

Ligament Strain Response Between Lower Extremity Contralateral Pairs During In Vitro Landing Simulation

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Background: Limb asymmetries, as determined through in vivo biomechanical measures, are known risk factors for anterior cruciate ligament (ACL) injury. Previous cadaveric studies have shown a lack of significant differences in ligament strain between contralateral lower extremities when identical kinematics were simulated on specimens. Recent methodological developments have applied in vivo knee kinetics to exert landing forces on cadaveric lower extremities to mimic ACL injury events, but it is unknown whether contralateral limbs fail in a consistent manner during impact simulator testing.

Hypothesis: It was hypothesized that contralateral lower extremities would not exhibit side-to-side differences in ligament strains. Furthermore, it was hypothesized that failure loads and failure locations would be independent of limb dominance.

Study Design: Controlled laboratory study.

Methods: Fourteen pairs of cadaveric lower extremities were obtained from an anatomic donations program (8 female, 6 male; mean \pm SD: age, 41.7 \pm 8.1 years; mass, 86.8 \pm 27.0 kg; body mass index, 29.4 \pm 9.0 kg/m²). A mechanical impact simulator was used to re-create the impulse ground-reaction force generated during an in vivo landing task. Ligament strains were recorded by differential variable force transducers implanted on the ACL and medial collateral ligament (MCL).

Results: No significant differences were observed in peak ACL or peak MCL strain for 5 loading conditions. Fisher exact tests of independence revealed that limb dominance was independent of both load at failure and failure location.

Conclusion: There were no significant differences in ACL and MCL strain values between limb sides during in vitro impact simulation testing. This finding indicates that limb dominance does not influence the failure threshold of the ACL, since there was no significant difference in failure strains. The functional mechanics of the ACL are comparable between contralateral pairs from the same healthy specimen.

Clinical Relevance: Injury mechanisms and intra-articular mechanics cannot be ethically studied in an in vivo setting. The current study provides additional insight into limb asymmetry that is observed among athletes in clinical sports medicine settings.

Keywords: anterior cruciate ligament; injury simulation; knee ligament biomechanics; contralateral pairs

In the United States, approximately 250,000 anterior cruciate ligament (ACL) injuries occur annually.²¹ Despite an abundance of research into injury mechanisms, risk factors, and prevention strategies, ACL injuries continue to occur in the athletic population.^{11,17,18,26} A recent study reported that over a 21-year period, the incidence rate of ACL injury in female athletes remained steady.²⁹ Limb asymmetries, as determined by biomechanical measures during in vivo investigations, have been identified as risk factors for primary and secondary ACL injury.^{19,27} In a prospective study, side-to-side differences in knee

abduction moment (KAM) during a drop vertical jump assessment were significantly greater in athletes who subsequently suffered an ACL injury versus noninjured athletes.¹⁹

Although in vivo investigations can identify potential mechanisms of injury, it is difficult to determine how individual anatomic structures respond to various external conditions, such as applied loads and rotations, in vivo. A few studies have measured ligament strain in vivo by surgically implanting a strain transducer in the ACL.^{10,12} A study with implanted strain transducers showed that isolated anterior shear loading and internal torque increased ACL strain in nonweightbearing and weightbearing positions.¹⁵ However, varus-valgus moments increased ACL strain only in the weightbearing positions. These results supported the

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protective function of the ACL in control of knee kinematics and reaffirmed the importance of application of these loads during clinical diagnosis of an ACL injury (eg, Lachman test). However, this technique has a limited ability to examine dynamic athletic tasks owing to the invasive nature of the differential variable force transducer (DVFT) implantation procedure. In addition, only tasks that elicit minimal risk of injury can be investigated. In vitro studies permit an improved examination of the response of individual structures in the lower extremity with systematic repeatability, as well as the ability to explore failure mechanics during dynamic tasks, which cannot ethically be done in vivo.

Previous cadaveric studies have shown an absence of significant differences in ligament strain between contralateral pairs when identical kinematics from athletic tasks captured in vivo were applied to the specimen via a 6 degrees of freedom robot.³ However, these simulations were conducted during controlled athletic tasks that presented no risk of injury to the soft tissue structures of the knee joint.⁶ Recent methodological developments apply in vivo knee kinetics to exert comparable landing forces on cadaveric lower extremities to mimic the high-risk mechanics known to contribute to ACL injury.^{8,23} This methodology presents a novel tool to investigate ligamentous strain response while the specimen's knee remains structurally intact and constrained in a physiologically relevant manner. Application of multiplanar loads via a combination of anterior tibial shear force (ATS), KAM, and internal tibial rotation (ITR) moment significantly increases ACL strain and can cause ACL failure.^{8,9,22,30} Injury outcomes that resulted from the application of this novel methodology, via demonstration using cadaveric models, support multiplanar knee valgus collapse as a primary mechanism of ACL injury.^{9,19,22,24} Moreover, ACL disruption patterns were reported to be independent of applied loading conditions. However, it remains unknown if contralateral ACLs respond and subsequently fail in a consistent manner when external loads are applied. Attaining this knowledge is important to biomechanics investigations because many testing methodologies are destructive and limit the capacity for repeated measures.⁴ Accordingly, it is critical to appreciate how comparable the results from contralateral pairs are through identical testing and subsequent statistical analysis.

Thus, the objective of this study was to compare strain responses in knee ligaments between contralateral lower extremity pairs during simulated in vitro landings. It was hypothesized that contralateral lower extremities would

not exhibit side-to-side differences in ligament strains. Furthermore, it was hypothesized that failure loads and failure locations would be independent of limb dominance.

METHODS

Fourteen pairs of fresh-frozen cadaveric lower extremities (8 female, 6 male; mean \pm SD: age, 41.7 \pm 8.1 years; mass, 86.8 \pm 27.0 kg; body mass index, 29.4 \pm 9.0) were obtained from an anatomic donations program (Anatomic Gifts Registry). Inclusion criteria for cadaveric specimens were as follows: (1) between 18 and 52 years old, (2) passed all serology tests, (3) no documented history of knee surgery or trauma, (4) no chemotherapy treatments lasting >1 month, and (5) no documented bed rest for >1 month prior to death. Specimen preparation methods previously reported in the literature were followed.⁸ Briefly, soft tissue was removed from the femur, which was sectioned 20 cm proximal to the superior aspect of the patella. The femoral shaft was then potted in polyester resin. The quadriceps and hamstrings tendons were isolated and clamped to hydraulic actuators to simulate muscle loads that act across the knee joint in vivo. These loads were presented in a 1:1 quadriceps:hamstrings ratio. The musculature of the shank and foot remained intact. Two portals were cut into the knee capsule just medial and lateral to the patellar tendon. The knee joint cavity was then cleaned of adipose tissue to expose the ACL and medial collateral ligament (MCL) so that 3-mm microminiature DVFTs (LORD Microstrain) could be implanted in the ligaments and respective ligament strains could be measured.^{8,10,14,24}

A novel mechanical impact simulator⁸ was used to simulate the impulse ground-reaction force generated during an in vivo landing task (Figure 1). External KAM, ATS, and ITR loads were applied to the specimen in a randomized order. These external load magnitudes were derived from 3-dimensional kinetic data that were previously collected in vivo from a cohort of 67 healthy athletes after completing a drop vertical jump task.⁸ The loads were categorized into tertiles (33%, 67%, 100%) that correspond to the respective loading magnitude observed from our in vivo population cohort (Table 1) and are referred to as *population percentages*. Each loading condition is reported as a percentage, not absolute magnitude, in the order of KAM_ITR_ATS.

If a specimen survived the subfailure protocol, external weight was added to match 0.5 \times body weight, and load magnitudes were increased in 20% increments (maximum

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Ethical approval was not sought for the present study.

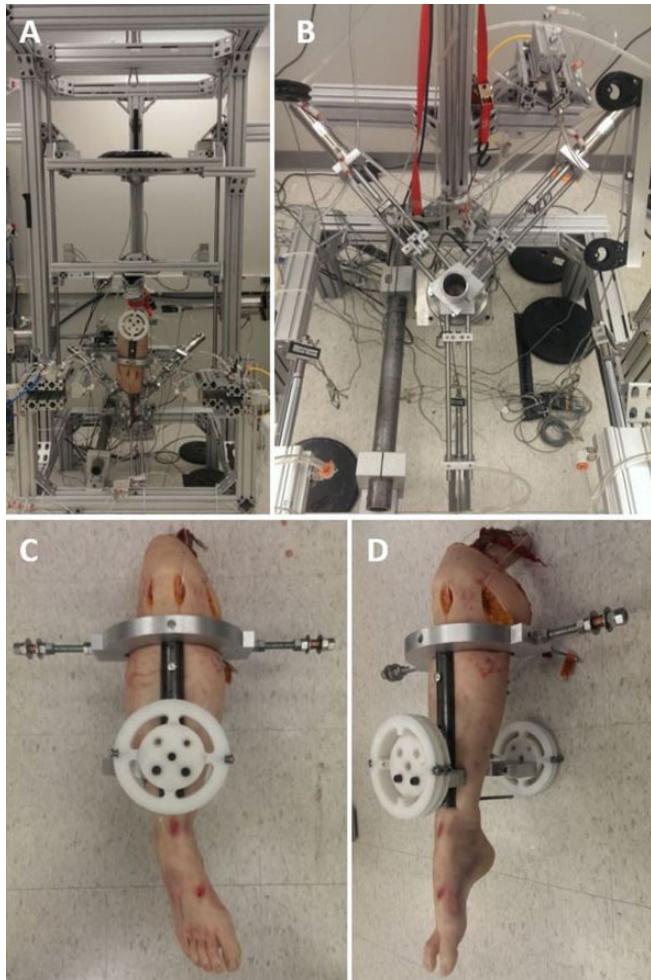


Figure 1. Mechanical impact simulator. (A) Frontal view of the entire simulator with a specimen ready for testing, with the knee locked at 25° of flexion to mimic in vivo initial contact position.^{1,2} (B) Top view of the 6-axis load cell, potting cut, and muscle actuators. (C) Frontal and (D) sagittal views of the tibial fixture mounted on a specimen. Figure reproduced from Bates et al.⁸ Used with permission from Elsevier.

load 300_300_300) between impacts until failure was achieved. Ligament strains were recorded by DVRTs implanted on the ACL and MCL.^{8,10,14,24} After testing was completed, a board-certified orthopaedic surgeon (A.J.K.) evaluated each specimen to determine the injuries sustained to the primary structures in the knee joint. Injuries occurring in the proximal or distal quarter of the ACL were considered femoral or tibial side, respectively, while the remaining 50% of the ligament was considered midsubstance. Any clinical score ≥ 2 was considered an injury as prescribed by the orthopaedic surgeon (A.J.K.).

Analyses of ligament strains were performed between dominant and nondominant sides, as reported in the specimen profile provided by the anatomic donations program. Ligament strains for no load (000_000_000), low risk (033_033_033) medium risk (067_067_067), high risk

TABLE 1
External Loads Applied to Specimen That Correspond to Population Percentages of In Vivo Recorded Kinetics From a Cohort of Athletes Completing Drop Vertical Jump Tasks⁸

Population Percentage	Knee Abduction Moment, N·m	Internal Tibial Rotation, N·m	Anterior Tibial Shear Force, N
0	1.7	1.0	47
33	13.5	9.7	64
67	26.8	18.6	80
100	57.3	53.7	196

(100_100_100), and failure trials were analyzed, for a total of 5 loading conditions. During the trial where specimen failure occurred, DVRT data are unreliable owing to artifactual strain gauge displacement that may result in invalid data during a ligament rupture. Therefore, DVRT data from the trial immediately preceding the failure trial were utilized for failure strain analysis. Given the randomized nature of the testing protocol, if 1 of the 4 specified trials (0%, 33%, 67%, 100%) was not completed on both limbs of a contralateral pair prior to failure, that risk classification was excluded from analysis for that pair.

An analysis of variance test (load \times strain) with a Bonferroni correction determined significant differences in strain between contralateral pairs, which set significance at $\alpha < .016$. Three separate analyses of variance for each ligament (ACL, MCL) were performed for percentage strain as well as change in strain from initial contact (defined as *peak strain* – *strain at initial contact*) and from baseline (*peak strain* – *strain at baseline*). Baseline was defined as the strain of the ligament prior to the application of any external loads (KAM, ITR, ATS). Initial contact was defined as the point at which the vertical ground-reaction force was ≥ 25 N. Statistical analysis was performed in JMP (v 10; SAS Institute Inc). Two separate Fisher exact tests of independence were run to investigate the relationship between limb side and failure load and between limb side and failure location ($\alpha < .05$).

RESULTS

Contralateral pairs exhibited no significant differences in peak ACL strain ($F_{4,50} = 0.3653$, $P = .83$) or peak MCL strain ($F_{4,50} = 0.2180$, $P = .93$) during a simulated landing (Table 2). Similarly, contralateral pairs exhibited no significant differences for changes in ACL strain from initial contact ($F_{4,50} = 0.6046$, $P = .66$), MCL strain from initial contact ($F_{4,50} = 0.5335$, $P = .71$), ACL strain from baseline ($F_{4,50} = 0.6673$, $P = .62$), or MCL strain from baseline ($F_{4,50} = 0.2028$, $P = .94$) (Tables 3 and 4).

Contralateral pairs tended to fail at similar externally applied loads and with similar pathologies (Table 5). Fisher exact test demonstrated that limb dominance was independent of the failure load ($P = .103$). Similarly, limb dominance was independent of failure location ($P > .999$). All failures were ACL related or a bone fracture; additionally, a total of 11 specimens experienced MCL failure. MCL outcome was

TABLE 2
Peak Strain for ACLs and MCLs^a

Loading Condition ^b : Ligament	Peak Strain, Mean ± SD, %	
	Dominant	Nondominant
000_000_000 (n = 10)		
ACL	4.72 ± 3.37	12.54 ± 9.99
MCL	1.73 ± 1.50	1.46 ± 1.30
033_033_033 (n = 11)		
ACL	6.15 ± 4.16	12.91 ± 8.65
MCL	1.95 ± 2.00	1.41 ± 1.14
067_067_067 (n = 10)		
ACL	6.34 ± 3.57	12.69 ± 8.45
MCL	2.30 ± 2.34	1.78 ± 1.70
100_100_100 (n = 7)		
ACL	10.05 ± 5.22	12.33 ± 9.39
MCL	3.24 ± 2.78	4.04 ± 3.32
Failure (n = 13)		
ACL	12.11 ± 3.54	16.37 ± 10.83
MCL	4.87 ± 3.90	3.93 ± 3.38

^aACL, anterior cruciate ligament; MCL, medial collateral ligament.

^bEach loading condition is reported as a percentage and is formatted in the order of KAM_ITR_ATS (knee abduction moment, internal tibial rotation, anterior tibial shear force).

TABLE 3
Change in Strain for ACL and MCL Ligaments
(Strain_{Peak} – Strain_{IC})^a

Loading Condition ^b : Ligament	Change in Strain, Mean ± SD, %	
	Dominant	Nondominant
000_000_000 (n = 10)		
ACL	2.13 ± 1.33	8.94 ± 8.71
MCL	1.41 ± 1.61	0.84 ± 0.70
033_033_033 (n = 11)		
ACL	3.34 ± 2.19	8.50 ± 7.54
MCL	1.52 ± 1.36	1.20 ± 1.09
067_067_067 (n = 10)		
ACL	3.01 ± 1.38	7.58 ± 6.63
MCL	1.79 ± 1.73	1.47 ± 1.54
100_100_100 (n = 7)		
ACL	3.80 ± 1.78	4.76 ± 3.15
MCL	1.15 ± 0.94	2.28 ± 1.73
Failure (n = 13)		
ACL	5.21 ± 3.47	9.29 ± 9.90
MCL	2.08 ± 2.95	2.07 ± 1.67

^aACL, anterior cruciate ligament; IC, initial contact; MCL, medial collateral ligament.

^bEach loading condition is reported as a percentage and is formatted in the order of KAM_ITR_ATS (knee abduction moment, internal tibial rotation, anterior tibial shear force).

congruent in 11 of 14 contralateral pairs (7 pairs with no MCL failure, 4 pairs with MCL failure in both specimens). The remaining 3 contralateral pairs were split, with 1 MCL failure in one side but not the contralateral.

TABLE 4
Change in Strain for ACL and MCL Ligaments
(Strain_{Peak} – Strain_{Baseline})^a

Loading Condition ^b : Ligament	Change in Strain, Mean ± SD, %	
	Dominant	Nondominant
000_000_000 (n = 10)		
ACL	2.15 ± 1.33	8.92 ± 8.71
MCL	1.41 ± 1.61	0.82 ± 0.69
033_033_033 (n = 11)		
ACL	3.55 ± 2.09	8.48 ± 7.54
MCL	1.71 ± 1.85	1.22 ± 1.08
067_067_067 (n = 10)		
ACL	3.73 ± 1.57	8.57 ± 7.59
MCL	2.12 ± 2.28	1.59 ± 1.72
100_100_100 (n = 7)		
ACL	6.39 ± 1.78	7.30 ± 3.98
MCL	2.82 ± 2.71	3.61 ± 3.00
Failure (n = 13)		
ACL	8.06 ± 3.62	11.23 ± 9.15
MCL	3.61 ± 3.16	3.41 ± 3.06

^aACL, anterior cruciate ligament; MCL, medial collateral ligament.

^bEach loading condition is reported as a percentage and is formatted in the order of KAM_ITR_ATS (knee abduction moment, internal tibial rotation, anterior tibial shear force).

DISCUSSION

The objective of the current study was to compare ligament strain responses between contralateral lower extremities during simulated in vitro landings. Limb asymmetries are known to occur during in vivo athletic movement analysis; however, it remains unknown if the asymmetries persist during in vitro simulated athletic movements. The present simulation limited joint position in the sagittal plane, applied known external loads to represent muscle forces, and applied an impulse force representative of a drop vertical jump landing. The findings indicated that contralateral limbs did not exhibit significant differences in peak ACL strain or peak MCL strain at 5 loading conditions, including injury; thus, our hypothesis that there would be a lack of differences between contralateral pairs was not rejected. These findings are consistent with a previous investigation of contralateral differences that used in vivo kinematics to drive robotic simulations of noninjurious sidestep cutting and drop vertical jump tasks.³ The robotics investigation similarly reported no differences in peak ligament strains between contralateral limbs. Together, the findings from the current study and the robotics investigation suggest a lack of differences between contralateral pairs when athletic task simulations are driven by in vivo kinematics or in vivo kinetics.

Mean peak ACL strain was greater than mean peak MCL strain for all 5 conditions studied, which agrees with trends reported in previous studies.^{7,28} Peak ACL strain (change from baseline) in the trial just prior to failure was lower in the current study for dominant and nondominant sides

TABLE 5
Failure Load and Board-Certified Surgeon Description of Specimen ACL Failure Location^a

Specimen (Sex)	Dominant Side		Nondominant Side	
	Loading Condition ^b	Location	Loading Condition ^b	Location
1 (F)	033_100_067	Femoral side	100_067_067	Femoral side
2 (F)	033_067_000	Femoral fracture	067_033_000	Midsubstance
3 (M)	120_120_120	Femoral side	160_160_160	Midsubstance
4 (M)	220_220_220	Midsubstance	100_100_100	Femoral side
5 (F)	100_100_100	Femoral side	180_180_180	Femoral side
6 (M)	160_160_160	Femoral side	200_200_200	Femoral side
7 (F)	067_000_033	Femoral side	067_067_033	Femoral side
8 (M)	120_120_120	Femoral side	100_067_067	Femoral side
9 (M)	140_140_140	Femoral side	220_220_220	Femoral side
10 (M)	120_120_120	Femoral side	200_200_200	Femoral side
11 (F)	033_100_067	Femoral side	100_100_067	Tibial side
12 (F)	Survival^c	N/A	000_033_000	Femoral side
13 (F)	100_067_100	Femoral side	033_033_033	Femoral side
14 (F)	033_100_067	Femoral side	300_300_300	Midsubstance

^aUnless noted, all specimen failures are specific to the ACL. Bolded text indicates that the specimen survived through complete subfailure protocol. ACL, anterior cruciate ligament; F, female; M, male; N/A, not applicable.

^bEach loading condition is reported as a percentage and is formatted in the order of KAM_ITR_ATS (knee abduction moment, internal tibial rotation, anterior tibial shear force).

^cThis specimen survived the entire subfailure and failure protocol (maximum load, 300_300_300).

than that reported via a similar impact simulation methodology (8.06% [dominant] and 11.23% [nondominant] vs 18.7%, respectively).²⁴

Previous impact-driven injury simulators were designed around hanging static weights mounted to pulley systems.^{22,24,28} Accordingly, each trial would take several minutes to set up while weights were attached to the specimen. This delay potentially allowed for the introduction of creep and elongation to the viscoelastic structures of the knee. In our pneumatic-driven mechanical impact simulator, an entire trial, including the application of external loads, lasts 3 seconds.⁸ This shorter duration better represents the physiologic timing of external load application during landing and may have consequently limited the ultimate strain observed as compared with previous testing. Previously reported mean peak ACL strain was within the range reported in the current study for 0% load trials (6.8% [peak strain] vs 2.15% and 8.92% [dominant and nondominant, respectively]).²²

The mean peak ACL strain (6.1%) reported from a kinematic-driven robotic simulation of a drop vertical jump landing was within the range of peak ACL strains reported in the current study for the dominant limb at the varying loading conditions (2.15%-8.06%).⁷ However, the mean peak MCL strain (0.7%) from the robotic simulation was lower than the range of peak MCL strains reported in the current study for the dominant limb (1.41%-3.61%).⁷

Note that failure pathologies were consistent between sides for most contralateral pairs. Of the 28 specimens, 15 survived to the failure protocol (ie, 100_100_100). Interestingly, 12 of these 15 specimens represented 6 contralateral pairs where both limbs survived the complete subfailure loading protocol and were subjected to the failure testing protocol. Fisher exact test of independence revealed that

limb dominance was independent of load at failure and failure location. These results agree with a previous study reporting that ACL disruption patterns were independent of applied loading conditions.²⁴ This finding indicates that failure loads and patterns are not dependent on limb dominance. ACL ruptures may incur secondary injuries to secondary knee structures and can involve bone bruise patterns.^{9,13,16,20}

A previous study reported a relationship between clinically representative tibial plateau injury locations and ACL injury mechanisms.²⁴ However, in the current study, tibial plateau injury patterns were not analyzed. Tibial plateau injuries are the least common clinical presentation of ACL injury, approximately accounting for only 4% of injuries.³³ In the present cohort, only 1 specimen (3.6%) presented with a tibial-side ACL rupture.

Note that failure of 1 specimen was not due to ACL rupture but rather a femoral fracture. This specimen exhibited an intact ACL structure in posttesting orthopaedic examinations. Furthermore, 1 specimen survived the entire subfailure and failure protocol (maximum load, 300_300_300). The non-ACL failure specimen and the survival specimen were included in the failure characterization analysis to represent the most comprehensive comparison of failure mechanisms observed. The remaining 26 specimens exhibited clinically representative ACL failures, most commonly femoral avulsions. This represents a successful rupture rate of 93% in the present cohort, and the present injury locations correlate better with the clinical presentation of in vivo ACL injuries than previous simulations of ACL injury.^{24,32,33} The current failure rate corresponds with the 87% rupture rate for the full cohort of tested specimens (including noncontralateral pairs).⁹

The current study is not without its limitations. Since a randomized loading protocol was used to test each specimen to failure, not all specimens were subjected to all loading conditions analyzed in the present study. Therefore, the number of lower extremity pairs varies for the different conditions. Ligament strain was not assessed in response to varus moment or external rotation torque in the current protocol. Moreover, femoral notch width is a potential anatomic factor that may contribute to ACL injury risk.¹⁸

Notchplasty procedures were performed on the majority of specimens to ensure that bony structures did not potentially inhibit DVRT implantation or impinge the DVRT during the testing protocol. As performed, these procedures were used to remove a small volume of bony tissue from inside the femoral notch to allow free movement of the DVRT without damaging the tibiofemoral contacting surface of the cartilage on the femoral condyle. Thus, femoral notch width could not have been assessed between contralateral pairs. In addition, DVRTs are known to have large variability with respect to measured strain values when implanted in soft tissue structures.^{5,7,9,28}

DVRT variability may artifactually limit significance in peak ligament strains. Thus, change in strain was analyzed to minimize the effect of DVRT variability as well as biological variability in the baseline ligament strain of each specimen. Change in strain from initial contact was defined as the difference between peak strain and strain at initial contact, when the vertical ground-reaction force component first equaled or exceeded 25 N. Similarly, change in strain from baseline was defined as the difference between peak strain and strain at baseline, when the specimen was in a neutral position prior to the application of any external loads. In agreement with peak strain findings, no significant differences were found between contralateral pairs for change in strain of the ACL or MCL. This further supports the notion that contralateral pairs fail to exhibit differences in strain response when external loads are applied.

Additional limitations include specimen age, lack of direct measurement of ligament loads, and cadaveric application of muscle loads. The mean \pm SD age of an ACL tear across a whole population is 29.4 ± 11.7 years.³¹ The mean age of our cadaveric specimens is slightly outside this standard deviation (41.7 ± 8.1 years), and tissue mechanical properties are known to degrade with age. However, this is a problem inherent to cadaveric investigation, and the relatively young population in the present study is more representative than much of the existing literature conducted on older specimens. Additionally, it is possible that age may have contributed to the femoral fracture, as that specimen was the oldest in this study at 51 years. Given the destructive nature of our testing protocol, we were unable to perform a selective cutting procedure to quantify forces within the ACL and MCL.²⁵

Additionally, we were unable to measure and thus execute subject-specific muscle activation patterns during our simulations. Novel techniques to resolve these limitations would improve the physiologic accuracy of impact simulations and would be useful future contributions. Regarding power, the post hoc effect size in ACL strain during failure trials was 0.42. To achieve 0.80 power with $\alpha = .05$ at this

effect size would require 77 specimens. The current investigation experimented on 28 specimens and was thus underpowered, with an achieved power of 0.57. Unfortunately, young, relatively healthy cadaveric specimens are difficult and expensive to obtain. To achieve the desired statistical power would have required an inordinate investment of time and expense.

CONCLUSION

Findings from this investigation demonstrate that limb dominance does not affect the failure threshold of the ligament or failure location, as no differences in ligament strain were observed between dominant and nondominant sides. This indicates that limb asymmetry is not solely determined by the structure of the ligament but rather by the product of multiple extrinsic factors and loading mechanisms that influence ACL response. Furthermore, this study agrees with previous literature indicating that contralateral limbs are representative of each other during in vitro testing.³ Direct comparisons of ligament behavior can be made between contralateral sides in future studies.

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