Original Research

Do Sex-Specific Differences Exist in ACL Attachment Location?

An MRI-Based 3-Dimensional Topographic Analysis

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Background: Female sex is an independent risk factor for an anterior cruciate ligament (ACL) injury, as the incidence of an ACL rupture is 4- to 6-fold higher in female athletes compared with their male counterparts. The ACL attachment location as a potential risk factor for the increased ACL rupture rate in women has never been reported in the literature.

Purpose/Hypothesis: The purpose of the present study was to investigate the 3-dimensional topographic anatomy of the ACL bundle attachment in female and male patients, with and without an ACL rupture, and identify potential sex-related differences. We hypothesized that the ACL attachment location would be significantly different between men and women, in both the intact- and ruptured-ACL states.

Study Design: Cross-sectional study; Level of evidence, 3.

Methods: Magnetic resonance images of the knee from 90 patients (55 men, 35 women) with a ruptured ACL and 90 matched controls (55 men, 35 women), who suffered a noncontact knee injury without ACL rupture, were used to create 3-dimensional models of the femur and tibia. The ACL bundles' origin and insertion were outlined on each model, and their location was measured using an anatomical coordinate system. A 2-way analysis of variance was used to compare the ACL attachment location between male and female patients, with and without an ACL rupture.

Results: No significant differences were found between female and male participants regarding ACL attachment location (femoral origin and tibial insertion). Patients with a ruptured ACL demonstrated a significantly different ACL origin compared with the participants with an intact ACL by an average difference of 8.9% more posterior ($P < .05$) and 4.0% more proximal ($P < .05$) in men and 13.0% more posterior ($P < .05$) and 5.5% more proximal ($P < .05$) to the flexion-extension axis of the knee in women.

Conclusion: The ACL attachment location should not be considered a risk factor for the increased ACL rupture rates in female compared with male athletes. However, a more posterior and proximal location of the femoral ACL origin might be a predisposing factor to an ACL rupture regardless of sex.

Keywords: anterior cruciate ligament; anteromedial bundle; posterolateral bundle; tibial insertion; sex; female

Anterior cruciate ligament (ACL) injury is a common cause of disability in young, physically active patients, and a significant risk factor for posttraumatic osteoarthritis.[15] According to current estimates, more than 250,000 ACL ruptures occur every year in the United States,[23] and more than 2 million occur worldwide.[20] Female sex is an independent risk factor for an ACL rupture, as the ACL rupture rate is 4- to 6-fold higher in female athletes compared with their male counterparts.[16,21] Since the number of women participating in sports has increased by more than 900% in high school and 500% in collegiate athletics over the past few decades,[4] ACL rupture is becoming a near-epidemic health issue for female athletes.[6] Furthermore, female patients demonstrated significantly worse outcomes and higher ACL graft rupture rates than male patients after an ACL reconstruction.[22]

Several factors have been proposed to explain the increased incidence of ACL injury in female athletes, and they are commonly classified as anatomical,[8] neuromuscular,[1] and hormonal.[14] Regarding the anatomical factors, several geometrical knee differences[12] and ACL sizes[2] (including length, volume, and cross-sectional area) have

The Orthopaedic Journal of Sports Medicine, 8(11), 2325967120964477
DOI: 10.1177/2325967120964477
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been reported between men and women. However, the ACL attachment as a potential risk factor for an increased ACL rupture between men and women has never been reported in the literature.

The purpose of the present study was to investigate the 3-dimensional (3D) topographic anatomy of the ACL bundle attachment in female and male patients, with and without an ACL rupture, and identify potential sex-related differences. We hypothesized that the ACL attachment location would be significantly different between men and women, in both the intact- and ruptured-ACL states.

METHODS

Study Design and Patient Selection

The present single-center, retrospective study was approved by a regional ethical committee. After receiving informed consent, we reviewed the medical records and magnetic resonance imaging (MRI) scans of 90 patients with a ruptured ACL (55 men, 35 women; average age, 26 years [range, 16-45 years]) and 90 controls with an intact ACL who were matched for sex, age, and body mass index. Inclusion criteria were patients younger than 45 years with no history of previous trauma or surgery on the injured knee and with MRI that were performed within 1 month of injury. Exclusion criteria were patients with poor-quality MRIs that did not allow identification of the ACL footprint or reconstruction of the 3D models. The control group included patients with no history of knee problems (pain, instability, surgery) who suffered a noncontact knee injury and received an MRI, which did not demonstrate an ACL or ALL rupture.

MRI Characteristics and Image Processing

All patients underwent MRI using a 3.0-T MR Scanner (Achieva; Philips Healthcare). Proton density–weighted turbo spin-echo (TSE) SPAIR (SPectral Attenuated Inversion Recovery) T1 sagittal plane images (slice thickness, 1 mm; voxel size, 3.29 $\times$ 0.22 $\times$ 0.22 mm) and T1 high-resolution TSE coronal plane images (slice thickness, 1 mm; voxel size, 0.12 $\times$ 2.74 $\times$ 0.12 mm) were obtained. The 2 MRI stacks were combined to yield volumetric data with a voxel size of 0.22 $\times$ 0.25 $\times$ 0.24 mm (Figure 1A) using commercial software (AMIRA 6.5, FEI SVG; Thermo Fisher Scientific). Using the same software, the 3D surface of the tibia with its articular cartilage was reconstructed according to a previously validated and published method.[3] The femoral origin and tibial insertion areas of the anteromedial (AM) and posterior-lateral (PL) bundles were digitized, and their centers were calculated (Figures 1 and 2). Finally, the surface models were imported to a self-developed MATLAB script (MathWorks) for subsequent analyses. The accuracy of this technique is expected to be less than 1 mm based on the study of Han et al,[5] who compared the open cadaveric measurements with 1.5-T 3D MRI measurements and demonstrated that the paired differences in femoral length and width between the 2 methods were 1 and 2 mm, respectively.

Anatomical Coordinate System of the Distal Femur and Proximal Tibia

The anatomical coordinate system of the distal femur (fACS) was reconstructed following the recommendations of Miranda et al.[17] Briefly, 2 spheres were best-fit to the posterior articular surface of the medial and lateral condyles, respectively, using a Gauss-Newton nonlinear least-squares algorithm (Figure 1B). The radius of the best-fit sphere on the lateral femoral condyle was defined as the lateral femoral condyle width. The line connecting the centers of the best-fit spheres formed the medial/lateral (M/L) axis of the fACS and the flexion-extension axis (FEA) of the knee. The anterior/posterior (A/P) axis of the fACS was established by creating the best-fit cylinder of the femoral shaft and then taking the cross-product of the central cylinder axis with the M/L axis. The proximal/distal (P/D) axis of the fACS was defined by the cross-product of the M/L axis with the A/P axis. The origin of the fACS was defined as the midpoint of the intersections of the M/L axis with the most medial and most lateral points of the distal femur, respectively.

The anatomical coordinate system of the proximal tibia (tACS) was reconstructed following a previously established method.[11] Briefly, 2 ellipses were best-fit to the articular surface of the medial and lateral tibial plateau, respectively, using a Gauss-Newton nonlinear least-squares algorithm (Figure 2B). The line connecting the centers of the best-fit ellipses formed the M/L axis of the

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Final revision submitted April 21, 2020; accepted June 1, 2020.

One or more of the authors has declared the following potential conflict of interest or source of funding: This project was sponsored by the National Natural Science Foundation of China (31771017, 31972924), the Science and Technology Commission of Shanghai Municipality (16441908700), the Innovation Research Plan supported by the Shanghai Municipal Education Commission (ZXWF082101), the National Key R&D Program of China (2017YFC0110700, 2019YFC0120600), and the Interdisciplinary Program of Shanghai Jiao Tong University (ZH2018QNA06, YG2017MS09). AOSSM checks author disclosures against the Open Payments Database (OPD). AOSSM has not conducted an independent investigation on the OPD and disclaims any liability or responsibility relating thereto.

Ethical approval for this study was obtained from the Ethics Committee of Northwest and Central Switzerland (project ID, 2018-01410).

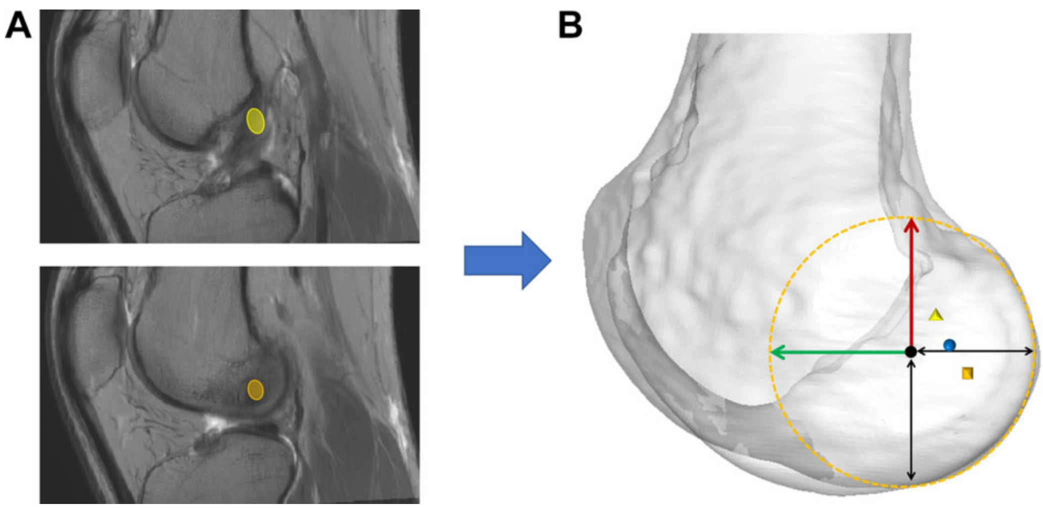

Figure 1. Left knee with an intact anterior cruciate ligament (ACL) in a male participant. (A) High-resolution volumetric magnetic resonance (MR) data were created after merging sagittal and coronal MR stacks. The femoral origins of the anteromedial (AM) and posterolateral (PL) bundles are marked with yellow and orange ellipses, respectively. (B) A 3-dimensional surface model of the distal femur with an anatomical coordinate system was constructed. The origin of the coordinate system is shown with a black dot, the red arrow indicates the proximal/distal axis, and the green arrow indicates the anterior/posterior axis. The lateral femoral condyle width, defined as the radius of the best-fit sphere in the lateral condyle, is shown with black arrows. The centroid of the AM bundle (yellow triangle), that of the PL bundle (orange square), and the femoral origin of the ACL as a single bundle (blue circle) are also marked.

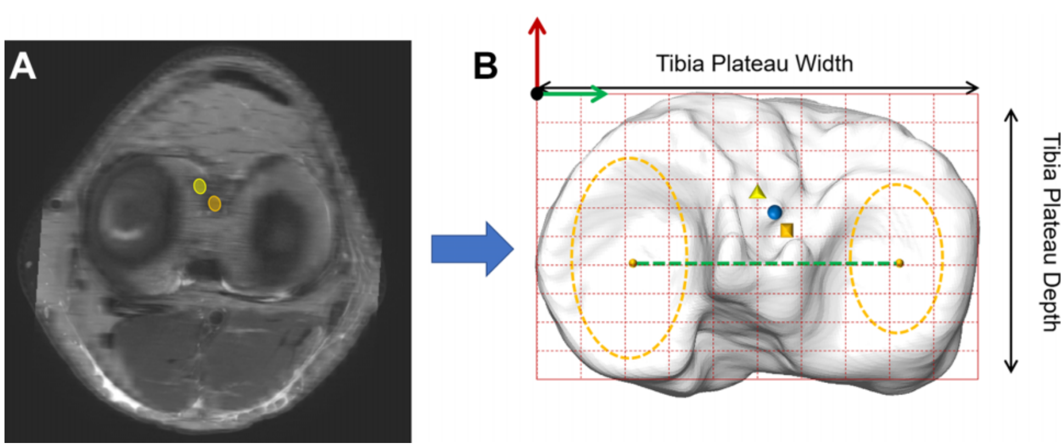

Figure 2. . Left knee with an intact anterior cruciate ligament (ACL) in a male participant. (A) High-resolution transverse magnetic resonance (MR) image. The tibial insertions of the anteromedial (AM) and posterolateral (PL) bundles are marked with yellow and orange ellipses, respectively. (B) A 3-dimensional surface model of the proximal tibia with an anatomical coordinate system was reconstructed. The origin of the coordinate system is shown with a black dot, the red arrow indicates the anterior/posterior axis, and the green arrow indicates the medial/lateral axis. A line connecting the center of the best-fit ellipses on the articular surface of the medial and lateral tibial plateau was drawn (dashed green line), and within this best-fit plane, a bounding box, defined by the depth and width of the tibial plateau, was created. The origin of the anatomical coordinate system of the proximal tibia (tACS) was then moved to the most anterior and medial point of the bounding box. The centroid of the AM bundle (yellow triangle), that of the PL bundle (orange square), and the femoral origin of the ACL as a single bundle (blue circle) are also marked.

tACS; the midpoint of the line was the tibia center. The cross-product of the M/L axis and the proximal tibial long axis formed the A/P axis of the tibia. The cross-product of the M/L and A/P axes formed the P/D axis. A plane was then best-fit to the surface of the tibial plateau. The tibia plateau depth was defined as the A/P distance between the anterior border of the tibial plateau (where the plateau edge drops down to the shaft) and the posterior border of the tibial plateau. Similarly, the tibial plateau width was defined as the M/L distance between the medial and lateral border of the tibial plateau. Within the plane, a bounding box was defined by the depth and width of the tibial plateau. The

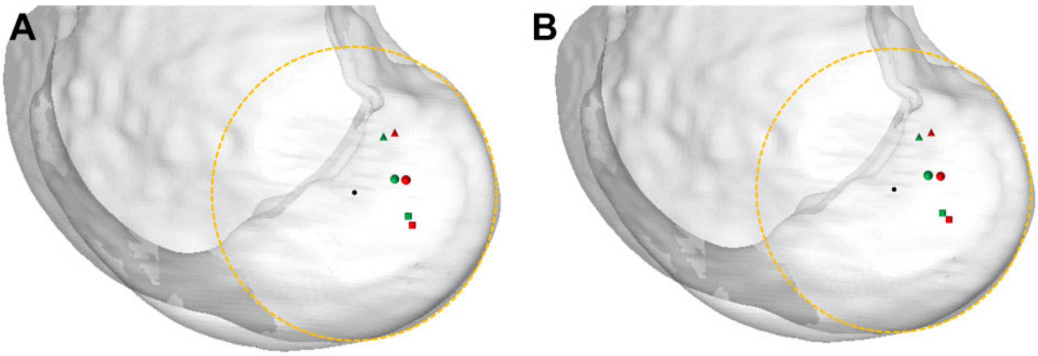

Figure 3. Left distal femur demonstrating the mean normalized femoral origins of the anterior cruciate ligament (ACL) as a single bundle (green circle), anteromedial (AM) bundle (green triangle), and posterolateral (PL) bundle (green square) in (A) men and (B) women with an intact ACL, as well as the femoral origins of the ACL as a single bundle (red circle), AM bundle (red triangle), and PL bundle (red square) in (A) men and (B) women with a ruptured ACL.

origin of the tACS was then moved to the most anterior and medial point of the bounding box (Figure 2B).

Statistical Analysis

As manual digitization was involved in the determination of the origin and attachment of the ACL bundles, the intra- and interobserver reliabilities of the measurements were evaluated by 2 independent blinded observers using single-measure intraclass correlation coefficients (ICCs) with a 2-way random-effects model for absolute agreement.

A post hoc power analysis was performed to estimate the statistical power (1-β), with medium effect size and $\alpha = .05$ using statistical power analysis software (G*Power Version 3.1; Franz Faul, Universität Kiel). Descriptive statistics included means, standard deviations, and ranges for continuous variables, and frequencies and percentages for discrete data. All parameters were tested with the Kolmogorov-Smirnov test for normality. A 2-way analysis of variance was adopted to compare the ACL attachment locations between male and female patients, with and without an ACL rupture. All the statistical analyses were performed using SPSS Version 23 software (IBM Corp).

RESULTS

Power Analysis and Intra- and Interobserver Reliability

The statistical power for detecting a 1-mm difference between the ACL attachment locations of male and female patients for 35 participants in the female group and 55 participants in the male group was 85%. The intra- and interobserver ICCs ranged from 0.85 to 0.99 (excellent) reliability for all measurements.

Femoral ACL Origin as a Single Bundle

In female and male participants with an intact ACL, the normalized A/P femoral ACL origin was located at a mean of 23.5% ± 5.0% and 26.3% ± 4.1% posterior to the FEA of the knee, respectively ($P = .3$), and the normalized P/D femoral ACL origin was located at a mean of 19.7% ± 4.2% and 18.6% ± 3.1% proximal to the FEA, respectively ($P = .61$). In female and male patients with a ruptured ACL, the normalized A/P femoral ACL origin was located at a mean of 36.5% ± 5.1% and 35.2% ± 4.1% posterior to the FEA, respectively ($P = .57$), and the normalized P/D femoral ACL origin was located at a mean of 14.2% ± 3.4% and 14.6% ± 3.1% proximal to the FEA of the knee, respectively ($P = .86$) (Figure 3). Significant differences were observed between both female and male patients with a ruptured ACL compared with female and male patients with an intact ACL (Table 1). The femoral origins of the AM and PL bundles are also summarized in Table 1.

Tibial ACL Insertion as a Single Bundle

In female and male participants with an intact ACL, the normalized A/P tibial ACL insertion was located at a mean of 37.5% ± 5.0% and 38.5% ± 4.8% of the tibial plateau depth, respectively ($P = .34$), and the normalized M/L tibial ACL insertion was located at a mean of 47.6% ± 3.6% and 46.5% ± 3.6% of the tibial plateau width, respectively ($P = .20$). In female and male patients with a ruptured ACL, the normalized A/P tibial ACL insertion was located at a mean of 40.2% ± 5.1% and 39.4% ± 6.1% of the tibial plateau depth, respectively ($P = .50$), and the normalized P/D tibial ACL insertion was located at a mean of 48.4% ± 4.7% and 47.8% ± 3.8% of the tibial plateau width, respectively ($P = .52$) (Figure 4). The tibial insertions of the AM and PL bundles are also summarized in Table 2. No significant differences were observed between patients with a ruptured versus an intact ACL.

DISCUSSION

Female athletes have demonstrated a 4- to 6-fold increased risk of an ACL injury compared with their male counterparts who participate in the same sport.[16,21] Although several risk factors have been proposed over the past years to

TABLE 1
Summary of Femoral ACL Origin in Male and Female Patients With and Without an ACL Rupture[a]

Parameter (%)	ACL Intact			ACL Ruptured		
	Men	Women	P Value	Men	Women	P Value
A/P ACL origin (SB)	26.3 ± 4.1[b]	23.5 ± 5.0[c]	.30	35.2 ± 4.1[b]	36.5 ± 5.1[c]	.57
P/D ACL origin (SB)	18.6 ± 3.1[b]	19.7 ± 4.2[c]	.61	14.6 ± 3.1[b]	14.2 ± 3.4[c]	.86
A/P AM–bundle origin	18.2 ± 5.3[b]	16.3 ± 4.2[c]	.36	24.9 ± 6.7[b]	23.8 ± 6.2[c]	.55
P/D AM–bundle origin	42.6 ± 8.1	41.9 ± 7.6	.77	45.8 ± 8.1	45.0 ± 7.4	.77
A/P PL–bundle origin	32.9 ± 8.9	30.9 ± 8.2	.40	35.2 ± 9.7	34.9 ± 8.2	.92
P/D PL–bundle origin	16.1 ± 4.4[b]	16.7 ± 5.3[c]	.77	22.9 ± 6.1[b]	21.7 ± 5.4[c]	.59

[a]Data are reported as the mean ± SD of the normalized values. ACL, anterior cruciate ligament; AM, anteromedial; A/P, anterior/posterior; P/D, proximal/distal; PL, posterolateral; SB, single bundle.
[b]Significant difference between men with an intact ACL and men with a ruptured ACL ($P < .01$).
[c]Significant difference between women with an intact ACL and women with a ruptured ACL ($P < .01$).

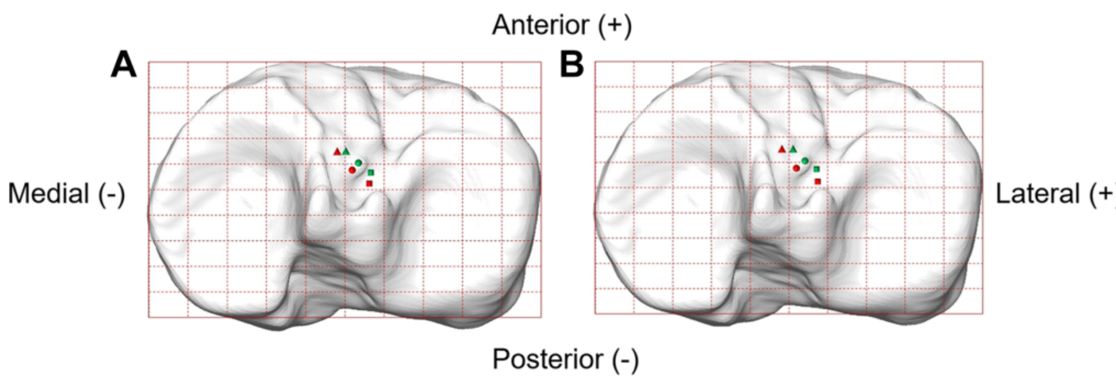

Figure 4. Left proximal tibia demonstrating the mean normalized tibial insertion of the anterior cruciate ligament (ACL) as a single bundle (green circle), anteromedial (AM) bundle (green triangle), and posterolateral (PL) bundle (green square) in (A) men and (B) women with an intact ACL, as well as the tibial insertion of the ACL as a single bundle (red circle), AM bundle (red triangle), and PL bundle (red square) in (A) men and (B) women with a ruptured ACL.

explain this discrepancy in ACL injury between sexes, the ACL attachment location as a potential risk factor for the increased incidence of ACL rupture in women has never been investigated. Therefore, the purpose of the present study was to analyze the 3D topographic anatomy of the ACL bundle attachment, in both men and women, with and without an ACL rupture, and identify potential differences. The results of the current study demonstrated that no sex-specific differences exist in the ACL attachment location. However, significant differences were found regarding the femoral ACL origin between men with a ruptured ACL and men with an intact ACL, as well as between women with a ruptured ACL and women with an intact ACL.

Several studies have reported significant sex-specific differences in the anthropometric characteristics of the ACL and the knee joint. Chandrashekar et al[2] reported that in 10 female cadavers, the ACL was significantly smaller in length, cross-sectional area, volume, and mass compared with 10 male cadavers. As a result, the ACL from women exhibited 8.3% lower strain, 14.3% lower stress, and 9.43% lower strain energy density at failure and, most importantly, a 22.49% lower modulus of elasticity. Kiapour et al,[9] using porcine animal models, reported that female knees were smaller, with steeper lateral tibial slope, thinner medial femoral cartilage, lower ACL yield load, and greater laxity (at 30° and 90°) compared with the knees of their male counterparts. Several authors have described sex-specific anthropomorphic differences in the distal femoral condyles[13] and proximal tibia.[26] In the present study, we hypothesized that because of the variable morphology of the distal femur and proximal tibial between male and female knees, sex-specific differences in the ACL attachment location would exist. However, the results of the current study demonstrated that no sex-specific differences exist in ACL attachment location and, therefore, the ACL attachment location should not be considered a risk factor for the increased ACL rupture rates in female compared with male athletes.

Multiple anatomical differences of the tibiofemoral joint between ACL-ruptured and healthy knees have been reported in the literature. Specifically, Park et al,[18] in an MRI analysis of 120 patients with an ACL injury and 106 participants without an ACL injury, demonstrated a significant difference in notch width and notch width index between groups, with a more significant difference in female patients compared to males. Pfeiffer et al[19] reported an increased posterior depth of the lateral condyle in patients

TABLE 2
Summary of the Tibial ACL Insertion in Male and Female Patients With and Without an ACL Rupture[a]

	ACL Intact			ACL Ruptured		
Parameter (%)	Men	Women	*P* Value	Men	Women	*P* Value
A/P ACL insertion (SB)	38.5 ± 4.8	37.5 ± 5.0	.34	39.4 ± 6.1	40.2 ± 5.1	.50
M/L ACL insertion (SB)	46.5 ± 3.6	47.6 ± 3.6	.20	47.8 ± 3.8	48.4 ± 4.7	.52
A/P AM–bundle insertion	34.6 ± 6.6	34.2 ± 6.7	.81	34.4 ± 4.6	34.2 ± 4.7	.85
M/L AM–bundle insertion	48.0 ± 4.9	48.3 ± 4.3	.83	50.3 ± 3.6	51.3 ± 3.3	.23
A/P PL–bundle insertion	43.0 ± 5.5	42.3 ± 5.4	.60	47.5 ± 4.2	7.6 ± 4.1	.94
M/L PL–bundle insertion	56.9 ± 4.9	57.5 ± 4.7	.57	56.5 ± 3.0	57.7 ± 3.9	.59

[a]Data are reported as the mean ± SD of the normalized values. ACL, anterior cruciate ligament; AM, anteromedial; A/P, anterior/posterior; M/L, medial/lateral; PL, posterolateral; SB, single bundle.

with a ruptured ACL compared with the control group. Hodel et al[7] reported that patients with an ruptured ACL demonstrated a smaller lateral femoral condyle index compared with those with an intact ACL. Sturnick et al[25] found that female patients with an increased lateral tibial plateau slope had an increased risk for an ACL rupture; these authors[24] also reported that men with an increased medial tibial spine volume had a decreased risk of ACL injury. In the present study, patients with a ruptured ACL demonstrated a significantly different femoral ACL origin compared with participants with an intact ACL by an average difference of 8.9% more posterior and 4.0% more proximal to the FEA in men and 13.0% more posterior and 5.5% more proximal to the FEA in women, suggesting that a more posterior and proximal location of the femoral ACL origin might be a predisposing factor to an ACL rupture.

The present study should be interpreted in light of its potential limitations, mostly inherent to the MRI identification of the ACL attachments. Although the gold standard technique is cadaveric dissection with histologic analysis, it is nearly impossible to preselect cadaveric knees with a ruptured ACL, owing to the absence of the cadaver's medical history. Because we were able to obtain high-quality 3D images after combining the sagittal and coronal plane images, the ACL bundle attachments were visible and distinct in all of the patients in the current study. Also, identification of the ACL bundle attachment in ACL-injured knees can be difficult because of tissue disruption and rapid deterioration of the ACL stump after rupture. However, in the present study, only patients with high-quality MR images obtained within 1 month of injury (to reduce the risk of not identifying the ACL footprint due to ACL stump deterioration) were included. The ACL bundle attachments were visible and distinct in these patients. Finally, all the participants in the present study were White, thus the results of the present study might not reflect the ACL bundle anatomy of the Black or Asian population, as ethnic-specific anatomical variations of the knee have been reported.[10]

CONCLUSION

The current study investigated the 3D topographic anatomy of the ACL bundle in male and female participants with and without an ACL rupture. No sex-specific differences existed in the ACL attachment location, however significant differences were found regarding the femoral ACL origin between patients with a ruptured ACL and those with an intact ACL, independent of sex. The results of the present study suggest that the ACL attachment location should not be considered a risk factor for the increased ACL rupture rates in female compared with male athletes. However, a more posterior and proximal location of the femoral ACL origin might be a predisposing factor to ACL rupture, regardless of sex.

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