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Risk of Anterior Cruciate Ligament Fatigue Failure Is Increased by Limited Internal Femoral Rotation During In Vitro Repeated Pivot Landings

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Abstract

Background—A reduced range of hip internal rotation is associated with increased peak anterior cruciate ligament (ACL) strain and risk for injury. It is unknown, however, whether limiting the available range of internal femoral rotation increases the susceptibility of the ACL to fatigue failure.

Hypothesis—Risk of ACL failure is significantly greater in female knee specimens with a limited range of internal femoral rotation, smaller femoral-ACL attachment angle, and smaller tibial eminence volume during repeated in vitro simulated single-leg pivot landings.

Study Design—Controlled laboratory study.

Methods—A custom-built testing apparatus was used to simulate repeated single-leg pivot landings with a 4×-body weight impulsive load that induces knee compression, knee flexion, and internal tibial torque in 32 paired human knee specimens from 8 male and 8 female donors. These test loads were applied to each pair of specimens, in one knee with limited internal femoral rotation and in the contralateral knee with femoral rotation resisted by 2 springs to simulate the active hip rotator muscles' resistance to stretch. The landings were repeated until ACL failure occurred or until a minimum of 100 trials were executed. The angle at which the ACL originates from the femur and the tibial eminence volume were measured on magnetic resonance images.

Results—The final Cox regression model ($P = .024$) revealed that range of internal femoral rotation and sex of donor were significant factors in determining risk of ACL fatigue failure. The specimens with limited range of internal femoral rotation had a failure risk 17.1 times higher than

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did the specimens with free rotation ($P = .016$). The female knee specimens had a risk of ACL failure 26.9 times higher than the male specimens ($P = .055$).

Conclusion—Limiting the range of internal femoral rotation during repetitive pivot landings increases the risk of an ACL fatigue failure in comparison with free rotation in a cadaveric model.

Clinical Relevance—Screening for restricted internal rotation at the hip in ACL injury prevention programs as well as in individuals with ACL injuries and/or reconstructions is warranted.

Keywords

anterior cruciate ligament; fatigue; knee; hip; femoroacetabular impingement

Injuries to the anterior cruciate ligament (ACL) continue to pose significant health and financial burdens due to their short- and long-term consequences,²⁹ especially in young women, who are at greater risk of ACL injury.³⁹ Although research has long been directed at elucidating noncontact ACL injury mechanisms, the role of repetitive loading has received little attention.³³ Many joints in the human body are susceptible to repetitive loading injuries, including the wrist,¹¹ shoulder,³ elbow,¹⁰ intervertebral disc,³⁸ and hip.⁵ In fact, failures due to tissue fatigue have been reported in the leporine medial collateral ligament⁴¹ and the human extensor digitorum longus tendon.³⁰ As for the knee and the ACL, the current dogma is that injury results from a single loading rather than repetitive loading. However, athletes appear to rupture their ACL during maneuvers that they have performed numerous times before—maneuvers such as jump landings and plant-and-cut movements.^{17,26} Only recently has evidence emerged of tissue fatigue as an ACL failure mechanism: ACL rupture occurred with cyclic loading of a magnitude that if repeated only once or twice would not injure the ACL in a cadaveric model.²⁰ Greater impact load and smaller ligament cross-sectional area were identified as contributing factors to the risk of ACL fatigue injury.²⁰

Additional factors that can reduce ACL fatigue life, however, remain unknown. First, limited range of internal rotation at the hip has been shown to be a contributing factor to ACL injury risk.^{6,9} Restrictions in internal femoral rotation designed to mimic limited ranges of hip internal rotation have been shown to increase ACL strain in cadavers during simulated single-leg pivot landings.⁴ Hence, limited hip internal rotation might be expected to decrease ACL fatigue life by increasing ligament loading. Second, the angle at which the ACL originates from the femur may affect the ACL fatigue life. In an in vitro model in which human knee specimens were cyclically loaded, this femoral-ACL attachment angle was significantly more acute in specimens that exhibited a tear of the posterolateral (PL) bundle or a permanent elongation of the ACL than those that did not sustain an ACL failure.²³ An acute attachment angle appears to induce a stress concentration at the femoral enthesis, as shown in silico.²³ The femoral-ACL attachment angle, therefore, may be directly related to ACL fatigue life. Third, the size of the tibial eminence could also be directly related to ACL fatigue life given that this bony structure was found to be smaller in ACL-injured individuals than in healthy, uninjured controls,¹⁴ especially in male patients.³⁵ The tibial eminence may act as a bony restraint against internal tibial rotation, and thus a

small eminence may provide less resistance to such axial rotation. A smaller restraint to internal tibial rotation would increase the risk of ACL injury because a combination of knee axial compression force, internal tibial torque, and knee abduction moment is likely the worst-case loading scenario for the ACL, as tested in vitro and in silico.^{8,22,25,28,32} Hence, limited hip internal rotation, a small femoral-ACL attachment angle, and a small tibial eminence volume may contribute to ACL injury risk because these factors may decrease the fatigue life of the ACL by increasing ACL load during each loading cycle.

The purpose of this study, therefore, was to determine the effect of limited range of internal femoral rotation, sex, femoral-ACL attachment angle, and tibial eminence volume on in vitro ACL fatigue life during repetitive simulated single-leg pivot landings. This landing model is representative of the period in vivo before any accumulated microdamage can be repaired. A custom-built in vitro knee-testing apparatus^{4,20,25} was used to simulate single-leg pivot landings in paired knees, with one knee from each pair loaded with limited internal femoral rotation and the other knee with free femoral rotation. We tested the primary hypothesis that the risk of ACL failure would be significantly greater with limited range of internal femoral rotation than with free rotation. We also tested the secondary hypotheses that female sex, a smaller femoral-ACL attachment angle, and a smaller tibial eminence volume would increase risk of ACL failure in comparison with male sex, a larger attachment angle, and a smaller tibial eminence volume, respectively.

METHODS

Specimen Procurement and Preparation

To determine the sample size required to test our hypotheses, 2-sided 2-group survival analyses based on exponential survival ($\alpha = 0.05$; $1 - \beta = 0.80$) were performed with unpublished pilot survival data (ie, group exponential parameters; hazard ratios). These data were obtained from 6 pairs of knee specimens (3 male and 3 female donors) by using the same methods described herein. Because power analyses available for survival data are limited to dichotomized data, only range of internal femoral rotation and sex were included as independent variables to predict risk of ACL failure. This power analysis provided a conservative estimate because it could not account for the presence of paired knees, which have greater correlation than unpaired knees. These a priori power analyses revealed a total sample size of 4 and 17 knee specimens for the internal femoral rotation and sex variables, respectively. Given the conservative nature of these power analyses and the fact that an equal number of female and male knee specimens was preferred, 16 pairs of fresh-frozen knee specimens, for a total of 32 specimens from 8 male (mean $\pm$ SD: age, 42.4 ± 16.6 years; height, 1.75 ± 0.06 m; mass, 71.3 ± 8.5 kg) and 8 female (age, 47.6 ± 11.1 years; height, 1.65 ± 0.08 m; mass, 53.5 ± 8.4 kg) donors, were procured for this study. No scars indicative of knee surgery, no evidence of joint degeneration, and no joint deformity, as assessed with magnetic resonance imaging (MRI) and visual inspection, were present in the knee specimens.

The knee specimens were stored in a freezer at -20°C until dissection, MRI, and testing. The specimens were removed from the freezer 48 hours before dissection and thawed at room temperature. They were dissected down to the knee joint capsule, leaving intact its

ligaments, as well as the tendons of the quadriceps (rectus femoris), medial hamstrings (semitendinosus, semimembranosus, gracilis), lateral hamstrings (biceps femoris), medial gastrocnemius, and lateral gastrocnemius. After dissection, each knee specimen underwent MRI and then was mechanically tested on a later day. The dissected specimens were stored in the freezer until 24 hours before testing. Immediately before testing, the proximal femur and the distal tibia and fibula were cut to a length of 20 cm each, from the joint line. Then, each bone extremity was potted in polymethylmethacrylate.

Experimental Design and Protocol

A cross-sectional, matched-pair design was used to test the hypotheses. From each donor, one knee specimen was randomly assigned to a pivot landing with a limited range of internal femoral rotation and the paired knee specimen to a pivot landing with free range of femoral rotation. Each session began with 5 nonpivot trials that served 2 purposes: (1) to precondition the knee specimen and (2) to determine the height from which the weight needed to be dropped from the top of the testing apparatus to simulate a jump landing with a ground-reaction force approximating 4 times body weight ($4 \times BW$), $\pm 10\%$. During these preconditioning trials, only an impulsive compression force and knee flexion moment were produced (no axial tibial torque). After this set of trials, pivot trials were executed (compression, flexion moment, and internal tibial torque), approximately 1 minute apart, until ACL failure occurred or a minimum of 100 trials was achieved.²⁰ For the knees with limited range of femoral rotation, the femoral rotation device was locked. For the knees with free range of femoral rotation, the femoral rotation device was unlocked. ACL failure was defined as either a macroscopic failure of the ligament or a 3-mm increase in cumulative anterior tibial translation, as previously defined²⁰ and accepted clinically.⁷ The presence of macroscopic failure was assessed when a sudden increase in the range of anterior tibial translation occurred ($> 10\%$, based on pilot work), and failure was confirmed, along with injury location, by visual inspection.

Magnetic Resonance Imaging

Before testing, each knee specimen was placed in a coil in full extension and scanned with a 3.0-T MRI system (Ingenia model; Philips Medical Systems), using a 3-dimensional T2-weighted, proton-density sequence with the following parameters: repetition time, 1000 milliseconds; echo time, 35 milliseconds; slice thickness, 0.7 mm; pixel spacing, 0.49×0.49 mm; spacing between slices, 0.35 mm; field of view, $330 \times 200 \times 96$ mm (inferior-superior, anterior-posterior, medial-lateral, respectively).

From the MRIs, the angle at which the ACL originates from the femur, termed here the *femoral-ACL attachment angle*, and the volume of the tibial eminence were measured by use of OsiriX software (v 4.1.2; www.osirix-viewer.com). For the femoral-ACL attachment angle, the images were reconstructed to create oblique-sagittal and oblique-frontal planes, which ran parallel to the longitudinal axis of the ACL. In the oblique-sagittal view, the oblique-frontal slice running through the midportion of the ACL was identified (Figure 1A, white line). From that oblique-frontal slice, the femoral-ACL attachment angle was measured. Specifically, we calculated the angle between (1) a line drawn along the edge of the lateral femoral condyle where the ACL inserts and (2) a line along the longitudinal axis

of the proximal 25% of the ACL (Figure 1A, α). For the tibial eminence volume, all frontal plane slices in which this structure was present were identified. From these slices, the area of the tibial eminence proximal of a line connecting the most superior points of the medial and lateral tibial plateau was outlined (Figure 1B). Tibial eminence volume was calculated by OsiriX, which multiplied, for each slice, the outlined area by the sum of slice thickness and slice spacing and then added each slice volume to obtain total volume. All measurements were made by the same investigator. Intra-observer reliability of the measurements was assessed by measuring the variables 3 times, on different days, for each specimen and calculating the intraclass correlation coefficients (ICCs). The ICCs for the MRI measurements were excellent, with 0.78 for the femoral-ACL attachment angle and 0.88 for the tibial eminence volume.

Knee Testing Apparatus

The dissected and imaged knee specimens were inverted and mounted in a modified Withrow-Oh testing apparatus²⁵ in 15° of knee flexion. This apparatus simulated a single-leg pivot jump landing with a ground-reaction force approximating 4×BW by impacting the distal end of the tibia and producing an impulsive compression force, knee flexion moment, with and without internal tibial torque (pivot and nonpivot trials, respectively). Specifically, a weight (Figure 2) was dropped onto the tibia from a height that was determined by trial and error during the nonpivot trials and that achieved a 4×BW loading magnitude, as measured by a 6-axis load cell at the proximal femur (Figure 2, *L*). Internal tibial torque was produced with a tibial torsion device (Figure 2), which was either locked to simulate a non-pivot landing or unlocked to simulate a pivot landing.⁴ Axial femoral rotation was controlled by a novel femoral rotation device (Figure 2) at the proximal end of the femur. As previously described,⁴ the device consisted of a circular plate, which rotated in the transverse plane, and 2 pretensioned springs (spring rate, 16.8 N/mm; McMaster-Carr) to resist axial rotation. To model limited internal femoral rotation, the femoral rotation device was locked with a steel stop. To model adequate rotation, the steel stop was removed from the device to allow free femoral rotation. In this condition, rotation was only resisted by the femoral rotation device's springs, which simulated the tensile resistance of the hip rotator muscles to stretch. Knee muscle tension and tensile resistance to stretch were modeled by means of pretensioned elastic structures (ie, woven nylon cord) connected to the tendons of the quadriceps and medial and lateral ham-strings and gastrocnemii with cryoclamps (Figure 2). Before every trial, the quadriceps muscle-tendon unit and the ham-strings and gastrocnemii muscle-tendon units were pretensioned to ~180 N and ~70 N, respectively.²⁴ Tension of the muscle-tendon units was measured at 2 kHz by 5 uniaxial load cells (Transducer Techniques) attached, in series, to the woven nylon cords and cryoclamps.

Tibiofemoral kinematic values were recorded at 400 Hz via an optoelectronic imaging system (Optotrak Certus; Northern Digital) that tracked the 3-dimensional (3D) location of 6 infrared-emitting diodes. Three diodes were affixed to the femoral segment, with 3 other diodes affixed to the tibial segment, in a configuration that defined the sagittal, frontal, and transverse planes of each segment. The 3D coordinates of the femoral and tibial diodes were used to quantify the knee rotations and translations. Meanwhile, 3D forces and moments

produced at the distal tibia and proximal femur were recorded at 2 kHz via two 6-axis force sensors (Figure 2, *L*) (Advanced Manufacturing Technology Inc).

Data Processing

The 3D coordinates of the infrared-emitting markers, as acquired by the motion capture system, were low-pass filtered using a Butterworth filter (fourth order; cutoff frequency, 20 Hz). From the markers' 3D coordinates, in addition to the coordinates of the knee's origin—defined as the roof of the femoral notch and digitized before the landing trials—3D rotations and translations were calculated by use of the method described by Grood and Suntay.¹³ Femoral rotation was defined with respect to the testing apparatus, whereas tibial rotations and translations were defined with respect to the femur. Kinematic data were calculated as relative and/or cumulative changes in rotations and translations. A “relative” measurement was defined relative to the data point at time 0 (initial contact) of the trial of interest. A “cumulative” measurement was defined relative to the data point at time 0 of the first pivot trial. All load cell data were also low-pass filtered with a Butterworth filter (fourth order; cutoff frequency, 70 Hz).

The main outcome measure was the number of trials executed until ACL failure occurred or until a minimum of 100 pivot trials was reached. From each trial, the range of internal femoral rotation was extracted as the main independent variable. Peak relative and cumulative anterior tibial translations were also extracted to assist in determining ACL failure, as well as peak relative and cumulative internal tibial rotations.

Statistical Analysis

The hypotheses were statistically tested by means of Cox regression models with shared frailty (to account for paired knee specimens). Specifically, the primary hypothesis was tested with a model that predicted ACL failure risk with internal femoral rotation (dichotomized and coded as 1 = free and 2 = locked) as the predictor variable. The secondary hypothesis was tested with the full model, which included internal femoral rotation, sex of donor, femoral-ACL attachment angle, and tibial eminence volume as the predictor variables. A final model was selected based on the variables that best predicted risk of ACL failure. Additionally, the mean loading conditions (peak landing force, peak internal tibial torque, range of internal femoral rotation) and knee kinematics (peak relative and cumulative anterior tibial translation, peak relative and cumulative internal tibial translation) were compared between groups via 1-way analyses of variance (ANOVAs) to gain insight into the biomechanical differences between conditions. An alpha level below .05 indicated statistical significance.

RESULTS

Eight of the 32 knee specimens that were tested failed during the repetitive pivot landings: 7 specimens loaded with limited internal femoral rotation (“locked” condition) and only 1 specimen loaded with free rotation. The failed specimens included 5 female knees, which failed at a mean ($\pm$ SD) of 15 ± 13 loading cycles, and 3 male knees, which failed at a mean of 84 ± 41 cycles. There was 1 complete ACL tear, 2 partial ACL tears, 2 permanent

elongation failures, and 3 tibial avulsions (Table 1). On average, $3.3^{\circ} \pm 0.6^{\circ}$ and $14.1^{\circ} \pm 2.5^{\circ}$ of internal femoral rotation occurred during the pivot landings with limited and free rotation, respectively. Loads applied to the knee specimens during the nonpivot and pivot trials, as well as the knee kinematics during the pivot trials, are presented in Table 2. Of note, the mean landing force and the average peak relative and cumulative anterior tibial translations were significantly greater during the pivot landings with limited rotation than with free rotation (Table 2).

The primary finding of this study is that the knee specimens with limited range of internal femoral rotation during repetitive in vitro pivot landings had a risk of ACL failure 8.3 times higher in comparison with the specimens with free rotation, when only this predictor variable was included in the statistical model (Wald $\chi^2 = 3.90$; $P = .048$) (Table 3, model 1; Figure 3). The full statistical model, which included internal femoral rotation, sex of donor, femoral-ACL attachment angle, and tibial eminence volume, did not significantly predict ACL failure risk (Wald $\chi^2 = 7.82$; $P = .098$) (Table 3, model 2). Although internal femoral rotation and sex of donor were found to be significant predictors in the full model, femoral-ACL attachment angle and tibial eminence volume did not significantly predict ACL failure risk. The best and final statistical model, therefore, only included internal femoral rotation and sex of donor as predictors of ACL fatigue failure risk (Wald $\chi^2 = 7.50$; $P = .024$) (Table 3, model 3). When accounting for sex, risk of ACL failure was 17.1 times higher in the knee specimens loaded with a limited range of internal femoral rotation than in those loaded with free rotation. When accounting for femoral rotation, the female knee specimens had a risk of ACL failure 26.9 times higher than the male specimens (Table 3), although this did not reach statistical significance.

DISCUSSION

The question addressed by the present study was whether limited range of internal femoral rotation, sex, femoral-ACL attachment angle, and tibial eminence volume affect the in vitro ACL fatigue life during repetitive simulated single-leg pivot landings. The main finding of the study is that limiting rotation increases the risk of an ACL fatigue failure, which suggests that constraining the available range of hip internal rotation during single-leg pivot landings increases the risk of sustaining an ACL rupture.

The primary hypothesis was supported: an in vitro repeated pivot landing model with a limited range of internal femoral rotation would have a significantly greater risk of ACL failure than that with free rotation. ACL failure risk was more than 8 times greater when internal femoral rotation was limited and more than 17 times greater when accounting for sex of donor. It is telling that only 1 knee specimen failed when internal femoral rotation was only resisted by springs, whereas 7 specimens failed when femoral rotation was locked. In addition, it is noteworthy that all ACLs that failed via a macroscopic tear ruptured at the femoral enthesis, especially of the PL bundle. Given the current literature,^{4,20} this is not surprising. In a similar in vitro repeated pivot landing model, landing impact force was found to be related to ACL injury risk.²⁰ Specifically, a $1 \times \text{BW}$ increase in impact force increased injury risk by more than 32-fold, with impact force acting as the surrogate measure for ACL stress.²⁰ In fact, many materials are known to fail under a number of

loading cycles that is inversely related to the tensile stress applied to them.¹⁸ And most recently, it has been shown that peak ACL strain increased in cadaver-simulated pivot landings as the available range of internal femoral rotation was decreased.⁴ With ACL strain being positively related to ACL stress,²⁷ the results presented in the current study were expected; the number of loading cycles to failure was expected to decrease with limited femoral rotation. Because the same energy was applied to both knees within a pair (ie, same drop height and drop weight) and thus in both internal femoral rotation conditions, larger landing forces and marginally larger internal tibial torques during the landings with limited rotation were mainly due to less energy being absorbed during femoral rotation in these landings. Greater loading translated into greater anterior tibial translation and marginally greater internal tibial rotation, which are known to increase ACL loading.²⁵ A more detailed biomechanical explanation is presented elsewhere.⁴ This may explain why athletes with decreased range of hip internal rotation have a greater risk of sustaining an ACL injury.^{6,9}

Our results corroborate recently published evidence that the human ACL is susceptible to a repetitive loading injury²⁰ and that the femoral enthesis, especially that of the PL bundle, is at risk of injury.^{20,34} This may explain why athletes seem to rupture their ACL during maneuvers that they have performed over and over again.^{17,26} So-called “fatigue” injuries have been reported in the leporine medial collateral ligament⁴¹ and the human extensor digitorum longus tendon.³⁰ Although tendons can repair and adapt to loading, their ability to do so deteriorates when tissue damage is too severe.¹ High ACL loading magnitudes and/or frequencies may induce tissue damage in vivo that is beyond the ACL's ability to adapt, thus leading to an accumulation of microdamage and then failure. Such a mechanism has been described in rat patellar tendon¹ and may occur in the ACL for several reasons: the ACL's lack of ability to remodel,²¹ the similar collagen composition of ligament and tendon,² and collagen's slow turnover rate.³⁷ If the ACL is indeed susceptible to fatigue-type failures in vivo, injury prevention efforts should focus on limiting the frequency of high ACL loading maneuvers, thereby improving the fatigue life of the ACL. This may mean improving the functional range of motion available in a hip that has restricted internal rotation to reduce ACL loading⁴ or reducing the frequency of certain athletic maneuvers known to greatly increase load on the ACL, similar to the limit imposed on Little League pitchers in regard to the number of pitches allowed per day. Furthermore, the PL bundle may be at greater risk because of its significant role in resisting loads, especially internal tibial torque, when the knee is near full extension during pivot landings.^{12,16} It is unknown, however, why the ACL's femoral enthesis is particularly vulnerable to failure in comparison with the tibial enthesis.

One part of our secondary hypothesis, that the female specimens would have a significantly greater risk of ACL failure in comparison with the male specimens, was not supported. Although including sex of donor in our statistical model improved it and the female ACLs had a risk of failure nearly 27 times greater than the male ACLs, sex of donor failed to reach statistical significance by a small margin ($P = .055$). We believe that the small number of ACL failures—only 5 female and 3 male ACLs failed out of a total of 32 ACLs—contributed to a lack of statistical power to reveal significant sex differences. However, a shorter fatigue life may explain why the ACL injury rate of women is 2 to 5 times greater

than that of men.³⁶ The female ACLs were expected to fail in fewer cycles than the male ACLs because of sexual dimorphism in ACL size¹⁹ and ultrastructure¹⁵ and/or knee joint structure.¹⁹ For example, Lipps et al^{19,20} found not only that female knee specimens have a smaller ACL cross-sectional area than male specimens but also that a smaller ACL cross-sectional area increases risk of a fatigue-type failure in a similar in vitro model. ACL cross-sectional area was not included in our regression model because we did not want to decrease its statistical power, especially given that this variable has already been shown to affect ACL injury risk during in vitro repeated pivot landings.²⁰

The other part of our secondary hypothesis, stating that femoral-ACL attachment angle and tibial eminence volume would have a significant effect on ACL failure risk, was also not supported. Although an acute femoral-ACL attachment angle and a smaller tibial eminence volume may increase one's risk of sustaining an ACL injury,^{23,35} these variables were not found to significantly influence risk of ACL failure (Table 3, model 2). With regard to femoral-ACL attachment angle, its effect on injury risk may be specific to the type of failure pattern, with a smaller angle being a risk factor for partial or complete tears but not for tibial avulsions, for example. Thus, pooling the data of all failed knee specimens may have masked any present effect. For instance, the knee specimens that failed via a tibial avulsion appeared to have greater attachment angles than all other failed specimens (mean $\pm$ SD, $34.6^\circ \pm 4.9^\circ$ vs $19.9^\circ \pm 5.5^\circ$) (Table 1). Isolating the specimens that failed via a complete or partial rupture at the femoral enthesis revealed smaller angles in these specimens in comparison with the specimens that did not fail ($18.6^\circ \pm 5.8^\circ$ vs $25.4^\circ \pm 9.1^\circ$) (Table 1). Unfortunately, the small number of ACL failures did not allow us to analyze the data based on failure type. Similar data patterns were noticed with the tibial eminence volume data, with knee specimens that failed via tibial avulsion having a relatively small volume in comparison with all other failed specimens ($1.23 \pm 0.17 \text{ cm}^3$ vs $1.58 \pm 0.38 \text{ cm}^3$) (Table 2). We note that an ACL failure via a tibial avulsion is not the most common type of ACL injury among the population at greatest risk. This probably stems from the specimens having been harvested from older donors (45.0 ± 13.9 years). Hence, pooling the data of all failed knee specimens may have masked any present effect of tibial eminence volume. Another reason for the lack of significant effect may be due to methodological reasons. Recently published data revealed that only the volume of the medial tibial eminence was inversely related to ACL injury risk, and in male patients only.³⁵ In the present study, volume was measured for the entire tibial eminence. Again, the small number of ACL failures did not allow us to analyze the data based on sex of donor.

We acknowledge several limitations of the present study. First, we investigated an ACL failure mechanism—ligament fatigue—with an in vitro model, which precludes the possibility of studying any adaptive biological response. Although the remodeling rate of the human ACL, whether intact or partially injured, is unknown, we know that no remodeling occurs in the completely ruptured human ACL²¹ and that type I collagen has a slow turnover rate.³⁷ For these reasons, we believe that the role played by biological healing and remodeling is minimal over periods of days or even weeks; hence, the results obtained from our in vitro model reflect behavior before any such remodeling can occur. Second, knee specimens were harvested from older donors, although the younger population sustains ACL injuries most frequently.³¹ Hence, results cannot necessarily be generalized to this latter

population. The number of cycles to failure may have been underestimated because of the lower quality structural and mechanical properties of the older ACL.⁴⁰ The number of ACL failures via a tibial avulsion may have been overestimated. We believe, however, that the general qualitative trends remain valid. Third, a small number of ACL failures occurred, which may have skewed the distribution of failure types. Fourth, only 2 internal femoral rotation conditions (“locked” and “free”) were included in our experimental design. But we consider our paired knee specimen design one of the strengths of this study because it reduced the effect of interspecimen variability. Although we cannot make definite conclusions about the relation between ACL failure risk and other available ranges of internal femoral rotation not tested herein, we have no reason to believe that a negative relation would not continue to exist if other available ranges of motion that fall within the condition tested (eg, $\sim 3^{\circ}$ - 14°) had been included. This is especially true considering that a similar relation has been reported between available range of internal femoral rotation and peak ACL strain during in vitro simulated pivot landings⁴ and considering that strain affects a ligament's potential for injury.⁴⁰ Additionally, because our limited internal femoral rotation condition modeled a hip with nearly no rotation, which was halted abruptly, thus representing a worst-case scenario, the hazard ratios reported herein cannot necessarily be generalized to in vivo landing scenarios. Fifth, only the monoarticular actions of the muscles were simulated in our in vitro model.

Our results confirm previous findings that the human ACL is susceptible to fatigue failure when loaded repeatedly under large loads.²⁰ This suggests that limiting the frequency of high-impact loading cycles and/or improving the fatigue life of the ACL as part of an ACL injury prevention program warrants further investigation. Our results also suggest that landing with a limited available range of hip internal rotation decreases the ACL's fatigue life. Hence, improving the functional range of motion available at the hip should decrease injury risk. This supports the justification for screening for restricted internal rotation at the hip as part of ACL injury prevention programs and evaluation protocols for individuals with ACL injuries and/or reconstructions. This is particularly true for women, because the female knee specimens tended to have a greater risk of ACL failure than the male specimens.

CONCLUSION

Limiting the range of internal femoral rotation increases the risk of sustaining an ACL fatigue failure during pivot landings in a cadaveric model.

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Figure 1.

(A) Example of the femoral-ACL attachment angle measurement. Left: oblique-sagittal MRI showing the location of the oblique-frontal slice (white line, at midportion of the ACL) that was used to measure the angle. Right: oblique-frontal MRI showing the definition of the femur-ACL attachment angle (α). (B) Example of the tibial eminence (TE) measurement. Frontal plane MRI showing the outlined area of the TE, which was multiplied by the sum of the slice thickness and slice spacing to obtain each slice's TE volume. Total TE volume was calculated by taking the sum of the TE volume of all slices.

Figure 2. Sagittal plane diagram of the in vitro testing apparatus used to simulate single-leg pivot landings (left) and a top view of the femoral rotation device (right). The position of the specimen and the device at peak relative internal femoral rotation during the trials with limited and free femoral rotation is represented by the solid and transparent portions of the diagram, respectively. *L*, 6-axis load cell.

TABLE 1

List of the Specimens Tested, Status of Internal Femoral Rotation, Number of Cycles to Failure, Description of the Failure Pattern, and Morphological Data^a

Specimen ^b	Internal Femoral Rotation	Cycles to Failure ^c	Failure Pattern ^d	Femur-ACL Angle, deg ^e	Tibial Eminence Volume, cm ³
M01149					
Left knee	Free	—	Did not fail	14.3	1.16
Right knee	Locked	127	Permanent elongation	17.3	1.24
M01431					
Left knee	Locked	80	Permanent elongation	26.4	2.03
Right knee	Free	—	Did not fail	23.9	1.98
F02341					
Left knee	Free	—	Did not fail	27.3	1.11
Right knee	Locked	38	Tibial avulsion	30.1	1.39
M02867					
Left knee	Free	—	Did not fail	19.4	1.27
Right knee	Locked	—	Did not fail	30.6	1.54
F10496					
Left knee	Locked	—	Did not fail	22.3	1.04
Right knee	Free	—	Did not fail	19.2	1.03
F20661					
Left knee	Locked	14	Complete tear at femoral enthesis	22.8	1.72
Right knee	Free	—	Did not fail	25.9	2.11
M21514					
Left knee	Locked	—	Did not fail	27.5	1.40
Right knee	Free	—	Did not fail	26.3	1.69
M22806					
Left knee	Free	—	Did not fail	30.7	1.41
Right knee	Locked	—	Did not fail	25.8	1.12
M30734					
Left knee	Free	—	Did not fail	22.7	2.07
Right knee	Locked	—	Did not fail	23.7	2.02
F34422					
Left knee	Free	—	Did not fail	19.6	1.22
Right knee	Locked	—	Did not fail	29.4	1.04
M34494					
Left knee	Locked	45	Partial tear of PL bundle at femoral enthesis	20.9	1.79
Right knee	Free	—	Did not fail	23.6	1.83
F34516					
Left knee	Free	—	Did not fail	30.4	1.06

Specimen ^b	Internal Femoral Rotation	Cycles to Failure ^c	Failure Pattern ^d	Femur-ACL Angle, deg ^e	Tibial Eminence Volume, cm ³
Right knee	Locked	7	Partial tear of PL bundle at femoral enthesis and midsubstance	11.9	1.13
F34568					
Left knee	Locked	—	Did not fail	14.5	0.88
Right knee	Free	—	Did not fail	28.5	1.18
F40036					
Left knee	Locked	6	Tibial avulsion	33.9	1.05
Right knee	Free	10	Tibial avulsion	39.7	1.25
M40061					
Left knee	Locked	—	Did not fail	26.3	1.06
Right knee	Free	—	Did not fail	32.2	1.33
F71125					
Left knee	Free	—	Did not fail	21.1	1.12
Right knee	Locked	—	Did not fail	25.2	1.26

^a ACL, anterior cruciate ligament; PL, posterolateral.

^b F, female donor; M, male donor.

^c Includes the 5 nonpivot trials at the beginning of each testing session. Dashes indicate nonfailure.

^d Permanent ACL elongation was defined as a 3-mm increase in cumulative anterior tibial translation relative to the first pivot trial.

^e Specimen knee flexion angle in the magnetic resonance imaging system was standardized, with all specimens imaged in full extension.

TABLE 2

Loading Applied to Knee Specimens and Their Kinematic Responses^a

Biomechanical Variable	Locked IFR	Free IFR	P Value
Nonpivot trials			
Loading			
Peak landing force (×BW)	4.2 ± 0.4	4.2 ± 0.2	.754
Pivot trials			
Loading			
Peak landing force (×BW)	5.0 ± 0.7	4.5 ± 0.5	.026 ^c
Peak internal tibial torque, N·m	31.3 ± 5.9	27.8 ± 5.5	.096
Knee kinematics ^b			
Peak relative anterior tibial translation, mm	8.2 ± 1.6	6.7 ± 1.1	.003 ^c
Peak cumulative anterior tibial translation, mm	8.9 ± 1.7	7.3 ± 1.2	.004 ^c
Peak relative internal tibial rotation, deg	19.7 ± 3.6	17.5 ± 2.9	.072
Peak cumulative internal tibial rotation, deg	21.6 ± 3.9	19.6 ± 2.9	.100

^aData are reported as mean ± SD. BW, body weight; IFR, internal femoral rotation.^bFor each specimen, peak values of all pivot trials, excluding the trial during which ACL failure occurred, were averaged.^cStatistically significant difference between groups ($P < .05$).

TABLE 3Results of Cox Regression Models With Shared Frailty^a

Predictor Variable	Hazard Ratio	95% CI	P Value
Model 1			.048 ^b
Internal femoral rotation	8.30	1.02-67.85	.048 ^b
Model 2			.098
Internal femoral rotation	13.13	1.32-130.96	.028 ^b
Sex	8.89	1.17-67.72	.035 ^b
Femoral-ACL attachment angle	1.12	0.93-1.36	.237
Tibial eminence volume	9.23	0.74-114.98	.084
Model 3			.024 ^b
Internal femoral rotation	17.09	1.70-171.85	.016 ^b
Sex	26.93	0.94-773.18	.055

^a ACL, anterior cruciate ligament.^b Statistically significant ($P < .05$).