and are common findings in painful knees but also commonly occur in pain-free knees in middle aged and older people.^{5 6} Such joint damage is often present without a history of distinct trauma but is considered to be of a “degenerative” nature and indicative of early knee osteoarthritis.⁵ Thus, middle aged patients with knee pain and meniscal tears should be considered as having early stage osteoarthritis and be treated according to clinical guidelines for knee osteoarthritis, starting with information, exercise, and often weight loss.⁹⁷

Unanswered questions and future research

Available evidence supports the reversal of a common medical practice.⁹⁸ However, disinvestment of commonly used procedures remains a challenge, and use of arthroscopy seems to be undiminished, in analogy with use of vertebroplasty following the publication of trials showing absence of benefit of this procedure.^{98 99} Surgeon confirmation bias in combination with financial aspects and administrative policies may be factors more powerful than evidence in driving practice patterns.^{23 100–103}

What is already known on this topic

- ▶ Arthroscopic knee surgery is frequently and increasingly used to treat middle aged and older patients with persistent knee pain
- ▶ All but one published randomised trials have shown no added benefit for arthroscopic surgery over that of the control treatment, but many specialists are convinced of the benefits of the surgical intervention

What this study adds

- ▶ Interventions that include arthroscopy are associated with a small benefit and with harms; the small benefit is inconsequential and of short duration
- ▶ The benefit is markedly smaller than that seen from exercise therapy as treatment for knee osteoarthritis
- ▶ These findings do not support the practice of arthroscopic surgery as treatment for middle aged or older patients with knee pain with or without signs of osteoarthritis

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Contributors JBT, CBJ, EMR, and LSL all participated in the conception and design of the study. JBT, CBJ, and LSL were responsible for acquisition of data. CBJ did the analysis, and JBT, EMR, and LSL took part in the interpretation of the analysis. JBT and LSL drafted the manuscript. All authors critically revised the manuscript for important intellectual content and approved the final version of the manuscript. LSL is the guarantor.

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Ethical approval Not required.

Data sharing Statistical code and dataset are available from the corresponding author.

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