Patellofemoral osteoarthritis is prevalent and associated with worse symptoms and function after hamstring tendon autograft ACL reconstruction

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ABSTRACT
Objectives To evaluate the compartmental distribution of knee osteoarthritis (OA) after anterior cruciate ligament reconstruction (ACLR), to determine if patellofemoral or tibiofemoral OA is more strongly associated with knee symptoms and function, and to evaluate the contribution of associated injuries and surgical delay to the development of OA.

Methods This cross-sectional study recruited 70 participants who underwent hamstring tendon (HT) ACLR 5–10 years previously. Radiographic OA was assessed according to the Osteoarthritis Research Society International (OARSI) criteria. Knee symptoms were assessed with the Knee Injury and Osteoarthritis Outcome Score (KOOS) and Anterior Knee Pain Scale (AKPS), while function was assessed with three lower limb tasks (hop-for-distance, one-leg rise and side-hop). Multivariate and binary logistic regression analyses were performed to assess the relationship between OA and symptomatic/functional outcomes and associated injuries/surgical delay, respectively.

Results Radiographic OA was observed in the patellofemoral (47%) and tibiofemoral joints (31%). Pain, symptoms and quality of life on the KOOS and the AKPS were associated with severity of patellofemoral OA (standardised regression coefficient \( \beta = -0.3 \) to \(-0.5\), \( p=0.001 \) to \(0.042\)), whereas only the KOOS-pain subscale was associated with tibiofemoral OA (\( \beta = -0.3\), \( p=0.037\)). For each functional task, greater patellofemoral OA severity was associated with worse performance, independent of tibiofemoral OA severity (\( \beta = -0.3 \) to \(-0.4\), \( p=0.001 \) to \(0.026\)). Medial meniscal and patellofemoral chondral lesions at surgery were associated with tibiofemoral and patellofemoral OA development at follow-up, respectively, while a longer surgery delay was associated with patellofemoral OA.

Conclusions Patellofemoral OA is common following HT ACLR and is associated with worse knee-related symptoms, including anterior knee pain, and decreased functional performance.

INTRODUCTION
Knee osteoarthritis (OA) frequently develops after anterior cruciate ligament (ACL) injury, 1 with personal, societal and financial impacts in young adults. Restoration of knee stability with an ACL reconstruction (ACLR) does not reduce the rate of radiographic OA development or improve short-term or long-term symptom outcomes. 2, 3 Indeed, an ACLR may even propagate the development of knee OA. 4 While the association between ACLR and knee OA has focused mostly on the tibiofemoral joint, our recent review reported that patellofemoral OA is common after ACLR (median prevalence of 36%) 5 and is frequently associated with pain. 6, 7 Patellofemoral OA is typically reported after a bone-patellar tendon-bone (BPTB) autograft ACLR, 6, 8 which may alter patellofemoral alignment and cartilage contact. 9 The prevalence and clinical impact of patellofemoral OA following the popular hamstring tendon (HT) autograft ACLR has rarely been investigated.

While patellofemoral and tibiofemoral OA often coexist, 10 the relative contribution of compartment-specific OA severity to symptoms and function after ACLR is not known. Knowing whether the patellofemoral or tibiofemoral compartment impacts more strongly on symptoms and function may direct treatment decisions and encourage compartment-specific management strategies. Potential confounders for the development of OA after ACLR are concomitant injury to either the meniscus or articular cartilage and the time between injury and ACLR. While meniscal injury is a potent risk factor for the development of tibiofemoral OA, 2 its relationship to patellofemoral OA remains controversial. 11–13 Similarly, there are contradictory reports of concurrent chondral lesions being associated with the long-term development of OA in the respective compartment. 14, 15 Finally, there are paradoxical reports for the influence of ACLR delay and OA aetiology, 11, 14–16 demonstrating a need to explore the duration of surgical delay and compartmental OA prevalence.

This study aimed to (1) describe the compartmental distribution of radiographic knee OA; (2) determine the relationship between patellofemoral and tibiofemoral OA severity and the severity of knee symptoms and functional performance after ACLR; and (3) determine if duration of surgical delay or meniscal/chondral injury observed at the time of ACLR is associated with the development of patellofemoral or tibiofemoral OA, using a cohort of individuals 5–10 years post-HT autograft ACLR.

METHODS
Participants
All individuals who had undergone a primary ACLR using a single-bundle four-strand HT autograft by one surgeon in Melbourne 5–10 years previously were identified from patient files. Letters of invitation were sent to all potentially eligible participants. Participants were included if they were aged at least 18 years at the time of surgery and...
had no history of injury/surgery to either knee prior to ACL rupture. Exclusion criteria were: (1) ACLR revision or arthroplasty; (2) inability to understand written and spoken English; and (3) pregnancy or breast-feeding. Approval was granted from the University of Melbourne Human Research Ethics Committee, and all participants provided written informed consent.

Surgery and rehabilitation
All ACLR surgeries were performed by a single surgeon (HGM) at a median of 3 months after the injury (range 2 weeks–28 years). A quadrupled HT graft of semitendinosus/gracilis was performed arthroscopically. The HT autograft was procured through a 3 cm incision near the tibial tubercle using a tendon harvester (Linvatec, Largo, Florida, USA). The graft (approximately 22 cm in length) was then doubled over two pull-out lead sutures. The tibial and femoral tunnels were drilled in the anatomical footprint of the native ACL with the use of a drill guide. Femoral fixation was achieved with an Endobutton (Acufex, Smith & Nephew, Andover, Massachusetts, USA) and tibial fixation with a 7–9 mm interference screw (RCI, Smith & Nephew, Andover, Massachusetts, USA). Graft tensioning was performed by hand in full knee extension. Meniscal tears were treated at the time of ACLR with partial resection or fixation when indicated by clinical and/or arthroscopic assessment. All patients were referred to physiotherapy for appropriate rehabilitation, including early weight-bearing, range of movement and neuromuscular retraining and graduated return to functional activities and sport.16

Primary outcome measures
Radiography
All participants underwent radiographic assessment of the ACLR knee undertaken in weight-bearing, with the knee flexed 30–40° and feet externally rotated 10°. Radiographic disease severity of the patellofemoral joint was assessed from skyline radiographs,17 while the tibiofemoral joint was assessed from a posteroanterior radiograph. Osteophytes and joint space narrowing (JSN) were scored in the patellofemoral and tibiofemoral compartments using the Osteoarthritis Research Society International (OARSI) atlas on a scale from 0 to 3 (0=normal, 1=mild, 2=moderate and 3=severe). Based on previous reports, we considered radiographic OA to be present if any of the following criteria were achieved in the patellofemoral or medial or lateral tibiofemoral compartments: JSN of grade 2 or higher, sum of osteophyte grades ≥2 or grade 1 JSN in combination with a grade 1 osteophyte.8, 10 We measured OA severity using the osteophyte grade in each compartment, since osteophytes are more strongly associated with knee pain and symptoms than other features such as JSN.14 We measured OA severity using the osteophyte grade in each compartment, since osteophytes are more strongly associated with knee pain and symptoms than other features such as JSN.14

All radiographs were assessed by two independent trained observers (KMC and MM). Both raters were blinded to clinical outcomes, with a consensus meeting used to resolve any discrepancies. Inter-rater reliability (κ coefficients) for OARSI scoring of patellofemoral and tibiofemoral radiographic features on a subset of 39 participants was 0.75 (95% CI 0.70 to 0.85) and 0.84 (95% CI 0.77 to 0.92), respectively.

Patient-reported outcomes
The Knee Injury and Osteoarthritis Outcome Score (KOOS) was used to assess patient-reported outcomes on five subscales: KOOS-pain, KOOS-symptoms, function in activities of daily living (KOOS-ADL), function in sport and recreation (KOOS-SR) and knee-related quality-of-life (KOOS-QOL).21 Each subscale addresses symptoms over the previous week and a normalised score was calculated for each subscale (100 represents no symptoms and 0 represents maximum symptoms). To assess specific patellofemoral symptoms, the Anterior Knee Pain Scale (AKPS; 0–100) was used,22 where a maximum score of 100 represents no patellofemoral symptoms.

Functional outcomes
The hop for distance test and the side-hop test, which are established tests of functional capacity in ACLR populations,23 were used to assess lower limb function. The maximum number of one-leg rises performed at a controlled speed from a standardised height plinth (knee at 90° flexion in sitting) was also recorded (one-leg rise test).24 The one-leg rise test is a global measure of lower-limb function and endurance and has been found to predict the development of radiographic knee OA in middle-aged people with chronic knee pain.24

Secondary outcome measures
Participant characteristics and knee motion
Participant characteristics including age, height and weight were recorded. Maximum range of knee flexion and extension was measured in supine position using a goniometer,25 and knee laxity with the KT-1000 arthrometer by one independent assessor (CCHL). The Tegner Activity Scale was used to assess the participant’s activity level.26

Concomitant injuries at surgery
Damage to the meniscus or articular cartilage observed at the time of ACLR was assessed from the surgical files of all participants. Meniscal injury was defined as any meniscal tear requiring surgery.10 Chondral injury was defined with Outerbridge classification as any damage ≥grade 2.14

Data analysis
Differences in demographic and clinical data between those with and without OA were determined using Student’s t tests or Mann-Whitney U tests as appropriate. Multivariate regression analyses, with both patellofemoral and tibiofemoral OA severity included in each model, were used to examine the relative contribution of compartment-specific OA severity (ordinal data 0–3) and symptoms and function. A similar approach with ordinal data has previously been performed to determine factors related to knee alignment27 and load.28 Regression models were analysed to ensure that general assumptions, including multicolinearity assumptions, were met. Participant characteristics that were univariately correlated with dependent variables were included as covariates (p<0.05). For chondral/meniscal injuries identified at surgery and surgical delay, OR and 95% CI were calculated for the presence of OA in each knee compartment using binary logistic regression analyses adjusted for age and gender. ACLR was classified as early (<6 weeks from injury), intermediate (6 weeks to 1 year from injury) or late (>1 year from injury). Statistical analyses were performed with SPSS for Windows V.21.0 software (SPSS, Chicago, Illinois, USA), with α set at 0.05.

RESULTS
Of the 743 invitation letters sent to potentially eligible participants, 103 were returned to the sender (change of address). Of the remaining 638 participants, 81 (13%) contacted the researchers; 4 were excluded due to bilateral ACLR, 2 due to ACLR revision surgery and 1 due to a patellectomy. After...
radiological assessment, a further four participants were excluded due to insufficient radiographic quality. Of the 70 eligible participants with radiographs, 42 (60%) were men. Mean (±SD) age was 42±10 years, time from surgery 7±2 years, height 1.7±0.1 m and weight 81±16 kg. Sixty participants completed the patient-reported outcomes (KOOS and AKPS) and 65 completed the functional assessment.

Distribution of radiographic OA
Thirty-three (47%) participants had radiographic patellofemoral OA and 22 (31%) had radiographic tibiofemoral OA (figure 1). Mild (grade 1, n=35; 50%) and moderate (grade 2, n=17; 24%) osteophytes were most commonly observed. Those with OA (either patellofemoral or tibiofemoral) were significantly older and less active than those without OA (table 1).

Relationship between compartment-specific OA severity, symptoms and function
Multivariate regression analyses, with patellofemoral and tibiofemoral OA severity as well as appropriate covariates (participant characteristics that were univariately correlated with dependent variables) included in each model (table 2), revealed that greater patellofemoral and tibiofemoral OA severity were associated with worse KOOS-pain. Greater patellofemoral OA severity was independently associated with worse KOOS-symptoms, KOOS-QOL and AKPS (table 2). Greater patellofemoral OA severity was also associated with lower performance on the three functional tasks, while tibiofemoral OA severity was not independently associated with any functional task (table 2).

Concomitant injuries and surgical delay
Patellofemoral chondral damage and medial meniscal injury observed at the time of surgery increased the odds of developing patellofemoral OA and medial tibiofemoral OA at follow-up, respectively (table 3). The presence of tibiofemoral OA was not associated with timing of ACLR; however, patellofemoral OA was more common in those who had a delayed ACLR compared to those who underwent an early ACLR (table 3).

DISCUSSION
The present study provides unique insights into the individual contribution of patellofemoral and tibiofemoral OA severity to symptoms and functional performance after ACLR. Patellofemoral OA (47%) was more common than tibiofemoral OA (31%) 5–10 years after ACLR, with OA being frequently isolated to the patellofemoral joint (20%). This compartmental distribution pattern of OA reflects previous community-based studies, and is identical to the reported prevalence from BPTB ACLR, suggesting that a HT autograft does not protect the patellofemoral joint from degenerative change. Our recent literature review proposed a number of explanations for the high rate of patellofemoral OA after ACLR, including concomitant damage to the patellofemoral compartment at the time of injury, which we confirmed in the current study and altered frontal and transverse plane knee kinematics, which we observed in our recent kinematic study. While it is possible that knee movement restrictions and prolonged quadriceps weakness also contribute to patellofemoral OA development, we did not observe any movement deficits in those with patellofemoral OA and muscle strength was not specifically evaluated. The prevalence of tibiofemoral OA in our study is similar to that in other studies with a 5-year to 10-year follow-up of HT ACLR. Lower rates of patellofemoral and tibiofemoral OA after ACLR have also been reported in the literature, which most likely reflect the different radiological methods and structural features of OA assessed. We chose to define OA using the OARSI atlas because other classification systems are limited to the tibiofemoral joint or JSN. It is also possible that the high prevalence of OA in our study may relate to the older age (mean 35 years) at surgery of our cohort, especially as our results (table 1) support previous findings that older age at ACLR predicts OA.

Debate surrounds the impact of radiographic knee OA severity on pain and function. We found that KOOS-pain was influenced by combined compartmental disease severity, while subscales such as KOOS-symptoms and KOOS-QOL were influenced by increasing patellofemoral OA severity alone. Not unexpectedly, worse score on the AKPS, used predominantly for patellofemoral pain conditions, was only associated with increasing patellofemoral disease severity. The KOOS-ADL subscale was not associated with severity of OA in either compartment, which may partly relate to this subscale’s measurement properties. The KOOS-ADL subscale was the only one that did not satisfy the regression assumptions due to its large ceiling effect, a feature observed in other studies. The greater association of patellofemoral OA severity with most patient-reported outcomes, even when tibiofemoral changes were accounted for,
may reflect the findings in community-based studies, which suggest that the patellofemoral joint may be a more potent source of knee OA symptoms than the tibiofemoral joint. It is possible that, for people who have undergone ACLR, interventions targeting the patellofemoral joint may have a greater impact on KOOS-symptoms and KOOS-QOL than those targeting the tibiofemoral joint. Considering the bias of ACLR rehabilitation programmes towards addressing tibiofemoral symptoms and function, further investigation is required.

### Table 2  Multivariate regression analyses of the association between the Knee Injury and Osteoarthritis Outcome Score subscales, the Anterior Knee Pain Scale and functional tasks with patellofemoral and tibiofemoral OA severity (grade 0–3)

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Independent variable</th>
<th>β</th>
<th>B</th>
<th>95% CI of B</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>KDOS-pain</td>
<td>Patellofemoral OA</td>
<td>−0.3</td>
<td>−3.6</td>
<td>−7.0 to −0.1</td>
<td>0.042</td>
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<td></td>
<td>Tibiofemoral OA</td>
<td>−0.3</td>
<td>−3.8</td>
<td>−7.3 to −0.2</td>
<td>0.037</td>
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<td>KDOS-symptoms</td>
<td>Patellofemoral OA</td>
<td>−0.4</td>
<td>−7.0</td>
<td>−12.3 to −1.7</td>
<td>0.011</td>
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<tr>
<td></td>
<td>Tibiofemoral OA</td>
<td>−0.2</td>
<td>−3.2</td>
<td>−8.6 to 2.3</td>
<td>0.251</td>
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<td>KDOS-ADL</td>
<td>Patellofemoral OA</td>
<td>−0.2</td>
<td>−3.5</td>
<td>−9.9 to 2.8</td>
<td>0.268</td>
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<tr>
<td></td>
<td>Tibiofemoral OA</td>
<td>0.0</td>
<td>0.6</td>
<td>−5.9 to 7.1</td>
<td>0.850</td>
</tr>
<tr>
<td>KDOS-SR</td>
<td>Patellofemoral OA</td>
<td>−0.2</td>
<td>−3.2</td>
<td>−9.0 to 2.7</td>
<td>0.281</td>
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<td>Tibiofemoral OA</td>
<td>−0.3</td>
<td>−5.8</td>
<td>−11.8 to 0.2</td>
<td>0.058</td>
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<td>KDOS-QOL</td>
<td>Patellofemoral OA</td>
<td>−0.5</td>
<td>−13.0</td>
<td>−20.3 to −5.8</td>
<td>0.001</td>
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<tr>
<td></td>
<td>Tibiofemoral OA</td>
<td>−0.2</td>
<td>−5.8</td>
<td>−13.2 to 1.6</td>
<td>0.124</td>
</tr>
<tr>
<td>AKPS</td>
<td>Patellofemoral OA</td>
<td>−0.5</td>
<td>−8.0</td>
<td>−12.8 to −3.3</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Tibiofemoral OA</td>
<td>−0.1</td>
<td>−1.8</td>
<td>−6.6 to 3.1</td>
<td>0.468</td>
</tr>
<tr>
<td>Hop for distance*</td>
<td>Patellofemoral OA</td>
<td>−0.3</td>
<td>−13.6</td>
<td>−23.6 to −3.5</td>
<td>0.009</td>
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<td></td>
<td>Tibiofemoral OA</td>
<td>−0.2</td>
<td>−7.9</td>
<td>−18.0 to 2.2</td>
<td>0.123</td>
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<td>Side hop*</td>
<td>Patellofemoral OA</td>
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<td>−6.5</td>
<td>−10.1 to −3.0</td>
<td>0.001</td>
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<tr>
<td></td>
<td>Tibiofemoral OA</td>
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<td>−2.0</td>
<td>−5.6 to 1.6</td>
<td>0.260</td>
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<tr>
<td>One-leg rise†</td>
<td>Patellofemoral OA</td>
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<td>−11.8 to −0.8</td>
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<td>Tibiofemoral OA</td>
<td>0.0</td>
<td>0.1</td>
<td>−5.6 to 5.7</td>
<td>0.980</td>
</tr>
</tbody>
</table>

N=60 for patient-reported outcomes, N=65 for functional tasks.
*Adjusted for height, age and gender.
†Adjusted for weight.
β, standardised regression coefficient; ADL, function in activities of daily living; AKPS, Anterior Knee Pain Scale; B, unstandardised regression coefficient; KOOS, Knee Injury and Osteoarthritis Outcome Score; OA, osteoarthritis; QOL, quality of life; SR, function in sport and recreation.

Patellofemoral OA severity was independently associated with poorer performance on all three functional tasks. One factor that may underpin this finding is quadriceps strength. Although we did not measure quadriceps strength, patellofemoral OA and associated structural features have been associated with lower quadriceps function.39–41 Furthermore, any quadriceps strength benefits of a HT, compared to BPTB autografts,42 resolve at 12 months postsurgery42 with no difference observed up to 10 years postsurgery.32 Therefore, it is plausible that quadriceps weakness was a feature of patellofemoral OA after HT autograft, contributing to decreased performance on the functional tasks. The probability of radiographic OA progression in these individuals could be heightened by quadriceps weakness.41 43

Patellofemoral chondral injuries noted at surgery significantly increased the odds of patellofemoral OA at the 5-year to 10-year follow-up, which is consistent with previous reports.14 In contrast, we found no association between chondral injuries and tibiofemoral OA. Owing to our relatively low numbers, further larger studies are needed to confirm the presence or absence of associations between tibiofemoral chondral lesions and OA, particularly in the lateral compartment where we observed large CIs. This is important, since previous studies provide conflicting results on the association between chondral damage and tibiofemoral OA.11 14 44 Our results support previous reports of an association between medial meniscectomy and tibiofemoral OA in the respective compartment,5 14 but not an association with lateral meniscectomy. However, we did not confirm previous findings of an association between meniscectomy and patellofemoral OA following ACL injury.9 11 The association between meniscal injury and long-term patellofemoral OA development is likely to be mediated by other factors, such as altered loading patterns, that require further investigation.

We observed that those who underwent an early ACLR developed less patellofemoral OA than those who waited 1 year or...
more for an ACLR. This relationship was not observed in the tibiofemoral compartment. Our findings are consistent with previous reports of a relationship between patellofemoral OA and cartilage damage and longer duration from injury to ACLR.\textsuperscript{11, 14, 45} While this may indicate that surgical delay is suboptimal for patellofemoral joint health, the patellofemoral cartilage has been shown to continue to deteriorate despite an ACLR\textsuperscript{46–48} and randomised controlled trials are required to determine whether reconstruction reduces the long-term development of patellofemoral OA.

Physical activity assessed with the Tegner Activity Scale was lower in those with knee OA (median 4) compared to those free of OA (median 5). While measuring and quantifying physical activity remains a challenge, post hoc analysis revealed that the difference in Tegner scores was mostly observed in those with patellofemoral OA, as those with patellofemoral OA did not differ in activity level from those with no OA (data not presented). Physical activity may protect the patellofemoral joint of uninjured knees by decreasing the rate of patellar cartilage volume loss over time.\textsuperscript{49} However, Neuman et al\textsuperscript{45} found that individuals with patellofemoral OA 13 years after ACLR rated higher on the Tegner Activity Scale than those with no OA. Physical activity levels before and after ACLR, as well as the extent of postoperative rehabilitation performed, may be confounding factors in the development of patellofemoral OA. However, owing to the retrospective nature of the current study, no data on these factors were available. Perhaps staying physically active is a risk factor for patellofemoral OA after ACLR because of the altered patellofemoral loading patterns that occur after injury and persist following ACLR.\textsuperscript{6}

The present study has limitations. While participants were self-selected, which may have resulted in a selection bias towards those with more symptoms and functional limitations, the OA prevalence was similar to previous reports.\textsuperscript{6, 8, 30–32} The relatively large number of invitation letters that did not reach potential participants (n=105, 14%) occurred due to individuals changing address since surgery, which is common in individuals of this age group. Although not strictly interval data, for the purposes of evaluating their relative contribution to symptoms and function, tibiofemoral and patellofemoral OA severity were treated as such in the regression models.\textsuperscript{27, 28} Furthermore, this was a cross-sectional study, and thus we did not have information on baseline (preinjury or pre-ACLR) radiographic status. It is possible that the presence of OA in this cohort may have been pre-existing and not associated with the ACL injury or reconstruction. However, no overt degeneration was observed arthroscopically at the time of ACLR, and the rate of patellofemoral and tibiofemoral OA found in the current study is much higher than that observed in the uninjured contralateral knee of patients 12 years after ACLR of a similar age (2.5%\textsuperscript{7} and 15%,\textsuperscript{1} respectively), making it unlikely that the prevalence of OA was independent of ACLR. Considering our findings of high patellofemoral OA, future prospective studies evaluating the development of OA after ACLR should also investigate the patellofemoral joint.

Orthopaedic and sports medicine clinicians should be aware of the high prevalence of patellofemoral OA (47%) and tibiofemoral OA (31%), 5–10 years after HT autograft ACLR. Importantly, patellofemoral OA severity was associated with worse symptoms and decreased functional performance, independent of tibiofemoral OA severity. Although most radiographic changes observed in the patellofemoral joint were mild, clinicians should consider the patellofemoral joint during postoperative rehabilitation, in an attempt to address long-term symptoms and degenerative joint disease.
Original article


