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No negative effect on patient-reported outcome of concomitant cartilage lesions 5–9 years after ACL reconstruction

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Abstract
Purpose To compare patient-reported outcome 5–9 years after anterior cruciate ligament (ACL) reconstruction in patients with and without a concomitant full-thickness [International Cartilage Repair Society (ICRS) grade 3–4] cartilage lesion.
Methods This is a prospective follow-up of a cohort of 89 patients that were identified in the Norwegian National Knee Ligament Registry and included in the current study in 2007, consisting of 30 primary ACL-reconstructed patients with a concomitant, isolated full-thickness cartilage lesion (ICRS grade 3 and 4) and 59 matched controls without cartilage lesions (ICRS grade 1–4). At a median follow-up of 6.3 years (range 4.9–9.1) after ACL reconstruction, 74 (84 %) patients completed the Knee Injury and Osteoarthritis Outcome Score (KOOS), which was used as the main outcome measure. Secondary outcomes included radiographic evaluation according to the Kellgren–Lawrence criteria of knee osteoarthritis (OA).
Results At follow-up, 5–9 years after ACL reconstruction, no statistically significant differences in KOOS were detected between patients with a concomitant full-thickness cartilage lesion and patients without concomitant cartilage lesions. Radiographic knee OA of the affected knee, defined as Kellgren and Lawrence ≥ 2, was significantly more frequent in subjects without a concomitant cartilage lesion ($p = 0.016$).
Conclusion ACL reconstruction performed in patients with an isolated concomitant full-thickness cartilage lesion restored patient-reported knee function to the same level as ACL reconstruction performed in patients without concomitant cartilage lesions, 5–9 years after surgery. This should be considered in the preoperative information given to patients with such combined injuries, in terms of the expected outcome after ACL reconstruction and in the counselling and decision-making on the subject of surgical treatment of the concomitant cartilage lesion.
Level of evidence Prognostic; prospective cohort study, Level I.

Keywords Anterior cruciate ligament · Reconstruction · Cartilage lesion · Outcome · KOOS

Introduction

Anterior cruciate ligament (ACL) injuries are often associated with other knee injuries. The prevalence of concomitant partial-thickness and full-thickness cartilage lesions at the time of anterior cruciate ligament reconstruction (ACLR) has been reported to be 20.2 and 6.4 %, respectively, in the Norwegian and Swedish knee ligament registries [24], and similar rates have been found in the USA [19]. Even though concomitant cartilage lesions at the time of ACLR have shown to be a predictor of later knee osteoarthritis (OA) [6, 14, 15, 18], reports on patient-reported outcomes are conflicting. The current literature includes several studies reporting no negative effects of concomitant cartilage lesions on patient-reported outcome after ACLR

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[26, 27, 29]. In contrast, two of the most comprehensive studies performed on this topic [5, 22] both conclude that full-thickness cartilage lesions present at the time of ACLR predict inferior patient-reported outcome 2–6 years after surgery.

The current study is the second report on a longitudinal follow-up of a cohort of ACL-injured patients with a concomitant full-thickness cartilage lesion [International Cartilage Repair Society (ICRS) grade 3–4] [3] and a matched control group of ACL-injured patients without cartilage lesions (ICRS grade 1–4), as described in the index study by Hjermundrud et al. [13]. In the first prospective evaluation of this cohort, at a median follow-up of 2.1 years after ACLR, patients with a concomitant cartilage lesion fared worse in terms of patient-reported outcome and improvement during the follow-up period, compared to the control group [23].

The main purpose of the present study was to broaden the knowledge on midterm to long-term prognosis after ACLR in patients with concomitant full-thickness cartilage lesions, and by that, support decision-making regarding different treatment options, and information to the patients. Consequently, the cohort was prospectively followed for 5–9 years after ACLR to investigate whether there at follow-up were any differences in patient-reported outcome in patients with and without a concomitant full-thickness cartilage lesion. To our knowledge, this is one of very few level-1 prognostic studies on this subject matter. The null hypothesis was that the patient-reported outcome would be similar for patients with a concomitant full-thickness cartilage lesion compared to patients without cartilage lesions 5–9 years after ACLR.

Materials and methods

All patients were included from the Norwegian National Knee Ligament Registry (NKLR) which was established in June 2004 with the main objectives to register all surgical procedures performed on knee ligaments, and prospectively monitor the outcome, including revisions or any type of reoperations [10]. As a part of the immediate postoperative registration of patient, knee and surgery specific variables, the surgeons grade concomitant focal cartilage lesions according to the ICRS guidelines [3]. The Knee Injury and Osteoarthritis Outcome Score (KOOS) [21] is used as the patient-reported outcome measure in the NKLR and is administered to the patients prior to ACLR and at subsequent follow-ups. KOOS is a self-administered questionnaire consisting of 42 questions distributed between five separately scored subscales: Pain, Other Symptoms (Symptoms), Activities of Daily Living (ADL), Function in Sport and Recreation (Sport/Rec) and Knee-Related Quality of Life (QoL). Each subscale score is converted to a 0 (worst) to 100 (best) scale. It is considered to be a valid, reliable and responsive assessment tool for patients with ACL and cartilage injury [1, 4, 7, 21].

The data assembly is voluntary and entrants complete an informed consent form prior to surgery, allowing for later use of their registry data, including the KOOS questionnaire. The baseline national compliance rates of primary ACLR have been reported as 86–97 % for the registration form and 88 % for the KOOS questionnaire [11, 30].

A search performed among the 4849 primary ACLRs reported to NKLR by the end of 2007 identified 30 patients that met all of the following inclusion criteria: A full-thickness cartilage lesion (ICRS grade 3 or 4), age less than 40 years, no associated ligament or meniscus injury, no previous knee surgery, less than 12 months from ACL injury to ACLR and a complete preoperative KOOS questionnaire [13, 23]. These 30 patients constituted the study group.

For each patient in the study group, two control patients with an isolated ACL injury and no cartilage lesion of any ICRS grade were included from the NKLR by the end of 2007, generating 60 control patients. Apart from having no cartilage lesion, the control patients had to meet the same inclusion criteria as for the study group. The control patients were matched to the study patients according to age, gender, days from injury to surgery and type of graft. One control patient was excluded from the index data due to an incomplete preoperative KOOS questionnaire, leaving a control group of 59 patients.

In the study group, 22 (73 %) patients had a concomitant full-thickness cartilage lesion measuring 2 cm^2 or less, and 8 (27 %) were >2 cm^2. 20 (67 %) cartilage lesions were located in the medial tibiofemoral compartment, 6 (20 %) in the lateral femoral compartment and 4 (13 %) in the patellofemoral compartment. 23 (77 %) patients in the study group underwent ACLR without performing any simultaneous cartilage procedure, while a cartilage procedure was performed in 7 of the patients at the time of ACLR. Of these 7, 4 patients had a debridement procedure and 3 patients underwent a microfracture procedure.

Follow-up

At a median follow-up of 6.3 years (range 4.9–9.1), KOOS data were obtained from 75 (84 %) of the original 89 patients in the cohort. All 30 patients in the study group returned their KOOS questionnaires at follow-up, but one patient had to be excluded due to missing KOOS data from both matched controls. That study patient had a cartilage lesion <2 cm^2, localized to the lateral compartment. 13 patients in the control group were considered as lost to follow-up as they did not respond to reminders by postal mail or telephone, and one patient was because of

medical reasons unable to complete the KOOS questionnaire. The patients that were excluded at follow-up ($n = 2$) or lost to follow-up ($n = 13$) were also withdrawn from the preoperative KOOS data. Thus, KOOS data from 29 study patients and 45 control patients were available for statistical analysis.

Following repeated requests, 19 patients in the study group and 22 patients in the control group were available for radiographic examination at follow-up. The median time from surgery to radiographic examination was 8.2 years (range 6.4–9.8) for the study group and 8.4 years (range 6.7–9.8) for the control group. Standing radiographs were graded independently and blinded to group assignment by two of the authors (SU and JHR). Grading was done according to the original Kellgren and Lawrence criteria of knee (tibiofemoral) OA (0 normal to 4 severe) [16]. In cases of inconsistency in grading between the two evaluators, radiographs were reassessed and consensus agreement made.

Auxiliary data were assembled by questionnaires returned by postal mail or by patient interviews and included Tegner activity score [2, 28], height, weight and smoking status. At follow-up, these patient characteristics, together with age, gender distribution, time from injury to surgery, duration of the follow-up period and the ACL graft used were comparable between the study group and the control group, as outlined in Table 1. Moreover, all patients answered questions regarding any new traumas to the knee and/or any additional surgical procedures performed during the follow-up period.

Table 1 Characteristics of the study groups at follow-up

	Study group ($n = 29$)	Control group ($n = 45$)
Age (years)[a] ($n = 74$)	34.9 (6.8)	34.7 (7.4)
Follow-up (years)[a] ($n = 74$)	6.8 (1.5)	6.1 (1.3)
Time from injury to surgery (months)[a] ($n = 74$)	5.5 (2.5)	5.5 (2.6)
Gender[c] ($n = 74$)		
Females	8 (28)	13 (29)
Males	21 (72)	32 (71)
Right/Left ($n = 74$)	16/13	29/16
Body mass index[a] ($n = 73$)	25.1 (2.7)	25.5 (3.9)
Graft type[c] ($n = 74$)		
Hamstring tendons	17 (59)	25 (56)
Patella tendon/other	12 (41)	20 (44)
Smoking status[c] ($n = 72$)		
Non-smokers	22 (76)	35 (81)
Tegner activity level score[b] ($n = 51$)	4 (1–9)	4 (1–9)

[a] Mean and (standard deviation)

[b] Median and (range)

[c] Number and (percentages)

The study was approved by the Regional Ethical Committee of South-Eastern Norway, University of Oslo, ID 2013/180b.

Statistical analysis

The KOOS QoL subscale is regarded as the most sensitive when evaluating ACL-injured patients [21] and was consequently defined as the primary outcome measure.

Comparisons between the two groups within the cohort were performed using paired samples t test, and all mean differences and mean changes measured by KOOS are given with 95 % confidence intervals (CIs). In cases where KOOS were available for both control patients, the data were regarded as clustered and the average score were used in the analysis [17]. The significance of the observed between-group difference of proportions of radiographic OA was analysed using Fisher's exact test. Level of significance was defined as $p \leq 0.05$. According to the power analysis, 26 pairs of patients were needed at follow-up to detect a change or difference in KOOS QoL of 10 points given a power of 0.80, a significance level of 0.05 and a standard deviation (SD) of the difference between the study patients and the control patients of 17.2, which was the SD of the difference between the groups preoperatively [13, 23].

IBM® SPSS® (Statistical Package of Social Sciences) software version 22.0 was used for all statistical analysis.

Results

The mean KOOS scores at preoperative and at follow-up for the study group (ACL-injured patients with a concomitant full-thickness cartilage lesion, $n = 29$) and the control group (ACL-injured patients without cartilage lesions, $n = 45$) are presented as KOOS profiles in Fig. 1. As shown in Table 2, there were no statistically significant between-group differences in KOOS scores at preoperative, nor at follow-up. Correspondingly, when comparing the change over time (from preoperative to follow-up) in KOOS scores between the two groups, no significant differences were found (Table 2).

Table 3 displays the mean changes in KOOS scores from preoperative to follow-up in each group. The control group reported significant improvements in all KOOS subscales, while this was only true for the KOOS subscales pain, sport/rec and QoL in the study group. In both groups, the most prominent improvement from preoperative to follow-up was observed in the primary outcome measure KOOS QoL.

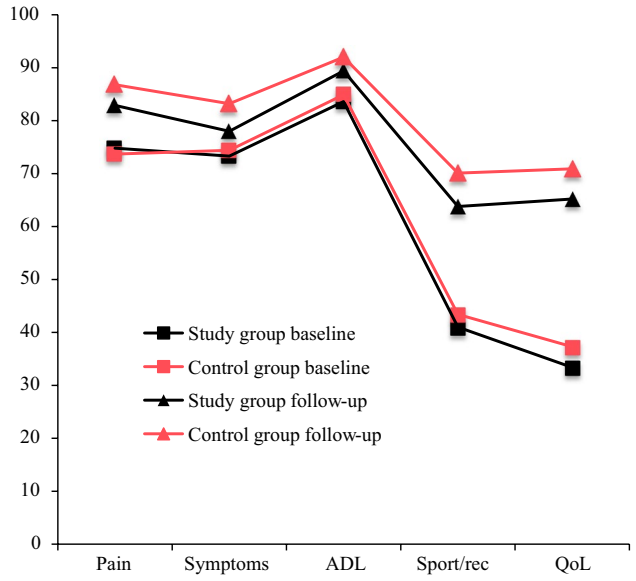

Fig. 1 Profiles of mean Knee Injury and Osteoarthritis Outcome Score (KOOS) of the study group (with a concomitant full-thickness cartilage lesion) and the control group (without concomitant cartilage lesions) at preoperative and at median 6.3-year follow-up after anterior cruciate ligament reconstruction

Radiographic OA was defined as Kellgren and Lawrence ≥grade 2 and was detected in the affected knee in 12 of the 19 patients available for radiographic follow-up in the study group and in 21 of the 22 patients available for radiographic follow-up in the control group ($p = 0.016$). The corresponding numbers for the contralateral, unaffected knees were 5 out of 19 and 9 out of 21, respectively. There were non-significant between-group differences in radiographic OA of the unaffected knee. The distribution of the assigned grades of radiographic OA of the affected knees is shown in Fig. 2.

During the follow-up period, 7 patients (24 %) in the study group and 10 patients (22 %) in the control group underwent a total of 23 subsequent knee surgeries (Table 4).

Discussion

The main finding of the present study is that concomitant full-thickness cartilage lesions present at the time of ACLR did not show to be a significant prognostic factor associated with patient-reported outcome 5–9 years after surgery.

Although the study group reported marginally inferior crude mean scores in all KOOS subscales compared to the control group at follow-up, the differences were not statistically significant. Given the knowledge that the outcomes differed significantly in favour of patients without concomitant full-thickness cartilage lesions in the short to mid-term evaluation (median 2.1 years) [23], the convergence in KOOS scores over time is somewhat surprising and certainly must have occurred after the first evaluation and up to the current 5–9-year follow-up. The convergence in KOOS scores is largely explained by a slight deterioration of outcomes in the control group and a continued improvement in the study group, as revealed when comparing the KOOS scores at the current follow-up to the short to mid-term follow-up. A decrease in the mean between-group difference was observed in all KOOS subscales from the 2.1-year follow-up to the current 5–9-year follow-up, the most prominent being KOOS QoL with a decline from 17.2 (95 % CI 4.2–30.1) to 5.7 (95 % CI −9.7 to 21.0) and KOOS Sport/Rec 19.8 (95 % CI 5.3–34.3) to 6.3 (95 % CI −8.6 to 21.2).

Possible explanations for this initial divergence, and later convergence in KOOS scores between the two groups, are not to be found among some of the known factors of importance on the outcome after ACLR, such as BMI, activity level, time from injury to surgery, age and gender, smoking status or choice of graft as all these factors are

Table 2 Mean difference between the study group and the control group in Knee Injury and Osteoarthritis Outcome Score (KOOS): at preoperative, follow-up and change over time

KOOS subscales	Preoperative		Follow-up		Change over time	
	Mean difference (95 % CI)	*p* value	Mean difference (95 % CI)	*p* value	Mean difference (95 % CI)	*p* value
Pain	1.1 (−7.1 to 9.3)	(n.s.)	−3.9 (−13.3 to 5.4)	(n.s.)	−4.6 (−14.6 to 5.4)	(n.s.)
Symptoms	−1.1 (−8.7 to 6.4)	(n.s.)	−5.2 (−15.3 to 4.9)	(n.s.)	−5.2 (−16.2 to 5.8)	(n.s.)
ADL	−1.3 (−7.5 to 4.9)	(n.s.)	−2.6 (−10.7 to 5.5)	(n.s.)	−2.1 (−11.2 to 7.1)	(n.s.)
Sport/Rec	−2.4 (−15.3 to 10.5)	(n.s.)	−6.3 (−21.2 to 8.6)	(n.s.)	−4.7 (−19.9 to 10.6)	(n.s.)
QoL	−3.9 (−10.6 to 2.8)	(n.s.)	−5.7 (−21.0 to 9.7)	(n.s.)	−1.9 (−17.7 to 13.9)	(n.s.)

Mean difference = study group minus control group

Change over time = follow-up minus preoperative

CI confidence interval, *p* level of significance, *n.s.* non-significant, *ADL* activities in daily living, *QoL* quality of life

Table 3 Mean change over time in Knee Injury and Osteoarthritis Outcome Score (KOOS) of the study group and the control group

KOOS subscales	Study group		Control group	
	Mean change over time (95 % CI)	*p* value	Mean change over time (95 % CI)	*p* value
Pain	8.1 (0.5 to 15.7)	0.038	12.7 (5.6 to 19.7)	0.001
Symptoms	4.7 (−3.3 to 12.7)	(n.s.)	9.9 (2.0 to 17.8)	0.016
ADL	5.7 (−1.0 to 12.5)	(n.s.)	7.8 (1.4 to 14.2)	0.019
Sport/Rec	22.8 (11.5 to 34.1)	<0.001	27.4 (16.0 to 38.9)	<0.001
QoL	31.8 (21.3 to 42.3)	<0.001	33.7 (23.6 to 43.8)	<0.001

Mean change over time = follow-up minus preoperative

CI confidence interval, *p* level of significance, *n.s.* non-significant, *ADL* activities of daily living, *QoL* quality of life

evenly distributed between the two groups both preoperatively and at follow-up.

Radiographic knee OA was the only factor differentiating the two groups at follow-up, as a significant higher proportion of knee OA among the control patients was detected. That finding might explain the downtrend in KOOS scores in the control group from the 2.1-year follow-up to the current 5–9-year follow-up, and the subsequent convergence in KOOS scores. Even though conflicting evidence exists on the association between radiographic knee OA and patient-reported outcome, it has been shown that high-grade radiographic OA negatively affects all KOOS subscales at long-term follow-up [20]. Hence, the significant between-group difference in radiographic OA, in favour of the study group, was an unanticipated finding as concomitant full-thickness cartilage lesions at the time of ACLR are shown to be a risk factor for later OA [14, 15]. The current study design does not allow for assessment on the reasons why control patients more frequently developed radiographic OA, but the strict inclusion criteria might have been of importance. Moreover, the magnitude of loss to follow-up (radiographs of only 22 out of 59 controls) in regard to radiographic examination might have introduced an attrition bias.

The negative effect of concomitant full-thickness cartilage lesions on the short-term outcome after ACLR was reported in the 2.1-year follow-up of the current cohort [23] and is supported by similar findings in a large nationwide population-based cohort [22]. The number of studies investigating the effect of such lesions on the mid-term to long-term outcome after ACLR is limited, and the results are inconsistent. In a report by Widuchowski et al. [29], the authors conclude that deep cartilage lesions at the time of ACLR do not appear to affect clinical outcome at 10- and 15-year follow-up. Shelbourne et al. [26] found very little difference in the postoperative clinical course, up to 12 years after ACLR, between patients with and without a concomitant chondral defect. On the other hand, in a more recent report from the same author,

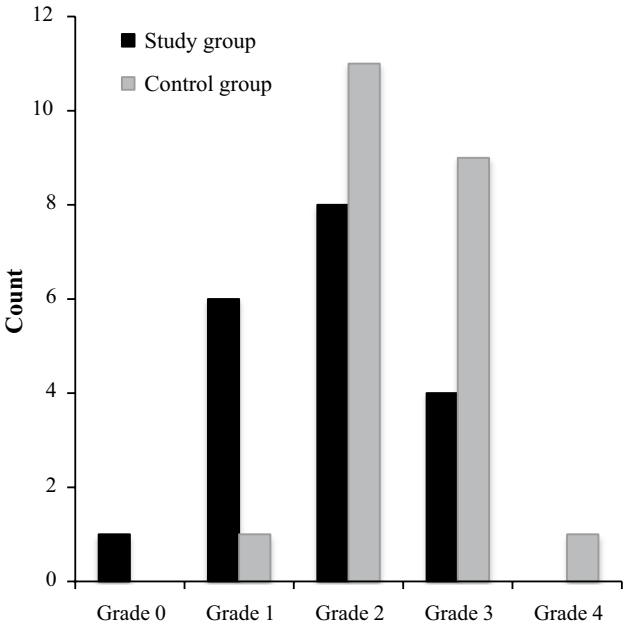

Fig. 2 Radiographic grading of knee osteoarthritis of the affected (ACL reconstructed) knee according to the Kellgren and Lawrence criteria

Table 4 Subsequent knee surgeries during the follow-up period

Procedures[a]	Study group[a]	Control group[a]
ACL revision/reconstruction	2	5
Meniscus surgery	3	4
Cartilage surgery[b]	4	0
Other/minor surgery[c]	3	2

[a] Frequency

[b] Debridement and/or microfracture

[c] Diagnostic arthroscopy and/or removal of cyclops formation and/or partial synovectomy

articular cartilage damage coupled with less than normal knee motion adversely affected the result >10 years after ACLR [25]. In a cohort study from the US Multicenter

Orthopaedic Outcomes Network (MOON) regarding this issue, Spindler et al. [27] found no significant influence of cartilage lesions on the 6-year outcome scores. However, by including 2 additional enrolment years and thereby increasing the sample size, Cox et al. [5] were able to perform a comprehensive, multivariable modelling of ACLR outcomes, identifying articular cartilage lesions as a significant predictor of impaired subjective outcome scores at 6 years. Nevertheless, as pointed out in a recent systematic review on this subject matter [9], considerable heterogeneity in patients, injuries and surgical factors exist among the different reports, making it difficult to directly compare the findings from these studies.

The rate of subsequent knee surgeries was higher than in the annual reports from the NKLR, but in line with the results from a recent large prospective cohort study from the USA [12].

The main strengths of the current study are its prospective design and the high overall follow-up rate (84 %). Moreover, the narrow inclusion criteria set, and the strict matching between the groups minimized confounding and most likely left the cartilage lesion as the only distinguishing factor. On the other hand, the use of these narrow inclusion criteria generated a patient sample of which the findings might not be generalizable to the general ACL-injured population. Others have shown that the potential of extrapolating results from clinical studies to the general population, in the case of knee cartilage injury, is limited [8].

The main limitation of the current study is the limited number of included patients. Although the sample size requirements from the power analysis (26 pairs of patients) were fulfilled, the increasing diversity in outcome scores during follow-up, as seen by the expansion in SDs over time, is indicative of the need of a larger sample size.

The findings at the different follow-ups of the current cohort illustrate the fact that patient outcome varies with time, and emphasize the importance of longitudinal study designs.

Moreover, it seems that a concomitant full-thickness cartilage lesion at the time of ACLR negatively affects restoration of knee function on short- to midterm basis, but levels out over time. Interestingly, even though most study patients did not receive any cartilage treatment at the time of ACLR, a continued improvement in KOOS scores over time was observed. That observation highlights the need of larger prospective cohort studies, or randomized controlled trials, to investigate the effectiveness of surgical intervention on these cartilage lesions.

The findings of the current study should be considered in the preoperative information given to patients with such combined injuries, in terms of the expected outcome after ACLR and the decision-making regarding surgical treatment of the concomitant cartilage lesion.

Conclusion

ACL reconstruction performed in patients with a concomitant full-thickness cartilage lesion restored patient-reported knee function, at 5–9-year follow-up, to the same level as ACL-reconstructed patients without such lesions. The data from the longitudinal follow-up of the current cohort suggest that patients with a concomitant full-thickness cartilage lesion can expect the patient-reported outcome to be significantly inferior at 2–5 years after surgery, but comparable to other ACL-reconstructed patients 5–9 years after surgery.

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Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

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