Purpose: We aimed to perform a systematic review of the literature concerned with timing of surgery after anterior cruciate ligament injury. Methods: A systematic electronic search in Medline through PubMed, Embase, and the Cochrane Library was carried out in October 2011. All English-language randomized controlled clinical trials, prospective comparative cohort studies, and prognostic and diagnostic studies published from January 1995 to August 2011 were eligible for inclusion. All articles addressing timing of surgery were eligible for inclusion regardless of injury-to-surgery interval, graft type, surgical technique, or rehabilitation. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist guided the reporting and data abstraction. Methodologic quality of all included articles was carefully assessed. Results: We included 22 articles (3,583 patients) in the systematic review. Study design, research methodology, surgical technique, and outcome measurements differed greatly among included articles. The injury-to-surgery interval, classified as early and delayed, ranged from within 2 days to 7 months and 3 weeks to 24 years, respectively. Eight articles promoted early reconstruction, whereas the majority of articles found no difference in outcome between early and delayed surgery. Two articles were inconclusive. Conclusions: There were few or no differences in subjective and objective outcomes related to timing of anterior cruciate ligament reconstruction. Level of Evidence: Level II, systematic review of Level I and II studies.

There is no consensus on whether early or delayed surgery of the anterior cruciate ligament (ACL) is preferable, nor is any there consensus on the classification of early and delayed time intervals. Recently published results are either inconsistent or inconclusive.1–6 Injury to the ACL is strongly associated with the development of osteoarthritis (OA),7–9 to which the non-reconstructed ACL-deficient knee is especially prone because an unstable knee is predisposed to cartilage lesions and meniscal tears, which are important predictors of OA.7,10,11 Theoretical advantages of early reconstruction are shorter rehabilitation period, faster return to previous sporting activities, and less risk of exposing the knee to subsequent injuries associated with recurring instability such as meniscal and chondral injuries, which predispose the knee to future OA. Delaying the ACL reconstruction allows for optimal restoration of range of motion and strength while also potentially minimizing the risk for arthrofibrosis.1,12

Smith et al.1 performed a systematic review and meta-analysis regarding timing of ACL reconstruction and found no difference in clinical outcome between patients who underwent early reconstruction (<3 weeks) and those with delayed reconstruction (>6 weeks). They observed several limitations to the current literature on this topic and recommended caution when interpreting the results. Therefore the purpose of this study was to perform a systematic review of the literature concerned with timing of surgery after ACL injury, by conducting an extensive electronic literature search including randomized controlled clinical trials, prospective comparative cohort studies, and prognostic and diagnostic studies. All topic-specific articles were included, regardless of injury-to-surgery interval, graft choice, surgical technique, or whether timing of surgery was a primary or secondary...
objective. The hypothesis was that delayed reconstruction produced more meniscal and chondral pathology, predisposing the knee to increased risk of future OA.

Methods

Protocol
This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.15

Eligibility Criteria
Reports of randomized controlled clinical trials, prospective comparative cohort studies, and diagnostic and prognostic studies written in English and published from January 1995 to August 2011 were eligible for inclusion. All articles addressing timing of surgery, both as primary and secondary objectives, were eligible for inclusion regardless of injury-to-surgery interval, graft type, open or arthroscopic surgery, primary repair or reconstruction, or rehabilitation. The population of interest was skeletally mature and ACL-deficient patients. The primary outcome measures of interest were meniscal and chondral pathology, as well as OA. Subjective and objective instability, return to previous work or sporting activities, pain, range of movement, rupture, and revision surgery, as well as clinical scores and questionnaires, were assessed as a secondary outcome measure.

Information Sources and Search
An extensive systematic electronic search in Medline through PubMed (January 1995 to August 2011), EMBASE (January 1995 to August 2011), and the Cochrane Library (January 1995 to August 2011) using MeSH terms was carried out in October 2011 by 2 experts in electronic search methods at the Gothenburg University Library. All English-language articles published from January 1995 to August 2011 were eligible for inclusion. The following search terms were used in the fields of title, abstract, and keywords: “anterior cruciate ligament” OR “ACL” AND “reconstruction” OR “surgery” AND “1995:3000.” The complete search string was as follows: (“Anterior Cruciate Ligament”[Mesh] OR “anterior cruciate ligament”[tiab] OR ACL[tiab]) AND (“Surgical Procedures, Operative”[Mesh] OR surgical[tiab] OR surgery[tiab] OR reconstruction[tiab] OR reconstructive[tiab] OR reconstructed[tiab]) AND (English[lang] AND (“1995”[PDAT] : “3000”[PDAT])). References lists of included articles were searched for possible additional articles not generated by the electronic search.

Study Selection
The first author (D.A.) and senior author (K.S.) performed the study selection, which was validated in duplicate. To assess data concerning timing of surgery, all articles generated by the electronic search were screened by reading the title, abstract, “Methods” section, and “Results” section. If initial screening failed to provide sufficient data for the purpose of inclusion or exclusion, the article was assessed in full text. The investigators were not blinded to author names and journal names during the process of screening and extracting data. Therapeutic studies with clinical outcome measures related to timing of surgery were included. Studies reporting on outcomes without clear clinical correlations, such as radiographic outcomes (e.g., assessments of screw or tunnel position) or thickness of neotendon (regrowth of the harvested hamstring tendons), were excluded. However, studies that reported on a combination of clinical outcomes and other outcomes such as biomechanics, radiographs, or histology were included. Prognostic studies were included if they presented a clear relation between surgery and clinical outcome, as well as potential prognostic factors. Diagnostic studies were included if they reported on therapeutic as well as diagnostic outcomes. Studies on animals, anesthesia and analgesia, biology and histology, cadavers, diagnostic tools, economics, epidemiology, imaging results without clinical outcome, multiple knee injuries, rehabilitation protocols, revision surgery, and skeletally immature patients were excluded. Studies that assessed or validated instruments or technicalities were excluded. Furthermore, editorials, letters, notes, proceedings, and conference abstracts were excluded.

Assessment of Risk of Bias in Included Studies
The methodologic quality of the included articles was assessed with reference to random sequence generation and concealment of allocation (selection bias), blinding (performance bias and detection bias), and loss of participants (attrition bias).

Data Extraction
The first author (D.A.) performed the process of data extraction using a standardized extraction sheet, obtaining data according to the PRISMA checklist.13 The senior author (K.S.) validated data extraction. Disagreements regarding article selection, data extraction, or assessments were resolved by discussion. Obtained data from included articles were as follows: participants, interventions, comparisons, outcomes, study design (PICOS), allocation, sample size, sample size calculation, bias, and length of follow-up.

Synthesis of Results
Statistical analysis of the data, for the purpose of a meta-analysis, was not possible because of substantial heterogeneity in study design, populations, and outcome measurements. Therefore a thorough assessment and best-synthesis approach were used to delineate
the research area by systematically presenting the available data in the current literature. Comparison of means was performed by use of the unpaired t test. Analysis was performed with IBM SPSS Statistics, version 20 (IBM, Armonk, NY).

Results
A total of 11,729 articles were identified by the initial electronic search. After removal of duplicates, sorting of studies, and subsequent screening, a total of 37 topic-specific articles addressing timing of surgery were identified. Fifteen articles did not provide sufficient demographic data on the interval between injury and surgery for inclusion in this review. Because of these shortcomings, 4 randomized controlled clinical trials, 14-17 10 prospective comparative cohort studies, 18-27 and one diagnostic study 28 were excluded. A total of 22 articles (3,583 patients) were included for final assessment in this systematic review (Fig 1). Ten studies were randomized controlled trials (1,065 patients). 29-33 Eleven studies were prospective comparative cohort studies (2,456 patients). 39-48 Only one prognostic study was included (62 patients). 49

Eight articles found early surgery after ACL injury to be a predictor of superior outcome. 29,31,33,36,40,41,47,49 However, study design, methodology, and surgical technique, as well as the primary research focus, differed greatly. The injury-to-surgery interval classified as early surgery varied from 1 to 5 months, whereas delayed surgery was classified as ranging from 3 months to 24 years after injury. Twelve articles found no significant differences in clinical outcome with regard to timing of surgery after ACL injury. Five of these articles focused primarily on the injury-to-surgery interval, 30,34,35,38,43 whereas one article compared early reconstruction with nonsurgical treatment but with optional delayed reconstruction if needed. 35 Concurrent with articles promoting early reconstruction, there was a wide range in the injury-to-surgery interval classification. Early surgery varied from within 48 hours to anywhere within 6 months, whereas delayed surgery was classified as ranging from 3 weeks to more than 13 years after injury. One article did not present the injury-to-surgery interval. 39 None of the included articles found evidence to support delayed reconstruction. Two articles were deemed inconclusive with regard to our research question. 9,44 Although there was a significant difference in surgical timing and outcome between study groups, the injury-to-surgery interval was never specifically analyzed without covariance of the primary outcome variable.

Seven articles assessed timing of ACL surgery as a primary objective, 30,34,35,38,40,42,43 and only the article by Ahlén and Lidén 40 found early surgery to be superior to delayed surgery measured with the Tegner and Lysholm scores. The remaining 6 articles did not find evidence to support a certain injury-to-surgery interval to be more beneficial when comparing meniscal and chondral lesions, radiographic OA, laxity, range of motion, Tegner and Lysholm scores, International Knee Documentation Committee score, and muscle strength. Three articles compared ACL surgery with conservative treatment and consistently found a growing number of patients (ranging from 23% to 37%) in the initially conservatively treated group who underwent delayed reconstruction of the ACL because of unacceptable symptomatic instability. 32,36,41 Furthermore, the number of meniscal injuries requiring surgery (resection or fixation) during follow-up was significantly higher in patients who underwent delayed reconstruction.

A total of 11 articles compared the risk for meniscal and chondral pathology in patients who underwent early and delayed reconstruction, respectively (Table 1). Five articles found an increased risk for subsequent intra-articular injuries when surgery was delayed. 29,32,36,41,43 Six articles found no such correlation. 31,33,36,40,42

Nine articles evaluated the incidence of radiographic OA as an outcome measure. 9,33,36,37,41,43,46,48,49 Four of these studies had long-term follow-up of at least 10 years. 36,46,48,49 The study with the longest follow-up, by Meunier et al., 36 showed that the subgroup of patients with late ACL reconstruction (range, 1 to 14 years) had a higher rate of radiographic OA compared with early reconstruction (63% [10 of 16] v 50% [21 of 42]). The other long-term studies did not present a clear relation between injury-to-surgery interval and OA. In the study by Oiestad et al., 9 the group with late ACL reconstruction had significantly more radiographic signs of OA. However, there were no differences in symptomatic OA, and interpretation was confounded by the fact that the group with late reconstruction had combined ACL and meniscal and/or chondral injuries. There were 3 midterm studies. In 2 of these studies, there was a positive correlation between longer injury-to-surgery interval and development of degenerative changes, 33,49 whereas one study found evidence to support the opposite. 41 The 2 short-term studies found no differences in degenerative changes between early and delayed reconstruction. 37,43

Discussion
This systematic review investigated the impact of timing of surgery on the outcome after ACL injury. The primary focus was on meniscal and chondral injury because of the known long-term effects and risk for OA. The main finding was that there appear to be few or no differences in subjective and objective outcomes related to surgical timing of ACL reconstruction. The secondary finding was that methodologic limitations and heterogeneity in the currently available literature complicated interpretation.
Smith et al.\(^1\) compared early versus delayed reconstruction in a systematic review and meta-analysis and found no difference in clinical outcome based on the injury-to-surgery interval while also commenting on the methodologic limitations in the literature. In contrast to Smith et al., our systematic review presented a more extensive literature search, which included articles on ACL surgery and categorized these into groups based on study design. Another important strength is the inclusion of all articles addressing timing of surgery, not just those addressing it as a primary objective. This is a crucial factor because a database search might not reveal all relevant variables in a study but might only show search results based on index
## Table 1. Study Characteristics

<table>
<thead>
<tr>
<th>Authors</th>
<th>Design</th>
<th>Early</th>
<th>Delayed</th>
<th>Sample Size</th>
<th>Follow-up Rate (%)</th>
<th>Sample Size Calculation</th>
<th>Graft Type</th>
<th>Follow-up</th>
<th>Increased Risk for Meniscal/Chondral Injury With Delayed Surgery Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barenius et al.²⁹</td>
<td>RCT</td>
<td>&lt;5 mo</td>
<td>&gt;5 mo</td>
<td>164</td>
<td>93 (n = 153)</td>
<td>No</td>
<td>PT/STG</td>
<td>8 yr</td>
<td>Yes</td>
</tr>
<tr>
<td>Bottoni et al.³⁰</td>
<td>RCT</td>
<td>9 d (2-17 d)</td>
<td>85 d (42-192 d)</td>
<td>70</td>
<td>99 (n = 69)</td>
<td>No</td>
<td>STG</td>
<td>1 yr</td>
<td>No</td>
</tr>
<tr>
<td>Eriksson et al.³¹</td>
<td>RCT</td>
<td>&lt;5 mo</td>
<td>&gt;5 mo</td>
<td>164</td>
<td>94 (n = 154)</td>
<td>No</td>
<td>PT/STG</td>
<td>31 mo</td>
<td>NA</td>
</tr>
<tr>
<td>Frobell et al.³²</td>
<td>RCT</td>
<td>&lt;10 wk</td>
<td>12 mo</td>
<td>121</td>
<td>100 (n = 121)</td>
<td>Yes (KOOS)</td>
<td>PT/STG</td>
<td>2 yr</td>
<td>Yes</td>
</tr>
<tr>
<td>Harilainen et al.³³</td>
<td>RCT</td>
<td>NA</td>
<td>NA</td>
<td>99</td>
<td>80 (n = 79)</td>
<td>Yes (Lysholm)</td>
<td>PT/STG</td>
<td>5 yr</td>
<td>NA</td>
</tr>
<tr>
<td>Marcacci et al.,³⁴</td>
<td>RCT</td>
<td>&lt;15 d</td>
<td>11 mo (3-21 mo)</td>
<td>82</td>
<td>100 (n = 82)</td>
<td>No</td>
<td>PT/fascia lata + LAD</td>
<td>5 yr</td>
<td>No</td>
</tr>
<tr>
<td>Meighan et al.³⁵</td>
<td>RCT</td>
<td>&lt;2 wk</td>
<td>8-12 wk</td>
<td>31</td>
<td>100 (n = 31)</td>
<td>No</td>
<td>HT</td>
<td>1 yr</td>
<td>No</td>
</tr>
<tr>
<td>Meunier et al.³⁶</td>
<td>RCT</td>
<td>NA</td>
<td>1-14 yr</td>
<td>100</td>
<td>88 (n = 88)</td>
<td>No</td>
<td>PT/iliotibial band/synthetic</td>
<td>15 yr</td>
<td>Yes</td>
</tr>
<tr>
<td>O’Neill³⁷</td>
<td>RCT</td>
<td>&lt;3 wk</td>
<td>&gt;3 wk</td>
<td>129</td>
<td>97 (n = 125)</td>
<td>No</td>
<td>PT/STG</td>
<td>42 mo</td>
<td>NA</td>
</tr>
<tr>
<td>Raviraj et al.³⁸</td>
<td>RCT</td>
<td>7 d (2-14 d)</td>
<td>32 d (29-42 d)</td>
<td>105</td>
<td>94 (n = 99)</td>
<td>Yes (ROM)</td>
<td>STG</td>
<td>32 mo</td>
<td>No</td>
</tr>
<tr>
<td>Aglietti et al.³⁹</td>
<td>PCS</td>
<td>NA</td>
<td>NA</td>
<td>75</td>
<td>100 (n = 75)</td>
<td>No</td>
<td>STG</td>
<td>2 yr</td>
<td>NA</td>
</tr>
<tr>
<td>Ahlén and Liden⁴⁰</td>
<td>PCS</td>
<td>3 mo (2-5 mo)</td>
<td>30 mo (24-48 mo)</td>
<td>61</td>
<td>100 (n = 61)</td>
<td>No</td>
<td>ST/STG</td>
<td>2 yr</td>
<td>No</td>
</tr>
<tr>
<td>Fithian et al.</td>
<td>PCS</td>
<td>&lt;3 mo</td>
<td>&gt;3 mo</td>
<td>287</td>
<td>73 (n = 210)</td>
<td>No</td>
<td>PT</td>
<td>6.6 yr</td>
<td>Yes</td>
</tr>
<tr>
<td>Hunter et al.</td>
<td>PCS</td>
<td>&lt;2 d, 3-7 d, 1-3 wk</td>
<td>&gt;3 wk</td>
<td>185</td>
<td>100 (n = 185)</td>
<td>No</td>
<td>PT</td>
<td>1 yr</td>
<td>No</td>
</tr>
<tr>
<td>Larkin and Barber-Westin⁴³</td>
<td>PCS</td>
<td>4 wk (1-8 wk)</td>
<td>44 mo (3-162 mo)</td>
<td>50</td>
<td>84 (n = 42)</td>
<td>No</td>
<td>PT</td>
<td>31 mo</td>
<td>Yes</td>
</tr>
<tr>
<td>Oiestad et al.³⁹</td>
<td>PCS</td>
<td>7.1 mo</td>
<td>42.4 mo</td>
<td>221</td>
<td>82 (n = 181)</td>
<td>No</td>
<td>PT</td>
<td>12 yr</td>
<td>NA</td>
</tr>
<tr>
<td>Pape et al.⁴⁴</td>
<td>PCS</td>
<td>&lt;2 wk</td>
<td>&gt;6 wk</td>
<td>58</td>
<td>93 (n = 54)</td>
<td>No</td>
<td>PT</td>
<td>1 yr</td>
<td>NA</td>
</tr>
<tr>
<td>Rose et al.⁴⁵</td>
<td>PCS</td>
<td>&lt;6 wk</td>
<td>&gt;6 wk</td>
<td>115</td>
<td>87 (n = 100)</td>
<td>No</td>
<td>PT/STG</td>
<td>1 yr</td>
<td>NA</td>
</tr>
<tr>
<td>Shelbourne and Gray⁴⁶</td>
<td>PCS</td>
<td>1.2 mo (1 d to 6 mo)</td>
<td>2.6 yr (0.3-24 yr)</td>
<td>1276</td>
<td>39 (n = 502)</td>
<td>No</td>
<td>ST</td>
<td>14 yr</td>
<td>NA</td>
</tr>
<tr>
<td>Wojtys and Huston⁴⁷</td>
<td>PCS</td>
<td>&lt;6 mo</td>
<td>&gt;6 mo</td>
<td>25</td>
<td>100 (n = 25)</td>
<td>No</td>
<td>PT</td>
<td>18 mo</td>
<td>No</td>
</tr>
<tr>
<td>Wu et al.⁴⁸</td>
<td>PCS</td>
<td>&lt;4 mo</td>
<td>&gt;4 mo</td>
<td>103</td>
<td>61 (n = 63)</td>
<td>No</td>
<td>PT</td>
<td>10 yr</td>
<td>NA</td>
</tr>
<tr>
<td>Keays et al.⁴⁹</td>
<td>Progn</td>
<td>NA</td>
<td>NA</td>
<td>62</td>
<td>90 (n = 56)</td>
<td>No</td>
<td>PT/STG</td>
<td>6 yr</td>
<td>NA</td>
</tr>
</tbody>
</table>

HT, hamstring tendon graft; KOOS, Knee injury and Osteoarthritis Outcome Score; LAD, ligament augmentation device; NA, data not available; PCS, prospective comparative cohort study; Progn, prognostic study; PT, patellar tendon graft; RCT, randomized controlled clinical trial; ROM, range of motion; ST, semitendinosus graft; STG, semitendinosus and gracilis graft.
information. This methodology significantly increased the workload but was chosen to accomplish better coverage of the databases used in the search.

The inclusion of all articles addressing the injury-to-surgery interval resulted in large variations in the classification of early and delayed surgery. Considering all articles, early surgery was classified as ranging from within 2 days to 7 months. Delayed surgery was classified as ranging from 3 weeks to 24 years after injury. By implication, a reconstruction classified as early in one study would have been considered as delayed in another study. These findings complicate the interpretation of the results. However, this is the actual reality in current ACL research and clinical settings, which is important to show and elucidate. This might be more important than to perform a meta-analysis of an arbitrarily constructed classification of early and delayed injury-to-surgery intervals because consensus or agreements are lacking.

Timing of Surgery

Among articles promoting early reconstruction, only the article by Ahlén and Lidén36,41 focused primarily on the timing of reconstruction, whereas 2 articles compared early reconstruction with initial nonsurgical treatment and optional delayed reconstruction.36,41 Ahlén and Lidén found more than 3 times as many medial meniscus injuries in the delayed group. However, there were no significant differences in meniscal or chondral damage at index surgery, in contrast to Meunier et al.36 and Fithian et al.,41 as well as Barenius et al.,29 who concluded that early surgery reduced the risk of instability and meniscal tears and subsequent meniscal surgery. This difference might be attributable to the small population size without a sample size analysis (type II error) and a shorter follow-up in the study by Ahlén and Lidén.

The study by Meunier et al.,36 with its long-term follow-up of 15 years, concluded that meniscectomy at index surgery was the most important predictor of OA in the knee, a finding supported by several other authors.3,48-50 Furthermore, 31% of the patients initially treated conservatively had to undergo surgical treatment because of instability, which is consistent with findings by Frobell et al.32 Interestingly, this finding was echoed in the study by Fithian et al.41 in which every third ACL reconstruction prevented one delayed surgery in moderate-risk patients (number needed to treat, 3). Apparently, the current literature supports the notion that although avoiding surgery might be a noble pursuit, avoiding risks with anesthesia and postoperative complications, as well as unnecessary economic expenses, the majority of the initially conservatively treated patients tend to undergo surgery sooner or later because of disabling instability.51

Eleven articles assessed differences in meniscal and chondral injuries between early and delayed ACL surgery. Among the 6 articles concerned with injury-to-surgery interval as a primary research question, 5 found no increased risk for subsequent intra-articular injuries with delayed surgery (Table 1). Bottoni et al.37 showed that meniscal and chondral injuries were comparable between early and delayed reconstruction, a finding supported by Meighan et al.,35 Marcacci et al.,34 and Raviraj et al.38 All articles were randomized controlled clinical trials with adequate randomization. However, the sample sizes were small, and only the study by Raviraj et al. performed a sample size calculation to be able to detect significant differences with regard to range of motion. More importantly, the difference in time span between early and delayed reconstruction was small, which might not be sufficient to detect progressive intra-articular injury to the menisci or cartilage. Interestingly, all studies that compared surgical with nonsurgical treatment (in which surgery was optional in patients in whom unacceptable disabling symptoms developed) showed that delayed surgery significantly increased the risk for meniscal and chondral injuries.32,36,41 a finding supported by both Barenius et al.29 and Larkin and Barber-Westin.43 Finally, studies that found no increased risk for intra-articular injuries with delayed surgery had a mean follow-up of 2.1 years (range, 1 to 5 years), whereas studies that detected significantly more meniscal and chondral injuries with delayed surgery had a longer mean follow-up of 6.8 years (range, 2 to 15 years) (P = .064). Recent studies also confirmed that surgical delay was a significant predictor of both meniscal and cartilage injury.4,5

The study by Frobell et al.32 concluded that early reconstruction was not superior to initial nonsurgical treatment with optional delayed reconstruction in the short-term. The article represents high methodologic quality with proper randomization. A sample size calculation was performed for the Knee Injury and Osteoarthritis Outcome Score, which was the primary outcome measurement. The follow-up rate was high. However, there is a concern with the markedly increased proportion of reconstructions in the optional delayed group at each interim visit. At the 6-month visit, 7% had undergone delayed reconstruction, increasing to 20% at 1 year of follow-up and 37% at the final 2-year follow-up. Frobell et al.51 have recently published midterm results from this study, which showed an additional increase to 51% at the 5-year follow-up. This gives rise to the question whether initial nonsurgical treatment in young adults with a high preinjury activity level is an acceptable treatment option. The continued follow-up of these participants is necessary to evaluate the long-term consequences of ACL deficiency. Finally, both subjective and objective
knee instability and meniscal signs and symptoms were more frequent in the optional delayed reconstruction group, which might be an important factor in the long-term development of symptomatic OA. However, other authors have not supported this finding. Interestingly, in the study by Larkin and Barber-Westin, almost every patient in the delayed group required meniscal surgery, which is consistent with previous reports that non-reconstructed ACL-deficient knees are highly predisposed to meniscal injury.  

In the 5-year follow-up by Frobell et al., the patients who underwent delayed reconstruction required significantly more meniscal surgical procedures on the index meniscus compared with patients who underwent early reconstruction.

Four articles focused primarily on factors related to the development of OA in the midterm and long-term and found that meniscal and chondral damage consistently produced a worse outcome both on objective measurements and on patient-reported outcomes, which was also supported by Barenbrug et al., Eriksson et al., and Meunier et al. These findings have previously been reported thoroughly by other authors. Harilainen et al. showed that a longer injury-to-surgery interval correlated with degenerative changes. Interestingly, they also found that delayed reconstruction correlated with a positive pivot-shift test 5 years after reconstruction, which previously has been shown to predict a worse long-term outcome.  

Six articles, not concerned with timing of surgery as a primary objective, did not present statistics on significant differences regarding the injury-to-surgery interval at baseline, which precludes conclusions regarding absence of differences in outcome. Furthermore, sample size calculations were not presented; hence the probability of a type II statistical error must be borne in mind.

<table>
<thead>
<tr>
<th>Limitation</th>
<th>No. of Trials</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT with inadequate randomization</td>
<td>3</td>
<td>30</td>
</tr>
<tr>
<td>RCT with no randomization method presented</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>No sample size calculation</td>
<td>19</td>
<td>86</td>
</tr>
<tr>
<td>No. of trials with no significant differences among study groups</td>
<td>12</td>
<td>55</td>
</tr>
<tr>
<td>No. of trials with no significant differences among study groups that did not have sample size calculation</td>
<td>10</td>
<td>83</td>
</tr>
<tr>
<td>No blinding</td>
<td>4</td>
<td>18</td>
</tr>
<tr>
<td>No blinding stated</td>
<td>14</td>
<td>64</td>
</tr>
<tr>
<td>Sample size of 0 to 49</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Sample size of 50 to 99</td>
<td>9</td>
<td>41</td>
</tr>
<tr>
<td>&lt;80% follow-up rate</td>
<td>4</td>
<td>18</td>
</tr>
</tbody>
</table>

**Table 2. Overview of Limitations**

**Quality Assessment**

This systematic review included randomized controlled trials, prospective comparative cohort studies, and prognostic studies encompassing both Level I and Level II evidence. However, articles considered as the highest level of evidence might be limited by methodologic errors, as previously reported by Andersson and colleagues. The majority of articles did not perform a sample size calculation, and in 83% of the trials, no significant differences were detected (Table 2). These articles did not present a sample size based on statistical power, allowing a type II statistical error to occur. Furthermore, 82% (n = 18) of the reviewed trials did not perform blinded follow-up assessments or did not present whether this was accomplished. Sample sizes were considered small (<100 subjects) in 50% of the trials. On the other hand, the follow-up rate was regarded as satisfactory. Long-term follow-up is important, especially when assessing clinical outcome and the development of OA, because the ACL-injured population often is young with a long life expectancy. In this systematic review the distributions of short-term, midterm, and long-term trials were 59%, 23%, and 18%, respectively (Table 3). From ideal, this distribution is, however, encouraging compared with numbers previously reported in the ACL literature.

**Limitations**

There are several important limitations to this systematic review. Only an electronic search was performed, and only 3 databases (Medline, EMBASE, and Cochrane Library) were used. Only articles published in English between January 1995 and August 2011 were included. Furthermore, articles assessing timing of surgery as a secondary objective were included. Finally, because of broad inclusion criteria for the purpose of a wide-range assessment of the subject, pooling of data into a meta-analysis was not possible because of substantial study heterogeneity.

**Conclusions**

This systematic review has shown that, on the basis of currently available literature, there appear to be few or no differences in subjective and objective outcomes related to timing of ACL reconstruction. However, there are indications that delaying reconstruction predisposes the knee to instability, meniscal injury, and chondral...
injury, which are the strongest predictors for future OA development. In the short-term and midterm, this development might not be symptomatic, but in the long-term, delaying reconstruction might place patients at risk of a potentially disabling disease.

References


