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Associations between inadequate knee function detected by KOOS and prospective graft failure in an anterior cruciate ligament-reconstructed knee

Lars-Petter Granan · Valborg Baste · Lars Engebretsen · Maria C. S. Inacio

Abstract

Purpose First, to evaluate whether the 2 year post-operative Knee injury and Osteoarthritis Outcome Score (KOOS) in primary anterior cruciate ligament reconstructions (ACLRs) was significantly different between patients that did not go on to have a subsequent revision after the 2 year post-operative control and the ones that did. Second, to test whether the "clinically failure" value of KOOS quality of life (QoL) < 44 was indicative of a clinically relevant difference in the risk of subsequent revision ACLR.

Methods ACLRs reported to the Norwegian Knee Ligament Registry between June 2004 and December 2009. 5,517 primary ACLRs with at least 2-year follow-up with KOOS QoL before revision surgery.

Results There were clinically significant differences, adjusted and unadjusted, in both the KOOS Sport and Recreation and QoL subscales in patients with a later revision surgery compared to those that did not have a revision surgery. In adjusted models, the risk of later ACLR revision was 3.7 (95 % CI 2.2–6.0) higher in patients with a 2-year KOOS QoL < 44 compared to patients with a KOOS QoL ≥ 44. For every 10-point reduction in the KOOS QoL, a 33.6 % (95 % CI 21.2–47.5 %) higher risk for later ACLR revision was observed.

Conclusions This study reveals an association between inadequate knee function, as measured by KOOS, and a prospective ACL-reconstructed graft failure.

Level of evidence Prognostic study (prospective cohort study), Level II.

Keywords Anterior cruciate ligament · Revision · Registry · Patient-reported outcome measures

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Introduction

Clinical tools capable of identifying inferior knee function after anterior cruciate ligament reconstruction (ACLR), so-called "clinical failures", are currently not available. While certain tools will assess physical characteristics of the knee, function does not always correlate to these measurements. Additionally, inferior knee function is not always the same as graft rupture; therefore, physical examination will not be sufficient to detect this problem either.

For years, the Knee injury and Osteoarthritis Outcome Score (KOOS) [8–10] values suggestive of clinical failures have been proposed, but no studies have actually quantified the likelihood of failure based on these proposed KOOS

values in ACLR patients. One such predefined treatment failure criterion, the KOOS quality of life (QoL) subscale score below 44, was proposed in 2010 by Frobell et al. [5]. To our knowledge, this cut-off has not been confirmed by other studies.

The purpose of this study was twofold. Firstly, to evaluate whether the 2 year post-operative KOOS in primary ACLRs was significantly different between patients that did not go on to have a subsequent revision after the 2 year post-operative control and the ones that did. Secondly, to test whether the "clinically failure" value of KOOS QoL < 44 was associated with an increased risk of subsequent failure.

The study hypothesis was that the 2-year ACLR follow-up with the KOOS is associated with subsequent revision and thus is justified for further scrutiny as a clinical prediction tool.

Materials and methods

A retrospective analysis of a prospectively followed sample from the Norwegian Knee Ligament Registry (NKLR) primary ACLR cohort registered from 7 June 2004 to 31 December 2009 was conducted ($n = 8,944$). All patients who underwent a primary ACLR and had a 2 year post-operative KOOS ($n = 5,517$) were included in the analysis. Each subscale was analysed separately, and the numbers of complete answers differ slightly between the subscales (data not shown). Patients revised within the first 2 years after their index ACLR ($n = 192$) were excluded from the analysis. The 3,154 patients that did not complete any of the subscales in the KOOS form are included in the non-responder analysis. Non-responders are those who did not answer the 2 years post-operative KOOS. All patients with revision surgery completed their follow-up KOOS prior to surgery.

The NKLR covers the population of Norway (5.0 million people) and collects information at 57 hospitals or surgery centres. It has reported >85 % voluntary participation since 2006 [6, 11]. Data collection for the NKLR has been described previously [6]. In brief, it is a paper-based registry with anonymous contribution by surgeons. The patient's social security number is used as the unique identifier of the patient by the registry. The NKLR includes follow-ups on all patients at 2 years post-operatively using the KOOS. All revisions are reported to the NKLR by the surgeons performing the surgery.

Information about age at time of surgery, sex, pre-operative and 2 year post-operative KOOS, time from completion of 2 year post-operative KOOS until censoring of data (i.e. 31 December 2011), or if the patient was recorded with a later ACLR revision surgery (defined as revision surgery performed more than 2 years after their index ACLR), was obtained from the NKLR. The patients were categorized into those that had a later ACLR revision and those that did not have any ACLR revision in the study period.

The KOOS includes 42 items in five separately scored subscales: pain, other symptoms, function in activities of daily living (ADL), function in sport and recreation (Sport/Rec), and knee-related QoL [9, 10]. The KOOS has shown acceptable test–retest reliability [9]. In this study, a clinically relevant difference in any KOOS subscale was considered to be a change in score of at least 10 points, in accordance with previous studies [8]. Since our study investigates revisions after ACLRs in a relative short time span, the latter two subscales (Sport/Rec and QoL) are found to be the most relevant to analyse [3, 7, 10] and therefore also the main focus.
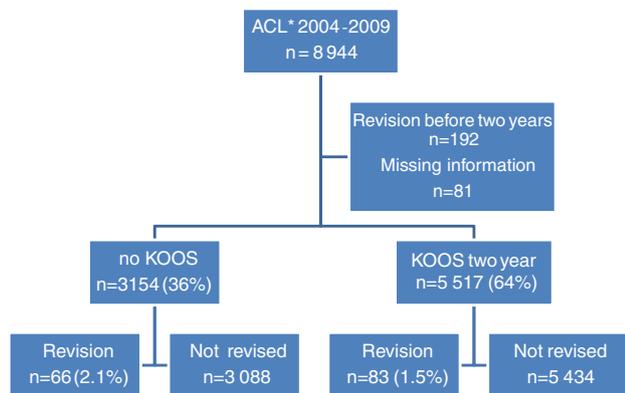
Participation in the NKLR is voluntary, for both surgeons and patients. Patients sign an informed consent form, and the NKLR is approved by the Norwegian Data Inspectorate as an extension of the Norwegian Arthroplasty Register concession. All data extracted from the NKLR are anonymized.

Statistical analysis

Descriptive statistics were given as mean values, standard deviations (SD) and percentages (%). Mean 2 year post-operative KOOS and 95 % confidence intervals (CI) were provided. To estimate mean KOOS differences between patients with revision and without ACLR revision, we used linear regression with and without adjustment for sex, age and pre-operative KOOS. Cox regression analyses were performed to estimate the hazard ratio (HR) with 95 % CI for revision for those with low KOOS QoL (<44) relative to high KOOS QoL (≥44). The "clinically failure" value of KOOS QoL < 44 was chosen due to the findings of Frobell et al. [5]. The Cox regression models were adjusted for sex, age and pre-operative KOOS QoL. Cox regression analyses were also used to make adjusted survival curves at a mean of the covariates. The numbers of included individuals in the adjusted analyses can vary slightly due to missing pre-operative KOOS information. Non-responders analyses, to determine whether patients who answered 2 years post-operative KOOS and those who did not answered were similar, were conducted with Chi-square tests for categorical variables and Student's t test for continuous variables. All tests were two sided and $\alpha = 0.05$. The data were analysed using IBM SPSS Statistics (version 20.0) and by R to provide survival plot (version 2.15.0 for Windows).

Results

The final study sample included 5,517 ACLR. Of these, 83 cases had a revision procedure after the completion of the 2-year KOOS (Fig. 1). Characteristics of the study sample are in Table 1 and Fig. 2. The mean follow-up of the primaries without revision was 54.4 months (SD = 18.9), and for the cases with later revisions the mean follow-up, time from ACLR to revision, was 40.0 months (SD = 13.2).
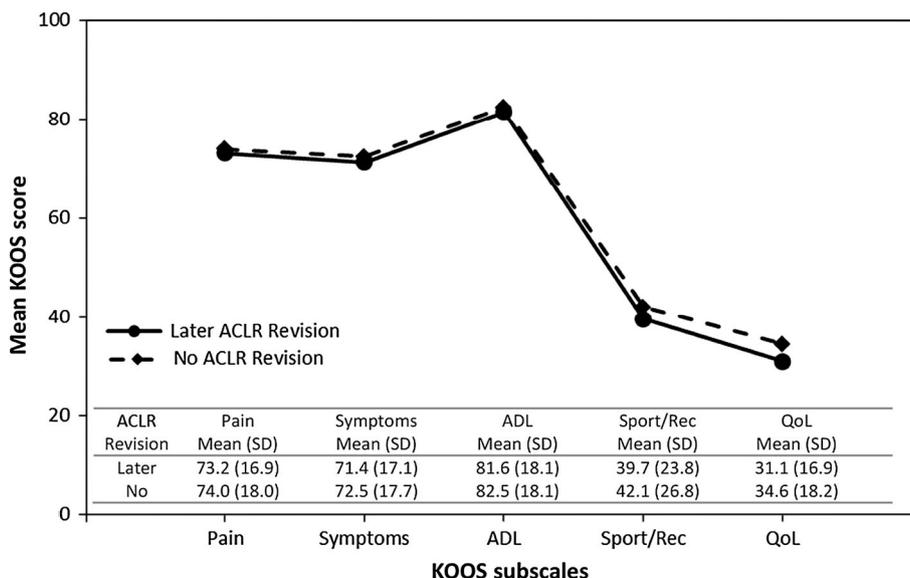

Fig. 1 Flowchart of inclusion and exclusion of patients

The mean score and mean differences in all the five KOOS subscales and 95 % CI by patient's revision status are in Table 2. For Sport/Rec and QoL subscales scores, the unadjusted and adjusted mean differences were more than 10 points higher in the non-revised group than in the revised group.

Figure 3 displays the survival curve of the 2-year follow-up KOOS QoL for those who score ≥44 points and <44 points. In age, sex and pre-operative KOOS-adjusted models, the risk of later revision was 3.7 (95 % CI 2.2–6.0) higher in patients with a 2-year KOOS QoL < 44 compared to patients with a KOOS QoL ≥ 44. In Table 3, this is also shown for the different age groups. The findings indicate also that the KOOS does not differ significantly between males and females (data not shown). A 33.6 % (95 % CI 21.2–47.4 %) higher risk for revision was observed for a 10-point reduction in the KOOS QoL.

Comparing non-responders and responders to the 2 year post-operative KOOS, there was a significantly higher occurrence of ACLR revision patients among the non-responders (2.1 %) compared with the responders (1.5 %, $p = 0.04$). There were also significantly more men (66.1 % vs. 52.3 %, $p < 0.001$) and lower mean age (27.6 vs. 29.2 years, $p < 0.001$) among the non-responders compared with responders, respectively.

Table 1 Study sample characteristics

	Later ACLR revision			No ACLR revision			Total		
	N	Mean	SD	N	Mean	SD	N	Mean	SD
Age	83	25.5	11.2	5,434	29.3	10.8	5,517	29.2	10.8
Males (%)	40 (48.2 %)			2,847 (52.4 %)			2,887 (52.3 %)		

ACLR anterior cruciate ligament reconstruction, *SD* standard deviation

Fig. 2 Study sample pre-operative KOOS subscales scores. *ACLR* anterior cruciate ligament reconstruction, *ADL* activities of daily living, *Sports/Rec* function in sport and recreation, *QoL* knee related quality of life, *KOOS* Knee injury and Osteoarthritis Outcome Score, *SD* standard deviation

Table 2 Mean 2 year post-operative KOOS and mean differences in KOOS between the non-revised and revised ACLR cases

KOOS subscale	Revised after 2-year KOOS	N	Mean score (95 % CI)	Unadjusted mean difference (95 % CI)	Adjusted[a] mean difference (95 % CI)
Pain	No	5,389	84.4 (84.0–84.9)	11.0 (6.2–15.7)	9.3 (5.7–12.9)
	Yes	81	73.4 (68.7–78.2)		
Symptoms	No	5,428	77.0 (76.5–77.4)	9.7 (5.1–14.2)	6.6 (2.6–10.7)
	Yes	83	67.3 (62.8–71.8)		
ADL	No	5,390	90.7 (90.3–91.1)	9.6 (4.6–14.6)	7.8 (4.7–10.9)
	Yes	81	81.1 (76.2–86.1)		
Sport/Rec	No	5,413	65.0 (64.3–65.7)	19.8 (12.9–26.7)	19.5 (13.4–25.7)
	Yes	82	45.2 (38.3–52.0)		
QoL	No	5,421	66.1 (65.4–66.7)	18.8 (12.6–25.1)	15.8 (10.4–21.3)
	Yes	83	47.2 (41.0–53.5)		

ACLR anterior cruciate ligament reconstruction, *KOOS* Knee injury and Osteoarthritis Outcome Score, *ADL* activities of daily living, *Sport/Rec* sports and recreation, *QoL* quality of life, *CI* confidence interval

[a] Adjusted for sex, age and pre-operative KOOS. $N = 4,716$
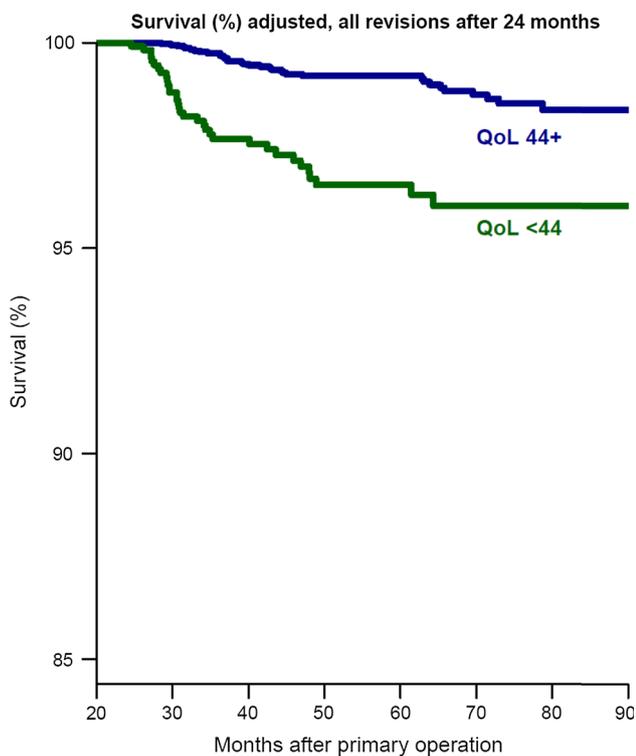
Fig. 3 Survival probability of ACLR by 2 year post-operative KOOS QoL subscale score. Cox regression results with adjustments for sex, age and pre-operative KOOS

Table 3 The 2-year adjusted hazard ratio for later revision in various age categories in patients with a 2-year KOOS QoL < 44 compared to patients with a KOOS QoL ≥ 44

Age group (years)	N	HR (95 % CI)
≤19	25	3.2 (1.4–7.1)
20–28	24	3.0 (1.3–7.1)
29–37	10	3.6 (1.0–13.5)
≥38	9	9.3 (1.8–47.8)
All	68	3.7 (2.2–6.0)

Adjusted for sex and pre-operative KOOS

KOOS Knee injury and Osteoarthritis Outcome Score, *QoL* quality of life, *HR* hazard ratio, *CI* confidence interval

patients who had a KOOS QoL < 44 at 2 years post-index ACLR was also observed.

The authors did not identify high-quality studies investigating the association between pre-operative KOOS in primary and revision ACLRs. Our findings are important because they show that a 2 year post-operative KOOS was low before revision of the ACLR. It is possible that this self-assessment tool, which is associated with subsequent graft failure, can be used to identify patients that need additional attention from their physician or physiotherapist. These patients could then be evaluated for clinical factors that might be addressed and improved by adequate rehabilitation. While graft failure is an irreparable condition, surgery is not the only remedy of this condition. A study by Eitzen et al. [4] has shown that patients, both potential copers and non-copers, are likely to respond to structured progressive rehabilitation. Theoretically, there is a possibility that subsequent revisions can be prevented.

The findings of this study support the hypothesis that KOOS QoL can be regarded as an indicator of clinical

Discussion

The most important finding of the present study was that the KOOS 2 years after a non-revised ACLR operation was significantly different between patients who went on to have a revision and those who did not have a revision during the study period. An increased risk of failure in

failure [5]. However, the used cut-off point (<44) may not be the most appropriate for identification of clinical failures. Because non-revised patients had a small confidence interval with the lower limit more than 20 points higher than the suggested clinical failure value. This suggested clinical failure value has never been validated and 22 % (1,188/5,421) of the non-revised patients scored <44 points on the KOOS QoL subscale. Nevertheless, at this time, there are no alternatives for graft failure indicator or a more suitable cut-off value to suggest as a replacement. Another important contribution from this study is that the analysis of risk of revision based on the KOOS QoL cut-off value revealed no differences between sexes, indicating that separate analysis might not be necessary in the future.

This study's major strength is that it is based on a national cohort of patients. A large number of contributing surgeons, hospitals and patient subgroups (various age and activity levels) were included in this study, creating a large representative sample of patients undergoing ACLR in community-based practices. The ability to generalize our findings to a large number of patient and surgeon/hospital settings increases the external validity of our findings. In addition, previous studies have compared NKLR with other registries and concluded that findings can be generalized to these registries [7, 8, 10]. Another important strength of this study is the high internal validity of the NKLR, which collects information on ACLRs prospectively, using standard data collection procedures, with agreed upon definitions, and validated outcome tools such as the KOOS.

The main limitations of this study are the selected sample of cases included and possibility of selection bias. Only 62 % of the overall registry cohort was included in the study due to missing 2 year post-operative KOOS. We tried to evaluate this selection bias by performing a non-responder analysis. While some statistically significant differences exist between the responders and non-responders, the authors do not believe these would influence the findings in any particular way. The group of patients with missing KOOS data were younger, more often male, and had more revisions than the ones that had the complete 2-year KOOS follow-up suggesting our estimations are more likely conservative. But these findings need to be confirmed in other studies. We adjusted for patient characteristics found to be associated with the KOOS and revision ACLR as well as the pre-operative KOOS; however, other variables not in the registry could also influence this relationship and could confound the findings of this study.

Another limitation of this study is the limited information on the temporal relationship of the events. There are no certainties regarding when the graft failure leading up to a revision happened in relation to when the 2-year follow-up KOOS data were collected. To address this, we reviewed the data on patients with ACLR revisions done within 6 months after completing the KOOS 2-year follow-up. These patients ($n = 23$) have a lower KOOS for all the subscales (data not shown) than patients with later revisions ($n = 60$). In addition, we analysed the risk of later revision in patients with a 2-year KOOS QoL < 44 in this subset of patients, compared to patients with a KOOS QoL $\geq$ 44, and found it to be consistently higher (HR = 2.4, 95 % CI 1.2–4.8). Since the KOOS is a patient-reported outcome measure and is not correlated to other clinical information, this may be considered as a limitation of the current study. The NKLR recorded the cause of failure, but even though there were no statistically significant difference between responders and non-responders (data not shown), the various sub-groups due to cause of failure are too small for further statistical analysis.

Future studies are needed to confirm these findings. Studies should also be conducted to investigate possible ACLR failure indicators earlier on after the procedure. This is very likely, since data from the Swedish knee ligament register did not find any clinically significant difference between one and 2 year post-operative scoring for any of the KOOS subscales [1, 2]. There should also be conducted studies in a non-operative ACL-injured patient cohort to investigate whether the KOOS also can predict insufficient clinical outcome in this patient population.

Since the human biology is both dynamic and complex, it might be too simple to believe that questionnaires will be able to predict individual future knee function and failure. The finding in this study, however, suggests that a simple questionnaire like the KOOS reveals an association between inadequate knee function and a prospective ACLR graft failure.

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