Greater magnitude tibiofemoral contact forces are associated with reduced prevalence of osteochondral pathologies 2-3 years following anterior cruciate ligament reconstruction

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Abstract

Purpose: External loading of osteoarthritic and healthy knees correlates with current and future osteochondral tissue state. These relationships have not been examined following anterior cruciate ligament reconstruction. We hypothesised greater magnitude tibiofemoral contact forces were related to increased prevalence of osteochondral pathologies, and these relationships were exacerbated by concomitant meniscal injury.

Methods: This was a cross-sectional study of 100 individuals (29.7±6.5 years, 78.1±14.4 kg) examined 2-3 years following hamstring tendon anterior cruciate ligament reconstruction. Thirty-eight had concurrent meniscal pathology (30.6±6.6 years, 83.3±14.3 kg), which included treated and untreated meniscal injury, and 62 (29.8±6.4 years, 74.9±13.3 kg) were free of meniscal pathology. Magnetic resonance imaging of reconstructed knees were used to assess prevalence of tibiofemoral osteochondral pathologies (i.e., cartilage defects and bone marrow lesions). A calibrated electromyogram-driven neuromusculoskeletal model was used to predict medial and lateral tibiofemoral compartment contact forces from gait analysis. Relationships between contact forces and osteochondral pathology prevalence were assessed using logistic regression models.

Results: In patients with reconstructed knees free from meniscal pathology, greater medial contact forces were related to reduced prevalence of medial cartilage defects (odds ratio(OR)=0.7, Wald $\chi^2(2)=7.9$, 95% confidence interval (CI)=0.50-95, p=0.02) and bone marrow lesions (OR=0.8, Wald $\chi^2(2)=4.2$, 95% CI=0.7-0.99, p=0.04). No significant relationships were found in the lateral compartment of these reconstructed knees. In reconstructed knees with concurrent meniscal pathology, no relationships were found between contact forces and osteochondral pathologies.

Conclusions: In patients with reconstructed knees free from meniscal pathology, increased contact forces were associated with fewer cartilage defects and bone marrow lesions in medial, but not, lateral tibiofemoral compartments. No significant relationships were found between contact forces and osteochondral pathologies in reconstructed knees with meniscal pathology for any tibiofemoral compartment. Future studies should focus on determining longitudinal effects of contact forces and changes in osteochondral pathologies.

Level of Evidence: Case series (Level IV).

Keywords: cartilage; defects; bone marrow lesions; anterior cruciate ligament; reconstruction; meniscus

Introduction

Anterior cruciate ligament (ACL) rupture is a debilitating intra-articular knee injury. It often occurs during sport participation, and primarily affects individuals 15-25 years of age [17]. The ACL-deficient knee may be managed through orthopaedic reconstruction (ACLR), the aims of which are to restore translational and rotational stability. Unfortunately, ACLR does not prevent early onset knee osteoarthritis (OA) [24], and the mechanisms of post-ACLR knee OA development are not fully understood.

When the ACL and meniscus are injury concurrently, risk of future knee OA is greater than following isolated ACL rupture [29]. Osteochondral pathologies, such as subchondral bone marrow lesions (BMLs) and cartilage defects, are more prevalent in meniscal-injured compared to isolated ACL injuries [42]. Long-term knee health may be compromised by the presence of osteochondral pathologies following ACLR, as BMLs are predictors of cartilage loss [20] and defect development [13], while cartilage defects predict cartilage thinning [9] and arthroplasty [10]. Thus, preventing osteochondral pathologies may protect ACLR knees from OA, but prevention mechanisms are unknown.

Over-loading the articular tissues, e.g., subchondral bone and cartilage, is a mechanism of OA development. In knees with, or at risk of, OA, greater loading has been associated with disease structural markers [11], severity [37], and progression [27, 35], as well as the clinical features of pain [39] and dysfunction [39]. Following ACLR, both external knee loads [33] and internal articular contact forces [33, 44] are lower in magnitude than in healthy control knees. Lower-than-normal articular contact forces have been associated with future onset of radiographic knee OA [44], and, in animals, loss of bone [1]. Critically, relationships between articular contact forces and osteochondral tissue state in human ACLR knees remain unexplored, as does the influence of meniscal injury on these relationships.

The primary aim of this study was to determine relationships between tibiofemoral contact forces and osteochondral pathologies (i.e., cartilage defects and BMLs) 2-3 years following isolated and meniscal-injury ACLR. We focused on contact forces produced during walking, because walking (i.e., the most common human locomotor task) was the major determinant of the habitual biomechanical environment at the knee. Given ACLR has been associated with greater risk of early onset knee OA [24], and increased loading of at-risk, or OA-afflicted, knees has been associated with more osteochondral pathologies [11, 35], we hypothesized greater contact forces were related to greater cartilage defect and BML prevalence, and these relationships were exacerbated by meniscal injury. This study was the first investigation into relationships between contact forces and osteochondral pathologies in ACLR knees, and may help focus post-operative rehabilitation toward contact forces.

Materials and methods

This cross-sectional study was performed at two universities with institutional human research ethics approval (PES/36/10/HREC and 0932864.3). Prior to testing, participants provided their informed written consent. One hundred ACLR patients were tested: 18-42 years of age, body mass index $\leq$34 kg·m^{-2}, no neuromusculoskeletal or cardiovascular conditions, no lower-limb trauma since ACL injury, and no clinician- or self-diagnosed OA anywhere within the body. Participants were recruited from clinic records of our orthopaedic partners. Gait analysis and medical imaging were completed 2-3 years following ipsilateral hamstring tendon ACLR, which was performed <6 months from initial ACL rupture. We excluded those with multiple ACLR (i.e., revision(s) or contralateral ACLR) and International Cartilage Repair Society (ICRS) cartilage defect grade >1 (assessed intra-operatively during ACLR). We did not assess level of sport participation at the time of injury or at the time of laboratory testing.

Anterior cruciate ligament reconstruction procedure

Reconstructions were performed by one of five fellowship-trained orthopaedic surgeons, specializing in ACLR. Reconstructions were arthroscopically-assisted, with outside-in tibial drilling followed by either trans-tibial (~50% of all participants) or anteromedial portal femoral drilling. Irrespective of femoral drilling technique, the goal was to place the intra-articular femoral aperture over the anteromedial aspect of the native ACL's "footprint". Semitendinosus and gracilis tendons were harvested through a 3-4 cm incision over the *pes anserinus*, and used to create a 4-strand autograft. An appropriately sized Closed Loop Endobutton (Smith and Nephew Endoscopy, Mass, USA) was used to establish femoral fixation, while tibial fixation was achieved with an interference screw. Meniscal repair was undertaken if the surgeon deemed the lesion repairable and a stable repair construct with an element of vascularity could be achieved. If these conditions were not met, but the lesion was deemed stable through probing, it was left in place, otherwise, it was resected. Henceforth, ACLR with meniscal pathology will known as 'meniscal-injured ACLR', including those with repaired, resected, or untreated meniscus injury, and ACLR without meniscal pathology as "isolated ACLR".

The day following surgery participants left hospital and were instructed to return to full weight bearing with unrestricted range of motion as tolerated. All participants, including those with meniscal pathology, immediately underwent accelerated criterion-based physical therapy [38] to restore knee range of motion and strength, with particular emphasis on vastus medialis recruitment. Participants were instructed to begin training on a stationary bicycle by post-operative week 4, and by 3-4 months were cleared for vigorous straight-line running. At 4 months, participants were cleared to commence sport-specific exercises. Throughout therapy, feedback on progress and exercise guidelines were provided to participants. If participants could complete scheduled rehabilitation exercises without evoking substantial pain or swelling, they were graduated to more challenging exercises.

Magnetic resonance imaging

Magnetic resonance imaging was performed at two different locations: one used a 1.5 T Signa (GE Healthcare, Wisconsin) unit and the other a 3.0 T Megenetom Verio (Siemens, Germany) unit. The ACLR knees were subjected to T_1-weighted 3-dimensional gradient recall in sagittal plane to image cartilage structure, and proton density (PD)-weighted fat-saturated spin echo in coronal plane to image subchondral BMLs. For the 1.5 T unit, the T_1-weighted sequences used 55° flip angle, 4.4 x 10^{-2} s repetition time, 1.2 x 10^{-3} s echo time, 1.6 x 10^{-2} m field of view, 1.5 x 10^{-3} m slice thickness, and 256×256 pixel matrix, while PD-weighted sequences used 155° flip angle, 4 s repetition time, 5 x 10^{-2} s echo time, 3 x 10^{-3} m slice thickness, 1.6 x 10^{-1} m field of view, and 256x256 pixel matrix. For the 3 T unit, T_1-weighted sequences used 10° flip angle, 1.25 x 10^{-2} s repetition time, 4.9 x 10^{-3} s echo time, 1.6 x 10^{-1} m field of view, 1.5 x 10^{-3} m slice thickness, and 512×512 pixel matrix, while PD-weighted sequences used 155° flip angle, 2.64 s repetition time, 3.7 x 10^{-2} s echo time, 3 x 10^{-3} m slice thickness, 1.6 x 10^{-1} m field of view, and 256x256 matrix.

Cartilage defects and bone marrow lesions assessment

Osteochondral pathologies were assessed by a trained examiner with >10 years of experience assessing osteochondral pathologies from MRI. The examiner was blind to participant characteristics and meniscal injury status. Cartilage defects were assessed using ICRS score: 0 (normal), 1 (focal blistering and intra-cartilaginous low-signal intensity area with intact surface and base), 2 (surface or base irregularity and <50% thickness loss), 3 (deep lesions >50% thickness loss) and 4 (full-thickness focal defects or subchondral bone exposure due to wear). Cartilage defect prevalence was defined as ICRS score >1 for ≥2 consecutive sagittal plane MR images. Inter-rater reliability for cartilage defect assessment, expressed as intra-class correlation coefficients, was 0.85-0.93 [9]. The BMLs were assessed using the MRI Osteoarthritis Knee Score [19], which determined the extent of involvement in 10 knee

subregions. The BMLs were scored: 0 (none), 1 (<1/3 of subregion volume), 2 (1/3–2/3 of subregion volume), and 3 (>2/3 of subregion volume). The BML prevalence was defined as grade >1 on >2 consecutive coronal plane MR images. Intra- and inter-rater reliability of BML assessment, expressed as weighted kappa-values, were 0.50-1.00 and 0.67-1.00, respectively [42]. For these same ACLR participants, cartilage defect and BML prevalence has been previously reported, as have cartilage volume and tibial plateau bone area [42] (summarized in Table 2). Briefly, isolated and meniscal-injured ACLR knees in this study had more cartilage defects and BMLs compared to healthy knees from a control sample of healthy knees. Meniscal-injured ACLR knees had greater prevalence of medial tibial and femoral cartilage defects compared to isolated ACLR knees (not listed in Table 2, see [42]). There were no differences in cartilage volume, tibial bone area, and BML prevalence between isolated and meniscal-injured ACLR knees.

Gait analysis

Within a week of MRI, participants underwent laboratory-based gait analysis wherein full-body motion, ground reaction forces (GRFs), and surface electromyograms (EMGs) were concurrently and synchronously acquired. Participants walked over-ground at their self-selected pace wearing a full-body retro-reflective marker set [33]. Three-dimensional instantaneous marker positions were acquired using 10- or 12-camera Vicon (Oxford Metrics Group, UK) motion capture systems sampling at 200 or 120 Hz, respectively. The GRFs were acquired using two (Kistler Instrumente, Switzerland) or three (Advanced Mechanical Technology, USA) ground-embedded force platforms sampling at 1000 or 2400 Hz, respectively. Surface EMGs were acquired from 8 major muscles of the affected knee using Wave Wireless (Zero Wire, Aurion, Italy) or Telemyo 900 (Noraxon, Arizona, USA) systems sampling at 1000 or 2400 Hz, respectively. The skin surface was prepared consistent with recommendations from the 'Surface Electromyography for the Non-Invasive Assessment of

Muscles' project (http://www.seniam.org/). Circular pre-formed bipolar Ag/AgCl electrodes (Duo-Trode, Myotronics, USA) were applied atop medial and lateral gastrocnemii, hamstrings, and vasti, as well as rectus femoris and tensor fasciae latae.

Biomechanical modelling

Marker positions, GRFs, and EMGs were processed using custom Matlab (The Mathworks, USA) code. Marker positions and GRFs were digitally filtered using a 2nd order infinite impulse response low-pass Butterworth design. Data were filter-cascaded once to remove phase effects, and a cascade-adjusted 10 Hz cut-off applied. Each EMG was band-pass filtered (30-500 Hz), full-wave rectified, and low-pass filtered (6 Hz cut-off) to produce a linear envelope [23]. Amplitude of each linear envelope was scaled to its maximum, identified from maximal exertion isometric contractions performed on a seated dynamometer (Biodex, NY, USA) and dynamic motor tasks.

Gait biomechanics were determined using OpenSim [12] v3.2. A customized anatomic model was linearly scaled using pairs of prominent landmarks and joint centres [33]. Tendon and muscle force-length relationships are not necessarily preserved during this linear scaling [43]. To resolve this issue, we optimized tendon slack and optimal muscle fibre lengths for the 11 knee-spanning muscle tendon unit actuators (MTUAs) to preserve the dimensionless tendon and muscle fibre force-length relationships from the template model [28]. We then used OpenSim inverse kinematics, inverse dynamics, and muscle analysis tools to determine model kinematics, external kinetics, and MTUA kinematics (i.e., lengths and moment arms), respectively.

Gait biomechanics, MTUA kinematics and parameters, as well as conditioned EMGs were used to calibrate an EMG-driven model [23] with embedded tibiofemoral contact model [16, 45]. Prior to calibration, model representation of ACLR semitendinosus was modified [32] to reflect

post-harvest structure [22]. The EMG-driven model predicted medial and lateral tibiofemoral contact forces (N). As these participants did not have instrumented knee implants, it is not possible to measure tibiofemoral contact force predict error. However, similar previous studies conducted on individuals with instrumented prosthetic knee implants [16] found root mean squared errors of ~140-300 N and 250-280 N for medial and lateral tibiofemoral compartments, respectively. Tibiofemoral contact forces were subsequently time normalized to 100% of gait cycle. Each participant's maximum contact forces were identified from the stance phase of three repeated walking trials. From these, means were calculated and used together with osteochondral pathology prevalence in subsequent statistical analyses.

Statistical analyses

As there is no prior study of effects of tibiofemoral contact forces on osteochondral pathologies in ACLR knees, we conducted a power analysis [14] based on reported relationships between tibiofemoral contact stresses and osteochondral pathologies in at-risk knees [35]. We used average odds ratios of effects of contact stresses on osteochondral pathologies (i.e., 4.25). Forty-six participants were required to achieve 5% alpha error and 95% statistical power using a two-tailed, normally distributed, logistic regression analysis. Statistical analyses were performed using SPSS v22 (IBM, NY, USA). Logistic regressions were used to assess relationships between contact forces and osteochondral pathology. Contact forces were used as predictors of prevalence of cartilage defects and BMLs in the respective tibiofemoral compartments of isolated and meniscal-injured ACLR knees. In meniscal-injured ACLR knees, we examined the compartment where meniscal injury had occurred. Those with bilateral (i.e., medial and lateral compartment) meniscal injuries were included in regression models for both compartments. Results were reported per unit increase of 10% mean bodyweight of the entire

cohort of ACLR participants (i.e., 77 N).

Results

General characteristics of these ACLR participants have been reported [42] (summary in Table 1). Isolated and meniscal-injured ACLR participants were of similar age and height, and the groups contained similar proportions of males and tested right lower-limbs. Meniscal-injured ACLR participants had greater body mass (83.3±14.3 kg) and body mass index (26.9±4.1 $kg \cdot m^{-2}$) compared to isolated ACLR participants (74.9±13.3 kg, 24.2±2.8 $kg \cdot m^{-2}$) (both $p<0.001$). Isolated and meniscal-injured participants received ACLR at similar times following initial ACL injuries, and participated in this study at similar times following ACLR. Approximately 44% of isolated and 59% of meniscal-injured ACLR participants received transtibial femoral drilling, the remainder performed with anteromedial portal technique.

The meniscal injuries present in this cohort of ACLR knees are reported in Table 3. Lateral meniscus injuries were most common, with 25 instances in 38 meniscal-injured ACLR knees. Of these 25 lateral meniscal injuries, 12 were treated with resection while no other meniscal pathology was present. The remainder (i.e., 12 of 38 cases) consisted of isolated or combined untreated tears, repairs, and/or resections to either or both menisci.

In isolated ACLR knees, greater magnitude medial contact forces were significantly associated with decreased odds of prevalence of medial cartilage defects (odds ratio (OR)=0.7, Wald $\chi^2(2)=7.9$, 95% confidence interval (CI)=0.50-95, p=0.02) and medial BMLs (OR=0.8, Wald $\chi^2(2)=4.2$, 95% CI=0.7-0.99, p=0.04). In the lateral compartment of isolated ACLR knees, no significant relationships were found between contact forces and either cartilage defects or BMLs (Table 4). In meniscal-injured ACLR knees, no significant relationships were found between contact forces and cartilage defects or BMLs in any compartment.

Discussion

The main finding was that 2-3 years following ACLR greater medial contact forces were associated with fewer medial cartilage defects and medial BMLs, but, in ACLR knees with meniscal pathology, no significant relationships were found. This was the first study to report relationships between tibiofemoral contact forces and osteochondral pathologies in ACLR knees, but due to cross-sectional study design, causal relationships were not established. Rehabilitation clinicians may consider focusing on restoring tibiofemoral contact force magnitudes following ACLR, provided patients' menisci were uninjured. Future studies should determine longitudinal effects of contact forces on osteochondral pathologies in ACLR knees.

Participants with many or severe tibiofemoral osteochondral pathologies may have used movement strategies to minimize their contact forces due to pain. In individuals with structural and symptomatic medial knee OA, those with higher levels of pain walk with smaller knee adduction moments (KAMs), and increase their KAMs when administered analgesics [21]. However, not all individuals can lower their tibiofemoral contact forces, even when guided by established strategies [30]. Moreover, knee pain and dysfunction scores were similar between the ACLR cohorts in this study [42], as were external (i.e., spatiotemporal parameters, knee kinematics, and knee moments) and internal (e.g., tibiofemoral contact forces) knee biomechanics [32]. Thus, pain does not appear to explain group-level relationships between contact forces and osteochondral pathologies. Nonetheless, individuals may subtlety change their gait biomechanics, undetected by biomechanical analysis, and/or fail to report knee pain or dysfunction. Therefore, we cannot conclude greater contact forces *caused* reduced osteochondral pathologies, but highlight the disparate relationships between ACLR groups.

In ACLR knees free of meniscal pathology, greater medial contact forces were associated with fewer medial cartilage defects, but in meniscal-injury ACLR knees, relationships were non-significant, conflicting with our hypothesis. We expected relationships similar to those reported

for OA knees, where current joint structure [11] and future degeneration [34, 35] positively related to KAM and tibiofemoral contact stresses, respectively. Below we outline how our results may be reconciled with the literature. First, KAM is the sum of all body, inertia, muscle, contact, and passive soft tissue loads acting about the knee's frontal plane, but does not quantify internal load sharing (e.g., articular contact, muscles and ligaments). Indeed, correlations between KAM and tibiofemoral contact forces vary across individuals [26, 33, 40] and tasks [33], and changing KAM through intervention does not necessarily result in concomitant changes to contact forces [41]. Thus, KAM is not suited to studying influence of contact loading on articular tissues. Second, Segal and colleagues are the only team, prior to this study, to have used advanced computational models to predict tibiofemoral contact loading in this context. They developed subject-specific anatomic models, which were both computationally efficient and verified against finite element simulations (an impressive achievement), and found contact stresses predicted incident symptomatic knee OA [34] and osteochondral pathologies [35]. However, they applied a half-bodyweight vertical compressive force to their knee model, which both substantially underestimates applied force magnitudes during daily tasks (i.e., 2-3 bodyweights during walking [6, 15] and >8 bodyweights during sporting tasks [33]) and radically simplifies the loading profile (i.e., knee sustains 6 generalized loads during dynamic tasks). Moreover, their knee model was evaluated in neutral static posture without muscular loading, which varies between individuals and control tasks [7] and is influenced by pathology [18]. Nonetheless, Segal and colleagues found strong predictive relationships between contact stresses and disease development (i.e., odds ratios >4) [34, 35], perhaps due participant age and structural knee state.

When the structural state of articular tissues is compromised (e.g., aged or traumatized joints), impaired tissues cannot withstand daily mechanical demands leading to degeneration. Segal et al [34, 35] examined a cohort from the Multicenter Osteoarthritis Study (MOST), which

sampled community members with frequent knee symptoms and/or at risk of developing knee OA. Compared to those who did not develop knee OA over 15 months, those who developed knee OA had greater baseline tibiofemoral contact stresses (+0.54±0.77 MPa). Their results were consistent previous analysis from the MOST cohort [36], which revealed standing static varus knee deformity (i.e., surrogate medialized tibiofemoral loading) was associated with incident medial knee damage. Segal et al [35] also found baseline contact stresses predicted worsening of cartilage damage and BMLs, consistent with Miyazaki et al [27] who showed greater KAMs predicted medial joint space narrowing. However, the above cited studies [27, 34-36] examined individuals with, or at risk of, knee OA and who were substantially older than our study participants (current study: 29.8±6.4 vs 60±7.5 [36], 67.8±7.5 [34], 63.5±8.4 [35], and 69.7±7.5 [27] years of age). Generally, following ACL injury individuals are at elevated risk for knee OA development [24, 29], but, at testing, participants in this study had no clinician- or self-diagnosed knee OA [42] and were not obese (Table 1), nor did they have notable cartilage pathology at surgery. This suggests patient age may influence response of tibiofemoral cartilage and bone to contact forces. If so, physical rehabilitation following ACLR should be tailored to patient age, i.e., different for a 16 compared to 60 year old patient.

In ACLR knees free from meniscal pathology, greater medial tibiofemoral contact forces were associated with fewer medial BMLs, but in meniscal-injury ACLR knees, relationships were non-significant, conflicting with our hypothesis. Recent systematic review with meta-analysis [3] found two eligible studies [4, 5] examining relationships between external knee loads (i.e., KAM) and BMLs. Bennell and colleagues [5] found medial knee OA patients with larger KAM impulse had more medial BMLs, but did not find associations with 12 months BML progression [4]. However, both studies [4, 5], as well as Segal et al [35], examined individuals with older knees who had [4, 5], or were at risk of [35], medial knee OA. Our study is first to report relationships between tibiofemoral contact forces and BMLs in a young population (~30

years old), first to report these relationships in ACLR knees, and first to report potential protective influence of contact forces on BMLs. If greater medial contact forces do, in fact, protect ACLR knees from medial BMLs this would have implications for knee health because BMLs predict degeneration [13, 31]. These results should be considered cautiously, because the cross-sectional study design does not permit drawing causal links. For example, BMLs and other osseous injuries are not visible during arthroscopy, meaning BMLs assessed 2-3 years post-ACLR may have developed before, during, or after initial ACL injury or ACLR, worsened in the intervening 2-3 years, and/or contributed to cartilage defects [13].

There are several study limitations to consider. First, reconstructions for ~50% of participants (~44% in isolated and ~59% from meniscal-injured groups) were performed using transtibial femoral drilling, the remainder with an anteromedial technique. The effect of femoral drilling technique on transverse plane tibial stability is contentious. Some report no differences in passive internal and external tibial rotation between reconstructed and intact contralateral knees following transtibial femoral drilling [2], and no differences in direct comparisons with anteromedial femoral drilling [25]. However, meta-analysis indicates anteromedial femoral drilling results in superior clinical outcomes, including passive internal and external tibial rotation stability [8]. Femoral drilling technique may influence contact forces and hence relationships to osteochondral pathologies, but has not been demonstrated. Second, ACLR patients enrolled in standardized post-operative physical therapy, but we do not know compliance with, or progression through, therapy. Third, we did not assess levels of pre-injury or return-to sport participation, and do not know if these factors influenced contact forces and/or prevalence of osteochondral pathology. Fourth, neuromusculoskeletal models cannot currently be directly validated, as concurrent *in vivo* measures of muscle forces and articular contact forces from native intact human joints do not exist. However, EMG-driven models accurately predict external joint moments [23] and tibiofemoral contact forces (measured by

instrumented prosthetic implants [15, 16]), providing confidence in our model. Fifth, cross-sectional study design means we cannot establish causal relationships between osteochondral pathologies and contact forces. Although we excluded those with arthroscopically visible cartilage damage, not all cartilage injuries are identifiable during arthroscopy (e.g., lateral compartment cartilage indentation injuries) and BMLs are undetectable through visual inspection. Lack of pre- or peri-operative research-grade knee MRI means we cannot rule out presence of osteochondral pathologies at surgery, which could influence post-ACLR gait biomechanics and relationships to osteochondral pathologies. Future studies should consider using research-grade MRI following ACL injury, and again at ACLR, to robustly screen for osteochondral pathologies. Finally, we grouped heterogeneous meniscal injury and treatment types to facilitate analysis, but this rendered analysis insensitive to potential meniscal injury-specific relationships between contract forces and osteochondral pathology. However, due to the number of different meniscal injury and treatment types, this study was not powered to investigate them independently, but this is valid topic for future investigation.

Conclusion

In isolated ACLR knees, increased medial contact forces were associated with fewer medial cartilage defects and medial BMLs. If meniscal injury had been sustained, no significant relationships between contact forces and osteochondral pathologies were found.

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461 Table 1. Demographics, anthropometrics, and gait spatiotemporal parameters for isolated and
462 meniscal-injured ACLR participants.

	Isolated ACLR (n=62)	Meniscal-injured ACLR (n=38)
Males, n (%)	42 (68)	24 (63)
Age, years (std)	29.8 (6.4)	30.6 (6.6)
Mass, kg (std)	74.9 (13.3)	**83.3 (14.3)[t]**
Body mass index, $kg \cdot m^{-2}$ (std)	24.2 (2.8)	**26.9 (4.1)[t]**
Height, m (std)	1.75 (0.09)	1.76 (0.06)
Injury to surgery, years (std)	0.20 (0.11)	0.24 (0.17)
Surgery to testing, years (std)	2.5 (0.4)	2.6 (0.5)
Transtibial drilling, n (%)	25 (40)	17 (45)
Right knees tested, n (%)	32 (52)	17 (44)
Gait speed, $m \cdot s^{-1}$ (std)	1.4 (0.2)	1.4 (0.2)
Stride length, m (std)	1.5 (0.1)	1.5 (0.1)
Stride time, s (std)	1.1 (0.06)	1.1 (0.05)
Stride rate, $strides \cdot min^{-1}$ (std)	0.9 (0.05)	0.9 (0.04)

463 [t]Significantly different from the isolated ACLR group, $p<0.05$.

Table 2. Tibia cartilage volumes and bone plateau areas, as well as tibiofemoral cartilage defects and bone marrow lesions, specific to medial and lateral tibiofemoral compartments.

	Tibiofemoral compartment	Isolated ACLR (n=62)	Meniscal-injured ACLR (n=38)	p value
Tibia cartilage volume (mm^3±std)	Medial	2164±651	2214±595	NS
	Lateral	2921±846	2880±797	NS
Tibia plateau area (mm^2±std)	Medial	2223±335	2327±300	NS
	Lateral	1313±209	1289±186	NS
Cartilage defects (knees with prevalence, %)	Medial	22, 35%	22, 58%	**0.02***
	Lateral	49, 62%	32, 84%	**0.02***
Bone marrow lesions (knees with prevalence, %)	Medial	39, 63%	28, 74%	NS
	Lateral	40, 65%	19, 50%	NS

Prevalence of a cartilage defect or bone marrow lesions was defined as a grade >1 on at least two consecutive MR images using the respective grading standards. *Statistically significant ($p<0.05$) differences in proportion of knees with prevalence of osteochondral pathology between isolated and meniscal-injured ACLR, using an unadjusted χ^2 test. NS – Non-significant result.

471 Table 3. Breakdown of injury type in ACLR knees with meniscal pathology.

Meniscal injury type	Prevalence, n (%)
Untreated medial tear	4 (11)
Untreated lateral tear	6 (16)
Medial resection	5 (13)
Lateral resection	12 (32)
Untreated medial tear + lateral resection	2 (5)
Medial + lateral resections	1 (3)
Medial resection + lateral repair	1 (3)
Medial repair + untreated medial tear	4 (11)
Lateral repair + untreated lateral tear	3 (8)
Total (n)	38

472 Percentages for each injury type do not sum to 100% due to rounding.

473 Table 4. Relationships between tibiofemoral contact forces and both cartilage defects and bone
474 marrow lesions in isolated and meniscal-injured ACLR knees.

ACLR type	Osteochondral pathology	Tibiofemoral compartment	Odds ratio	p-value	95% confidence interval	
					Lower Bound	Upper Bound
Mensical-injured	Cartilage Defects	Medial	0.9	NS	0.6	1.2
		Lateral	1	NS	0.7	1.6
	Bone Marrow Lesions	Medial	0.9	NS	0.7	1.1
		Lateral	1.4	NS	0.9	1
Isolated	Cartilage Defects	**Medial**	**0.7**	**0.02***	**0.50**	**0.95**
		Lateral	0.9	NS	0.7	1.2
	Bone Marrow Lesions	**Medial**	**0.8**	**0.04***	**0.7**	**0.99**
		Lateral	1.1	NS	0.8	1.6

475 *Significant association of maximum walking tibiofemoral contact forces with the prevalence
476 of the relevant articular tissue pathology. NS – non-significant result.