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TITLE

Are knee biomechanics different in those with and without patellofemoral osteoarthritis after anterior cruciate ligament reconstruction?

RUNNING TITLE

Patellofemoral OA biomechanics after ACL reconstruction

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CONFLICT OF INTEREST

Nil

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ABSTRACT

Objectives. Patellofemoral osteoarthritis (PFOA) is prevalent following anterior cruciate ligament reconstruction (ACLR). This study aimed to investigate differences in transverse plane rotation between knees with varus and valgus alignment during gait in people with and without PFOA after ACLR.

Methods. Thirty-six individuals who were a mean nine ($\pm$ two) years post-ACLR (18 radiographic PFOA; 18 no knee OA) participated in this cross-sectional study. Knee internal-external rotation angles were measured using a three-dimensional motion analysis system during walking and running. Weight-bearing frontal plane knee alignment, measured with an inclinometer, was used to classify participants as having varus or valgus alignment. Two-way analysis of covariance was used to assess the effect of both PFOA and frontal plane knee alignment on dynamic knee internal-external rotation.

Results. Significant interactions were found between PFOA status and frontal plane alignment on knee internal-external rotation angles during walking ($p=0.019$) and running ($p=0.002$). Tests of simple effects revealed that during walking, individuals with valgus alignment and PFOA demonstrated a mean 3.9° (95% confidence interval [95%CI] 0.7, 7.1) less knee internal rotation than those with valgus alignment and no OA. During running this difference increased to 6.1° (1.8 10.4). For individuals with varus alignment, no significant effects were observed.

Conclusion. Less knee internal rotation during gait was found in individuals with PFOA and valgus alignment. A rotational shift of this magnitude may be sufficient to initiate or accelerate patellofemoral cartilage degeneration. Prospective studies are required to determine if these altered kinematic patterns result from, or contribute to, PFOA development after reconstruction.

SIGNIFICANCE AND INNOVATIONS

1. After ACLR, individuals with patellofemoral OA and valgus aligned knees demonstrated significantly less knee internal rotation during walking and running.
2. These kinematic characteristics may contribute to the high prevalence of patellofemoral OA after ACLR.

Anterior cruciate ligament (ACL) reconstruction (ACLR) is a well-established risk factor for the development of tibiofemoral osteoarthritis (OA) (1). However, our recent review also highlights that patellofemoral OA (PFOA), either isolated or combined with tibiofemoral OA, is prevalent, affecting a median 47% (range 12–76%) of people more than ten years after ACLR (1). To our knowledge, the mechanisms underpinning the high rate of PFOA after ACLR have not been evaluated, but appear to be independent of graft type (1). Changes to tibiofemoral biomechanics that occur following ACL injury and persist after ACLR may be related to the development of PFOA.

Two biomechanical characteristics observed after ACLR with potential to adversely affect the patellofemoral joint include increased transverse plane knee external rotation (i.e., external rotation of the tibia relative to the femur) and increased frontal plane knee valgus (2,3). Whilst it is known that knee external rotation is increased after ACLR compared to the uninjured knee (3) and healthy controls (2) during gait, increased knee valgus has only recently been reported (2). Due to the intimate relationship between the patellofemoral and tibiofemoral joints, the presence of increased knee external rotation with valgus alignment may increase lateral patellar tilt and/or rotation (4,5). Such changes may heighten lateral patellofemoral load and potentially increase PFOA risk (6). The aim of this cross-sectional study was to investigate differences in transverse plane rotation between knees with varus and valgus alignment during walking and running in people with and without PFOA after ACLR. We hypothesised that individuals with PFOA and knee valgus would exhibit less knee internal rotation during gait.

Patients and Methods

Participants

Participants were recruited retrospectively from our clinical study (7), investigating PFOA prevalence after ACLR (n=70). Ethical approval was granted from the University of Melbourne Human Research Ethics Committee and participants provided written informed consent. All participants had a primary arthroscopic single-bundle ACLR with a hamstring-tendon autograft (four-strand semitendinosus/gracilis) performed by a single experienced orthopaedic surgeon between 2000–2007. An EndoButton (Acufex, Smith & Nephew, Andover, MA) was used for proximal fixation and an absorbable interference screw (RCI, Smith & Nephew) for tibial fixation, with tunnels at the anatomical footprint of the native ACL. All participants completed a similar post-operative rehabilitation protocol, including early weight-bearing, range of movement and neuromuscular retraining as well as a graduated return to sport. We attempted to contact all participants with either PFOA (n=33) or no OA (n=34) from our previous study (7). Those who met the following inclusion criteria were invited to participate: aged ≥ 18 years at the time of ACLR, no report of graft rupture, revision surgery or arthroplasty on the ACLR knee, not currently affected by pain/condition restricting walk/run ability (obvious limp or >2 out of 10 pain on visual analogue scale during walk/run), and not currently pregnant or breastfeeding. Participants with meniscal or chondral lesions at the time of, or following, ACLR (Table 1), or contralateral knee injury were not excluded.

Participants underwent bilateral radiographic examination (weight-bearing posteroanterior and lateral views and non-weight bearing 30° flexion skyline view). Osteophytes and joint space narrowing (JSN) in the patellofemoral and tibiofemoral compartments were graded on a four-point scale according to the Osteoarthritis Research Society International (OARSI) atlas (8) (from 0=no change to 3=severe change) by the senior

author (KC), who has >10 years of radiographic evaluation experience, was blind to kinematic data, and has acceptable inter-rater reliability for scoring knee radiographs ($\kappa=0.745-0.843$) (7). Radiographic PFOA, defined as a patellofemoral osteophyte or JSN grade ≥ 2 or grade 1 JSN in combination with a grade 1 osteophyte, was based on previously defined criteria (9). Those with more severe tibiofemoral than PFOA in the ACLR knee were excluded. No OA was defined as not meeting OA criteria in either compartment.

Procedure

All eligible participants completed quantitative gait analysis. Demographic data (age, sex, height, weight), time between injury and surgery, activity level (Tegner) and weight-bearing frontal plane knee alignment were recorded prior to gait analysis. Frontal plane alignment of the ACLR knee was classified as varus or valgus (no participant had neutral alignment) as these are considered two entities that affect knee loads (especially patellofemoral loads) and OA risk differently (6). Specifically, the angle between the tibial tuberosity and mid-point of the talar neck was measured with a digital inclinometer with feet positioned on a template (feet shoulder-width apart, 10° external rotation) as previously validated (10).

Kinematic data of the ACLR knee were acquired using reflective markers placed at specific anatomical landmarks on the pelvis and lower-limbs (11). Marker trajectories were captured from 9 cameras at 120Hz (VICON, Oxford Metrics). A static trial was collected to calibrate relevant anatomic landmarks and establish joint centres (11), while knee flexion-extension axis was determined using dynamic optimisation (12). Participants wore standardised running sandals (NIKE, Straprunner V) and after several practice trials were asked to walk at a comfortable self-selected speed followed by running between 2.5–

3.5m.s⁻¹ until a minimum of three trials were captured for both gait speeds. A moderate running speed was selected to allow sufficient distance for safe acceleration/deceleration.

For a trial to be considered successful, total foot contact needed to occur on a force plate (Advanced Mechanical Technology, Inc.) embedded in the floor. Participants were given feedback to ensure designated running speed was met. Marker trajectories were filtered using Woltring's general cross-validatory quintic smoothing spline with a 15mm predicted mean squared error.

A biomechanical model of the pelvis and lower limbs (11) was used to calculate average knee internal-external rotation angle during time normalised stance phase (0-100%) of walking and running (foot contact to toe-off). Knee internal rotation was defined as internal rotation of the tibia relative to the femur. All computations were performed using Bodybuilder (VICON, Oxford Metrics).

Differences in demographic data between those with and without PFOA were evaluated using chi-square tests for binary data, and independent samples t-tests or Mann-Whitney-U tests for continuous data, where appropriate. Two-way univariate analyses of covariance (ANCOVA) (covariates: age, sex or BMI when different between OA groups) were used to assess the interaction between the effects of frontal plane knee alignment and OA status on knee internal-external rotation angles as well as main effects during walking or running. Tests of simple effects compared knee internal-external rotation angles between people with and without PFOA for varus and valgus knees separately. Significance was set at 0.05 with Bonferroni correction for number of pairwise comparisons completed ($n=2$) for simple effects analysis ($p<0.025$). Between-group effect sizes were calculated for differences between those with and without PFOA in those with varus and valgus knees separately using the standardised mean difference (SMD) (mean difference divided by standard

deviation), with 0.2, 0.5 and 0.8 considered small, medium and large effect size, respectively. Important statistical assumptions for univariate ANCOVA, including data normality, linearity and equality of variance, were met. Statistical analyses were performed with SPSS V21.0 (SPSS, Chicago, IL).

Results

Of the participants with either PFOA (n=33) or no OA (n=34) in the ACLR knee from our previous study, six (9%) were unable to be contacted, 10 (15%) declined to participate due to time commitments, two (3%) had relocated, three (4%) reported revision surgery, three (4%) had other conditions affecting their running ability and one (1%) was pregnant.

Following radiographic evaluation, six (9%) people had developed more severe tibiofemoral OA than PFOA in the ACLR knee and were excluded. Thus, 36 participants (PFOA=18; no OA=18) underwent quantitative gait analysis. Of those with PFOA, 10 (56%) had isolated PFOA and 8 (44%) had combined patellofemoral/tibiofemoral OA. PFOA was evenly distributed between medial and lateral patellofemoral compartments. Apart from those with PFOA being older ($p=0.029$), no significant differences existed between the groups (Table 1). Four participants had an ACL injury, while eight participants had radiographic OA (six isolated PFOA, two combined OA), in the contralateral knee. All participants with contralateral knee OA, except one, had PFOA in the index (ACLR) knee. Importantly, the contralateral knee was asymptomatic in all participants (i.e., did not affect walk/run ability).

TABLE ONE HERE

Univariate ANCOVA revealed a significant interaction between frontal plane knee alignment and OA status for knee internal-external rotation angles during walking ($p=0.019$) and running ($p=0.002$) when adjusted for age (Figure 1). No significant main effects were observed ($p>0.2$). Tests of simple effects revealed that, in walking, individuals with valgus alignment and PFOA demonstrated a mean 3.9° (95%CI: 0.7, 7.1) less knee internal rotation than those with valgus alignment and no OA with a moderate effect size ($p=0.019$, $SMD=0.60$). During running this difference was 6.1° (1.8, 10.4) with a larger effect size ($p=0.007$, $SMD=0.71$) (Figure 2). For individuals with varus alignment, those with PFOA had greater knee internal rotation than those without OA, but this comparison was not significant (walking: mean difference 1.3° (-1.8, 4.3); $p=0.393$; $SMD=0.20$, and running: mean difference 3.4° (-0.7, 7.5); $p=0.096$; $SMD=0.39$) (Figure 2).

FIGURE ONE HERE

FIGURE TWO HERE

Discussion

Our main finding was that people with PFOA after ACLR who exhibit static valgus alignment display less knee internal rotation during gait compared to those with no OA. Furthermore, this difference was more evident during running than walking. The combination of knee valgus and less internal rotation can increase patellofemoral malalignment and load (5,7) and may partially explain the high rates of PFOA observed after ACLR (1). Indeed, similar changes in patellar orientation and patellar cartilage contact have

been observed in younger individuals within the first year following ACLR during a single-leg lunge (13).

Rotational differences of approximately 5° between the ACLR and uninjured contralateral knee have been previously observed during walking (2,3). Our findings suggest that the relationship between altered knee internal-external rotation and patellofemoral joint integrity appear to be dependent on frontal plane knee alignment. This result is not surprising given that knee valgus also increases lateral patellar facet load (5) and is associated with a 1.6 fold increase in progression of lateral PFOA (6). Moreover, the relationship between PFOA, knee valgus and internal rotation appears to be greater during higher-impact tasks such as running, which may be related to the observed association between PFOA and higher activity levels after ACLR (9). Less knee internal rotation combined with knee valgus may lead to lateral patellar displacement with a subsequent shift in cartilage contact to areas of the patella unaccustomed to such loads. However, since this was a cross-sectional study, it is not known if the observed biomechanical alterations preceded PFOA development or if they reflect altered movement patterns as a consequence of PFOA. Importantly, all ACLRs were performed by a single experienced orthopaedic surgeon, minimising the variability in surgical technique and its potential influence on knee rotation kinematics.

The influence of concomitant injuries to menisci and patellofemoral cartilage on knee kinematics was not specifically investigated. Meniscectomy and cartilage pathology at the time of ACLR did not affect OA rates at follow-up (Table 1). However, OA affects many tissues, including the meniscus, cartilage, subchondral bone and synovium. As such, it was not possible to delineate the effects of individual tissue pathology. Indeed, meniscal,

cartilage and ACL pathology are often subclinical (i.e., asymptomatic) and thus could be confounding factors for any OA study.

This study has several limitations. As the participants were 7–12 years after reconstruction, several participants had ACL injuries ($n=4$) and OA ($n=8$) in the contralateral knee. Thus, it was not possible to use the contralateral knee as an uninjured control. However, a contralateral ACL injury is unlikely to have a direct influence on the kinematics of the index knee (14). Second, due to the cross-sectional nature of the current study, it was not possible to demonstrate a causal relationship between ACLR and PFOA development. Importantly, excluding those with greater tibiofemoral than PFOA increases the likelihood that our findings are not compounded by more severe tibiofemoral OA, which is a limitation of many clinical OA studies. Finally, whilst an *a priori* power calculation was not possible due to the dearth of literature on knee internal-external rotation kinematics in people with PFOA, the study was sufficiently powered except for the test of simple effects for those with and without PFOA during running in varus aligned knees ($p=0.096$).

If larger prospective studies determine that less knee internal rotation in those with valgus aligned knees is a risk factor for PFOA development, then surgical techniques that can minimise rotational abnormalities, such as double-bundle ACLR, may increase longevity of patellofemoral cartilage. Targeted rehabilitation programs addressing neuromuscular deficits associated with abnormal knee internal-external rotation and prophylactic knee braces represent other possible interventions for optimising knee rotation kinematics (15,16).

In summary, for individuals with knee valgus alignment, those with PFOA had significantly less knee internal rotation than those without OA during walking and running, while no significant differences were observed in knee kinematics for individuals with knee

varus alignment. Prospective studies are required to establish if these parameters precede, or result from, PFOA development so that subsequent surgical and/or rehabilitation strategies can be pursued to ultimately reduce the incidence of PFOA following ACLR.

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 submitted for publication. 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.

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

Acquisition of data. Culvenor, Schache, Crossley.

Analysis and interpretation of data. Culvenor, Schache, Vincenzino, Collins, Crossley.

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Table I. Demographic, alignment and gait velocity characteristics

Variable		PF OA (n=18)	No OA (n=18)	P value
		Mean (SD)	Mean (SD)	
Sex (male (%))		10 (56)	11 (61)	0.735¥
Age (years)		47 (10)	40 (9)	0.029
BMI (kg.m ⁻²)		27.3 (3.8)	26.6 (4.1)	0.577
Time since ACLR (years)		10 (2)	9 (2)	0.229§
Tegner activity scale*		6 [3 – 9]	6 [3 – 9]	0.923§
Injury to ACLR duration (months)*		4 [0.25 – 240]	3 [1 – 216]	0.986§
Frontal plane alignment (valgus (%))		10 (56)	7 (39)	0.317¥
Walk speed (m.s ⁻¹)*		1.5 [1.3 – 1.8]	1.6 [1.4 – 1.9]	0.343
Run speed (m.s ⁻¹)*		3.0 [2.6 – 3.4]	3.0 [2.6 – 3.5]	0.687
Concomitant injuries£				
Medial meniscectomy, n (%)		8 (44)	5 (28)	0.298¥
Lateral meniscectomy, n (%)		3 (17)	1 (6)	0.298¥
Patellofemoral chondral, n (%)		4 (22)	3 (17)	0.674¥
OA severity€, n (%)				
Patellofemoral	0	0 (0)	10 (56)	NA
	1	0 (0)	8 (44)	
	2	8 (44)	0 (0)	
	≥3	10 (56)	0 (0)	
Tibiofemoral	0	3 (17)	15 (83)	NA
	1	9 (50)	3 (17)	
	2	1 (5)	0 (0)	
	≥3	5 (28)	0 (0)	

PF, patellofemoral; OA, osteoarthritis; BMI, body mass index; SD, standard deviation; kg, kilograms; m, metres; s, seconds; Patellofemoral chondral, ≥grade 2 Outerbridge;

€ OA severity = sum of OARS atlas osteophyte score

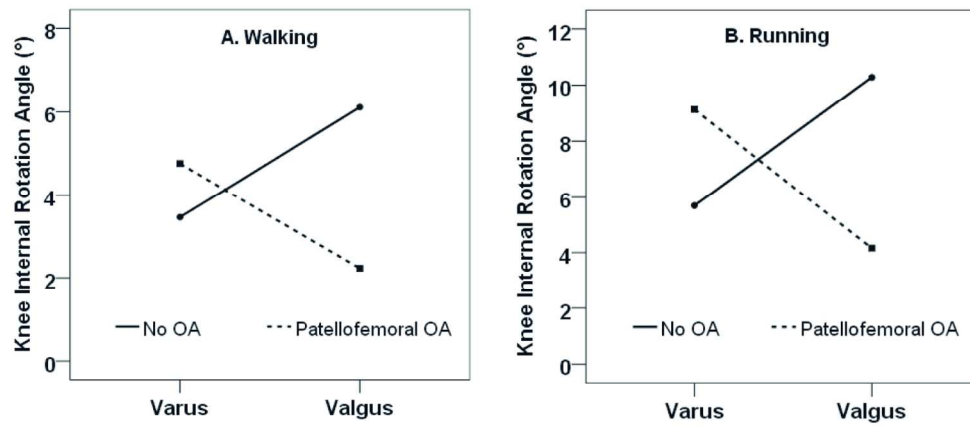
£ Concomitant injuries at time of ACLR or subsequent surgery; * median [range]; § Mann-

Whitney-U as data not normally distributed; ¥ chi-square test for binary data

Figure Legends

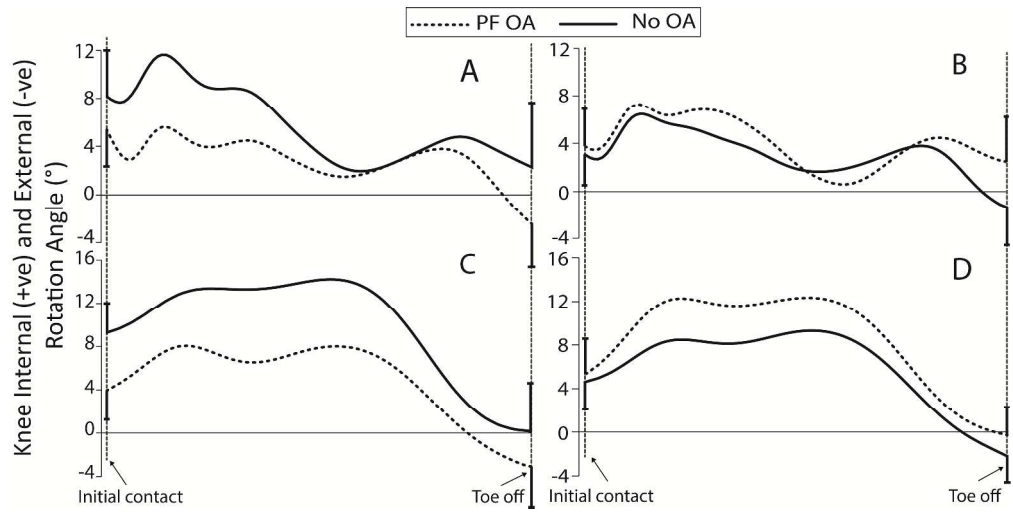
Figure I. Interaction plots showing the effects of frontal plane knee alignment and OA status on dynamic knee internal-external rotation angles during walking (A) and running (B), after adjustment for participant age ($p=0.019$ and 0.002 , respectively).

Figure II. Ensemble curves for average knee internal-external rotation angle, with error bars displaying 95% confidence intervals for initial contact and toe-off. Valgus aligned knees ($n=17$) during walking (A); and running (C). Varus aligned knees ($n=19$) during walking (B); and running (D).



Interaction plots showing the effects of frontal plane knee alignment and OA status on dynamic knee internal-external rotation angles during walking (A) and running (B), after adjustment for participant age ($p=0.019$ and 0.002 , respectively).
138x65mm (300 x 300 DPI)

Accepted



Ensemble curves for average knee internal-external rotation angle, with error bars displaying 95% confidence intervals for initial contact and toe-off. Valgus aligned knees (n=17) during walking (A); and running (C). Varus aligned knees (n=19) during walking (B); and running (D).
401x200mm (300 x 300 DPI)

Accepted