TITLE
Early patellofemoral osteoarthritis features 1 year after anterior cruciate ligament reconstruction predict symptoms and quality of life at 3 years

RUNNING TITLE
Impact of OA features following ACLR on KOOS

AUTHORS
Adam G Culvenor\textsuperscript{1,2,3} PT, PhD; Natalie J Collins\textsuperscript{1,4} PT, PhD; Ali Guermazi\textsuperscript{5} MD, PhD; Jill L Cook\textsuperscript{2,6} PT, PhD; Bill Vicenzino\textsuperscript{1} PT, PhD; Kay M Crossley\textsuperscript{1,2} PT, PhD

1. The University of Queensland, School of Health and Rehabilitation Sciences, Division of Physiotherapy, Brisbane, Queensland, AUSTRALIA
2. La Trobe University, School of Allied Health, College of Science, Health and Engineering, Melbourne, AUSTRALIA
3. Institute of Anatomy, Paracelsus Medical University Salzburg & Nuremberg, Salzburg, AUSTRIA
4. The University of Melbourne, Department of Mechanical Engineering, Parkville, AUSTRALIA
5. Boston University School of Medicine, Department of Radiology, Boston, USA
6. Monash University, Department of Physiotherapy, School of Primary Health Care, Melbourne, AUSTRALIA

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CORRESPONDING AUTHOR
Professor Kay M Crossley
School of Allied Health
La Trobe University, Melbourne 3086, Australia
Telephone: +61 3 94793902; Fax: +61 3 94795768; Email: k.crossley@latrobe.edu.au

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CONFLICT OF INTEREST
Ali Guermazi is the president of Boston Imaging Core Lab, LLC, and is a consultant to Merck Serono, Genzyme, OrthoTrophix, and TissueGene. These sources had no involvement in study design, interpretation of data, writing of the manuscript or the decision to submit the manuscript for publication. All other authors declare no conflict of interest.

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ABSTRACT

Objective. To determine if the presence of MRI osteoarthritis (OA) features in the patellofemoral or tibiofemoral joint (i.e. bone marrow lesions, cartilage lesions, osteophytes) and/or functional impairments, 1-year following anterior cruciate ligament reconstruction (ACLR), can predict Knee injury and Osteoarthritis Outcome Score (KOOS) at 3-years.

Methods. 93 participants (mean age 29±9 years, 56 [60%] men) who had undergone MRI examination and functional testing at 1-year post-ACLR, completed the KOOS at 3-years post-surgery. Multivariate regression models evaluated the prognostic capacity of compartment-specific osteochondral OA features, scored using the MRI OA Knee Score (MOAKS), and functional performance (hop for distance, one-leg-rise), to predict outcome on four KOOS-subscals (pain, symptoms, sport/recreation, quality of life [QOL]).

Results. Presence of patellofemoral cartilage lesions 1-year post-ACLR predicted worse score on all KOOS-subscals at 3-years (p≤0.01). Regression coefficients (B), 95% confidence intervals (CI): symptoms -5.1 (-9.1, -1.2); pain -4.0 (-6.7, -1.4); sport/recreation -6.7 (-11.0, -2.4); QOL -8.6 (-15.1, -2.1). No significant associations were found between tibiofemoral MRI features and knee symptoms. Poorer performance on the one-leg-rise test predicted worse KOOS-quality of life (B -6.5, 95%CI -12.4, -0.5, p=0.03).

Conclusion. The presence of a patellofemoral articular cartilage lesion and lower one-leg-rise performance at 1-year post-surgery are prognostic for poorer 3-year outcome following ACLR. Particular attention to patellofemoral compartment lesions and functional capacity is warranted during post-operative rehabilitation programs, as these features represent potential targets for therapy aimed at minimizing symptomatic disease progression in these young adults.
SIGNIFICANCE AND INNOVATIONS

1. Patellofemoral, but not tibiofemoral, articular cartilage lesions and reduced functional performance (one-leg rise task) 1-year post-ACLR predict poor 3-year self-reported outcome.

2. A greater emphasis may need to be placed on the patellofemoral joint during post-operative rehabilitation.

3. These imaging and clinical features represent potential targets for therapy aimed at minimizing symptomatic disease progression in young adults post-ACLR.
Anterior cruciate ligament (ACL) injuries constitute a high risk for incident radiographic knee osteoarthritis (OA), irrespective of management (1, 2). Yet, the link between radiographic and clinical features of knee OA is inconsistent, and may reflect lack of sensitivity in detecting early OA changes (i.e. radiography identifies bony abnormalities, not antecedent changes in cartilage) (3, 4). Magnetic resonance imaging (MRI) enables the assessment of pre-radiographic OA features early in the course of disease and may elucidate features of early symptomatic disease following ACLR.

Using MRI, we recently revealed prevalent pre-radiographic osteochondral (i.e. bone marrow lesions [BMLs], cartilage lesions) OA features in young adults 1-year following ACLR (5). Such early OA features may predict the development, or persistence, of knee symptoms. It is known that similar MRI features predict symptoms in older cohorts over a one and 5-year period (6, 7). However, in young adults following trauma, the natural history of osteochondral lesions differ, which may impact symptomatic outcomes. For example, post-traumatic BMLs are more likely to resolve compared to idiopathic BMLs in radiographic OA (8, 9), likely due to greater water content and unsaturated lipids (10).

Physical performance testing is recommended to assess lower-extremity function after ACLR and can have important prognostic implications. Functional impairments such as limb asymmetry observed on hop tests can predict self-reported knee function six months post-ACLR (11). The one-leg-rise test (tested 37 weeks post-ACL injury) can also predict self-reported knee symptoms 2 and 5-years post-ACL injury (ACL-deficient and ACLR individuals combined) (12). Thus, it is possible that functional impairments at 1-year might also predict knee symptoms at 3-years, in an ACLR population. Importantly, functional impairments are modifiable (13), providing a promising target for therapy.
Identifying MRI features and functional impairments following ACLR as prognostic factors will aid in developing therapy to retard the progression of symptomatic disease in young active adults. The current study aimed to determine if compartment-specific osteochondral lesions (i.e. BMLs, cartilage lesions, osteophytes) or functional impairments, 1-year following ACLR could predict self-reported Knee injury and OA Outcome Score (KOOS) at 3-years. A secondary aim was to compare KOOS results 1 and 3-years post-ACLR to population norms to provide context to the KOOS results reported by ACLR participants. Based on previous longitudinal studies in older adults free of radiographic OA (6, 7), and prospective studies post-ACL injury (12), we hypothesized that individuals with MRI pathology or functional impairments evident at 1-year post-surgery would exhibit worse results on the KOOS 3-years post-ACLR. We also hypothesized that KOOS results 1 and 3-years post-ACLR would be similar to population norms.

MATERIALS AND METHODS

Participants and procedures

Consecutive patients who had undergone primary single-bundle hamstring-tendon autograft ACLR by either one of two orthopaedic surgeons (>150 ACLRs annually) between July 2010 and August 2011, and were aged 18-50 years at time of surgery, were eligible for inclusion. Detailed descriptions of baseline inclusion and exclusion criteria, ACLR technique and post-operative rehabilitation have been published previously (5). Briefly, exclusion criteria included individuals with a history of knee injury/symptoms prior to ACL injury, >5-years between ACL injury and reconstruction, and any secondary injury/surgery to the ACLR knee. Ethics approval for this prospective study was granted by The University of Melbourne and
University of Queensland Human Research Ethics Committees, and participants provided written informed consent prior to participation.

Baseline assessment was conducted 1-year post-ACLR (range 11-15 months), and consisted of OA features on MRI, functional performance and knee symptoms (KOOS). Follow-up assessment was conducted 2-years after baseline (3-years post-ACLR), and consisted of KOOS only. In addition to the exclusion criteria for the baseline assessment (5), participants reporting any new knee injury or surgery (defined as a knee injury for which medical attention was sought), or any other condition affecting normal daily function since the 1-year post-ACLR evaluation, were excluded from this prospective study.

MRI acquisition and interpretation

Unilateral MRI knee examinations were performed using a 3.0T system (Philips Achieva, The Netherlands) with a 16-channel knee coil (Invivo, Gainesville, Florida, USA). Our imaging protocol consisted of a three-dimensional proton-density VISTA sequence acquired at 0.35mm isotropically (TR/TE 1300ms/27ms, 150mm² field of view (FOV) (acquisition time: 6:18mins). An additional sagittal short-tau inversion-recovery (STIR) sequence was deployed to reduce artefacts in the phase encoding direction arising from metallic hardware. The STIR sequence was acquired at 2.5mm thickness and 1.2mm slice gap. An inversion time of 180ms was applied with TR/TE 3850ms/30ms, FOV 160mm² (acquisition time 3:18mins). We also obtained an axial proton-density turbo spin echo (TSE) sequence with imaging parameters of TR/TE 3850ms/34ms, slice thickness 2.5mm, slice gap 2.0mm, and FOV 140mm² (acquisition time: 2:06mins).
The MRI scans were read by a musculoskeletal radiologist (AG) with 14-years of experience and established reliability in semi-quantitative MRI evaluation of knee OA using the MRI OA Knee Score (MOAKS) (weighted κ 0.54 to 1.00) (14). Briefly, the knee was divided into 14 subregions to score specific osteochondral features related to OA including BMLs (assessed using STIR and TSE sequences) and articular cartilage lesions (assessed using isotropic VISTA sequence). Osteophytes were also scored at specific locations in the tibiofemoral and patellofemoral compartments on isotropic VISTA sequence. The central and posterior femoral subregions and all tibial subregions (anterior, central and posterior) were used to assess the presence of BMLs and articular cartilage lesions in the tibiofemoral compartment. For patellofemoral OA features, the medial and lateral femoral trochlea and patella were assessed. Bone marrow lesions were scored based on the size relative to each subregion (0=none, 1=<33%, 2=33–66%, and 3=>66%). Articular cartilage damage was scored as partial- or full-thickness loss based on: i) size of any cartilage loss (including partial and full-thickness loss) as a percentage of surface area as related to the size of each individual region; and ii) percentage full-thickness cartilage loss of the region (0=none, 1=<10% of region of cartilage surface area, 2=10-75% of region of cartilage surface area, 3=>75% of region of cartilage surface area). Osteophytes were scored based on size (0=none, 1=small, 2=medium, and 3=large) (14). The MRI reader was blind to arthroscopic findings and any meniscal or chondral surgical intervention at the time of ACLR. The severity of each OA feature in this cohort has recently been reported (5). For the current study, the presence/absence (i.e. 0 vs ≥1) of each compartment-specific OA feature was used in primary analyses (e.g. medial/lateral trochlea and medial/lateral patella combined for patellofemoral OA features). Secondary analyses were conducted using OA feature severity score. Participant age, sex, height, and weight were recorded at the time of MRI, and body mass
index (BMI) calculated. From the assessment of radiographs, little radiographic OA (<5%) was observed (5).

**Functional performance**

The hop for distance, an established test of functional capacity in ACLR populations (15), was used to assess functional performance of both lower limbs. The longest of three trials was recorded from the toe at take-off, to the heel at landing, without subsequent smaller hops. The left limb was always tested first, and hands were held behind the back. We calculated the limb symmetry index (LSI), reported as a percentage (ACLR knee ÷ contralateral knee x 100). The LSI results were dichotomized for statistical analyses based on the commonly used cut-off to define functional recovery (≥90%) (12).

The maximum number of one-leg-rises performed at a controlled speed from a standardized height plinth (knee at 90° flexion in sitting) was also recorded (one-leg-rise test) (16). Results were dichotomized (≥22 or <22 rises), as this cut-off has been found to predict the development of radiographic knee OA in middle-aged people with chronic knee pain (16).

**Self-reported knee symptoms, function and quality of life**

The KOOS was used to assess patient-reported outcomes on four subscales: pain, symptoms, function in sport and recreation (KOOS-SR), and knee-related quality-of-life (KOOS-QOL) (17). Participants responded with respect to their knee condition over the previous week, and a normalized score was calculated for each subscale (100 represents no knee problems and 0 represents extreme knee problems). Due to ceiling effects observed in young active populations for the activities of daily living subscale of KOOS (18), this subscale was not evaluated. One-year post-ACLR, the KOOS was completed in person (pen and paper), while
at 3-years post-ACLR, the KOOS was completed via an online portal (MySQL, Oracle Corporation, California, USA) with identical instructions to the original paper version. KOOS has demonstrated test-retest reliability between paper and electronic formats (ICC>0.96) (19). Participants without access to email at follow-up (n=5) were mailed a hard copy of the KOOS to complete and return by post. Although the minimal clinical important difference is not known, a change in KOOS score of ≥10 has been suggested to represent a clinically significant difference (20).

Data analysis

Descriptive statistics were used to describe demographic characteristics and KOOS values 1 and 3-years post-ACLR, and to compare KOOS values to population-based normative data from similarly aged men and women (18-34 years) (those with an injury history not specifically excluded) (21). Dependent variables were KOOS subscales 3-years post-ACLR. Multivariate regression analyses evaluated whether compartment-specific osteochondral MRI features (BMLs, articular cartilage lesions, osteophytes) or functional performance (hop for distance, one-leg-rise) 1-year post-ACLR predicted 3-year KOOS values. Consistent with previous analyses for patellofemoral features (22), we adjusted all multivariate models for age, sex, BMI, and the presence of tibiofemoral osteochondral features (BMLs, articular cartilage lesions, and osteophytes). We also adjusted for baseline KOOS values, similar to other longitudinal ACLR studies (12). The same analyses were performed for associations with tibiofemoral features (adjusted for age, sex, BMI, patellofemoral osteochondral features, and baseline KOOS values). Standardized β values, unstandardized B values, 95% CIs and p-values were reported. The unstandardized B value represents the difference in KOOS when the outcome of interest is present (compared with absent). Regression models were analyzed to ensure that general assumptions, including multicollinearity assumptions, were met. We
examined the data for outliers by examining the regression residuals. Observations with standardized residuals greater than ±3 were excluded from the analysis since these few extreme data points may exert undue influence on the regression results (23). One outlier who reported considerable deterioration for all KOOS subscales for no apparent reason was excluded from all analyses. No more than two outliers were excluded from any analysis. Sensitivity analyses were also conducted by: i) including all participants, and ii) additionally adjusting for physical activity 1-year post-ACLR (assessed with Sports Activity Classification) (24), to evaluate the influence of outlying participants and activity level, respectively. All statistical analyses were completed using SPSS statistical software V.22.0 (SPSS, Chicago, Illinois, USA), with α set at 0.05.

RESULTS

Participants
Detailed results of participant recruitment into the previous cross-sectional study, which forms the baseline for this prospective study (i.e. 1-year post-ACLR), appear elsewhere (5). Briefly, of the 187 individuals who underwent an ACLR in the study period and met eligibility criteria, 111 (59%) participated in the 1-year post-ACLR assessment. There was no difference in age, sex, time from injury to ACLR or rate of concomitant injuries between eligible participants who did and did not participate in the 1-year post-ACLR assessment (p>0.05) (5). Of these 111 participants, 106 (95%) completed the KOOS 3-years following ACLR; the remaining 5 could not be contacted. After excluding 13 (12%) participants because of further knee injury and/or surgery (ruptured autograft=2, secondary meniscal surgery=6, contralateral ACL rupture=4, contralateral meniscectomy=1), a total of 93 participants, of whom 56 (60%) were men, were included in the final analysis. The median (interquartile range [IQR]) age at surgery and time from injury to ACLR was 26 (13) years.
and 3 (5) months, respectively. At the time of ACLR arthroscopy, 15 (16%) had evidence of a tibiofemoral chondral lesion and 9 (10%) a patellofemoral chondral lesion of ≥grade II Outerbridge, while 33 (35%) had a concurrent meniscectomy. The 1-year post-ACLR assessment took place at a mean ± standard deviation (SD) of 13 ± 1 months post-operatively, while the 3-year post-ACLR assessment was conducted at a mean 36 ± 1 months post-operatively. There was no difference in age, sex, BMI, time from injury to ACLR, rate of concomitant injuries, 1-year post-ACLR KOOS values or MRI characteristics between those who were included and those who were excluded from the final analysis (p>0.05).

Knee symptoms 1 and 3-years post-ACLR

One-year post-ACLR, all KOOS values were below normative data from 134 individuals of similar age (18-34 years) (21) (Table 1). Only KOOS-QOL had a difference from normative values that was greater than the suggested clinically significant difference of 10 points (20). Three-years post-ACLR, KOOS values were similar or higher than normative scores (Table 1). The greatest difference remained in KOOS-QOL, but this difference was <10 points.

TABLE ONE HERE

MRI features 1-year post-ACLR

Of the 93 participants included in the current prospective study, patellofemoral BMLs, articular cartilage lesions and osteophytes were observed in 20 (22%), 43 (46%), and 43 (46%) knees, respectively (Figure 1). Examples of patellofemoral articular cartilage lesions observed appear in Figure 2. The corresponding rates of tibiofemoral MRI features were 29 (31%), 38 (41%), and 41 (44%).

FIGURE ONE HERE
FIGURE TWO HERE

Functional performance 1-year post-ACLR

The mean±SD LSI for the hop for distance was 88.4±15.9%. Fifty-seven (61%) participants had a LSI ≥90%. The median (lower and upper IQR) number of one-leg-rises on the ACLR limb was 26 (10-50). Fifty-four (58%) participants performed ≥22 one-leg-rises.

MRI features as predictors of KOOS at 3-years post-ACLR

The presence of an articular cartilage lesion in the patellofemoral compartment was the only MRI feature 1-year post-ACLR to predict KOOS values at 3-years. Specifically, patellofemoral articular cartilage lesions were a significant predictor of worse score on all four KOOS subscales (Table 2). Secondary analyses of OA feature severity (i.e., ordinal data), confirmed these results (Figure 1), and with the exception of KOOS-symptoms (p=0.15) these findings did not change on sensitivity analyses (including all outliers and adjusting for physical activity). The effect of a patellofemoral cartilage lesion was strongest on KOOS-QOL, with cartilage lesion presence resulting in a KOOS-QOL score 8.6 points lower (compared with no cartilage lesion). Tibiofemoral BMLs, cartilage lesions or osteophytes did not significantly predict 3-year KOOS (p>0.05). The only tibiofemoral feature that trended towards being associated with KOOS was cartilage lesions (KOOS-QOL β=0.2, B=5.6, 95% CI -0.1 to 11.3, p=0.06). The positive regression coefficient indicates that a tibiofemoral cartilage lesion approached significance for predicting better KOOS-QOL. All other unstandardized regression coefficients for tibiofemoral features ranged from -1.8 to 2.6 (standardized regression coefficients -0.1 to 0.1), indicating a much smaller influence on 3-year KOOS than patellofemoral cartilage lesions.
Functional performance tests as predictors of KOOS at 3-years post-ACLR

The inability to perform ≥22 one-leg-rises 1-year post-ACLR was a significant predictor of worse KOOS-QOL at 3-years post-surgery (p=0.03) (Table 3), even after including outliers in sensitivity analyses and adjusting for physical activity (p=0.04). Median KOOS-QOL values and interquartile ranges for those able and unable to perform ≥22 one-leg-rises appear in Figure 3. The hop for distance was not a significant predictor of 3-year KOOS (Table 3).

DISCUSSION

In this study of knees with prevalent MRI pathology and little or no radiographic OA 1-year following ACLR, the presence of MRI detectable patellofemoral articular cartilage lesions was the only feature to predict KOOS 3-years post-ACLR. Functionally, worse performance on the one-leg-rise test predicted a lower knee-related QOL. These findings emphasize the clinical importance of MRI detected damage to the patellofemoral joint following ACLR and highlight the possible consequences of functional performance deficits at 1-year post-ACLR.

Few longitudinal studies have evaluated the relationship between MRI features and self-reported knee symptoms, function or QOL following ACLR. Among these prognostic evaluations, neither articular cartilage lesions nor BMLs observed pre-operatively predicted...
International Knee Documentation Committee (IKDC) subjective scores 1-year (25) or 12-years (26) post-ACLR. The issue with these prior studies is that the relationship with knee symptoms was evaluated only with tibiofemoral osteochondral MRI features. While these results are consistent with our finding of no relationship between tibiofemoral osteochondral features and KOOS, our evaluation of patellofemoral features allowed us to identify an important prognostic feature in these young adults at risk of radiographic OA. Specifically, the presence of a patellofemoral articular cartilage lesion was associated with worse scores on KOOS subscales. Specifically, those with a patellofemoral cartilage lesion had KOOS results ranging from 4.0 to 8.6 points lower than those without a patellofemoral cartilage lesion. Patellofemoral cartilage lesions had the strongest effect on KOOS-QOL and KOOS-SR, with differences greater than the respective subscale’s minimal detectable change, indicating a real difference (27). While the patellofemoral joint has gone largely unrecognized in ACLR studies (28), our results extend previous cross-sectional post-ACLR radiographic data (29), and MRI studies in older adults that reveal patellofemoral osteochondral pathology to have a greater association with knee symptoms than tibiofemoral osteochondral pathology (30, 31).

Given the association between patellofemoral pathology and KOOS subscales, a greater emphasis may need to be placed on the patellofemoral joint during post-operative rehabilitation. Modifications to typical rehabilitation exercises aimed at minimizing patellofemoral load have been proposed (32, 33) and, in combination with interventions with known efficacy in atraumatic patellofemoral pain populations (34), should be considered by clinicians. While the ability of non-surgical strategies to alter patellofemoral cartilage lesions is not known, the severity of cartilage lesions is low and hence, potentially modifiable (35). There is promising evidence that specific neuromuscular exercises can improve knee cartilage quality (glycosaminoglycan content) in middle-aged adults following partial
meniscectomy (36). Structured, individualized rehabilitation is also effective at improving self-reported knee symptoms and function (IKDC score) in young adults with a cartilage lesion (13). The effect of such strategies on knee symptoms in those with a tibiofemoral cartilage lesion may be less clear given that a trend towards a positive association between tibiofemoral cartilage lesions and QOL was observed. The use of non-surgical strategies to improve knee symptoms in those with a patellofemoral (and tibiofemoral) articular cartilage lesion after ACLR should be considered clinically, and evaluated in clinical trials.

The finding of no association between the presence of a BML or osteophyte in either knee compartment and KOOS 2-years later extends short-term (pre-operative to 1-year post-ACLR) (25) and long-term (preoperative to 12-years post-ACLR) (26) prospective MRI data from the tibiofemoral joint alone. These results contrast the longitudinal studies of BMLs in older, non-traumatic knees with and without radiographic OA, which typically find BMLs to be a source of pain (6, 7, 37). Thus, the lack of association between BMLs and knee symptoms in the current study supports spectral imaging data showing that post-traumatic BMLs have distinct biochemical properties from idiopathic BMLs, and are more likely to resolve (10). Larger BMLs may persist and be associated with future knee symptoms; however, most of the BMLs we observed were small (5). Similarly, the high-resolution MRI scans may have detected small, pre-clinical osteophytes, and the progression of these following ACLR is not known. In the short-term (over 2-years), BMLs and osteophytes do not appear to impact significantly on patient-reported pain, symptoms, sport function and QOL.

Performance on the one-leg-rise test was the only functional performance outcome to predict worse knee symptoms or function. Specifically, the inability to complete ≥22 one-leg-rises 1-
year after ACLR led to a KOOS-QOL score 6.5 points lower than those who performed ≥22 one-leg-rises. This finding extends recent data reporting that post-rehabilitation one-leg-rise LSI results (using a method of lowest height that can rise on one leg) predicted KOOS at 2 and 5-years post-ACL injury managed conservatively or surgically (12). The one-leg rise test consists of an everyday functional task – sit-to-stand. Inadequate one-leg rise (sit-to-stand) performance represents a relative functional disability, and in young ACLR populations, who typically derive much pleasure and self-worth from competing in competitive sport (38), this is likely associated with inferior performance, driving the lower QOL that we observed. While individual hop tests (hop for distance, 6m timed hop) can predict self-reported knee function (IKDC score) 1-year following ACL injury (39) and reconstruction (11), the results of the current study and others (12) indicate that functional capacity may be important determinants of future knee symptoms and QOL. The modifiable nature of these factors point to the importance of optimizing functional performance during post-operative rehabilitation.

It is important to acknowledge that one to two participants who had scores that were large outliers (deteriorated in KOOS-pain 29% and 21%) did have an undue influence on outcomes and were therefore excluded. With a larger sample and greater statistical power, these outliers would likely pose less of an issue. While there were no demographic differences between those who did and did not participate in baseline assessment, it is not known if patients with worse symptoms were more or less likely to participate, which may have confounded results.

The form of patient-reported outcome administration differed between assessments at 1-year (pen and pencil) and 3-years after ACLR (web-based). However, web-based administration of the KOOS has been shown to be equivalent to the traditional pen and paper administration (19). The KOOS reports outcomes during the previous week, and as such may be influenced by recent changes in physical activity or comorbidities. Because only mild impairments
existed on most subscales of the KOOS, which were similar to data from population norms (21) and Scandinavian ligament registries (1-2 years post-ACLR) (40), a ceiling effect may have occurred and contributed to the few associations we observed. Importantly, we adjusted our results for baseline KOOS values as well as BMI, age and sex. Although we analyzed measures of functional performance, specific qualitative control, such as knee valgus/internal rotation collapse, was not assessed, but may be linked to patellofemoral dysfunction post-ACLR (41). Finally, too few site-specific OA features (i.e., medial/lateral patella or trochlea) existed to perform statistical analyses of features in different patellofemoral locations, and without follow-up MRIs, we could not be certain of the structural progression of the lesions we observed 1-year post-ACLR. Further imaging follow-up of this cohort in the coming years will reveal important insights into the progression of these post-traumatic MRI features of disease, and the potential relationship with KOOS values.

The presence of a patellofemoral articular cartilage lesion and lower performance on the one-leg-rise test have important prognostic implications for symptomatic outcomes following ACLR. Particular attention to patellofemoral compartment lesions and functional capacity is warranted during post-operative rehabilitation programs, as these features represent potential targets for therapy aimed at minimizing symptomatic disease progression in these young adults.
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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Crossley had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis (e-mail: k.crossley@latrobe.edu.au).

Study conception and design. Culvenor, Collins, Cook, Crossley.

Acquisition of data. Culvenor, Collins, Guermazi, Crossley.

Analysis and interpretation of data. Culvenor, Collins, Guermazi, Vicenzino, Crossley

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COMPETING INTEREST STATEMENT

Ali Guermazi is the president of Boston Imaging Core Lab, LLC, and is a consultant to Merck Serono, Genzyme, OrthoTrophix, and TissueGene. These sources had no involvement in study design, interpretation of data, writing of the manuscript or the decision to submit the manuscript for publication. All other authors declare no conflict of interest.
REFERENCES


FIGURE LEGENDS

Figure 1. Patellofemoral OA feature severity and relationship to KOOS subscales. Data represent median and interquartile range. P-values represent significant results from analyzing OA feature severity in multivariate regression, adjusting for age, sex, body mass index, tibiofemoral OA features and baseline KOOS subscale score. KOOS, Knee injury and Osteoarthritis Outcome Score; SR, function in Sport and Recreation; QOL, quality of life; BML, bone marrow lesion.

Figure 2. Examples of MR images showing patellofemoral articular cartilage lesions that were predictive of Knee injury and Osteoarthritis Outcome Score results: A) Sagittal STIR MRI shows diffuse superficial patellar cartilage damage grade 3.0 without full-thickness defect (arrow); B) Axial proton density-weighted MRI shows full-thickness focal defect patellar cartilage damage graded 1.1 (arrow).

Figure 3. KOOS-QOL median and interquartile range for those able and unable to perform ≥22 one-leg rises. KOOS, Knee injury and Osteoarthritis Outcome Score; QOL, quality of life.
### Table 1. KOOS scores for participants included at both 1 and 3-years post-ACLR (n=93)

<table>
<thead>
<tr>
<th>Variable</th>
<th>One year post-ACLR</th>
<th>Three years post-ACLR</th>
<th>Normative scores Paradowski et al. (2006)(19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>KOOS-symptoms</td>
<td>83.0 ± 13.6</td>
<td>88.0 ± 11.0</td>
<td>88.2 ± 13.6</td>
</tr>
<tr>
<td>KOOS-pain</td>
<td>90.9 ± 9.1</td>
<td>94.8 ± 7.2</td>
<td>92.2 ± 12.8</td>
</tr>
<tr>
<td>KOOS-SR</td>
<td>81.7 ± 16.6</td>
<td>90.2 ± 11.0</td>
<td>85.8 ± 20.9</td>
</tr>
<tr>
<td>KOOS-QOL</td>
<td>68.6 ± 18.0</td>
<td>79.9 ± 15.3</td>
<td>84.4 ± 19.7</td>
</tr>
</tbody>
</table>

Values are mean ± standard deviation. KOOS, Knee injury and Osteoarthritis Outcome Score; SR, sport and recreation; QOL quality of life; ACLR, anterior cruciate ligament reconstruction
Table 2. Multivariate regression analyses of the associations between the presence of patellofemoral MRI features assessed 1-year post-ACLR and KOOS values assessed 3-years post-ACLR (n=93)

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Patellofemoral bone marrow lesions§</th>
<th>Patellofemoral articular cartilage lesions§</th>
<th>Patellofemoral osteophytes§</th>
</tr>
</thead>
<tbody>
<tr>
<td>KOOS-symptoms*</td>
<td>-0.1</td>
<td>-0.3</td>
<td>-0.2</td>
</tr>
<tr>
<td>KOOS-pain#</td>
<td>0.0</td>
<td>-0.2</td>
<td>0.0</td>
</tr>
<tr>
<td>KOOS-SR#</td>
<td>-0.2</td>
<td>-0.3</td>
<td>-0.1</td>
</tr>
<tr>
<td>KOOS-QOL*</td>
<td>0.0</td>
<td>-0.3</td>
<td>-0.1</td>
</tr>
</tbody>
</table>

Adjusted for age, sex, body mass index, MRI features in the tibiofemoral compartment and baseline KOOS subscale score.

§ reference group = no pathology; * one outlier excluded; # two outliers excluded. CI, confidence interval; β, standardized regression coefficient; B, unstandardized regression coefficient; KOOS, Knee injury and Osteoarthritis Outcome Score; SR, sport and recreation; QOL, quality of life.
Table 3. Multivariate regression analyses of the associations between functional performance assessed 1-year post-ACLR and KOOS values assessed 3-years post-ACLR (n=93)

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Hop for distance*</th>
<th>One-leg-rise§</th>
</tr>
</thead>
<tbody>
<tr>
<td>KOOS-symptoms*</td>
<td>β = 0.0, B = -0.9, 95% CI = -4.7 to 2.9, p = 0.63</td>
<td>β = 0.0, B = -0.3, 95% CI = -4.0 to 3.4, p = 0.87</td>
</tr>
<tr>
<td>KOOS-pain#</td>
<td>β = -0.1, B = -0.8, 95% CI = -3.3 to 1.7, p = 0.53</td>
<td>β = -0.1, B = -1.5, 95% CI = -4.0 to 1.0, p = 0.23</td>
</tr>
<tr>
<td>KOOS-SR#</td>
<td>β = -0.1, B = -1.6, 95% CI = -5.7 to 2.5, p = 0.45</td>
<td>β = 0.0, B = -0.3, 95% CI = -4.5 to 3.9, p = 0.88</td>
</tr>
<tr>
<td>KOOS-QOL*</td>
<td>β = -0.1, B = -3.7, 95% CI = -10.0 to 2.6, p = 0.24</td>
<td>β = -0.2, B = -6.5, 95% CI = -12.4 to -0.5, p = 0.03</td>
</tr>
</tbody>
</table>

Adjusted for age, sex, body mass index, and baseline KOOS subscale score.

§ reference group = hop for distance ≥90% limb symmetry index, and one-leg-rise test ≥22 rises; * one outlier excluded; # two outliers excluded. CI, confidence interval; β, standardized regression coefficient; B, unstandardized regression coefficient; KOOS, Knee injury and Osteoarthritis Outcome Score; SR, sport and recreation; QOL, quality of life.
Patellofemoral OA feature severity and relationship to KOOS subscales. Data represent median and interquartile range. P-values represent significant results from analyzing OA feature severity in multivariate regression, adjusting for age, sex, body mass index, tibiofemoral OA features and baseline KOOS subscale score. KOOS, Knee injury and Osteoarthritis Outcome Score; SR, function in Sport and Recreation; QOL, quality of life; BML, bone marrow lesion.

229x162mm (300 x 300 DPI)
Examples of MR images showing patellofemoral articular cartilage lesions that were predictive of Knee injury and Osteoarthritis Outcome Score results: A) Sagittal STIR MRI shows diffuse superficial patellar cartilage damage grade 3.0 without full-thickness defect (arrow); B) Axial proton density-weighted MRI shows full-thickness focal defect patellar cartilage damage graded 1.1 (arrow).
KOOS-QOL median and interquartile range for those able and unable to perform ≥22 one-leg rises. KOOS, Knee injury and Osteoarthritis Outcome Score; QOL, quality of life.
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Author/s:
Culvenor, AG; Collins, NJ; Guermazi, A; Cook, JL; Vicenzino, B; Whitehead, TS; Morris, HG; Crossley, KM

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Date:
2016-06-01

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