

## Incidence of Knee Osteoarthritis after Anterior Cruciate Ligament Injury- A Systematic Review

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### Abstract

**Background:** This is a systematic review of studies on the prevalence and risk factors of knee osteoarthritis more than four years following anterior cruciate ligament tear.

**Methods:** A systematic search was performed in PubMed, EMBASE and AMED. Inclusion criteria were studies involving patients with isolated anterior cruciate ligament injury or combined with other knee meniscal or ligaments injuries treated by operative or non-operative methods and assessed by radiological clinical evaluation tools and radiological classification systems. Coleman modified score was used to assess the methodological quality of the included studies.

**Results:** Five prospective, three of which were randomised controlled trial, and three retrospective studies were included. All studies were of good quality with Coleman modified score higher than 55. The mean score was 76 prevalence of knee OA following ACL injuries, varying between 0% and 59%. Meniscal injury and duration between injury and surgery were found to be the most common risk factors for knee OA following ACL injury.

**Conclusion:** This systematic review of good quality studies suggests that the prevalence rates of knee osteoarthritis after anterior cruciate ligament reconstruction varies between 0 to 59% Patients with combined ACL and meniscal injury. There was wide variation in the reported knee OA prevalence. These variations are attributed to factors such as differences in study population, study design, participant's level of activity, reconstruction approaches, post-operative rehabilitation programme and radiological classification used. Overall, the modified Coleman methodology score was high for the included studies. Only one study included non-operatively treated patients making comparison between the outcome of operative and non-operative approach difficult.

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

### I. Introduction:

The ACL is a strong ligament connecting the femur to the tibia. Anatomically, it has two bundles, the Antero-medial, which originates from the proximal part of the femoral insertion to the antero-medial part of the tibial insertion. This bundle becomes loaded and stretched during knee flexion, and the poster-lateral bundle inserts into the postero-lateral part of the tibial plateau which gets loaded and stretched during knee extension<sup>1</sup>. The main function of the ACL is to support and stabilise the tibia from anterior displacement relative to the femur as well as stabilise internal and external rotation, valgus and varus movements of the tibia over the femur<sup>2</sup>. ACL injury is one of the most common injuries to ligaments of the knee and accounts for approximately 30 injuries per 100,000 of the population<sup>3</sup>. However, there are more than 100,000 new ACL injuries that happen each year<sup>4</sup> (Agel et al., 2005). ACL is a common injury for those playing sport and among the general public. It is more common in the 15-25 age group<sup>4</sup>, particularly those involved in pivoting sports like football, tennis. Seventy percent of ACL injuries happen in non-contact situations when the player lands with external rotation of the tibia in relation to the femur with the knee fully extended<sup>5</sup>. Research shows that women are at higher risk than men<sup>4,6</sup>.

In people with ACL injuries, knee function impairment might be demonstrated in the form of limited ROM, muscle weakness and pain leading to limitation of daily living or sports activities<sup>7</sup>. One of the most reported consequences of an ACL injury is lack of dynamic knee stability, where stability of the joint is not held during fast changes of position during open and closed chain activities<sup>8</sup>. Quadriceps are some of the most affected muscles following an ACL injury and reconstruction<sup>9</sup>. ACL Reconstruction has a range detrimental effect on joint function such as: reduced muscle function, reduced ROM and neuromuscular deficits<sup>10</sup>. Joint effusion is found to be associated with reduced knee function as well<sup>11</sup>

The long term effect of ACL reconstruction and rehabilitation on knee function has been discussed extensively in the literature. <sup>12</sup>Deehan conducted a case series study, which demonstrated the 15 year outcome of ACL reconstruction with emphasis on knee functions for 90 patients who had isolated ACL injury. The study used a good range of outcome measures including ROM, Lachman and pivot shift tests, single leg hop test, lysholm knee score, radiographic assessment and International Knee Documentation Committee evaluation. Study results

indicated good ligament stability, ROM and subjective outcome measures at 15 years after surgery with kneeling pain as a common persistent problem. The radiological assessment has indicated signs of OA, although the severity of these signs was not associated with the level of joint stability. 13 Daniel conducted a prospective study to investigate the fate of 292 patients who had ACL injuries. These patients were treated either surgically or non-surgically. The study results indicated that in the five-year follow-up all the participants who were treated by non-surgical approaches returned to normal sports activities, and those who underwent reconstruction developed a higher level of OA compared with the non-operated patients. ACL Injuries can be clinically treated by conservative rehabilitation or surgical repair followed by post-surgical rehabilitation. The clinical decision regarding which treatment pathway is usually made by the surgeon and the patient<sup>14</sup>. Conservative, on-surgical, rehabilitation aims to restore the joint dynamic stability and function, through strength and neuromuscular training<sup>2</sup>. Quadriceps weakness is evident after anterior cruciate ligament (ACL) injury, which might affect the knee function post operatively<sup>15</sup>. Knee osteoarthritis (KOA) is one of the major causes of pain and physical disability in older adults. This is a dynamic disease that is metabolically active and includes both destruction and construction mechanisms that could be activated by injuries from either biochemical or mechanical events<sup>1</sup>. No definitive treatment was found to be superior and the patho-mechanics are still not well understood<sup>1,16</sup>. There are a range of structural changes associated with knee OA, which include damage or loss of articular cartilage, remodelling and sclerosis of the subchondral bone, subchondral cysts formation and osteophyte formation<sup>17</sup>.

## II. Materials And Methods

### Aims of the study

- To review the reported prevalence of knee OA after ACL injuries treated with conservative treatment or surgery with a follow-up more than four years.
- To evaluate the reported risk factors for knee OA following ACL injury.

Literature search

S.N	Table 1 : Search Terms	
1	Anterior cruciate ligament	13259
2	Knee joint	62929
3	Knee Joint OR ligament	108585
4	Knee injuries	24488
5	Osteoarthritis	53943
6	Epidemiologic studies	1574831
7	Epidemiology	1612945
8	Retrospective studies	481967
9	2 OR 5	104397
10	1 Or 3 Or 4	77474
11	6 Or 7	2701369
12	9 AND 10 AND 11	2896

**Table 1:** Search Terms

Systematic searches were carried out in the following databases: PubMed, Medline, CINHALL, AMED, OVID, Cochrane Library and PEDRO, from the inception of the databases to October 2013. MeSH terms and Boolean operators were used for journal articles related to ACL and osteoarthritis. The searches were conducted by the primary researcher. The search strategy and specific search terms used are explained in table (1). The abstracts of the search results were reviewed by the main researcher to identify the studies that match the inclusion criteria. If the information given in the abstract was not sufficient to make a decision, the full text version of the article was reviewed.

### Design:

Research methodology as the path to finding an answer to a research question<sup>18</sup>. Systematic review of the literature in this study attempts to answer the research question by systematically evaluating related literature. It summarises their results in order to identify the prevalence of knee Osteoarthritis following ACL injuries. Over 20,000 journals and two million articles are published every year. This increasing amount of available papers does not make it easy for health professionals to conclude clinical facts and recommendations. Therefore, systematic review is considered to be at the highest level of the evidence hierarchy<sup>19</sup> as it offers the researcher opportunity to contribute to the literature via exploring the available studies related to the topic of interest and conclude some evidence that could be applied in clinical practice<sup>20</sup>. The aim of the PRISMA Statement is to assist researchers with improving the reporting of systematic reviews and meta- analyses<sup>21</sup>. A critical literature review is a valuable scientific method to summarise, critically appraise and communicate the

results of available research<sup>22</sup>. Therefore, it is helpful in pooling together results from separately conducted research related to the prevalence of KOA following ACL injuries. In addition to the previous attributes, systematic reviews are important to identify gaps in the current literature and guide future research activities<sup>23</sup>.

### **Inclusion Criteria**

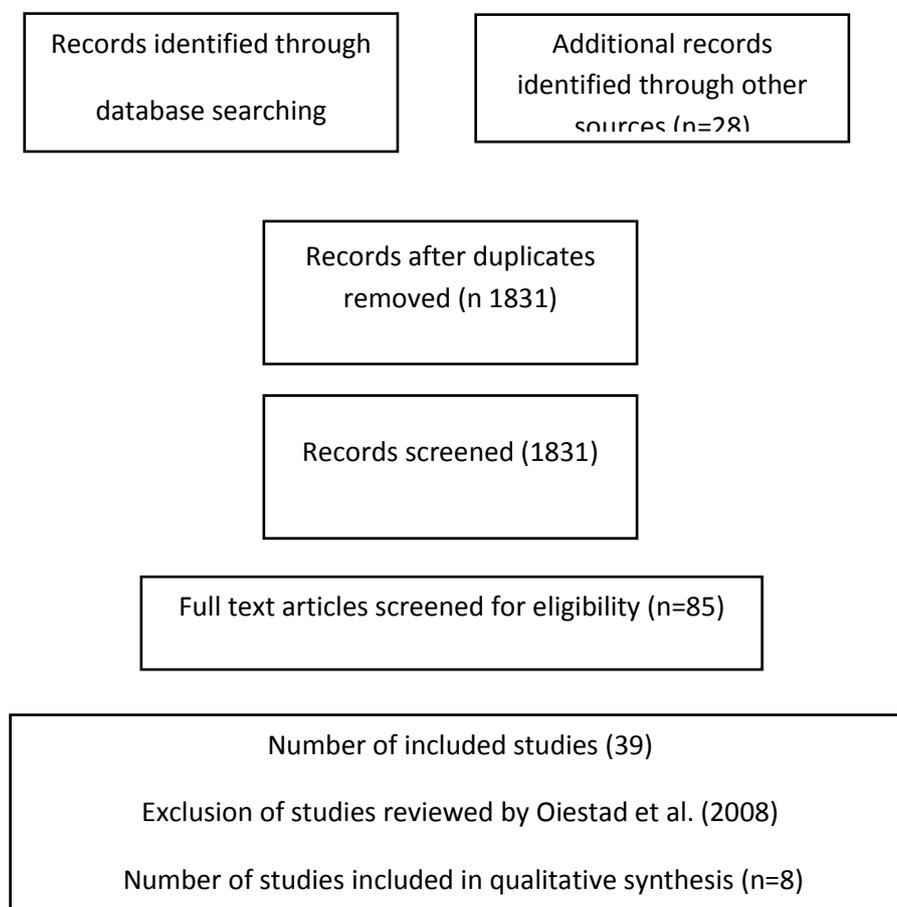
The inclusion criteria were prospective or retrospective studies in English or translated into English, published between 1960 and 2013. Studies might include male or female adult subjects with ACL injury and treated surgically by any type of technique or using any type of graft or treated non- surgically by rehabilitation programme. The follow-up time was more than four years.

### **Exclusion criteria**

The exclusion criteria were not prospective or retrospective case studies, and articles that reported individuals with ACL injury associated with fractures. These exclusion criteria were established to minimize the clinical heterogeneity of the review outcomes..

### **Search results:**

Figure 1 shows the results from the search strategy and the application of the PRISMA flow diagram<sup>24</sup>. A total of 2896 studies were identified using the search strategy from the inception of the databases until October 2013. After removing duplicates, 1831 studies were screened against the inclusion criteria, 85 full text articles were assessed for eligibility and finally 39 studies were identified. Studies that were included<sup>25</sup> were excluded to avoid duplication and finally four studies were assessed as prospective and three studies were assessed as retrospective.



**Figure 1**

Data collection and analysis: Data was read and collected by the main reviewer using data extractions form (see table 2).

**Table 2** Characteristics of Studies included in the Systematic Review

Authors	No. of Subjects	Description of Subjects	Additional Injuries and/or Re-injury at Follow-up	Follow-up, years	Initial Treatment of ACL	Radiologic Findings	CMS score
Song et al., 2013 Prospective RCT	112	80 male, 32 female; mean age=33.1y ACL injury confirmed on MRI or arthroscopically, with meniscus injury Or LCL or interchondroal injury	58with meniscal injury 18 had meniscal repair Meniscectomy	4	patients had either single or double bundled reconstruction BTB graft single bundled n=60 double bundled n= 52	single bundled group: grade 0=80,gradeI=21,grade II=7,gradeIII=4,grade IV = 0; Non operative group: grade0=8,gradeI=10, grade II=4,gradeIII=3,	76
Streich et al., 2013 Retrospective	40	12 Female 10 male Mean age 29 y isolated ACL injury	Excluded from study	10	Isolated ACL injury using quadrupled hamstring allograft	IKCD at 10 Y follow up 29 knees =normal Grade A 11 Knees=nearly normal Grade B	67
Soumalain et al 2012 Prospective	90	61 Male 29 Female Mean age = 33 ACL Injury confirmed on arthroscopy with meniscal injury	excluded from study	5	Patient had either single bundled or double bundled reconstruction n=30 single bundled n=60	KL Classification Grade 0= 25 Grade I =56 Grade II =9 Grade III and IV = 0	87
Strewer et al., 2011 et al., 2012 prospective	73	Median age=43y(range, 24-63y);46men,27 women; isolated ACL injury at presentation with no articular surface damage or meniscus lesions	Excluded from study	13	Isolated ACL-R using BTB graft	K/L classification 13.5-y=4.1%grade 0, 41.1% grade I, 32.9% grade II,16.4% grade III,	63
Streich et al., 2011 Retrospective	80	56 male 24 female mean age 25.8	excluded from study	15	isolated knee injury ACL reconstruction conservative treatment	IKDC at 15 y follow up 40 operative Grade B 42 non-operative Grade B 60 Operative Grade C 57 No-operative Grade C	65
Li et al., 2011 retrospective-case control	249	Not mentioned	Excluded from the study	7.8	Isolated ACL-R using Single bundle	K/L Classification Grade 0 =49% Grade 1=35% Grade 2=10%	85

						Grade 4= 2%	
Oiestad et al., 2010 Prospective	221	90 females, 120 males; mean age=39.1 isolated ACL or in combination with meniscus injury and/or chondral lesion and/or MCL injury, with uninjured contralateral knee	Isolated ACL injury in 82 patients, medial meniscus injury in 39 patients, lateral meniscus injury in 19 patients, medial and lateral meniscus injury in 26 patients, meniscus and MCL in 5 patients, meniscus and MCL and chondral lesion in 3 patients, meniscus and chondral lesion in 29 patients, chondral lesion only in 7 patients	12.5	ACL-Reconstruction using BTB graft (n= 181) and hamstring tendon autograft (n=29);137 partial meniscal resections and 13 meniscal sutures performed	Injured knee K/L=9% grade 0, 20% grade I, 47% grade II, 19% grade III, 5% grade IV	87
Keays et al., 2010 Prospective	56	18 Female 40 Male Mean age 27 y isolated ACL or in combination with meniscal or chondral injury.	Isolated ACL or combined with meniscal injury		ACL-Reconstruction using BTB graft (n= 29) and hamstring tendon autograft (n=29)	K/L= grade I= 48 % 12% grade II, 36% grade III	67

### III. Result

#### Review of the literature:

Overview of the studies

Studies were collected from PubMed, Medline, CINHALL, AMED, OVID, Cochrane Library and PEDRO databases. All studies were published in peer reviewed journals, e.g. American Journal of Sport Medicine and Physiotherapy. Eight studies were included in this review. The studies investigated the prevalence and risk factors for knee osteoarthritis following isolated ACL or combined with meniscal or chondral lesions. 921 subjects were included in this review with sample size ranging from 40 to 249 subjects with mean age of 25.8 to 39. The patients had either isolated ACL injury (n= 614 subjects) or ACL and associated injuries (n=307 subjects). ACL and associated injury were evaluated by clinical and radiologic methods or using both methods. The studies were conducted in the USA, Australia or European countries. All the studies used radiological assessment to evaluate KOA at the follow-up. One study included the radiological findings of 40 subjects who received non-operative treatment; seven studies included radiological assessment of 841 patients treated surgically; and three studies included radiological assessment of 40 subjects treated non-surgically and surgically<sup>26</sup>.

There were 881 patients treated surgically by different surgical approaches. Bone-patellar tendon-bone grafts were performed on 395 subjects, 98 subjects were surgically treated using hamstring tendon graft and 288 were treated by combination of both grafts. One study used single bundled and double bundled grafts. Forty patients were treated by non-operative methods<sup>26</sup>. This included physiotherapy and quadriceps and/or lower limb strengthening for a minimum of three months and or lifestyle modification instructions.

#### Methodological Quality

The results of the study quality assessments are presented in table 3. None of the studies scored the complete mark of 90 and fulfilled all the criteria. The highest score was 87, achieved 30, and the lowest score was 65<sup>26</sup>. The prospective studies achieved a mean modified CMS of 76, with a highest score of 87 and a lowest score of 67. The retrospective studies achieved a mean score of 72, with a highest score of 65 and a lowest score of 85. Studies that achieved scores above 55% were considered of high quality<sup>27</sup>.

Table 3

Study	Study size	Mean follow-up, years	No. of different treatment procedures	Type of study	Diagnostic certainty	Description of treatment given	Outcome criteria	Procedure for assessing outcomes	Description of subject selection process	Total Score
Song et al. (2013)	10	5	10	15	3	3	7	8	15	76
Striech et al. (2013)	7	5	10	0	5	3	7	12	18	67
Suomalainen et al. (2012)	10	5	10	15	5	5	7	12	18	87
Struwer et al. (2011)	10	5	10	0	5	3	7	5	18	63
Streich et al. (2011)	10	5	10	0	5	5	3	9	18	65
Lei et al. (2011)	10	5	10	15	5	3	7	12	18	85
Oiestad et al. (2010)	10	5	10	15	5	5	7	12	18	87
Keays et al. 2010	7	5	10	15	0	0	7	0	18	67

Table 4 Risk Factors for Development of Knee OA following ACL rupture

Study used Discriminate analysis	Strong Risk Factors
Striech et al (2013)	Meniscectomy-meniscal injury-duration between injury and surgery-BMI -Age
Keays et al 2010	Meniscectomy-meniscal injury-duration between injury and surgery

Table 5

*Modified Coleman Methodology Score (Oiestad et al 2008)*

Section	number or Factor	Score
<b>Criteria</b>		
<b>Part A</b>		
Only one score to be given for each section		
Study size: number of patients	>60 41-60 20-40 <20, not stated >4	10 7 4 0 5
Mean follow-up, years		
no. of different treatment procedures included in each reported outcome. More than 1 method may be assessed, but separate outcomes should be reported	1 procedure  More than 1 method but >90% of subjects undergoing the 1 procedure not stated, unclear, or <90% of subjects undergoing the 1 procedure	10  0
Type of study	prospective cohort study/randomized Retrospective cohort study	15 0
Diagnostic certainty	in all in >80% in <80%	5 3 0
Description of treatment given	Adequate (technique stated and necessary details of that type of procedure given)  r (technique only stated without Elaboration) Inadequate, not stated, or unclear	  5 0
<b>Part B</b>		
Scores could be given for each option in each of the 3 sections		
Outcome criteria	Outcome measures clearly defined Position Reported either inter-rater or intra-rater reliability Use of outcome criteria that has reported good reliability	4 3 3 3
procedure for assessing outcomes	Subjects recruited (results not taken from surgeons' files) investigator independent of surgeon/therapist Written assessment Completion of assessment by subjects themselves with minimal investigator assistance	5 4 3 3
Description of subject selection process	Selection criteria reported and unbiased Recruitment rate reported >80% Recruitment rate reported <80% Eligible subject not included In the study satisfactorily or 100% Recruitment	5 5 3 5
Total score/90		

The Critical Appraisal Skills Programme 10 Guide Questions (Table 5) was used to explore the strengths and weaknesses of a research paper. In the present literature review, each paper is analysed individually. The initial step in analysing a research is critiquing the aim or purpose of the study<sup>28</sup>. All the included studies demonstrated a very clear and well formulated title. It is important that a study has a well- defined title to attract more readers and give them a clear idea of the main objectives<sup>29</sup>. This could not occur if the title describes the study design, sample population, time and duration of the study. Observational study design is considered the most frequently used research method to observe prevalence and risk factors of pathologies<sup>30</sup>. Most of the follow-up studies on subjects with ACL injuries were either prospective or retrospective cohort studies with few RCTs as well. Cohort studies are characterised by observation of interventions, exposures or outcome over a certain period as they occur naturally from the time of inclusion<sup>31</sup>. A case-control design also includes observation of a control group without the exposure of interest. There are different factors that might affect the validity of cohort studies. This includes selection bias, confounding factors and possibility of high drop rate of participants at the follow-up. A common methodological bias issue related to long-term follow-up studies is the follow-up rate of the study participants. Follow-up rate might be affected by the difficulties of finding the study participants at the time of follow-up, participants' readiness and motivation to participate as well as cost related issue particularly for those who live a long distance away.

<sup>32</sup>This depends on the type of loss, whether it is systematic or random, i.e. considerable bias might be taken into account if there is a systematic loss of participants to follow-up of 20%. On the other hand, random loss to follow-up of up to 60% has been shown to give unbiased results. These figures might be different with RCTs in which 20% loss at follow-up or more is considered a real threat to the study validity<sup>33</sup>. The prospective cohort study design is the most adequate design for evaluating long-term knee function and development of knee OA in subjects with ACL injury and reconstruction.

Song et al., 2013

This prospective randomised controlled trial (RCT) study investigated whether double bundled ACL reconstruction is superior to single bundled technique to prevent OA or provide better stability and function. The study recruited 130 patients with unilateral ACL injury and no instability or previous radiological evidence of KOA (more than grade 2 Kellgren and Lawrance classification). The participants were prospectively randomised into a double bundled (n= 65) or single bundled (n=65) group. Degree of osteoarthritis was evaluated according to the Kellgren-Lawrance grade prior to the surgery and at the time of the follow-up four years later. The number of patients with one degree or more progression of OA from pre to post operation was determined. Lachman and pivot-shift tests were used to evaluate stability and Lysholm knee score, Tegner activity score and International Knee Documentation Committee (IKDC) subjective scale were used to evaluate the functional outcomes. Using a combination of reliable subjective scales and objective measures is essential to evaluate improvement in functional activities<sup>9</sup>. Six patients dropped at the time of the follow-up due to graft failure and had revision surgery. This drop rate is not big enough to produce bias<sup>33</sup>. Five patients (9.6%) in the double bundled group and six patients (10%) in the single bundled group showed more advanced OA radiological changes at the follow-up. Within six month of surgery, all patients regained full range of knee movement and no significant differences in stability were found. Also, functional scales did not show significant difference between groups in terms of changes in functional activities except for International knee Documentation Committee where (P=0.03). The time from injury to surgery, age at surgery and sex follow-up periods were not significantly different between the two groups and not considered as risk factors of KOA in this study. However, patients who underwent meniscectomy or meniscal repair showed more degenerative changes compared with those who did not (P=0.04). The authors clearly stated the aim of the study and established the rationale of conducting this research. They explored the available evidence that supports the prevalence of KOA following single bundled ACL reconstruction due to the post-surgical changes in knee kinematics. Considering the evidence from anatomical studies that suggest better knee kinematics following double bundled techniques, and the lack of randomised trial to investigate prevalence of KOA following the double bundled technique, the authors have used this as a basis to conduct the trial.

Streich et al., 2013

This retrospective study investigated the long-term outcome of ACL reconstruction using quadrupled semitendinosus tendon. The rationale behind the study was clearly explained by the authors. Patellar tendon bone allograft is widely used in ACL reconstruction, although it has several complications such as high incidence of anterior knee pain, quadriceps weakness and limited range of knee extension. Therefore, hamstring tendon allograft is becoming more popular. However, short- and long-term studies have indicated several postoperative complications associated with hamstring tendon allograft too, including hamstring weakness and increased joint laxity. That said, no studies have been conducted to investigate the long-term effect of hamstring tendon allograft using the quadrupled graft, which is stronger and bigger in size and might provide better results. There is need for such a study. In this study, 101 patients were diagnosed by clinical examination and confirmed

with arthroscopy, which improved the validity of the diagnosis. The patients underwent ACL reconstruction using the quadrupled hamstring graft, and those with chondral, ligamentous or meniscal injuries were excluded. This was helpful to produce a homogenous sample. In total, 59 patients participated. There was a random drop rate of 19 patients due to various reasons (the details of the dropped patients are mentioned by the authors). Details of the surgical procedure were clearly set out to help reproducibility. However, all surgeries were performed by one senior surgeon, and no details were given about surgeon experience. Final assessment at 10 years follow-up period was performed by two independent blinded observers to minimize bias. The assessment was conducted using radiographic examination following the International Knee Documentation Committee guidelines. 34Valley considered this classification as valid and reliable classification to assess knee degenerative changes. Lysholm and Tegner activity scores were used for clinical evaluation. Although the study has used the contralateral knee for comparison at the end of the follow-up period, it is not clear whether initial assessment was preoperatively conducted. This might raise questions regarding how improvement or deterioration could be accurately detected and might affect the validity of the study. The study mentioned what was permitted and when during the rehabilitation process, but no details were given about the rehabilitation setting, components of the exercise programme or the physiotherapists who supervised the rehabilitation programme. This seems to be an issue with all the previous studies and might negatively affect the reproducibility.

Statistical analysis and results were clearly discussed using graphs. Study results showed that 11 patients had mild evidence of degeneration and graded as B by the International Knee Committee Documentation. However, the rest of the sample was graded as A, which is normal. No patient was classified as grade C or D, which is defined as severely abnormal by the International Knee Committee Documentation guidelines. The study suggested negative correlation between pivot shift and clinical assessment score (IKDC and Lyshom scores), which is in line with previous findings and earlier research by the authors of this study<sup>35</sup>. Patients with negative pivot test had better results on IKDC and Lyshom scores and those with signs of rotational instability. The study also showed positive correlation between age and High BMI index and knee degenerative changes. Overall, the study was the first to investigate the long-term outcome of ACL reconstruction using quadrupled hamstring graft, although some issues might affect the reproducibility and generalisability of the study such as small sample size, methodological flaws related to lack of details regarding pre-operative clinical assessment, limited details of the rehabilitation process and surgeon experience. However, it opens the door for future research to be conducted using larger sample size.

### **Summary of the literature review**

All the studies demonstrated aim and objectives based on sound justification. No sample size calculation was performed in any of the included studies. Therefore, there was unjustifiable variation in sample size; number of subjects varied between 40 and 24936. The source of sample was stated in all the studies as well as inclusion and exclusion criteria. All studies mentioned the number of patients lost at follow-up and explained the causes of the drop rate at final follow-up. Description of the sample population was clear to help with the reproducibility of the study method in most of the studies. However, the details provided varied, with most of the studies giving a detailed description of the sample sex and mean age. Others provided further details about patient level of activities. Additionally, the studies used a range of reliable clinical and radiographic outcomes. Some studies used a wide range of measures<sup>37</sup>, while others used one measure to assess each aspect of the clinical examination<sup>37</sup>. All the studies clearly described the surgical procedures to improve reproducibility. However, all the studies except that of failed to provide information on surgeon experience<sup>38</sup>. Details of the post-operative rehabilitation programme consistently lacked details in all the studies except for Oiestad. Details of assessor blinding were considered in, but this was not considered in any other study<sup>39</sup>. Five studies used prospective study design, which was considered by a previous review as the most appropriate to investigate prevalence of OA following ACL rupture. This study design is superior to the retrospective design. The chances of recall bias and loss of participants at follow-up is less compared with retrospective study design<sup>40</sup>. Overall, the studies demonstrated different levels of methodological quality. A common issue which may have affected the reproducibility of these studies was limited detail as regards some parts of the methods such as post-operative rehabilitation, assessment procedures and lack of assessor blinding. This chapter summarised important points that included an overview of the main characteristics of the studies, the results of assessing the risk bias using the Modified Coleman Methodology Score and the methodological quality, outcomes and recommendations of each study.

## **IV. Discussion**

### **Summary of the main results**

Eight studies of good quality (Coleman Modified score CMS > 55) including a total of 921 subjects with ACL injury were included in this systematic review based on the inclusion criteria. Five of the studies were assessed to have a prospective study design, and three studies were assessed to have a retrospective study

design. The studies achieved a mean Coleman Modified score (CMS) of 74.6 of a total score of 90. The prospective studies disclosed higher methodological quality than did the retrospective studies. Mean modified CMS for the prospective studies was 76 and 47 for the retrospective studies.

In this review two different radiological classifications were used by the studies: International Knee Documentation Committee and Kellgren-Lawrance classification. In studies which used International Knee Documentation Committee grade (A), there was no evidence of radiological degeneration and grade D indicated severe degeneration. In studies which used Kellgren and Lawrence classification, grade 0 indicated no evidence of radiologic classification and grade IV indicated severe degeneration. To maintain consistency, Grade B in the International Knee Documentation Committee and Grade II in the Kellgren and Lawrence classification were considered as the cut-off grade to indicate degeneration at the follow-up evaluation<sup>41</sup>.

The reported prevalence of knee OA in this review varied between 0% and 59%. Five of the studies included subjects with isolated knee injuries and showed prevalence of knee OA of 0% (Soumalainen CMS score of 87) to 49% (Streich – SMS score of 65). Studies with subjects combining ACL and meniscal injury showed prevalence of knee OA which varied between 0% (Streich et al. 2013 – CMS score of 67) and 42.3 % (Oiestad CMS score of 87).

The study which included subjects with isolated knee injury and achieved second highest SCM score reported knee OA prevalence of 0%<sup>44</sup>. In comparison, the study with the highest CMS score and included subjects with combined ACL and meniscal injury reported a knee OA prevalence of 42.3%. In summary, the study results indicated that isolated ACL injury have low prevalence of radiologic knee OA compared with those with combined ACL and meniscal injury. Only one study with CMS score of 65 compared subjects treated by operative and non-operative approaches. The study reported no significant difference between the two groups with regard to the prevalence of knee OA.

The review of these results shows a wide range of variations in the reported knee OA prevalence. These variations might be attributed to different factors such as study population, study design, participant's level of activity, reconstruction approaches, post-operative rehabilitation programme and radiological classification used. These factors were considered by previous review. However, this review included more prospective studies; three were randomised controlled trials and the mean CMS score was higher than that of the study by the CMS score for the included studies in this review was relatively higher than those included.

One prospective case control study with CMS of 67<sup>42</sup> and one retrospective study with CMS score of 85% used regression analysis to identify risk factors for development of knee OA following ACL injury. Different risk factors were reported by these two studies; the strongest factors were concurrent meniscal injury, duration between injury and surgery and Body Mass Index (BMI). A previous review considered the same factors as strong predictors as well.

Although previous studies have highlighted the positive impact of post-operative rehabilitation on the outcome of ACL reconstruction<sup>43</sup>, most of the included studies did not highlight the possible effect of lack of supervised rehabilitation on the long-term clinical outcome. Future studies need to provide participants with comprehensive rehabilitation exercise programme in order to confirm post-operative rehabilitation as a possible risk factor for development of knee OA.

### **Implication of the study**

The results of this study, which indicate low to moderate prevalence of knee OA following ACL reconstruction, support the findings of previous reviews. In line with previous studies, this review reported meniscal injury and time between injury to surgery as strong predictors of knee OA following ACL injury. The implication of these results on the timing of surgical approach, surgery performed early after the incidence of ACL rupture, might prevent further damage to the meniscus and articular cartilage and, consequently, reduce the risk of arthritis and prevent reoccurrence of rupture. In addition, such immediate surgical interference will reduce the age at surgery and the risk of patello-femoral OA.

### **Strengths of the review**

One of the key strengths of this review is the inclusion of five prospective studies, three of which are randomised controlled trials. All studies including the three retrospective cohort studies scored over 55 in the Coleman modified score, which indicates good quality. Inclusion of good quality studies is important to reduce the biased outcomes<sup>44</sup>.

### **Limitations of the review**

The study has a few limitations that might affect its validity. The data search was conducted by the researcher; unfortunately, it was difficult due to time constraint to use an independent librarian to conduct the data search to ensure that all the relevant studies were included. Although the researcher took all the necessary measures to identify the relevant literature, as a novice researcher there is possibility of error or inaccuracy in the data search.

The researcher expanded the electronic search to cover the period from the inception of the included databases to October 2013, in order to identify any literature not included in the previous reviews. The screening of this large number of abstracts and main articles was a time consuming process. The researcher felt at the time that this would be helpful to improve the validity of the study. The search results identified the same studies included in the previous review. The researcher considers this as a beneficial learning experience and good attempt to improve the validity of the review. Due to time limitation, only one reviewer conducted the data extraction and quality scoring processes; this might affect the validity of the review due to increased risk of reviewer bias<sup>45</sup>. In this review a qualitative (narrative) analysis was conducted to analyse the findings of the studies and quality score. This method of analysis is considered to be subjective in nature as it reflects the reviewer's interpretation of the results, particularly in the absence of a peer reviewer, due to lack of statistical analysis. There were many variations among the studies which affected the data analysis process. Heterogeneity of the studies due to variable study design, assessment tools and population used in the trials made it difficult to conduct a quantitative analysis (meta-analysis) in addition to the narrative analysis in this review.

These variations in age and other variables in individual studies might lead to statistically heterogeneous outcomes. Clinical and statistical heterogeneity are closely related to each other<sup>46</sup>. Considering that ACL injury is more linked to sports related activities, patients with higher level of motivation and desire to return to sport early might be more willing to participate in such studies. Therefore, this might produce evidence of selection bias<sup>47</sup>.

### **Recommendations for future study**

Based on the results of this study, it is recommended that further prospective studies are conducted using less variables such as outcome measures, previous level of activity and age. Existence of such good quality trials will produce good quality meta-analysis studies. Such high level evidence is essential to guide change in clinical practice. Future studies might use regression analysis to investigate the risk factors for developing knee OA following ACL rupture. Although risk factor was a common aim among the studies in this review, only two studies used regression analysis to produce valid results.

### **V. Conclusion**

In conclusion, based on the quality assessment of the included studies and narrative analysis, the prevalence of knee OA was found to vary between 0 and 58% in this review. The highest prevalence was 49% reported by a retrospective study with Coleman modified score of 87%. Lowest prevalence was 0 and achieved by a prospective study with Coleman modified score of 85%. Different risk factors were considered as predictors of knee OA following ACL injury. Among these factors, meniscal injury, time between injury and surgery and BMI were found to be the strongest predictors. This review supports the evidence that the prevalence of knee OA following ACL injury is under 50% as described by a mixture of good quality prospective and retrospective studies. Future research might need to be prospective and pay more attention to the importance of post-operative rehabilitation and other variables that could lead to heterogeneity of the studies such as population and level of activities.

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