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Winner of the 2008 Systematic Review Competition

Knee Osteoarthritis After Anterior Cruciate Ligament Injury

A Systematic Review

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Background: This is a systematic review of studies on the prevalence of osteoarthritis in the tibiofemoral joint more than 10 years after an anterior cruciate ligament injury, the radiologic classification methods used, and risk factors for development of knee osteoarthritis.

Methods: A systematic search was performed in PubMed, EMBASE, and AMED. Inclusion criteria were studies involving patients with anterior cruciate ligament injury, either isolated or combined with medial collateral ligament or meniscal injury and either surgically or nonsurgically treated, and a minimum 10-year follow-up with radiologic assessment. Methodological quality was evaluated using a modified version of the Coleman methodology score.

Results: Seven prospective and 24 retrospective studies were included. The mean modified Coleman methodology score was 52 of 90. Reported prevalence of knee osteoarthritis for subjects with isolated anterior cruciate ligament injury was between 0% and 13%. For subjects with anterior cruciate ligament and additional meniscal injury, the prevalence varied between 21% and 48%. Seven different radiologic classification systems were used in the studies. Only 3 studies reported reliability results for the radiologic assessments. The most frequently reported risk factor for development of knee osteoarthritis was meniscal injury.

Conclusion: This systematic review suggests that the prevalence rates of knee osteoarthritis after anterior cruciate ligament reconstruction reported by previous reviews have been too high. The highest rated studies reported low prevalence of knee osteoarthritis for individuals with isolated anterior cruciate ligament injury (0%-13%) and a higher prevalence of knee osteoarthritis for subjects with combined injuries (21%-48%). Overall, the modified Coleman methodology score was low for the included studies. No universal methodological radiologic classification method exists, making comparisons of the studies and stating firm conclusions on the prevalence of knee osteoarthritis more than 10 years after anterior cruciate ligament injury difficult.

Keywords: anterior cruciate ligament injury; knee osteoarthritis; long-term follow-up

Anterior cruciate ligament (ACL) injuries occur primarily in young individuals involved in pivoting sports such as team handball, soccer, basketball, football, alpine skiing, and tennis.[11,25,85] An ACL injury is often associated with functional impairments and disabilities due to knee joint laxity, meniscal injuries, reduced quadriceps strength, and changes in knee joint loading, with subsequent development of knee osteoarthritis (OA).[4] Risk factors for posttraumatic knee OA are multifactorial; however, the primary risk factors frequently reported are meniscal injury at the time of reconstruction[2,81] and participation in high-level sports activities involving cutting, pivoting, and twisting.[4,56] No previous studies have shown that an ACL reconstruction prevents the development of knee OA.[16,46]

There are several studies evaluating the long-term consequences of an ACL injury.[§] Most of these studies involved heterogeneous populations with regard to treatment, activity levels, and whether the ACL injury was isolated or combined with meniscal injuries. Few long-term studies have evaluated homogeneous populations such as soccer and team handball players.[47,57,90] Consequently, the existing follow-up studies vary considerably concerning the reported

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[§]References 1, 9, 10, 16-19, 23, 26, 27, 32, 39-41, 44, 59, 64, 65, 70, 73, 74, 82.

prevalence of knee OA, with a prevalence ranging between 10% and 90%.[12,25,46] Clearly, it is difficult to draw firm conclusions with respect to the development of knee OA after an ACL injury, although it is commonly claimed that on average 50% of patients with ACL injury will develop knee OA in the long run.[46] For subjects with a combined ACL and meniscal injury, the prevalence of knee OA is claimed to be as high as 70% at 15 to 20 years after the injury.[25] However, to our knowledge, no systematic reviews on follow-up studies of more than 10 years, including methodological assessment score, have been published.

The purposes of this study were (1) to systematically review the reported prevalence of knee OA in the tibiofemoral joint more than 10 years after ACL injury, (2) to evaluate the radiologic classification methods used to verify radiologic knee OA, and (3) to evaluate the reported risk factors for knee OA in studies with a follow-up of more than 10 years after ACL injury.

METHODS

Study Selection

The inclusion criteria for studies in this systematic review were:

- Prospective or retrospective study designs
- Subjects with ACL injury treated surgically or nonsurgically
- Isolated ACL injury or ACL injury combined with meniscal and/or medial collateral ligament injury
- Radiologic assessment as one of the outcomes
- Follow-up time of a minimum 10 years after ACL injury
- Studies reported in English and Scandinavian languages

The exclusion criteria were:

- Studies not involving radiologic assessment
- Studies with a follow-up less than 10 years

Search Strategy

Systematic searches were carried out in August 2008 in 3 different databases: PubMed (from 1966), EMBASE (from 1980), and AMED (from 1985). The searches were performed with assistance from librarians at the Medical Library, Ullevaal University Hospital. The search strategy for PubMed is shown in Table 1. The PubMed search strategy was transferred into comparable search strategies in EMBASE and AMED. In addition, supplementary searches in PubMed, EMBASE, and AMED using "anterior cruciate ligament and osteoarthritis" were performed to find all available articles. The abstracts of the search results were reviewed. In cases in which the abstracts did not give full information about the inclusion criteria for this review, the full-text versions of the studies were reviewed. In addition, reference lists of relevant studies were reviewed to identify studies not found through the primary electronic searches.

TABLE 1
Specific Search Terms Used in PubMed[a]

Search Term	No.
Anterior cruciate ligament (MeSH) (1991)	6100
Knee joint (MeSH)	31 033
Ligaments, Articular (MeSH)	17 458
Knee joint OR Ligament, Articular (limits 1965-1990)	17 646
Knee Injuries (MeSH)	11 644
Osteoarthritis, Knee (MeSH) (1998)	4427
Osteoarthritis (MeSH)	32 158
Epidemiologic studies (MeSH) (1998)	1 048 164
Epidemiology (limits 1967-1997)	5202
2 OR 7 (Knee OA before 1998)	34 138
1 OR 4 OR 5 (ACL injury)	30 024
6 OR 10 (Knee OA)	38 484
8 OR 9 (Epidemiologic studies)	1 053 106
11 AND 12 AND 13 (Limits: Human, English, Danish, Norwegian, Swedish)	1769

[a]MeSH, medical subject heading; OA, osteoarthritis. 2 OR 7: Knee joint OR Osteoarthritis; 1 OR 4 OR 5: Anterior cruciate ligament OR [Knee joint OR Ligament, Articular] OR Knee injuries; 6 OR 10: Osteoarthritis, Knee OR [Knee joint OR Osteoarthritis]; 8 OR 9: Epidemiologic studies OR Epidemiology; 11 AND 12 AND 13: [Anterior cruciate ligament OR [Knee joint OR Ligament, Articular] OR Knee injuries] AND [Osteoarthritis, Knee OR [Knee joint OR Osteoarthritis]] AND [Epidemiologic studies OR Epidemiology].

Study Quality Assessment

A modified version of the Coleman methodology score (CMS)[14] was used to assess the methodological quality of the included studies. The CMS originally consisted of 10 criteria with a total score ranging from 0 to 100. A score of 100 indicated the most high-quality study with no confounding factors or other biases. The criteria were based on the CONSORT statement for randomized controlled trials.[5] The CMS was originally developed for surgical treatment of tendinopathy, but modified versions of the CMS have been used in other reviews.[38,87] In this systematic review, the CMS was modified to be suitable for cohort studies. The following criteria were altered for part A: (1) "Number of follow-up years" (question 2) was altered from 2 to 10 years, (2) "type of study" (question 3) was altered to give both prospective cohort studies and randomized controlled trials the highest score, (3) "description of treatment" (question 6) was altered from the term *surgical* to *treatment*, and (4) "description of postoperative treatment" (question 7) was removed. Part A gave a total score of 50. The following modifications were included in part B: (1) "Outcome criteria" (question 1) was altered; the original criterion concerning sensitivity was removed, and the score was given to studies that reported interrater or intrarater reliability for the radiologic assessments. Part B gave a total score of 40. The maximum score of the modified CMS was therefore 90. The modified CMS is listed in Appendix 1 (available online at http://ajs.sagepub.com/supplemental/). The

methodological quality of the included studies was assessed by 2 independent reviewers. Conflicting scores for the various items were discussed until consensus was reached.

Data Extraction

To evaluate the reported prevalence of knee OA, results from the radiologic assessments were extracted from the included studies. The data on knee OA were based on cutoff values for the different radiologic classification systems corresponding to Kellgren and Lawrence grade 2,[42] International Knee Documentation Committee (IKDC)[37] grade C, or Ahlbäck grade 1.[3] No cutoff for the CMS has been reported to define high or low methodological quality. It is suggested in the literature that a score of more than 55% of total score for other checklists is to be considered as high-quality studies.[89] In this systematic review, the prospective studies have been classified as high-quality studies.

RESULTS

Abstracts of 2199 studies were reviewed from the systematic searches. The systematic searches resulted in 1769 abstracts in PubMed and 85 abstracts in EMBASE. A search using the search terms *anterior cruciate ligament injury and osteoarthritis* identified 16 abstracts in AMED and 329 abstracts in PubMed. Based on the inclusion criteria, 33 studies were included. Seven studies were assessed as prospective,[19,31,45,53,60,67,93] and 26 studies were assessed as retrospective.[‖] Twenty-four studies were identified in PubMed, 2 studies were included from EMBASE, and 7 were identified by manual searches of journals and reference lists in relevant studies. These 7 studies did not appear in the systematic searches because of the missing citation term *osteoarthritis*. Two of the studies[51,83] were later excluded owing to use of the same study population as that of later published studies.[49,50] No additional studies were identified in AMED. Finally, 7 prospective studies and 24 retrospective studies were included. Only 1 of the prospective studies was a randomized study evaluating long-term results after primary repair or nonsurgical treatment of ACL injury.[53]

The characteristics of the studies are presented in Appendix 2 (available online at http://ajs.sagepub.com/supplemental/). The total number of subjects included was 3069, with sample sizes ranging from 24 to 328 patients. Twenty studies included radiologic assessment of 1114 surgically treated subjects, and 5 studies included radiologic assessment of 276 nonsurgically treated subjects. Three studies evaluated 517 surgically and nonsurgically treated subjects including radiologic assessment. Three studies included radiologic assessment of 273 nonsurgically and surgically treated separately. Hence, radiologic evaluation was carried out on 2180 of the included subjects, resulting in a radiologic follow-up rate of 71%. Eleven studies reported radiologic results for the contralateral knee, involving 666 knees. Surgical procedures for the ACL injury reported in the studies were primary repair with or without augmentations, bone–patellar tendon–bone grafts, looped semitendinosus tendon grafts, or fascia lata allografts. The mean follow-up time in the included studies was 13.7 years, with a variation from 10 to 27 years. Preinjury activity level was reported in 11 studies with a mean Tegner score of 6.7, with the lowest score of 5.7 and the highest score of 9. Fifteen studies reported follow-up activity level with a mean Tegner score of 5.1, with the lowest score of 3.7 and the highest score of 6.4 (Appendix 2).

Methodological Quality

The results of the study quality assessments are presented in Table 2. For part A, "type of study" and "number of treatment procedures" gave the lowest scores. For part B, the lowest scores were achieved for "outcome criteria" and "description of subject selection process." None of the studies fulfilled all the criteria (modified CMS of 90); however, 1 study revealed a modified CMS of 88.[60] The mean modified CMS was 52 ± 13, which corresponds to a CMS of 58 when transferred to a 0 to 100 score. The lowest score achieved was 22, and the highest was 88 (Table 3). The prospective studies achieved a mean modified CMS of 69, with a highest score of 88 and a lowest score of 61. The retrospective studies correspondingly achieved a mean modified CMS of 47, with a highest score of 59 and a lowest score of 22.

Prevalence of Knee OA

The overall prevalence of OA in the tibiofemoral joint varied between 1% and 100%. The corresponding prevalence in the contralateral knees revealed 0% to 38%. The prospective studies reported prevalences of knee OA between 1% and 100%, and the retrospective studies reported prevalences of knee OA between 13% and 100% (Table 3). Studies that reported results for isolated and combined ACL injuries separately reported knee OA between 0% and 39% and between 21% and 100%, respectively (Table 3). Two nonrandomized studies, 1 of which revealed the highest methodological score, reported a significant difference in knee OA development between nonsurgically treated and surgically treated.[43,60] No differences were reported for the prevalence of knee OA between surgically treated (29%-51%) and nonsurgically treated subjects (24%-48%) for other included studies.[22,43,47] Studies including subjects with a preinjury Tegner score of more than 7 or studies that included only soccer players reported a prevalence of knee OA between 8% and 100%.[47,49,53,61,90,93] Studies including subjects with lower preinjury Tegner scores reported a prevalence between 11% and 66%.[19,34,36,43,55,77,86,88]

Radiologic Classification Methods

Seven different radiologic classification methods were used in the 31 included studies. Five studies used the Fairbank classification system[20] with a reported prevalence

[‖]References 13, 22, 34, 36, 43, 47, 49-51, 54, 55, 58, 61-63, 68, 69, 75, 77-79, 83, 86, 88, 90, 94.

TABLE 2
Modified Coleman Methodology Score for Long-term Follow-up Studies on Subjects With ACL Injury

Section Score (Maximum)	Mean (SD)
Part A	
Study size (10)	8.0
Mean duration follow-up (5)	5.0
No. of treatment procedures (10)	6.1
Type of study (15)	3.4
Diagnostic certainty (5)	4.7
Description of surgical procedure (5)	3.9
Part B	
Outcome criteria (10)	4.9
Outcome measured clearly (4)	3.7
Reported interrater or intrarater reliability (3)	0.4
Use of outcome criteria that has reported good reliability (3)	0.8
Procedure for assessing outcomes (15)	9.2
Subjects recruited (5)	5.0
Investigator independent of surgeon/therapist (4)	2.1
Written assessment (3)	0.5
Completion of assessment by subjects themselves with minimal investigator assistance (3)	1.6
Description of subject selection process (15)	7.0
Selection criteria reported and unbiased (5)	2.7
Recruitment rate reported (≥80% = 5; <80% = 3)	3.6
Eligible subjects not included in the study accounted for (5)	0.7
Total part A (50)	31.1 (9.6)
Total part B (40)	21.1 (6.9)
Total score (90)	52.2 (12.4)

of knee OA between 8% and 100%.[13,22,63,69,93] Two studies used the Ahlbäck classification system[3] with a reported prevalence of knee OA between 11% and 44%.[19,34] Two studies reported a prevalence of knee OA between 16% and 50% using a combination of Fairbank classification system and Ahlbäck classification system.[49,53] The Kellgren and Lawrence classification system[42] was used in 5 studies,[31,43,77,79,88] and the Osteoarthritis Society Research International classification system[8] was used in 3 studies,[47,60,90] with a reported prevalence of knee OA of 24% to 48% and 16% to 48%, respectively. Ten studies used the IKDC classification system.[37] The reported prevalence of knee OA in these studies was between 1% and 100%.[¶] Four studies did not specify radiologic classification system but used a combination of joint space narrowing (JSN) and osteophyte formation.[50,58,61,62] These studies reported a prevalence of knee OA between 21% and 77% (Table 3). Most of the studies reported that the radiographs were performed with the patients in the standing position with full weightbearing (n = 30) and with a knee flexion angle of 15° to 45° (n = 17).

Risk Factors for the Development of Knee OA

Identification of risk factors using regression analysis was conducted in only 3 studies. Risk factors identified in these 3 studies were ACL surgery, age, body mass index,[43] <90% on single-legged hop test compared with the uninjured side 1 year after surgery,[67] loss of extension, and laxity.[75] In the remaining studies, risk factors were identified using group comparisons. Risk factors reported were meniscectomy, patients older than 25 years at injury, obesity, more than 6 months between injury and surgery, high level of sports activity, OA of the contralateral knee, chondral lesions, knee joint laxity, and duration of follow-up. Meniscal injury and meniscectomy were the most frequently reported risk factors (Table 3).

DISCUSSION

Thirty-one studies including a total of 3069 subjects with ACL injury were included in this systematic review based on the inclusion criteria. Seven of the studies were assessed to have a prospective study design, and 24 studies were assessed to have a retrospective study design. The studies achieved a mean modified CMS of 52 of a total score of 90. The prospective studies disclosed higher methodological quality than did the retrospective studies, with a mean modified CMS of 69 versus 47.

Prevalence of Knee OA

The reported prevalence of knee OA varied between 1% and 100% for the prospective studies and between 13% and 100% for the retrospective studies. Eight of the 31 included studies reported results separately for subjects with isolated ACL injury and subjects with combined ACL and meniscal injury.[34,45,47,58,60,78,90,93] For subjects with isolated ACL injury, the prevalence of knee OA varied between 0% and 39%, with a modified CMS of 47 to 88. The 3 prospective studies with the highest modified CMS[45,60,93] revealed a prevalence of knee OA of 0%, 8%, and 13%, respectively, for subjects with isolated injuries, whereas the 5 retrospective studies with lower modified CMS revealed a prevalence of knee OA of 13%, 31%, 39%, 13%, and 26%, respectively.[34,47,58,78,90] In addition, 2 of the other studies with high modified CMS included mostly subjects with isolated ACL injury. Pinczewski et al,[67] with a modified CMS of 67, reported a prevalence of knee OA of 1% to 3%. This study excluded patients with excision of more than one third of one meniscus at the time of the ACL reconstruction, and only 20% of the included subjects had meniscal injuries. Furthermore, the prospective study by Drogset et al,[19] with a modified CMS of 64, reported a prevalence of only 11%. This study included 30% of subjects with additional meniscal injuries. In summary, ACL injury with no additional meniscal injury seems to have low prevalence of radiologic knee OA in the tibiofemoral joint more than 10 years after injury (0%-13%). A previous review article suggested a prevalence of knee OA of 15% to 20% for isolated ACL injuries 15 to 20 years after ACL injury.[25] However, this was not a systematic review and did not include methodological assessment of the included studies.

For subjects with combined ACL and meniscal injuries, the reported prevalence of knee OA (21%-100%) was higher than were the results on subjects with isolated ACL

[¶]References 36, 45, 54, 55, 67, 68, 75, 78, 86, 94.

TABLE 3
Modified CMS, Prevalence of Knee OA, and Reported Risk Factors for Each Included Study Listed by Highest Score[a]

Study	Knee OA Prevalence (Contralateral Knee),[b] %	Reported Risk Factors for Knee OA	Part A (50)	Part B (40)	Total Score (90)
Neuman et al[60] (2008)	16; isolated/combined: 0/37; surgically treated: 35; nonsurgically treated: 11	Meniscectomy	50	38	88
Meunier et al[53] (2007)	30 (16); surgically treated: 29; nonsurgically treated: 31	Meniscectomy	38	34	72
Lebel et al[45] (2008)	17.8; isolated/combined: 13.6/21.5	Body mass index at index surgery; age at follow-up	50	17	67
Pinczewski et al[67] (2007)	Patellar/hamstrings tendon: 3/1	>90% difference in single-legged hop 1 year after surgery; additional surgery	40	27	67
Wu et al[93] (2002)	Isolated/combined: 8/100	Meniscectomy	50	15	65
Drogset et al[19] (2006)	11 (4)		40	24	64
Hanypsiak et al[31] (2008)	32 joint space narrowing; 48 Kellgren and Lawrence grade 2 or more; 30 no signs of OA	Meniscal tear	35	26	61
Salmon et al[75] (2006)	21	Meniscectomy; loss of extension, laxity	35	24	59
van der Hart et al[88] (2008)	45 (3)		32	27	59
Hart et al[34] (2005)	Isolated/combined: 13/44 (0)	Meniscectomy	29	29	58
Kessler et al[43] (2008)	Surgically treated: 45; nonsurgically treated: 24	Age; body mass index	35	22	57
Cohen et al[13] (2007)	40	Meniscectomy	35	21	56
Hertel et al[36] (2005)	24	Meniscal surgery	35	20	55
Segawa et al (2001)	37 (8.6)	Age, level of sports activity, meniscectomy, obesity, OA of contralateral knee	35	18	53
Seon et al[77] (2006)	43	Meniscal injury at index; >6 months from injury to reconstruction; age > 25 years at reconstruction	35	17	52
Lohmander et al[47] (2004)	48 (8); isolated/combined: 39/69; surgically/nonsurgically treated: 51/42	Meniscal surgery	33	18	51
Selmi et al[78] (2006)	28 (7); isolated/combined: 13.5/37.2	Laxity; medial meniscectomy; chondral lesions	35	16	51
von Porat et al[90] (2004)	41; isolated/combined: 31/59	Meniscal tear	18	33	51
Reid et al[69] (1992)	53	Duration of follow-up; meniscectomy	29	19	48
Nakata et al[58] (2008)	41; isolated/combined: 26/87	Meniscectomy	35	12	47
Yamaguchi et al[94] (2006)	71 (16)	Meniscectomy	32	15	47
Pritchard et al[68] (1995)	30	Meniscal surgery	29	15	44
Strand et al[86] (2005)	15 (3)	Advanced age at injury	25	19	44
Maletius and Messner[49] (1999)	30	Meniscal tear	22	21	43
Meystre et al[54] (1998)	20	Medial meniscectomy; chondral lesions	29	14	43
Fink et al[22] (2001)	Surgically treated: 50; nonsurgically treated: 48	Meniscal resection; for nonsurgery: high-risk pivoting sports	25	17	42
O'Brien[63] (1993)	100	Time since meniscectomy; obesity (>20% increase over ideal body weight)	18	24	42
Neyret et al[61] (1993)	77 (10)	ACL injury; length of follow-up; amount of tibial translation	27	14	41
Murray and Macnicol[55] (2004)	66 (38)		25	15	40
Noyes et al[62] (1983)	44	Time from injury; joint swelling for strenuous activities, for running activities, for stair climbing; giving way during walking	12	19	31
McDaniel and Dameron[50] (1983)	35.5	Overweight; meniscectomy; varus deformity	14	8	22

[a]CMS, Coleman methodology score; OA, osteoarthritis.
[b]Medial and/or lateral knee OA defined by cutoff values on the radiologic assessments corresponding to Kellgren and Lawrence grade 2, Ahlbäck grade 1, or International Knee Documentation Committee grade C.

injury. The studies with the highest modified CMS revealed a prevalence of knee OA in subjects with combined injuries between 21% and 48%.[31,45,53,60] The prospective study by Wu et al[93] reported a prevalence of knee OA of 100% for the group with complete meniscectomy in addition to the ACL injury. This study was not included in the data extraction because only 9 subjects were included in the combined group, and 4 of these 9 subjects had confirmed radiologic changes in the tibiofemoral joint at the time of the ACL reconstruction. Based on the other prospective high-quality studies not including subjects with radiologic changes at inclusion, the reported prevalence of knee OA for subjects with combined ACL and meniscal injuries was below 48% (Table 3). These results seem to be maintained when including results from the highest rated retrospective studies (Table 3).

Five of the included studies with a mean modified CMS of 62 reported a prevalence of knee OA for surgically treated and nonsurgically treated separately.[22,43,47,53,60] Two of the studies reported a significant difference in knee OA between surgically and nonsurgically treated subjects[43,60]; however, these studies were not randomized, and the surgically treated group in the highest rated study consisted of only 17 subjects.[60] No differences were reported for the prevalence of knee OA between surgically treated (29%-51%) and nonsurgically treated subjects with ACL injury (31%-48%) for the other studies. In the study by Meunier et al[53] (modified CMS of 72), one third of the subjects in the nonsurgically treated group underwent later ACL reconstruction due to instability problems. On the basis of these 5 studies, the studies that reported on subjects with nonsurgically treated ACL injury and those evaluating only subjects undergoing surgical treatment, no difference in the prevalence of knee OA between surgically and nonsurgically treated subjects can currently be shown. However, the data extracted in this systematic review revealed a tendency indicating that an ACL reconstruction as a single factor will not prevent the development of knee OA.

Eleven studies included in the present systematic review reported the prevalence of knee OA in the contralateral knee, which varied between 0% and 38% (Table 3). However, the study that reported a prevalence of 38% showed a modified CMS of only 40,[55] and the studies that reported a prevalence of 16%[53,94] included contralateral knees with both ACL ruptures and meniscectomies. The other 8 studies reported prevalence between 0% and 10%. Compared with the 1% to 2% prevalence of knee OA reported in the general age-matched population without ACL injuries,[72,92] this variation could suggest altered joint loading in the contralateral knee after ACL injury or that these patients are more disposed to knee injuries in the contralateral knee due to more participation in pivoting sports compared with the general age-matched population.

The variation in the reported prevalence of knee OA for the included studies is probably owing to several factors: different study designs and weak methodological quality, different surgical techniques or treatment procedures, as well as different radiologic classification systems used to evaluate knee OA.[46] The different study populations (subjects with isolated vs combined knee joint injuries, reinjured or surgically revised during the follow-up period, and subjects with different types and levels of sport activities) could probably also explain some of the variation and makes it hard to compare the study results.

Radiologic Classification Systems

Seven different radiologic classification systems were used in the 31 included studies. All the classification systems included evaluation of osteophyte formation, JSN, or both. However, the studies that reported joint space width did not describe the procedures used to measure joint space. The cutoff grade (grade 2) for defining knee OA for the original Kellgren and Lawrence classification system involved osteophyte formation and possible JSN.[42] This is different from the IKDC classification system and from the studies that use a combination of the Ahlbäck and Fairbank classification systems. These classification systems have cutoff grades for defining knee OA that involve JSN up to 50% compared with the contralateral knee and "moderate changes" as criteria. The Ahlbäck classification system emphasizes only JSN and not osteophyte formation for defining knee OA. Furthermore, at least 2 different ways of classifying grade 2 for the Kellgren and Lawrence classification system have been reported; the original Kellgren and Lawrence used the criteria "definite osteophytes and possible narrowing of joint space," and the newer versions have used "definite osteophyte, unimpaired joint space" and "minimal osteophytes, possible narrowing, cysts, and sclerosis" as criteria for grade 2.[15,76] Three of the 5 studies included in this systematic review that used the Kellgren and Lawrence classification system did not report which of these criteria they used for the grade 2 level.[31,43,77]

In this systematic review, we used the following cutoff values for defining knee OA: Kellgren and Lawrence grade 2, IKDC grade C, and Ahlbäck grade 1. However, these different classification systems cannot easily be compared. One study compared the Kellgren and Lawrence system grade 2 to 3 versus the Ahlbäck system grade 1, as well as the Kellgren and Lawrence system grade 3 to 4 versus the Ahlbäck system grade 1 to 2.[66] This study reported acceptable agreement between these 2 classification systems (κ of 0.76 and 0.78, respectively). Details on how to obtain reproducible images in each study and how to evaluate knee joint degeneration are insufficiently reported in the included studies.[48] Ideally, the studies should include both interrater and intrarater reliability data to enhance the reliability of the results.[75] Only 3 of the included studies in this systematic review reported reliability results for the raters who examined the radiographs.[60,75,90] Salmon et al[75] reported good agreement between the raters using the IKDC radiologic classification system. Von Porat et al[90] referred to high interrater-reliability results for the rater in their study and a rater from another study. However, it is unclear if the reliability results were for the Osteoarthritis Research Society International classification system, which was used in the included study, or if they were for another radiologic classification system. Neuman et al[60] reported good interrater reliability for JSN (κ = 0.78) and poor for osteophyte (κ = 0.52). Acceptable intrarater

reliability and poor interrater reliability[52] have been reported for the IKDC radiologic classification system.[35] For the Ahlbäck classification system, poor reliability results have been reported,[24] and 2 problems using this classification have been identified: first, whether a visible joint space represents remaining cartilage and, second, whether there is bone attrition.[91]

One single, experienced examiner should rate the radiographs to optimize the reliability using both the Ahlbäck classification and the IKDC classification system. The Kellgren and Lawrence classification system[42] has shown acceptable interrater and intrarater reliability, but it has also been criticized for its emphasis on osteophytes and that the system is relatively insensitive to assess changes in OA over time.[7] Thus, a condition with JSN but without osteophyte formation will not be defined as knee OA according to the Kellgren and Lawrence classification system, which is in contrast to the Ahlbäck classification system. We have not been able to find reliability studies for the Fairbank classification, which was originally used to evaluate patients who had undergone meniscectomy.[20] The Fairbank classification system has been criticized for overestimating the frequency of knee OA.[25] The variation in the reported prevalence of knee OA for the 5 studies using the Fairbank classification system (8%-100%) and for the 8 studies using the IKDC classification system (1%-100%) could partly be explained by poor reliability results. An internationally accepted, reliable, and valid radiologic classification system is clearly needed.

All studies included have defined knee OA exclusively using radiologic assessment. No studies included the American College of Rheumatology criteria clinical criteria for defining knee OA.[6] There are weak correlations between symptoms and radiologic changes for patients with knee OA.[30] Future studies should therefore include both clinical and radiologic criteria for defining knee OA after ACL injury or reconstruction.

Reported Risk Factors for Development of Knee OA After ACL Injury

Only 3 of the included studies used regression analyses to identify risk factors for development of knee OA after ACL injury. Pinczewski et al[67] reported the performance on the single-legged hop test 1 year after the injury as a significant predictor for the development of knee OA 10 years after injury. Kessler et al[43] found ACL surgery, age, and body mass index as significant risk factors for knee OA development after ACL injury. Salmon et al[75] reported that meniscectomy at the time of the ACL reconstruction, loss of knee extension, and increased knee joint laxity (Lachman test) were significant predictors for the development of knee OA 13 years after ACL reconstruction. Seon et al,[79,80] using group comparisons, identified that individuals older than 25 years at surgery, more than 6 months between injury and surgery, obesity, and additional meniscal injury were significant risk factors for the development of knee OA 11 years after ACL reconstruction. Nearly all the included studies reported that meniscal injury seemed to be a significant risk factor for the development of knee OA after ACL injury.

Previous studies have reported intra-articular injuries, age, sex, genetics, obesity, joint deformity, sports participation, and muscle weakness as risk factors for knee OA development.[21] Neither quadriceps strength nor returning to pivoting sports was examined as risk factors in the highest rated included studies.

On the basis of the studies included in this systematic review, we conclude that meniscal injuries and meniscectomy are well-documented risk factors for the development of knee OA after ACL injury. Factors such as ACL surgery, age, obesity, knee joint laxity, performance on hop tests, and loss of knee extension should be further documented to be considered as risk factors. To identify risk factors, multivariate regression analysis should be applied in future prospective cohorts with large numbers of subjects.[11]

Methodological Quality

This systematic review revealed a mean modified CMS of 52 of a total of 90. This score corresponds to 58 points when normalized to a 0 to 100 score. Other systematic reviews including other study populations have reported a mean CMS of 37 to 43.[14,38,87] The highest rated studies recently published confirmed the findings by Jakobsen et al,[38] who reviewed cartilage repair studies and found a significant correlation between CMS and publication year. The most frequent questions in the modified CMS that resulted in a low score were the following: "type of study," "outcome criteria," and "procedure for assessing outcome," which is in accordance with other systematic reviews.[38] Information based on subject recall in retrospective studies can be unreliable.[14] On the other hand, a retrospective study often requires only 1 follow-up, and larger sample sizes can be included. In a prospective cohort study, all data are collected with standardized methods, and this approach involves measuring potential risk factors before the development of knee OA.[11]

This systematic review suggests that previous reviews have reported too high a prevalence of knee OA after ACL reconstruction.[25,46,48,71] This study presents detailed data on the prevalence of knee OA after ACL injury and suggests that we should continue to report a low prevalence of knee OA after isolated ACL injury (0%-13%) and higher prevalence of knee OA in combined ACL and meniscal injuries (21%-48%). Furthermore, similar cutoff levels and criteria for radiologic knee OA should be used, Fairbank classification should not be used, and IKDC shows poor reliability results. In addition, clinical criteria based on the American College of Rheumatology criteria should be included for defining knee OA.

This systematic review has some limitations. The CMS was originally developed for reporting surgical outcome after patellar tendinopathy. This could limit the use for assessing the methodological quality of cohort studies involving both surgically and nonsurgically treated subjects with ACL injury. The methodological quality assessment

could have been done differently using another checklist.[33] Specific checklists for cohort studies and randomized controlled trials have been published[28,29]; however, these checklists involve mainly the same questions as those involved in the CMS: type of study, diagnostic certainty, how to measure outcome, follow-up rate, dropout analysis, and blinding. The strength of the CMS is the included clinical questions in addition to a total score given for methodological quality of each study. On the other hand, the weighting of the criteria included in the CMS can be questioned. For instance, in part B, concerning the question about recruitment rate, the highest score for 80% recruitment rate is 5, whereas it is 3 for studies with less than 80% recruitment rate. This means that studies with 50% loss to follow-up only will score 2 points less than will studies with 100% follow-up. The mean follow-up rate of subjects going through radiologic assessment was 71%, with a variation between 43% and 100%. More than 20% lost to follow-up may pose threats to the validity.[84] However, in prospective long-term cohort studies, higher dropout rates would be expected. Selection bias concerning study participants is a significant criterion regarding study quality. Those with the highest motivation for returning to sport or those with knee OA symptoms could be most willing to take part in the study.[48] The subject characteristics of the subsamples who went through radiologic assessment were usually poorly described concerning age, sex, activity levels, and reinjuries.

Because of the heterogeneity of the included studies, meta-analysis was not possible. Some of the studies did not primarily evaluate knee OA but had other main purposes. Publication bias could also be a problem, with respect to publishing the most interesting results. Finally, this review only included studies published in the English and Scandinavian languages.

In summary, the highest rated studies reported low prevalence of knee OA for individuals with isolated ACL injury (0%-13%) and a prevalence of knee OA between 21% and 48% for subjects with combined injuries. The highest rated study, by Neuman et al,[60] found no knee OA among the included subjects with nonsurgically treated ACL injury more than 15 years after the ACL injury. Meniscal injury at the time of ACL injury was most frequently associated with knee OA in studies with high and low modified CMS. On the basis of this systematic review with thorough examination of the methodological quality of the studies, we should discontinue reporting that subjects with ACL injury have a prevalence of knee OA between 50% and 100%. However, we need a common, reliable, and valid radiologic classification system to define knee OA after ACL injury in the future.

Future studies on reported incidence of knee OA should be prospective and evaluate subject characteristics, reinjuries, revision surgery, type and level of activity, quadriceps muscle strength, and other potential risk factors consecutively. We propose the following guidelines for future studies on the basis of the findings in the present systematic review:

1. They should be prospective studies with clearly defined aims and end points.
2. Clear inclusion and exclusion criteria: The recruitment rate should be reported, and attempts should be made to account for patients who are not included and those who are lost to follow-up.
3. One common radiologic classification system should be used and clearly reported. Reliability data should be reported for an independent, blinded examiner.
4. The rehabilitation protocol should be reported.
5. Regression analysis should be used to evaluate risk factors for knee OA after ACL injury or surgery on a representative sample.

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