Effect of Concomitant Cartilage Lesions on Patient-Reported Outcomes After Anterior Cruciate Ligament Reconstruction

A Nationwide Cohort Study From Norway and Sweden of 8470 Patients With 5-Year Follow-up

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Background: The effect of concomitant focal cartilage lesions on patient-reported outcomes after anterior cruciate ligament reconstruction (ACLR) remains to be determined.

Purpose: To evaluate the effect of concomitant partial-thickness (International Cartilage Repair Society [ICRS] grades 1-2) and full-thickness (ICRS grades 3-4) cartilage lesions on patient-reported outcomes 5 years after ACLR.

Study Design: Cohort study; Level of evidence, 2.

Methods: All patients who underwent unilateral primary ACLR registered in the Norwegian and Swedish National Knee Ligament Registries from 2005 to 2008 (n = 15,783) were included in the study. At 5-year follow-up, 8470 (54%) patients completed the Knee injury and Osteoarthritis Outcome Score (KOOS). Multivariable linear regression models were used to estimate the effect of concomitant partial-thickness and full-thickness cartilage lesions on patient-reported outcomes (KOOS) 5 years after ACLR.

Results: Compared with no concomitant cartilage lesions, both partial-thickness and full-thickness cartilage lesions were indicators of statistically significant adverse effects on the KOOS in the adjusted regression analysis at 5-year follow-up after ACLR.

Conclusion: ACL-injured patients with concomitant cartilage lesions reported worse outcomes and less improvement than those without cartilage lesions 5 years after ACLR.

Keywords: knee; anterior cruciate ligament (ACL); reconstruction; cartilage lesions; KOOS

Anterior cruciate ligament (ACL) injuries are associated with articular focal cartilage lesions. In reports from large, prospectively collected ACL cohorts such as the Norwegian National Knee Ligament Registry (NKLR), the Swedish National Knee Ligament Registry (SKLR), and the Kaiser Permanente Anterior Cruciate Ligament Reconstruction Registry in the United States, concomitant cartilage lesions were present in 27% and 23% of ACL reconstructions (ACLRs), respectively.[16]

Even though the presence of a cartilage lesion at the time of ACLR is known to be a significant predictor of premature radiographic knee osteoarthritis,[6,13-15,17] the previous literature is inconsistent and somewhat divergent when it comes to the effect on patient-reported outcomes. Some of the studies have found no adverse effects of concomitant cartilage lesions on patient-reported outcomes after ACLR,[2,25-28] while others have found that concomitant cartilage lesions are associated with inferior patient-reported outcomes.[7,21,23,24] Firm knowledge on the short- and long-term prognosis after ACLR in patients with these combined injuries is necessary if the information and advice given to the patient regarding treatment and expectations are to be optimal. Hence, there is a need for large population-based studies evaluating that subject matter.

The primary objective of the present prospective, nationwide population-based study was to evaluate the effect of concomitant focal partial-thickness (International Cartilage Repair Society [ICRS] grades 1-2) and full-thickness

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(ICRS grades 3-4) cartilage lesions on patient-reported outcomes as measured by the Knee injury and Osteoarthritis Outcome Score (KOOS) 5 years after ACLR.

METHODS

NKLR and SKLR

After obtaining approval from the institutional review board of Akershus University Hospital and the Regional Ethical Committee of South-Eastern Norway, University of Oslo, data were assembled from the NKLR and the SKLR. The NKLR was established in June 2004 and the SKLR in January 2005, with the main objective to register all surgical procedures performed on knee ligaments and to prospectively monitor outcomes on a nationwide scale.[10,11] The Swedish registry was based on the Norwegian registry, and there are no major cross-cultural differences in the data between the 2 countries.[11] In both registries, the surgeons' reporting rates are found to be satisfactory, with reporting rates above 85%.[1,11]

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.[4,5] Cartilage lesion size is reported as area <2 cm^2 or ≥ 2 cm^2. Concomitant cartilage lesions are treated at the discretion of the surgeon with, in descending order of frequency, no treatment, debridement, microfracture, or various other surgical techniques.

The KOOS is used as the patient-reported outcome measure in both the NKLR and SKLR. The questionnaire consists of 42 questions distributed between 5 separately scored subscales: Pain, Symptoms, Activities of Daily Living (ADL), Sport and Recreation (Sport/Rec), and Knee-Related Quality of Life (QoL); it is considered to be a valid, reliable, and responsive assessment tool for patients with ACL and cartilage injuries.[3,8,20] Data assembly is voluntary, and patients complete an informed consent form before surgery, allowing for later use of their registry data, including the KOOS questionnaire.

Patients

The current study is a longitudinal 5-year follow-up of a nationwide population-based cohort consisting of all patients who underwent unilateral primary ACLR between January 1, 2005, and December 31, 2008, and who were registered in the NKLR or SKLR. During this time frame, a total of 15,783 patients were prospectively registered. This patient cohort has previously been described in a study on the incidence and risk of full-thickness cartilage lesions in ACL-injured knees[22] and a study reporting on 2-year outcomes after ACLR in patients with concomitant meniscal and cartilage lesions.[23]

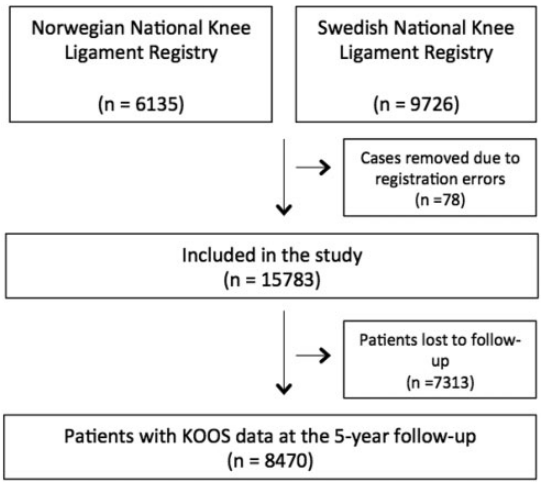

Figure 1. Flowchart of the patients during inclusion (2005-2008) and follow-up. KOOS, Knee injury and Osteoarthritis Outcome Score.

At a mean (±SD) follow-up of 5.1 ± 0.2 years and with a mean patient age of 33.8 ± 10.6 years, KOOS data were received from 8470 (54%) of the 15,783 patients. Of these, 3573 (42%) patients were from the Norwegian registry and 4897 (58%) patients from the Swedish registry. Patient flow during inclusion and follow-up is shown in Figure 1, and baseline characteristics at the time of ACLR for the patients included in the study cohort and for patients lost to follow-up are shown in Table 1. With the exception of sex and age, the baseline characteristics of the study population and those lost to follow-up were comparable. The patients available for follow-up tended to be older and to have a higher proportion of women compared with patients lost to follow-up.

In the present study, patients were categorized as having no concomitant cartilage lesion, partial-thickness cartilage lesions (ICRS grades 1-2), or full-thickness cartilage lesions (ICRS grades 3-4). Patients with more than 1 concomitant

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TABLE 1
Baseline Characteristics at the Time of ACL Reconstruction for Patients in the Study Cohort and Patients Lost to Follow-up[a]

	Study Cohort (n_1)	Lost to Follow-up (n_2)
Age at surgery, y, median (range), ($n_1 = 8470$; $n_2 = 7306$)	27 (9-69)	24 (8-64)
Time from injury to surgery, mo, median (range) ($n_1 = 8178$; $n_2 = 7072$)	9 (0-521)	9 (0-400)
Female sex ($n_1 = 8470$; $n_2 = 7313$)	4125 (49)	2573 (35)
Previous ipsilateral knee surgery ($n_1 = 8470$; $n_2 = 7313$)	2232 (26)	1914 (26)
Concomitant ligament injury[b] ($n_1 = 8470$; $n_2 = 7313$)	621 (7)	493 (7)
Concomitant meniscal lesion ($n_1 = 8470$; $n_2 = 7313$)	3688 (43)	3156 (43)
Concomitant cartilage lesion ($n_1 = 8470$; $n_2 = 7313$)	2248 (27)	1910 (26)
ACL graft ($n_1 = 8470$; $n_2 = 7313$)		
Hamstring tendon	6473 (76)	5762 (79)
Bone–patellar tendon–bone	1833 (22)	1383 (19)
Other/unknown	164 (2)	168 (2)
Preoperative KOOS value, mean ± SD		
Pain ($n_1 = 6070$; $n_2 = 4877$)	74.7 ± 17.6	73.9 ± 18.0
Symptoms ($n_1 = 6089$; $n_2 = 4893$)	71.4 ± 18.0	70.2 ± 18.0
Activities of Daily Living ($n_1 = 6062$; $n_2 = 4866$)	83.8 ± 17.4	82.9 ± 17.5
Sport and Recreation ($n_1 = 6031$; $n_2 = 4864$)	42.3 ± 27.1	41.8 ± 27.1
Knee-Related Quality of Life ($n_1 = 6067$; $n_2 = 4878$)	34.2 ± 18.2	33.5 ± 18.2

[a]Data are shown as n (%) unless otherwise indicated. ACL, anterior cruciate ligament; KOOS, Knee injury and Osteoarthritis Outcome Score.
[b]Medial collateral ligament, lateral collateral ligament, posterior cruciate ligament, or posterolateral corner.

cartilage lesion were categorized according to the lesion with the highest ICRS grade. The baseline characteristics as stratified by these categories are shown in Table 2. At baseline, it was a consistent finding that some of the between-group differences (age at surgery, time from injury to surgery, previous ipsilateral knee surgery, concomitant ligament and meniscal injury, meniscal resection, and cartilage lesion size ≥ 2 cm^2) were more pronounced with increasing depth (higher ICRS grade) of the cartilage lesion.

Statistical Analysis

SPSS software (version 24.0; IBM) was used for all statistical analyses. P values $<.05$ were considered statistically significant. Crude mean KOOS scores and standardized regression coefficients are presented with 95% CIs. Crude mean KOOS scores at 5-year follow-up were estimated and stratified by patients with partial-thickness cartilage lesions, those with full-thickness cartilage lesions, and those without any concomitant cartilage lesions.

Multivariable linear regression was used to assess the possible impact on prognosis, as measured by the KOOS at 5-year follow-up, of concomitant partial-thickness and full-thickness cartilage lesions. The results are presented both unadjusted and adjusted for possible confounding from sex, age at surgery (continuous variable), previous ipsilateral knee surgery (yes/no), concomitant ligament injury (yes/no), concomitant meniscal injury (yes/no), concomitant meniscal resection (yes/no), time from injury to surgery (continuous variable), and type of ACL graft (hamstring, patellar tendon, or other). In all regression analyses, the no concomitant cartilage lesion category was used as the reference for the effect of partial-thickness and full-thickness cartilage lesions. Cartilage lesion–specific characteristics such as area and location were not included as independent variables in the multivariable regression analysis for the reason that controlling for these variables would shift the regression model to focus on the effect of ACLR instead of the concomitant cartilage lesion.

To determine whether cartilage lesion size (<2 cm^2 or ≥ 2 cm^2) was a significant predictor of KOOS scores at 5 years after ACLR, separate multivariable regression analyses were performed for the subsets of patients with partial-thickness cartilage lesions and full-thickness cartilage lesions. The factor of interest (lesion size ≥ 2 cm^2) in these additional analyses was included as an independent variable together with sex, age at surgery (continuous variable), previous ipsilateral knee surgery (yes/no), concomitant ligament injury (yes/no), concomitant meniscal injury (yes/no), concomitant meniscal resection (yes/no), time from injury to surgery (continuous variable), and type of ACL graft (hamstring, patellar tendon, or other). Cartilage lesion area <2 cm^2 was used as a reference for the effect of lesion size on KOOS scores at 5-year follow-up.

RESULTS

Of the 8470 patients available for follow-up at 5 years, 2248 (27%) had ≥ 1 concomitant cartilage lesions at the time of ACLR: 1685 (20%) patients with ≥ 1 partial-thickness cartilage lesions (ICRS grades 1-2) and 563 (7%) patients with ≥ 1 full-thickness cartilage lesions (ICRS grades 3-4). There were a total of 2825 partial-thickness cartilage lesions and 656 full-thickness cartilage lesions. Of the 1685 patients with concomitant partial-thickness cartilage lesions, 591 (35%) had >1 cartilage lesion (ICRS grades 1-2). Of the 563 patients with full-thickness cartilage lesions, 74 (13%) had >1 full-thickness cartilage lesion, and 218

TABLE 2
Baseline Characteristics by Cartilage Status at the Time of ACL Reconstruction[a]

	Study Cohort (N = 8470)		
	No Cartilage Lesions (n = 6222)	Partial-Thickness Cartilage Lesions (n = 1685)	Full-Thickness Cartilage Lesions (n = 563)
Age at surgery, y, median (range)	25 (9-69)	32 (13-67)	37 (14-66)
Time from injury to surgery, mo, median (range)	8 (0-361)	13 (0-430)	18 (0-521)
Female sex	3143 (50)	730 (43)	252 (45)
Previous ipsilateral knee surgery	1347 (22)	635 (38)	250 (44)
Concomitant ligament injury[b]	398 (6)	156 (9)	67 (12)
Concomitant meniscal lesion	2468 (40)	893 (53)	327 (58)
Meniscal resection	1608 (26)	652 (39)	253 (45)
ACL graft			
Hamstring tendon	4728 (76)	1307 (78)	438 (78)
Bone–patellar tendon–bone	1356 (22)	361 (21)	116 (21)
Other/unknown	138 (2)	17 (1)	9 (1)
Area			
<2 cm^2	NA	1048 (62)	248 (44)
≥ 2 cm^2	NA	573 (34)	310 (55)
Not reported	NA	64 (4)	5 (1)
Location			
Patella	NA	393 (14)	67 (10)
Trochlea	NA	149 (5)	45 (7)
Medial femoral condyle	NA	1099 (39)	344 (52)
Lateral femoral condyle	NA	356 (13)	82 (13)
Medial tibial plateau	NA	411 (14)	66 (10)
Lateral tibial plateau	NA	417 (15)	52 (8)
Preoperative KOOS value, mean ± SD			
Pain	75.6 ± 17.1	73.6 ± 18.5	69.8 ± 19.4
Symptoms	72.0 ± 17.8	70.4 ± 18.1	67.9 ± 19.0
Activities of Daily Living	84.8 ± 16.8	81.9 ± 18.4	78.4 ± 19.2
Sport and Recreation	43.6 ± 26.9	39.7 ± 27.1	36.1 ± 27.1
Knee-Related Quality of Life	34.8 ± 18.0	33.1 ± 18.3	31.0 ± 18.7

[a]Data are shown as n (%) unless otherwise indicated. ACL, anterior cruciate ligament; KOOS, Knee injury and Osteoarthritis Outcome Score; NA, not applicable.
[b]Medial collateral ligament, lateral collateral ligament, posterior cruciate ligament, or posterolateral corner.

TABLE 3
Crude KOOS Scores by Cartilage Status at 5-Year Follow-up After Anterior Cruciate Ligament Reconstruction[a]

	No Cartilage Lesions (n = 5981-6199)	Partial-Thickness Cartilage Lesions (n = 1609-1684)	Full-Thickness Cartilage Lesions (n = 510-562)
Pain	86.2 (85.8-86.6)	85.3 (84.5-86.1)	79.7 (78.0-81.4)
Symptoms	79.7 (79.2-80.1)	79.3 (78.4-80.2)	74.2 (72.5-75.6)
Activities of Daily Living	92.1 (91.7-92.4)	90.6 (89.8-91.3)	86.0 (84.4-87.5)
Sport and Recreation	70.6 (69.9-71.2)	68.4 (67.1-69.6)	61.6 (59.2-64.0)
Knee-Related Quality of Life	67.2 (66.6-67.8)	66.3 (65.1-67.4)	60.0 (57.8-62.2)

[a]Data are shown as mean (95% CI). KOOS, Knee injury and Osteoarthritis Outcome Score.

patients (39%) had an associated partial-thickness cartilage lesion.

The crude mean KOOS scores at 5-year follow-up for patients with no concomitant cartilage lesions, patients with partial-thickness cartilage lesions, and patients with full-thickness cartilage lesions are outlined in Table 3. Compared with patients with partial-thickness cartilage lesions, and in particular patients without any cartilage lesions, patients with full-thickness cartilage lesions reported inferior crude mean values on all of the KOOS subscales at 5-year follow-up. Except for lower scores on the KOOS subscales of ADL and Sport/Rec, patients with partial-thickness cartilage lesions reported equal crude mean KOOS scores at follow-up compared with patients without any cartilage lesions.

The results from the multivariable regression analysis with the unadjusted and adjusted effects of

TABLE 4
Unadjusted and Adjusted Regression Analyses of the Associations Between KOOS Subscales and Partial-Thickness and Full-Thickness Cartilage Lesions at 5-Year Follow-up After Anterior Cruciate Ligament Reconstruction[a]

		Partial-Thickness Cartilage Lesions			Full-Thickness Cartilage Lesions		
KOOS Subscale	n	β	95% CI	*P* Value	β	95% CI	*P* Value
Pain							
Unadjusted	8425	–0.9	–1.8 to –0.1	.040	–6.6	–8.0 to –5.1	<.001
Adjusted	8091	–0.8	–1.7 to 0.1	.084	–6.0	–7.5 to –4.5	<.001
Symptoms							
Unadjusted	8445	–0.4	–1.4 to 0.6	.400	–5.5	–7.0 to –3.9	<.001
Adjusted	8107	–1.1	–2.1 to –0.1	.042	–6.5	–8.2 to –4.9	<.001
Activities of Daily Living							
Unadjusted	8425	–1.5	–2.3 to –0.7	<.001	–6.1	–7.3 to –4.9	<.001
Adjusted	8088	–0.7	–1.5 to 0.0	.067	–4.6	–5.9 to –3.3	<.001
Sport and Recreation							
Unadjusted	8100	–2.2	–3.6 to –0.8	.002	–8.9	–11.2 to –6.7	<.001
Adjusted	7779	–1.8	–3.2 to –0.3	.018	–8.1	–10.5 to –5.7	<.001
Knee-Related Quality of Life							
Unadjusted	8356	–0.9	–2.2 to 0.4	.170	–7.2	–9.3 to –5.1	<.001
Adjusted	8026	–1.5	–2.8 to –0.1	.033	–8.0	–10.2 to –5.7	<.001

[a]KOOS, Knee injury and Osteoarthritis Outcome Score.

TABLE 5
Adjusted Regression Analysis of the Associations Between KOOS Subscales and Cartilage Lesion Size at 5-Year Follow-up After Anterior Cruciate Ligament Reconstruction[a]

	Partial-Thickness Cartilage Lesions ≥2 cm^2				Full-Thickness Cartilage Lesions ≥2 cm^2			
KOOS Subscale	n	β	95% CI	*P* Value	n	β	95% CI	*P* Value
Pain	1561	–1.9	–3.7 to –0.1	.045	524	–0.7	–4.2 to 2.8	NS
Symptoms	1562	–2.3	–4.3 to –0.4	.019	526	–0.1	–3.6 to 3.5	NS
Activities of Daily Living	1561	–1.7	–3.3 to –0.1	.046	524	–0.7	–3.9 to 2.6	NS
Sport and Recreation	1494	–3.2	–6.0 to –0.4	.026	479	–4.2	–9.3 to 0.1	NS
Knee-Related Quality of Life	1543	–2.0	–4.6 to 0.6	NS	515	–2.0	–6.6 to 2.6	NS

[a]KOOS, Knee injury and Osteoarthritis Outcome Score; NS, not significant.

partial-thickness cartilage lesions and full-thickness cartilage lesions on each of the KOOS subscales are shown in Table 4. In the unadjusted analysis, with patients without concomitant cartilage lesions as the reference, partial-thickness cartilage lesions were significantly associated with inferior scores on all KOOS subscales except for Symptoms and QoL. In the adjusted analysis, partial-thickness cartilage lesions showed significant associations with inferior scores at follow-up on all KOOS subscales except for Pain and ADL. Full-thickness cartilage lesions were significantly associated with inferior scores on all KOOS subscales in both the unadjusted and the adjusted analyses.

As shown in Table 5, the subgroup multivariable regression analysis of patients with partial-thickness cartilage lesions (n = 1685), lesion size ≥2 cm^2 was significantly associated with inferior scores at 5-year follow-up on all KOOS subscales except for QoL. In the corresponding subgroup analysis of patients with full-thickness cartilage lesions (n = 563), no significant associations between lesion size and the KOOS subscales were detected (Table 5).

DISCUSSION

The main finding of the present study was that compared with patients with no concomitant cartilage lesions, those with cartilage lesions reported significantly inferior outcomes, as measured by the KOOS, at 5-year follow-up after ACLR. To date, this is the largest multivariable modeling of midterm outcomes in patients with this combined injury.

Both partial-thickness and full-thickness cartilage lesions were indicators of statistically significant adverse effects on the KOOS in the adjusted regression analysis. The minimal clinically important difference for the KOOS in the current population is not established, but a clinically meaningful difference or change in the KOOS score of at least 8 points is often used.[19] Though statistically significant, the observed adverse effects of partial-thickness cartilage lesions were small and likely without major clinical significance. However, the observed negative adjusted effects of full-thickness cartilage lesions were larger, with –8.1 and –8.0 points for the 2 most responsive KOOS subscales, Sport/Rec and QoL,

respectively. This is in line with the results from a recent comprehensive level 1 cohort study of 1512 ACL-reconstructed patients with 6-year follow-up by Cox et al,[7] in which concomitant cartilage lesions of Outerbridge grades 3 to 4 were a significant predictor of reduced KOOS and International Knee Documentation Committee (IKDC) scores. In contrast, in the only other level 1 prognostic study with >5 years' follow-up of these combined injuries, no negative effect of concomitant full-thickness cartilage lesions on the KOOS was detected 5 to 9 years after ACLR.[27] This diversity in the reported effects of concomitant cartilage lesions on patient-reported outcomes after ACLR is illustrative of the current literature on this subject matter, as some have found an association between cartilage lesions and patient-reported outcomes,[7,21,23,24] while others have found no such association.[2,25-28] As pointed out in a recent systematic review, considerable heterogeneity in patients, injuries, surgical factors, outcome measurements, and observation periods exists among the different reports, making it difficult to directly compare the findings from these studies.[9]

When comparing the adjusted negative effects of full-thickness cartilage lesions at the current 5-year follow-up with 2-year follow-up of this cohort,[23] with effect differences ranging from –1.7 to –2.7, more pronounced adverse effects of full-thickness cartilage lesions were found on all KOOS subscales at the 5-year follow-up. Consequently, not only did ACLR, in the short term, fail to restore knee function to the same level as patients without full-thickness cartilage lesions, but the divergence in knee function also seems to evolve with time, at least up to 5 years after surgery.

Aside from controlling for the variables included in the multivariable regression analysis, the current study design did not allow for an assessment on the reasons for this relative deterioration in patient-reported outcomes over time. However, the limited functional competence and durability of repair tissue after spontaneous or surgical cartilage repair are well known.[12] Moreover, others have shown that there is an increased risk of osteoarthritis associated with these cartilage lesions.[13,14] The subgroup analysis on the impact of lesion size on KOOS scores at 5-year follow-up indicates that lesions ≥ 2 cm^2 can predict inferior outcomes for patients with partial-thickness cartilage lesions. On the contrary, there was no significant association between lesion size and patient-reported outcomes 5 years after ACLR in patients with full-thickness cartilage lesions. However, firm conclusions regarding the effect of lesion size cannot be drawn from these results, as some information is lost in the dichotomization of lesion size into <2 cm^2 and ≥ 2 cm^2. In particular, exact information about small (<1 cm^2) and large (>4 cm^2) lesions would allow for more nuanced subgroup analyses.

The observational study design has limitations, as is the case with the current study. The main limitation of this study is the rate of loss to 5-year follow-up (46%), with the potential of introducing attrition bias. Although the baseline characteristics of the study cohort and those lost to follow-up were comparable in the majority of the reported variables, patients lost to follow-up were younger and had a higher proportion of men than the patients available for follow-up. On the other hand, those factors, together with other factors most likely to have affected the prognosis and outcome after surgery, were adjusted for in the multivariable regression analysis. Moreover, in a validation study from the Danish Knee Ligament Reconstruction Registry, the KOOS values from nonresponders were equivalent to those from responders, indicating that registry data could be valid despite a high rate of loss to follow-up.[18] Another limitation is the use of the KOOS as the only outcome measure. Additional outcome measures, such as radiographic assessments of osteoarthritis and activity level scores, could have reduced the potential risk of unmeasured predictors and confounders as well as potentially shed some light on the reasons for the findings of the current study. None of these additional parameters were recorded in either the NKLR or SKLR during the current study period. However, the reasons for choosing the KOOS as the patient-reported outcome measure in the registries, and its limitations, are carefully outlined and discussed in the previous literature.[10]

The main strengths of the present study are that patients from nationwide population-based registries were included, without restrictive inclusion or exclusion criteria, ensuring a large sample size and the representation of a wide range of patients, hospitals, and surgeons. This should in turn provide results that are applicable to a large group of orthopaedic patients and practices. In addition, the validity of the findings is strengthened by the comprehensive adjustment for predictors and confounders in the analyses. However, when using regression models to examine exposure-outcome associations, it is often a matter for discussion whether the appropriate confounders have been controlled for. As there are no standardized or validated sets of possible confounding variables considered to be requisite when developing such regression models, the choice of possible confounders in this study was based on the current literature, clinical assumptions, and available parameters recorded by the 2 national registries. Possible confounding variables such as smoking status, body mass index, and energy of the initial trauma were not included.

In summary, the main finding in the present study, that concomitant full-thickness cartilage lesions were an indicator of significant adverse effects on patient-reported outcomes 5 years after ACLR, should be taken into account and assist in counseling patients with this combined injury regarding the midterm prognosis after ACLR. Moreover, the results highlight the need for further research emphasizing the improvement of current treatment algorithms for patients with these combined injuries. In addition, future studies should distinguish the cartilage lesion depth, as this variable is significantly associated with patient-reported outcomes.

CONCLUSION

ACL-injured patients with concomitant full-thickness cartilage lesions reported worse outcomes and less improvement

than those without cartilage lesions 5 years after ACLR. There were no effects of lesion size on patient-reported outcomes in patients with full-thickness cartilage lesions. Concomitant partial-thickness cartilage lesions had statistically significant adverse effects on patient-reported outcomes at 5-year follow-up, but this finding may not be clinically significant. Cartilage lesion size ≥ 2 cm^2 was a significant predictor of inferior patient-reported outcomes at 5-year follow-up in patients with partial-thickness lesions.

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REFERENCES

1. Ahlden M, Samuelsson K, Sernert N, Forssblad M, Karlsson J, Kartus J. The Swedish National Anterior Cruciate Ligament Register: a report on baseline variables and outcomes of surgery for almost 18,000 patients. *Am J Sports Med*. 2012;40(10):2230-2235.
2. Barenius B, Forssblad M, Engstrom B, Eriksson K. Functional recovery after anterior cruciate ligament reconstruction: a study of health-related quality of life based on the Swedish National Knee Ligament Register. *Knee Surg Sports Traumatol Arthrosc*. 2013;21(4):914-927.
3. Bekkers JE, de Windt TS, Raijmakers NJ, Dhert WJ, Saris DB. Validation of the Knee injury and Osteoarthritis Outcome Score (KOOS) for the treatment of focal cartilage lesions. *Osteoarthritis Cartilage*. 2009;17(11):1434-1439.
4. Brittberg M, Peterson L. Introduction of an articular cartilage classification. *ICRS Newsletter*. 1998;1:5-8.
5. Brittberg M, Winalski CS. Evaluation of cartilage injuries and repair. *J Bone Joint Surg Am*. 2003;85(suppl 2):58-69.
6. Claes S, Hermie L, Verdonk R, Bellemans J, Verdonk P. Is osteoarthritis an inevitable consequence of anterior cruciate ligament reconstruction? A meta-analysis. *Knee Surg Sports Traumatol Arthrosc*. 2013;21(9):1967-1976.
7. Cox CL, Huston LJ, Dunn WR, et al. Are articular cartilage lesions and meniscus tears predictive of IKDC, KOOS, and Marx activity level outcomes after anterior cruciate ligament reconstruction? A 6-year multicenter cohort study. *Am J Sports Med*. 2014;42(5):1058-1067.
8. Engelhart L, Nelson L, Lewis S, et al. Validation of the Knee injury and Osteoarthritis Outcome Score subscales for patients with articular cartilage lesions of the knee. *Am J Sports Med*. 2012;40(10):2264-2272.
9. Filardo G, de Caro F, Andriolo L, Kon E, Zaffagnini S, Marcacci M. Do cartilage lesions affect the clinical outcome of anterior cruciate ligament reconstruction? A systematic review. *Knee Surg Sports Traumatol Arthrosc*. 2017;25(10):3061-3075.
10. Granan LP, Bahr R, Steindal K, Furnes O, Engebretsen L. Development of a national cruciate ligament surgery registry: the Norwegian National Knee Ligament Registry. *Am J Sports Med*. 2008;36(2):308-315.
11. Granan LP, Forssblad M, Lind M, Engebretsen L. The Scandinavian ACL registries 2004-2007: baseline epidemiology. *Acta Orthop*. 2009;80(5):563-567.
12. Hunziker EB, Lippuner K, Keel MJ, Shintani N. An educational review of cartilage repair: precepts & practice—myths & misconceptions—progress & prospects. *Osteoarthritis Cartilage*. 2015;23(3):334-350.
13. Janssen RP, du Mee AW, van Valkenburg J, Sala HA, Tseng CM. Anterior cruciate ligament reconstruction with 4-strand hamstring autograft and accelerated rehabilitation: a 10-year prospective study on clinical results, knee osteoarthritis and its predictors. *Knee Surg Sports Traumatol Arthrosc*. 2013;21(9):1977-1988.
14. Keays SL, Newcombe PA, Bullock-Saxton JE, Bullock MI, Keays AC. Factors involved in the development of osteoarthritis after anterior cruciate ligament surgery. *Am J Sports Med*. 2010;38(3):455-463.
15. Li RT, Lorenz S, Xu Y, Harner CD, Fu FH, Irrgang JJ. Predictors of radiographic knee osteoarthritis after anterior cruciate ligament reconstruction. *Am J Sports Med*. 2011;39(12):2595-2603.
16. Maletis GB, Granan LP, Inacio MC, Funahashi TT, Engebretsen L. Comparison of community-based ACL reconstruction registries in the U.S. and Norway. *J Bone Joint Surg Am*. 2011;93(suppl 3):31-36.
17. Murray JR, Lindh AM, Hogan NA, et al. Does anterior cruciate ligament reconstruction lead to degenerative disease? Thirteen-year results after bone-patellar tendon-bone autograft. *Am J Sports Med*. 2012;40(2):404-413.
18. Rahr-Wagner L, Thillemann TM, Lind MC, Pedersen AB. Validation of 14,500 operated knees registered in the Danish Knee Ligament Reconstruction Register: registration completeness and validity of key variables. *Clin Epidemiol*. 2013;5:219-228.
19. Roos EM, Lohmander LS. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Outcomes*. 2003;1:64.
20. Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee injury and Osteoarthritis Outcome Score (KOOS): development of a self-administered outcome measure. *J Orthop Sports Phys Ther*. 1998;28(2):88-96.
21. Røtterud JH, Risberg MA, Engebretsen L, Årøen A. Patients with focal full-thickness cartilage lesions benefit less from ACL reconstruction at 2-5 years follow-up. *Knee Surg Sports Traumatol Arthrosc*. 2012;20(8):1533-1539.
22. Røtterud JH, Sivertsen EA, Forssblad M, Engebretsen L, Årøen A. Effect of gender and sports on the risk of full-thickness articular cartilage lesions in anterior cruciate ligament-injured knees: a nationwide cohort study from Sweden and Norway of 15 783 patients. *Am J Sports Med*. 2011;39(7):1387-1394.
23. Rotterud JH, Sivertsen EA, Forssblad M, Engebretsen L, Aroen A. Effect of meniscal and focal cartilage lesions on patient-reported outcome after anterior cruciate ligament reconstruction: a nationwide cohort study from Norway and Sweden of 8476 patients with 2-year follow-up. *Am J Sports Med*. 2013;41(3):535-543.
24. Shelbourne KD, Gray T. Minimum 10-year results after anterior cruciate ligament reconstruction: how the loss of normal knee motion compounds other factors related to the development of osteoarthritis after surgery. *Am J Sports Med*. 2009;37(3):471-480.
25. Shelbourne KD, Jari S, Gray T. Outcome of untreated traumatic articular cartilage defects of the knee: a natural history study. *J Bone Joint Surg Am*. 2003;85(suppl 2):8-16.
26. Spindler KP, Huston LJ, Wright RW, et al. The prognosis and predictors of sports function and activity at minimum 6 years after anterior cruciate ligament reconstruction: a population cohort study. *Am J Sports Med*. 2011;39(2):348-359.
27. Ulstein S, Bredland K, Aroen A, Engebretsen L, Rotterud JH. No negative effect on patient-reported outcome of concomitant cartilage lesions 5-9 years after ACL reconstruction. *Knee Surg Sports Traumatol Arthrosc*. 2016;25(5):1482-1488.
28. Widuchowski W, Widuchowski J, Koczy B, Szyluk K. Untreated asymptomatic deep cartilage lesions associated with anterior cruciate ligament injury: results at 10- and 15-year follow-up. *Am J Sports Med*. 2009;37(4):688-692.