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Does surgery reduce knee osteoarthritis, meniscal injury and subsequent complications compared with non-surgery after ACL rupture with at least 10 years follow-up? A systematic review and meta-analysis

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ABSTRACT

Objective We compared long term follow-up from surgical versus nonsurgical treatment of anterior cruciate ligament (ACL) rupture regarding radiographic knee osteoarthritis, secondary surgery, laxity, and patient-reported outcome measures (PROMs).

Design Systematic review and meta-analysis.

Data sources Embase, Medline, CINAHL, and Cochrane Library databases.

Eligibility criteria for selecting studies Studies directly comparing the minimally invasive surgical treatment (arthroscopy/mini-arthrotomy) and nonsurgical treatment of ACL rupture with at least 10 years of follow-up in adult patients were included.

Results Five studies met the eligibility criteria. A meta-analysis revealed a higher risk of radiographic knee osteoarthritis and a lower risk of secondary meniscal surgery for patients in the surgical group. The risk of graft rupture/secondary ACL revision and secondary ACL reconstruction was equal in the surgical and nonsurgical groups. Knee laxity was lower among patients in the surgical group in four studies. No difference was found in the PROMs (i.e., International Knee Documentation Committee, Tegner, Knee Injury and Osteoarthritis Outcome, and Lysholm scores).

Conclusion The risk of radiographic knee osteoarthritis was higher, but the risk of secondary meniscal injury was higher 10 years after surgical treatment of ACL rupture. The risk of graft rupture/secondary ACL revision or secondary reconstruction was unrelated to treatment type. The degree of knee laxity was reduced after surgical treatment in comparison with nonsurgical treatment, while PROMs were similar. However, due to the methodological challenges highlighted in this systematic review, these findings must be interpreted with caution.
INTRODUCTION
Anterior cruciate ligament (ACL) rupture can be treated surgical or nonsurgical. Recent high-quality comparative studies using midterm follow-up have largely failed to show any clear advantage of surgical versus nonsurgical treatment on knee OA development and patient-reported outcomes measures (PROMs). Prior systematic reviews with long-term follow-up also lack evidence to support either surgical or nonsurgical treatment. However, a major problem with these comparative studies is the considerable number of patients who initially received nonsurgical treatment but later opted for surgical treatment and thereby make the consequences of the initial treatment harder to track. Another shortcoming of the existing comparative studies is selection bias, since patients with worse injuries (e.g., concomitant ligament, cartilage, and meniscal injuries) are generally initially treated with surgery.

Open ACL reconstruction is rarely performed today, and minimally invasive techniques are dominant in modern clinical practice. Most systematic reviews with long term follow-up include studies with open ACL reconstruction treatment, thereby limiting the generalizability and clinical relevance of the findings. Consequently, excluding open ACL reconstruction studies from this review will provide a more up-to-date picture.

The aim of this study was to systematically review the literature and compare minimally invasive surgical (i.e. arthroscopy or mini-arthrotomy) versus nonsurgical treatment in patients with ACL rupture who had at least 10 years of follow-up concerning the severity of radiographic knee OA, secondary ACL surgery and meniscectomy, knee laxity, and PROMs.
METHODS

Protocol and registration
This systematic review was performed according to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines.12 The protocol was registered in the international prospective register of systematic reviews, PROSPERO (CRD42019119468, 9 January 2019) and met all the eligibility criteria for protocol registration.

Eligibility criteria
The PICO was defined as primary ACL rupture in adults treated with either surgical or nonsurgical treatment with a minimum of 10 years of follow-up and radiographic knee OA, secondary surgery, laxity, and PROMs data.

Studies were included if they:
- Included a comparison of surgical and nonsurgical treatment of ACL rupture
- Covered the use of a minimally invasive surgical technique (arthroscopic or mini-arthrotomy)
- Included a minimum of 10 years of follow-up
- Included a patient mean age of ≥ 18 years

Studies were excluded if they:
- Were animal or cadaveric studies
- Were articles not in the English, German, or Scandinavian languages
- Included patients with prior major knee surgery

Published studies with levels of evidence I through IV were included with the exception of population-based cohort studies. Editorials and conference abstracts were also excluded.

Arthroscopic verification of ACL tear was not considered a surgical intervention.

Information sources and literature search
A literature search was performed in October 2018 among four electronic databases: Embase, Medline, CINAHL, and the Cochrane Library. In addition, the reference lists of relevant studies were screened for additional eligible articles. The search strategy included the key term ‘anterior cruciate ligament’ in combination with surgical and nonsurgical treatment search terms as well as outcomes. For the purpose of including all relevant literature, a sensitive search strategy was used:
Librarians at the University Library of Southern Denmark assisted in shaping and optimizing the search strategy.

**Study selection**

Search results were extracted to EndNote (Clarivate Analytics, Philadelphia, PA, USA), duplicates were removed, and the remaining articles were imported into Covidence (Veritas Health Innovation, Melbourne, Australia). Titles and abstracts were screened by two independent reviewers (TL and DM). The full versions of potential articles were read to determine eligibility. In case of multiple studies using same cohort data, the studies with longer follow-up time and primary focus on tibiofemoral OA were preferred and included. Conflicts were resolved with discussion among the review team (TL, DM, CJ, and BV).

**Data collection**

Data extraction was performed independently by the two aforementioned reviewers (TL and DM) and crosschecked for errors. A data extraction sheet was created for the purpose. Discrepancies were resolved by consensus.

**Data items**

The extracted data included: sex; age; body mass index (BMI); country; Tegner activity level\(^{13}\); time from injury to intervention; meniscal and/or chondral injuries; knee laxity as measured by a KT-1000 arthrometer\(^{14}\); secondary injuries and/or surgical interventions; surgical intervention (arthroscopically or mini-arthroscopy surgery, graft type, rehabilitation after surgery), nonsurgical intervention (rehabilitation)\(^{15}\), and measurements of knee OA, specifically radiographic, Knee Injury and Osteoarthritis Outcome Score (KOOS),\(^{15}\) International Knee Documentation Committee (IKDC) subjective score,\(^{16}\) and Lysholm scoring scale values.\(^{17}\)
Secondary interventions were defined as: ACL reconstruction in the nonsurgical group and ACL revision or graft rupture in the surgical group. These procedures are comparable as they are the manifestation of treatment failure of the primary intervention in both groups. Minimally invasive surgical treatment was defined as ACL reconstruction using either arthroscopically or mini-arthrotomy technique.

Cutoff values for knee OA for the different radiographic classification systems were, in accordance with prior studies,\textsuperscript{4} \textsuperscript{6} \textsuperscript{18} defined as: Kellgren and Lawrence system\textsuperscript{19} grade ≥ 2; IKDC qualification\textsuperscript{20} grade ≥ C; and, for the Osteoarthritis Society Research International (OARSI) classification system,\textsuperscript{21} a joint space narrowing (JSN) of grade 2, sum of marginal osteophyte grades ≥ 2, or a grade 1 JSN in combination with a grade 1 marginal osteophyte, respectively.

**Risk of bias in individual studies**

A methodological quality appraisal of the studies was performed using the Downs and Black checklist.\textsuperscript{22} The Downs and Black checklist is frequently employed method evaluate reporting, external validity, internal validity, confounding, bias, and statistical power that has been recognized as a comprehensive and suitable option for assessing systematic reviews in the appraisal of both nonrandomised and randomised controlled trials.\textsuperscript{23} In the present investigation, the item concerning sufficient power was modified to whether the study presented a sample size calculation or not. It was modified, because there were insufficient data to make an adequate power calculation. Items received one point if the criterion was met and zero points if not (one item could score two points). Zero points were given if the item was unable to be quantified. The lowest methodological quality score possible was zero points and the highest was 28 points. The two reviewers performed an appraisal of the studies. Any disagreements were solved by discussion.

**Summary measures and synthesis of results**

The outcomes measures were reported by study and meta-analysed using forest plots using RevMan 5.3 (The Nordic Cochrane Center, Copenhagen, Denmark). The intervention effect was expressed as a risk ratio (RR) including a 95% confidence interval. Statistical significance was defined as $p \leq 0.05$. Pooled data were assessed for heterogeneity using the chi-squared and I-squared tests. Heterogeneity was defined as ‘absent’ (0%–25%); ‘low’ (26%–50%), ‘moderate’ (51%–75%) or ‘high’ (76%–100%). A fixed-effects meta-analysis was performed when the I-squared test outcome was less than 50%.
RESULTS

Study selection
In total, 10,401 studies were initially included. Of those, 10,364 were excluded based on a review of their titles and abstracts and the full versions of the remaining 37 studies were assessed for further eligibility (Figure 1). During the full-text review, an additional 32 studies were excluded for the following reasons: open surgery (n = 12), not comparing surgery with nonsurgery (n = 8), conference abstract (n = 5), repeated study cohort (n = 3),24-26 less than 10 years of follow-up (n = 2), and population cohort based studies (n = 2). The remaining five studies7 8 27-29 fulfilled all of the eligibility criteria and so were included in this review.

Study characteristics
Of the five included studies, two were prospective,27 28 including one that was randomised,28 and three studies were retrospective.7 8 29 A total of 371 patients were included, with a distribution of 164 surgically and 207 nonsurgically treated patients, respectively (Table 1). Follow-up ranged from 10 to 20 years in length. All ACL ruptures were confirmed by magnetic resonance imaging,28 arthroscopy7 8 27 or either one.29 One study29 included a unique subgroup of patients—that is, high-level athletes defined by Tegner score of more than seven points (median of nine points). All retrospective studies were pair-matched with respect to age and sex of the included patients. Other matching factors applied included BMI, follow-up duration, and concomitant injuries. A summary of study and patient characteristics is presented in Table 1.

Table 1 Study and patient characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Study design</th>
<th>Follow-up (years)</th>
<th>Quality to surgery</th>
<th>n</th>
<th>Mean age (SD) at follow-up</th>
<th>Sex (M/F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kessler et al; 20087</td>
<td>Switzerland</td>
<td>Retrospective</td>
<td>11</td>
<td>N/A</td>
<td>60</td>
<td>30.7 (12.5-54)§ $</td>
<td>68/41§</td>
</tr>
<tr>
<td>Neuman et al; 200827</td>
<td>Sweden</td>
<td>Prospective</td>
<td>15</td>
<td>4 years $</td>
<td>22</td>
<td>42 (7)$</td>
<td>14/8 4/4</td>
</tr>
<tr>
<td>Streich et al; 20118</td>
<td>Germany</td>
<td>Retrospective</td>
<td>15</td>
<td>7.3 months $</td>
<td>40</td>
<td>26.0 (6.4)*</td>
<td>28/1 2/2</td>
</tr>
<tr>
<td>Tsoukas et al; 201628</td>
<td>Greece</td>
<td>Prospective randomised</td>
<td>10</td>
<td>6 weeks $</td>
<td>17</td>
<td>31 (20-36)$</td>
<td>17/0 17/0</td>
</tr>
</tbody>
</table>
Risk of bias in individual studies

Methodological quality was evaluated using the Downs and Black checklist, with zero to 28 points being possible but with the included studies ranging only from 14 to 18 points, with a mean score of 16.8 points (Table 1). Collectively, the studies achieved the highest scores for items one to 10 covering reporting. However, for items 21 to 27, concerning confounding/selection bias, the studies attained considerably lower scores. The specific scores given for the studies are available in Appendix 1.

Radiographic knee osteoarthritis

All five studies measured the severity of radiographic knee OA using either the Kellgren and Lawrence system, IKDC grading, or the OARSI atlas. The prevalence of OA ranged from 24% to 80% in the surgical groups and 11% to 68% in the nonsurgical groups (Table 2). A significantly lower prevalence of radiographic knee OA in favour of the nonsurgical groups was shown in two studies (p = 0.03 in both). The meta-analysis revealed that the risk of radiographic knee OA was higher in the surgical groups [RR: 1.42 (95% CI: 1.09–1.85)] (Figure 2).

Table 2 Radiographic knee osteoarthritis

<table>
<thead>
<tr>
<th>Study</th>
<th>Scoring system</th>
<th>Surgical</th>
<th>Non-surgical</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n</td>
<td>Grades</td>
</tr>
<tr>
<td>Kessler et al⁷</td>
<td>K&amp;L</td>
<td>60</td>
<td>27/6/25/2/0</td>
</tr>
<tr>
<td>Neuman et al²⁷</td>
<td>OARSI</td>
<td>17</td>
<td>N/A</td>
</tr>
<tr>
<td>Streich et al⁸</td>
<td>IKDC</td>
<td>40</td>
<td>14/11/3/12</td>
</tr>
<tr>
<td>Tsoukas et al²⁸</td>
<td>IKDC</td>
<td>17</td>
<td>N/A</td>
</tr>
<tr>
<td>Van Yperen et al²⁹</td>
<td>K&amp;L</td>
<td>25</td>
<td>1/4/16/3/0/(1)</td>
</tr>
</tbody>
</table>

K&L: 0/1/2/3/4/(Total knee arthroplasty)
IKDC: A/B/C/D
Secondary surgical interventions

Graft ruptures, secondary ACL reconstructions, and meniscectomies were reported in four studies (Table 3).7 8 28 29 Due to the study design for one investigation, the surgical group consisted of patients from the nonsurgical group who had undergone secondary ACL reconstruction27 and were not included in the analysis of secondary surgery. Only one study29 differentiated between lateral and medial meniscectomy. Two7 8 of four studies7 8,30,31 found a significantly reduced need for secondary meniscectomy in the surgical group as compared with in the nonsurgical group (both p < 0.03). Our meta-analysis revealed that the risk of graft rupture or secondary ACL revision was independent of treatment [RR: 0.90 [95% CI: 0.49–1.66]] (Figure 2). Separately, the risk of secondary meniscectomy was reduced significantly in patients who had surgical treatment [RR: 0.34 (95% CI: 0.20–0.58)] (Figure 2).

Table 3 Secondary surgical interventions

<table>
<thead>
<tr>
<th></th>
<th>Surgical</th>
<th>Non-surgical</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Graft rupture or ACL revision (%)</td>
<td>Meniscectomy (%)</td>
</tr>
<tr>
<td>Kessler et al7</td>
<td>6/68 (9)*</td>
<td>7/68 (10)*</td>
</tr>
<tr>
<td>Streich et al8</td>
<td>8/67 (12)*</td>
<td>4/40 (10)</td>
</tr>
<tr>
<td>Tsoukas et al28</td>
<td>0/17 (0)</td>
<td>0/17 (0)</td>
</tr>
</tbody>
</table>

* Excluded from study

Knee laxity

Knee laxity (side-to-side difference) was measured using a KT-1000 arthrometer in all studies.7 8 27-29 Knee laxity ranged from 1.5 to 5.3 mm in the surgical groups versus 2.1 to 5.7 mm in the nonsurgical groups. However, one study29 reported the number of patients with a side-to-side difference of more than 3 mm was 10 of 25 (40%) in the surgical group and 19 of 25 (76%) in the nonsurgical group (p = 0.013). Still, four of the five studies found significantly less knee laxity in the surgical group.7 27-29
Patient-reported outcomes measures
IKDC subjective score was reported in three studies,\textsuperscript{8,28,29} with one study reporting better scores for patients in the surgical group (p = 0.04) (Table 4).\textsuperscript{28} The KOOS score was reported in two studies\textsuperscript{27,29} wherein the nonsurgical group reported a significantly better score on the pain subscale than compared to the surgical group in one study (p = 0.35),\textsuperscript{27} while there was no significant difference between the two groups in the other study.\textsuperscript{29}

Table 4 Patient reported outcome measures (PROMs)

<table>
<thead>
<tr>
<th>Study</th>
<th>IKDC subj</th>
<th>Lysholm</th>
<th>Tegner</th>
<th>IKDC subj</th>
<th>Lysholm</th>
<th>Tegner</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Surgical</td>
<td></td>
<td></td>
<td>Non-surgical</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BL</td>
<td>FU</td>
<td></td>
<td>BL</td>
<td>FU</td>
<td></td>
</tr>
<tr>
<td>Kessler et al\textsuperscript{7}</td>
<td>N/A</td>
<td>N/A</td>
<td>5.4</td>
<td>N/A</td>
<td>N/A</td>
<td>5.9</td>
</tr>
<tr>
<td>Neuman et al\textsuperscript{27}</td>
<td>N/A</td>
<td>86 (16)</td>
<td>7^</td>
<td>N/A</td>
<td>82 (19)</td>
<td>7^</td>
</tr>
<tr>
<td>Streich et al\textsuperscript{8}</td>
<td>69.9 (17.0)</td>
<td>68.0 (19.8)</td>
<td>7.6 (1.5)</td>
<td>4.7 (1.8)</td>
<td>75.9 (13.1)</td>
<td>75.5 (15.9)</td>
</tr>
<tr>
<td>Tsoukas et al\textsuperscript{28}</td>
<td>86.7 (6.5)</td>
<td>N/A</td>
<td>7 (5-7)^</td>
<td>7 (5-7)^</td>
<td>77.5 (13)</td>
<td>N/A</td>
</tr>
<tr>
<td>Van Yperen et al\textsuperscript{29}</td>
<td>81.6 (59.8-89.1)*</td>
<td>86.0 (75.5-91.0)*</td>
<td>9 (7-9)*</td>
<td>5 (3-6)*</td>
<td>78.2 (61.5-92.0)*</td>
<td>89.0 (75.5-95.5)*</td>
</tr>
</tbody>
</table>

Data are presented as mean (SD) unless otherwise specified.
^Median (range)
*Median (interquartile range)
BL, Baseline; FU, Follow-up; N/A, Not available; IKDC subj, International Knee Documentation Committee subjective form

Intervention description
Surgical intervention was performed within a period of six weeks\textsuperscript{28} to four years\textsuperscript{27} after initial injury. Arthroscopic surgical technique was performed in four studies\textsuperscript{7,8,28,29} and mini-arthrotomy in one,\textsuperscript{27} respectively. Bone–patellar tendon–bone was the preferred graft for ACL reconstruction,\textsuperscript{7,8,27,29} whereas reconstruction with four-stranded semitendinosus– gracilis graft was performed in one study.\textsuperscript{28} All surgically treated patients in the five studies participated in exercise-based rehabilitation programs of various length and two studies used supervised physiotherapy.\textsuperscript{7,27}
In the nonsurgical group, all of the studies used physiotherapy-supervised rehabilitation, except for one subgroup in one study. Nonsurgical treatment was initiated shortly following the confirmation of diagnosis. Follow-up time for the rehabilitation was only reported in two studies. Instructions to gradually return to more strenuous physical activities were given to patients in both groups.

**DISCUSSION**

This systematic review included five studies comparing surgical versus nonsurgical treatment of ACL rupture with more than 10 years of follow-up. Two studies were prospective and three were retrospective. Methodological shortcomings were evident in all studies, as demonstrated by a mean quality score of 16.8 points out of 28 points possible.

Based on the available data of 164 surgically and 207 conservatively treated patients, the risk of radiographic knee OA was higher in the surgical group than in the nonsurgical group. The risk of secondary ACL reconstruction was independent of treatment, whereas secondary meniscectomies were performed significantly less frequently in the surgical group. Patients who underwent ACL reconstruction experienced significantly less knee laxity. The PROMs (i.e., Lysholm, IKDC, Tegner, and KOOS scores) were independent of group allocation.

**Radiographic knee osteoarthritis**

Our meta-analysis revealed a higher risk of knee OA in patients who had gone through surgery in comparison with those treated via rehabilitation alone. However, caution must be applied in the interpretation and conclusions of this meta-analysis. With the exception of the one randomised study, the patients treated surgically had more subjective knee instability preoperatively compared to those treated nonsurgically. The choice of treatment was based on the patient’s wishes as well as the treating surgeons’ advice. In two studies, patients who did not respond well to nonsurgical treatment underwent ACL reconstruction and were therefore included in the surgery group. In the decision-making process, the surgeons’ guidance may have influenced patients’ choice of treatment, as we do not know in what way the surgeons gave their advice, as the use of a valid shared-decision tool was not reported. Marx et al. found that American orthopaedic surgeons consider several factors when making a decision in favour of surgical treatment, as follows: giving way in daily activities, giving way in sporting activities, high-demand activity, recurrent swelling, radiographic knee OA, and repairable meniscal tear. These
findings suggest a general tendency toward treating the most extensive ACL injuries surgically, thus introducing a potential risk of selection bias and thereby skewing the results in favour of nonsurgical treatment. Earlier literature suggests that high-level pivoting sports and a higher activity level over time can lead to an increase in OA,31 possibly promoting more knee OA in the surgical group. This, however, is disputed by more recent literature, wherein opposite findings indicate that those who are more physical active and who returned to pivoting sports had better knee function and less radiographic knee OA.32 Streich et al.8 and Kessler et al.7 both excluded patients who received secondary ACL reconstruction. Kessler et al.7 excluded patients receiving both primary and secondary meniscectomies. In this study, more than double the number of patients was excluded from the nonsurgical group than the surgical group, thereby possibly skewing the outcomes of the groups during follow-up. Hence, a possible underestimation of knee OA in the remaining patients in the nonsurgical group could have occurred. This is also indicated by the methodological quality assessment, wherein the studies collectively had low scores in the items on confounding/selection bias. Conducting a randomized controlled trial (RCT) could help to solve this problem. However, this is difficult to complete due to ethical considerations and recruiting, as reported by Frobell et al.,33 who conducted the only RCT to date with five years follow-up comparing early rehabilitation and ACL reconstruction to rehabilitation and optional delayed ACL reconstruction.2 A discrepancy is present when comparing this study’s results to our meta-analysis, as Frobell et al. did not report more radiographic knee OA in the surgical group.2 A possible explanation for this variance is the shorter follow-up period of five years in Frobell et al.’s study versus the 10-year or more period in ours.2 This difference supports the assumption of the aforementioned selection bias of the included studies in this systematic review.

The reasoning behind choosing nonsurgical treatment is that neuromuscular and strength training can stabilise the knee by way of increased muscle strength and enhanced proprioception.34 With one exception,27 none of the included studies reported follow-up of physiotherapy treatment for more than three months. Likewise, the compliance rate for these patients remains unknown. This could result in an underestimation of the potential beneficial effect of consistent physiotherapy treatment.

All patients in the study by Neuman et al.27 with radiographic knee OA at follow-up had primary or secondary meniscectomy. A tendency was confirmed by van Yperen et al.,29 who found that 94% in the surgical group and 68% in the nonsurgical group, respectively, among those who underwent meniscectomy developed knee OA. These findings correspond to the findings of Øiestad et al.,4
who, in a large systematic review, identified a significantly higher prevalence of ACL injuries with concomitant meniscal injury versus without (0%–13% compared to 21%–48%). This underlines the fact that meniscal injury and meniscectomy are important risk factors for developing knee OA.

The only study with two follow-up time-points, by van Yperen et al.,29 showed that radiographic knee OA developed in 19 of 50 (38%) patients at 10 years of follow-up and in 37 of 50 (74%) patients at 20 years of follow-up. This corresponds with findings of a recent meta-analysis by Cinque et al.,35 who showed that the prevalence of posttraumatic radiographic knee OA developed significantly at five, 10, and 20 years after surgical treatment as follows: 11%, 21% and 52%. Long-term follow-up is therefore necessary to examine the real late consequences of ACL rupture.

The presence of radiographic knee OA in this review was determined by cutoff values utilized in three different classification systems. Two studies using the Kellgren and Lawrence approach7 29 and one using OARSI27 classified more patients with knee OA in the surgical groups, while two studies using IKDC8 28 found no difference between the groups. There are challenges that appear when comparing results among studies that employed different classification systems. For example, Culvenor et al.18 determined that, when using the OARSI classification system, radiographic knee OA was nearly twice as common as when the Kellgren and Lawrence classification was used. Likewise, in the study by the MARS group,36 differences in interobserver reliability were present (IKDC vs. Kellgren & Lawrence). Due to the limited number of studies, it was not possible to include only studies using a single classification system.

The findings of this review does not conclude on whether surgical or nonsurgical treatment is preferable based on the patient-reported outcomes. There were no associations between increased risk of radiographic knee OA and PROMs in the surgical group. These observations are similar to earlier findings by Barker et al.,37 who found no association between radiographic knee OA and PROMs.

Our findings also seem to be somewhat consistent with those of Øiestad et al.,38 who identified no significant association between radiographic OA and all subscales of KOOS, with the exception of KOOS symptoms. They did, however, find significantly more symptoms among those with severe radiographic knee OA.

**Secondary surgical intervention**

Our meta-analysis revealed patients presented a significantly lower risk of having secondary meniscal surgery when initially treated surgically. However, the risk of having secondary ACL injury or surgery was not highly different between the two groups. This is in contrast to earlier
findings by Chalmers et al. who, in their meta-analysis, found that surgical patients had less need of secondary ACL surgery. In a similar fashion, Sanders et al. found in their register-based study, with a mean follow-up of 14 years, that surgically treated patients had a significantly lower risk of experiencing secondary symptomatic knee OA, meniscal tear, and total knee alloplastic versus nonoperatively treated patients. This could explain why we did not find a similar trend as that seen by Sanders et al. and Chalmers et al. Selection bias could have resulted in an overestimation of secondary graft rupture in the surgical group, compared to the nonsurgical group, as the young and highly physical active patients most often receive surgical treatment, especially those who want to return to participation in high-level pivoting sports.

**Limitations and strengths**

There were several limitations in our study. The five studies included did not measure radiographic OA with same scoring system, making comparisons difficult. In similar fashion, the studies used different PROMs. Surgical interventions also differed regarding specific technical details. Likewise, nonsurgical (e.g., physiotherapy, bracing, nontreatment) approaches were not equal across studies in respect to follow-up time-points, program content, and supervision. Furthermore, no studies reported specific compliance rates with rehabilitation programs. The inclusion of a larger number of patients would have been preferable. Publication bias may have influenced the authors’ reporting in the various studies. Lastly, the studies included in this systematic review included populations from European countries only, resulting in more homogenous patient groups and possibly reducing generalisability to other parts of the world.

Notwithstanding these limitations, a strength of this review is that all reconstructive surgeries in our studies were performed by arthroscopy or mini-arthrotomy, minimally invasive techniques that are comparable and used in today’s practice. Only studies directly comparing surgical and nonsurgical treatment were included. Also, two independent reviewers conducted the systematic literature search, study selection, and data extraction.

Future studies should focus on limiting bias, preferably by conducting randomised clinical trials. Although difficult to achieve, nonrandomised studies should try to reduce the inherent bias of patients with more symptoms being treated surgically. Longer follow-up periods could help establish the two treatments’ association with knee OA over a life-span. Measurements of OA, both radiographic and subjective, should be similar.
CONCLUSION
The risk of radiographic knee osteoarthritis was higher, but the risk of secondary meniscal injury was lower 10 years after surgical treatment of anterior cruciate ligament rupture. The risk of graft rupture/secondary ACL revision or secondary reconstruction was unrelated to treatment type. The degree of knee laxity was reduced after surgical treatment in comparison with nonsurgical treatment, while patient-reported outcomes were similar. However, due to the methodological challenges highlighted in this systematic review, these findings must be interpreted with caution.

Contributors
BV conceived the project while BV and CJ led the design (intervention selection, patient population, data management, and statistical analyses). TL, DM, MAR, and LE contributed to the design. TL and DM performed the literature search, extraction of data, quality assessment of studies, and synthesis of the results and drafted the first manuscript. All authors (TL, DM, CJ, MAR, LE, and BV) provided critical intellectual input to the manuscript and read and approved the final version of the manuscript, agreeing to be accountable for all aspects of the work.

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Competing interests
All authors report no conflicts for the present work. Dr. Viberg reports personal fees for lectures from Zimmer Biomet and Osmedic Swemac outside the submitted work.

Patient consent for publication
None.

REFERENCES


22 Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health* 1998;52:377-84.


Figure 1 PRISMA flow diagram of search strategy

- Records identified through database searching (n = 15,266)
- Additional records identified through other sources (n = 0)

Records after duplicates removed (n = 10,401)

Records screened (n = 10,401)

- Full-text articles assessed for eligibility (n = 37)
- Full-text articles excluded, with reasons (n = 32)
  - Open surgery (n = 12)
  - Not comparing operative and non-operative (n = 8)
  - Conference abstracts (n = 5)
  - Same cohort as included study (n = 3)
  - Follow-up < 10 years (n = 2)
  - Population-based cohort studies (n = 2)

Studies included in qualitative synthesis (n = 5)

Studies included in quantitative synthesis (meta-analysis) (n = 5)
Figure 2 Meta-analysis

Radiographic knee osteoarthritis

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Surgery Events</th>
<th>Surgery Total</th>
<th>Non-surgery Events</th>
<th>Non-surgery Total</th>
<th>Weight</th>
<th>Risk Ratio M–H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kessler et al</td>
<td>27</td>
<td>60</td>
<td>12</td>
<td>49</td>
<td>25.4%</td>
<td>1.84 [1.04, 3.24]</td>
</tr>
<tr>
<td>Neuman et al</td>
<td>6</td>
<td>17</td>
<td>7</td>
<td>62</td>
<td>5.8%</td>
<td>3.13 [1.21, 8.08]</td>
</tr>
<tr>
<td>Striech et al</td>
<td>15</td>
<td>40</td>
<td>15</td>
<td>49</td>
<td>25.9%</td>
<td>1.23 [0.60, 2.39]</td>
</tr>
<tr>
<td>Tsoukas et al</td>
<td>4</td>
<td>17</td>
<td>5</td>
<td>15</td>
<td>10.2%</td>
<td>0.71 [0.23, 2.16]</td>
</tr>
<tr>
<td>van Yperen et al</td>
<td>20</td>
<td>25</td>
<td>17</td>
<td>25</td>
<td>32.7%</td>
<td>1.18 [0.84, 1.64]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>159</strong></td>
<td><strong>200</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
<td></td>
<td><strong>1.42 [1.09, 1.85]</strong></td>
</tr>
<tr>
<td>Total events</td>
<td>72</td>
<td>56</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Heterogeneity:</td>
<td>$X^2 = 6.44$, df = 4 (P = 0.17); $I^2 = 38%$</td>
<td></td>
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<tr>
<td>Test for overall effect:</td>
<td>$Z = 2.62$ (P = 0.009)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Graft rupture or subsequent ACL reconstruction

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Surgical Events</th>
<th>Surgical Total</th>
<th>Non-surgical Events</th>
<th>Non-surgical Total</th>
<th>Weight</th>
<th>Risk Ratio M–H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kessler et al</td>
<td>6</td>
<td>68</td>
<td>12</td>
<td>68</td>
<td>61.9%</td>
<td>0.50 [0.20, 1.26]</td>
</tr>
<tr>
<td>Streich et al</td>
<td>8</td>
<td>67</td>
<td>6</td>
<td>59</td>
<td>32.9%</td>
<td>1.17 [0.43, 3.19]</td>
</tr>
<tr>
<td>Tsoukas et al</td>
<td>0</td>
<td>17</td>
<td>0</td>
<td>15</td>
<td>Not estimable</td>
<td></td>
</tr>
<tr>
<td>van Yperen et al</td>
<td>4</td>
<td>25</td>
<td>1</td>
<td>25</td>
<td>5.2%</td>
<td>4.00 [0.48, 33.33]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>177</strong></td>
<td><strong>167</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
<td></td>
<td><strong>0.90 [0.49, 1.66]</strong></td>
</tr>
<tr>
<td>Total events</td>
<td>18</td>
<td>19</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Heterogeneity:</td>
<td>$X^2 = 3.74$, df = 2 (P = 0.15); $I^2 = 47%$</td>
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<tr>
<td>Test for overall effect:</td>
<td>$Z = 0.33$ (P = 0.74)</td>
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</tbody>
</table>

Subsequent meniscectomy

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Surgery Events</th>
<th>Surgery Total</th>
<th>Non-surgery Events</th>
<th>Non-surgery Total</th>
<th>Weight</th>
<th>Risk Ratio M–H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kessler et al</td>
<td>7</td>
<td>68</td>
<td>18</td>
<td>64</td>
<td>40.9%</td>
<td>0.39 [0.17, 0.87]</td>
</tr>
<tr>
<td>Streich et al</td>
<td>4</td>
<td>40</td>
<td>16</td>
<td>40</td>
<td>36.4%</td>
<td>0.25 [0.09, 0.68]</td>
</tr>
<tr>
<td>Tsoukas et al</td>
<td>0</td>
<td>17</td>
<td>0</td>
<td>15</td>
<td>Not estimable</td>
<td></td>
</tr>
<tr>
<td>van Yperen et al</td>
<td>4</td>
<td>25</td>
<td>10</td>
<td>25</td>
<td>22.7%</td>
<td>0.40 [0.14, 1.11]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>150</strong></td>
<td><strong>148</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
<td></td>
<td><strong>0.34 [0.20, 0.58]</strong></td>
</tr>
<tr>
<td>Total events</td>
<td>15</td>
<td>44</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Heterogeneity:</td>
<td>$X^2 = 0.56$, df = 2 (P = 0.75); $I^2 = 0%$</td>
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<tr>
<td>Test for overall effect:</td>
<td>$Z = 3.95$ (P &lt; 0.0001)</td>
<td></td>
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</table>