Combined Anatomic Factors Predicting Risk of Anterior Cruciate Ligament Injury for Males and Females

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Abstract:

Background: Knee joint geometry has been associated with risk of suffering an anterior cruciate ligament (ACL) injury; however, few studies have utilized multivariate analysis to investigate how different aspects of knee joint geometry combine to influence ACL injury risk.
Hypotheses: Combinations of knee geometry measurements are more highly associated with the risk of suffering a noncontact ACL injury than individual measurements, and the most predictive combinations of measurements are different for males and females.
Study Design: Case-control study; Level of evidence, 3.
Methods: A total of 88 first-time, noncontact, grade III ACL-injured subjects and 88 uninjured matched-control subjects were recruited, and magnetic resonance imaging data were acquired. The geometry of the tibial plateau subchondral bone, articular cartilage, and meniscus; geometry of the tibial spines; and size of the femoral intercondylar notch and ACL were measured. Multivariate conditional logistic regression was used to develop risk models for ACL injury in females and males separately.
Results: For females, the best fitting model included width of the femoral notch at its anterior outlet and the posterior-inferior–directed slope of the lateral compartment articular cartilage surface, where a millimeter decrease in notch width and a degree increase in slope were independently associated with a 50% and 32% increase in risk of ACL injury, respectively. For males, a model that included ACL volume and the lateral compartment posterior meniscus to subchondral bone wedge angle was most highly associated with risk of ACL injury, where a 0.1 cm^3 decrease in ACL volume (approximately 8% of the mean value) and a degree decrease in meniscus wedge angle were independently associated with a 43% and 23% increase in risk, correspondingly.
Conclusion: Combinations of knee joint geometry measurements provided more information about the risk of noncontact ACL injury than individual measures, and the aspects of geometry that best explained the relationship between knee geometry and the risk of injury were different

between males and females. Consequently, a female with both a decreased femoral notch width and an increased posterior-inferior–directed lateral compartment tibial articular cartilage slope combined or a male with a decreased ACL volume and decreased lateral compartment posterior meniscus angle were most at risk for sustaining an ACL injury.

Keywords: ACL injury | risk factors | anatomy | tibial geometry

Article:

Anterior cruciate ligament (ACL) tears are often debilitating and can lead to osteoarthritis, regardless of surgical or nonsurgical treatment.[10,19] This has served as the motivation for current research that has focused on determining intrinsic and extrinsic risk factors associated with an ACL injury to identify those at an increased risk. Understanding potential risk factors could aid in the development of intervention strategies that can be targeted at these individuals.[29,30]

Different characteristics of knee geometry have been identified as risk factors for ACL injury; however, it is important to appreciate that dissimilarities in knee geometry exist between males and females. In comparison with males, females have been shown to have an increased posterior-inferior–directed slope of the tibial plateau subchondral bone [14] and a decreased medial tibial plateau depth of concavity,[14] femoral intercondylar notch size, femoral condyle size,[8,23,39] and ACL size.[1,8] These differences often persist after controlling for subject body weight or height. This is a concern because when data from males and females are combined to study risk factors associated with ACL injury, sex-based differences may obscure the effects of sex-dependent risk factors. Risk factors that have similar effects in males and females may not be detected in analyses of combined data if low values for females correspond to high values for males or vice versa. Conversely, variables that differ greatly between males and females may falsely appear to have an effect on both sexes. This suggests that assessments of knee geometry as risk factors for injury should be completed separately for men and women.

Indeed, recent research has found different relationships between geometric measurements of the knee and risk of suffering an ACL injury between males and females.[3,16,37,40] For example, the posterior-inferior–directed slopes of the subchondral bone and articular cartilage surface of the tibial plateau lateral compartment have been found to be greater in female ACL-injured subjects compared with noninjured control subjects, while no differences were found between male ACL-injured and noninjured control subjects.[3,16,35,37] One study found that the lateral femoral condyle radius of curvature, the tibial plateau radius of curvature, and the tibial plateau anteroposterior length were each smaller in male ACL-injured subjects compared with uninjured control subjects while no differences were found between injured and uninjured females.[40] These differing associations underscore the importance of considering each sex separately while investigating risk factors for ACL injury. Further, these studies did not assess the independence of these risk factors or the risks associated with combinations of these risk factors.

Two studies have used multivariate analyses to investigate how different geometric measures of the knee act in combination to influence the risk of sustaining an ACL injury.[27,31] Simon et al[27] investigated a combination of measurements including the medial and lateral tibial plateau subchondral bone slopes, femoral intercondylar notch width at its posterior inlet and anterior outlet, and the volume of the ACL. Using combined data from males and females, they found that the width of the anterior outlet of the femoral notch was the most predictive risk factor and that prediction was not substantially improved when the volume of the ACL and the slope of the lateral tibial plateau were included in the risk model. Likewise, Sonnery-Cottet et al [31] used pooled data from males and females to study the combined effects of tibial plateau medial compartment subchondral bone slope and femoral notch width index (the notch width normalized by the overall bicondylar width of the femur) and found that they were both associated with the risk of suffering an ACL injury independent of each other. Thus, the combined associations provided a better fit than either measure alone and explained more of the risk associated with injury. These multivariate studies support the importance of investigating the combined associations between geometric measures of the knee and ACL injury risk. However, the inclusion of additional anatomic measurements to conduct a comprehensive assessment and analysis of risk factors for males and females separately could provide a more complete understanding.

Study design and methodologies have differed considerably between the investigations of knee structure and its association with risk of suffering an ACL injury, and this may explain, at least in part, the conflicting reports. Much of what is known regarding the relationship between knee morphometric measures and the risk of suffering an ACL injury comes from studies that suffer from confounding factors. Oftentimes investigations fail to match healthy control subjects to ACL-injured subjects. For example, control data have come from subjects that have a symptomatic knee [14,33,37] produced by a condition other than an ACL injury, and it is unknown how this may affect the geometry of the knee. In some studies, data of ACL-injured subjects are collected from their injured knee, and inherent to this approach is the assumption that the ACL injury does not modify knee geometry. [14,33,37] Studies often lack data to support this assumption.

The objective of this investigation was to build on our prior studies that examined the univariate effects of a wide selection of measurements of anatomic structures of knee geometry on the risk of suffering a noncontact ACL injury.[2,34,35,42] We report the results of analyses that combined these measurements to develop comprehensive multivariate risk models for predicting noncontact ACL injury. Separate models were developed for females and males because they differed significantly in some measurements and because our prior univariate analyses indicated that risk factors for ACL injury were different between females and males.[2,34,35,42] The hypotheses of this study were that there are combinations of knee geometry measurements that have significantly greater associations with the risk of suffering a noncontact ACL injury than individual measurements and that the most predictive risk models are different for males and females.

METHODS

This investigation was based on additional investigation of magnetic resonance imaging (MRI) data collected as a subset of an institutional review board–approved prospective cohort study with a nested matched case-control analysis,[13,28] where all subjects provided written consent before participation. Grade III, noncontact ACL injuries (occurring without direct force to the knee) were identified as they occurred in local high school and college-level athletics. The control subjects were selected from the same sports team that the case subjects participated on and were the same sex and were exposed to the same type of activity. ACL injuries were diagnosed by an orthopaedic surgeon and confirmed via MRI and arthroscopic visualization at the time of surgery. Imaging was completed on both knees of 88 ACL-injured (27 male, 61 female) and 88 control (27 male, 61 female) subjects using a Phillips Acheiva 3T MRI system (Phillips Medical Systems) while they were positioned supine with their knees in extension inside an 8-channel SENSE knee coil. Sagittal-plane 3-dimensional T1-weighted fast-field echo (FFE) scans (resolution: 0.3 × 0.3 mm, slice thickness 1.2 mm) and sagittal-plane 3-dimensional proton density weighted scans (resolution: 0.4 × 0.4 mm, slice thickness: 0.7 mm) were obtained. The same MRI system, technique to position and support the subject's legs, and approach to locate the planes in which the MRI data were acquired was used for all subjects. For ACL-injured subjects, MRIs were obtained after injury but before surgery to avoid image artifact that may have been produced by the presence of ACL graft fixation hardware. The demographic information of study participants, including time between the injury date and MRI scan, was presented in our previous publication.[2]

Our prior studies that focused on the relationship between geometric characteristics of knee and the risk of suffering a noncontact ACL injury in this cohort were based on investigation of 32 different MRI measurements.[2,34,35,42] All measurements were made from the MRI data by a single examiner, a basic scientist, who performed manual segmentation with a digitizing tablet (Wacom Technology Corp) using readily available DICOM viewer software (Pixmeo, version 5.5.1, www.osirix-viewer.com). The methods used to make the measurements described in this work were 3-dimensional and obtained in a standardized and reproducible manner, using bony/soft tissue landmarks and boundaries to outline and segment the variables of interest. Reliability was assessed with the use of variance component analysis to establish variability between subjects, between examiners, and within examiners and calculate intraclass correlation coefficients (ICCs) for both inter- and intraobserver reliability. Our prior work established that all measurements displayed good intraobserver reliability and slightly lower interobserver reliability, which was acceptable due to each measurement being made by a single examiner.[2,34,35,42] Three-dimensional measurements of the knee were made in reference to a 3-dimensional coordinate system that was located in bone to account for variable knee positioning in the MRI scanner system, and we established that this could be done in a reproducible manner.[3] Digitized data were exported and postprocessed using custom written MATLAB programs. Details of how these measurements were made and the reliability associated with each measurement have been presented for geometries of the femoral intercondylar notch,[42] ACL,[42] tibial spines,[34] the tibial plateau subchondral bone,2 and the articular cartilage and meniscus surfaces.[35]

Statistical Methods

ACL injury can produce changes in the geometry of the tibiofemoral joint, including changes to the subchondral bone, cartilage surface, and menisci.[3,38] The measurements of the femoral notch geometry were based on the location of the ACL, and measurements of the ACL size relied on the ACL being intact. Consequently, the uninjured knee of the ACL-injured subject and corresponding left or right knee of the control subjects were used to assess associations between knee geometry and ACL injury risk. The use of the uninjured knee of ACL-injured subjects as a surrogate for the geometry of the knee before injury was validated by prior work that demonstrated side-to-side symmetry of all measurements between the uninjured knees of control subjects who had no history of knee injury.[2,34,35,42]

Stepwise multivariate conditional logistic regression was used to identify the combinations of geometric measurements of the knee that were most highly associated with the risk of suffering an ACL injury for males and females as separate groups as well as combined. Our prior reports focused on analyses performed within sets of related measures to determine their independent associations with ACL injury risk.[2,34,35,42] Univariate analyses were conducted to identify which variables were strongly related to risk, the results of which are provided in Appendix Tables A1, A2, and A3 (available online at http://ajsm.sagepub.com/supplemental). To avoid including correlated measures that influenced that same risk of injury, multivariate analyses were conducted among similar anatomic measures to identify the variables that were independently associated with ACL injury risk. Those variables found to display the greatest independent association with risk of ACL injury in prior analyses were considered for inclusion in the multivariate models. These variables included measurements of femoral intercondylar notch width at the anterior “outlet,” the femoral intercondylar notch anteromedial ridge thickness, the volume of the ACL, tibial plateau lateral compartment subchondral bone slope, lateral compartment middle articular cartilage slope, lateral compartment meniscus-cartilage height, lateral compartment meniscus-bone angle, and the medial tibial spine volume. The summary statistics of the geometric measurements, which originated from their prior separate analyses, are provided in the Appendix as Table A4 (available online).[2,34,35,42] The variables in each set that had significant independent associations were then analyzed together using a forward stepwise selection procedure in which the variable with the most highly significant univariate association with ACL injury risk was entered into the model first. Variables were entered or removed from the model based on the significance of their associations with risk after adjustment for the variables already in the model. Only variables with $P < .05$ were retained in the final model, which provided the best fit to the data using the fewest variables. All analyses were performed using SAS version 9.2 statistical software (SAS Institute Inc).

Subject body weight (measured with a calibrated scale) and rotational position of the superior-inferior–directed axes of the tibia relative to the femur during data acquisition with MRI (established by measuring the angle of rotation between the medial-lateral directed axes of the tibial coordinate system relative to the femoral coordinate system) have been found to be significant covariates in earlier univariate analyses assessing the relationship between knee structure and the risk of suffering an ACL injury.[2] To investigate and control for the effects of these potential confounders, they were added to the final models obtained from the stepwise procedure described previously.

RESULTS

For females, the multivariate model that included the femoral notch width at the anterior outlet (NW_O; OR = 0.667 per mm increase, or inversely OR = 1.5 per mm decrease; $P = .004$) in combination with the lateral compartment middle cartilage slope ($L_{at}T_{ib}$MCS; OR = 1.324 per degree increase; $P = .0004$) was most highly associated with risk of ACL injury (Table 1 and

Figure 1). Thus, each millimeter decrease in the width of the femoral intercondylar notch at its anterior outlet and each degree increase in posterior-inferior–directed slope of the middle region of the articular cartilage surface in the lateral compartment of the tibia were associated with 50% and 32% increases in the risk of ACL injury, respectively.

TABLE 1
Best-Fit Multivariate Risk Model for Females[a]

Variable (Unit Change)	Odds Ratio (95% CI)	*P* Value
$L_{at}T_{ib}MCS$ (1°)	1.324 (1.135-1.546)	.0004
NW_O (1 mm)	0.667 (0.505-0.881)	.004

[a]Includes measures of lateral compartment middle region articular cartilage slope ($L_{at}T_{ib}MCS$) and the femoral intercondylar notch width at the anterior outlet of the anterior cruciate ligament (NW_O). Multivariate conditional logistic regression was performed using the uninjured knee of ACL-injured subjects and the corresponding knee of control subjects. Odds ratios and associated 95% CIs describe the effects of a unit increase from the mean for each variable on risk of suffering an ACL injury.

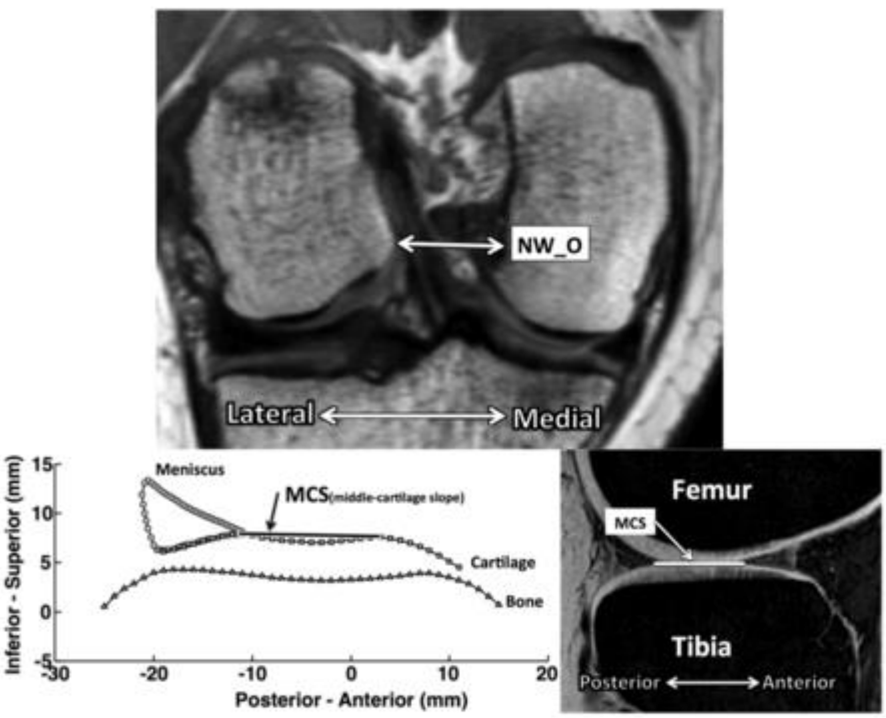

Figure 1. Measures most predictive of risk in females: the femoral intercondylar notch width at the anterior outlet of the anterior cruciate ligament (NW_O, top) and tibial plateau (T_{ib}) lateral compartment (L_{at}) middle region articular cartilage slope (MCS) displayed relative to postprocessed articular cartilage surface data (lower left) and in relation to MRI sagittal-plane image (lower right). Decreased notch width at its anterior outlet and increased lateral compartment middle cartilage slope were best associated with increased ACL injury risk in females.

For males, the multivariate model combining variables most predictive of injury included the volume of the ACL (ACL_VOL; OR = 0.697 per 0.1 cm^3 increase, or inversely OR = 1.43 per 0.1 cm^3 decrease; P = .013) and the lateral compartment meniscus-bone angle ($L_{at}T_{ib}MBA$; OR = 0.811 per degree increase, or inversely OR = 1.23 per degree decrease; *P* = .038) (Table 2 and Figure 2). Every 0.1 cm^3 decrease in ACL volume and each degree decrease in the wedge angle of the posterior aspect of the lateral meniscus was associated with 43% and 23% increases in risk of suffering an ACL injury, correspondingly.

TABLE 2
Best-Fit Multivariate Risk Model for Males[a]

Variable (Unit Change)	Odds Ratio (95% CI)	*P* Value
ACL_Vol (100 mm^3)	0.697 (0.523-0.928)	.013
$L_{at}T_{ib}MBA$ (1°)	0.811 (0.666-0.988)	.038

[a]Includes measures of anterior cruciate ligament volume (ACL_Vol) and the lateral meniscus wedge angle measured relative to bone ($L_{at}T_{ib}MBA$). Multivariate conditional logistic regression was performed using the uninjured knee of ACL-injured subjects and the corresponding knee of control subjects. Odds ratios and associated 95% CIs describe the effects of a unit increase from the mean for each variable on risk of suffering an ACL injury.

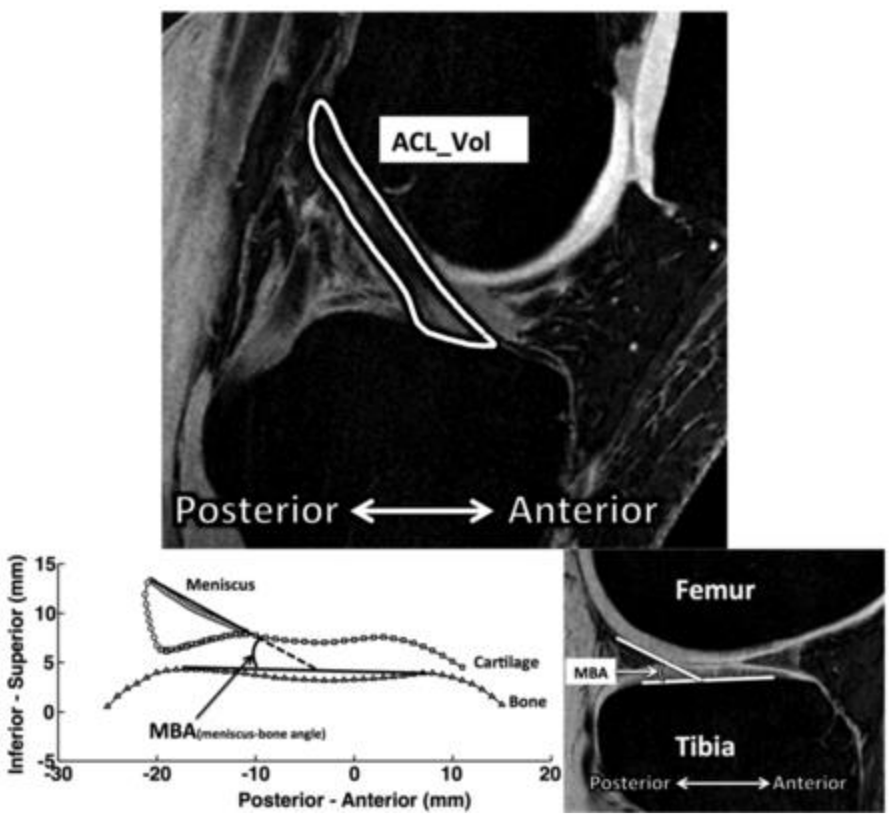

Figure 2. Measures most predictive of risk in males: the anterior cruciate ligament volume (ACL_Vol, top) and tibial plateau (T_{ib}) lateral compartment (L_{at}) meniscus-bone angle (MBA) displayed relative to postprocessed articular cartilage surface data (lower left) and in relation to MRI sagittal-plane image (lower right). Decreased anterior cruciate ligament volume and

decreased lateral compartment meniscus-bone angle were best associated with increased ACL injury risk in males.

When males and females were analyzed as a combined group, the lateral compartment middle cartilage slope, $L_{at}T_{ibia}MCS$ (OR = 1.216 per degree increase; *P* = .001), combined with the lateral compartment meniscus-cartilage height, $L_{at}T_{ibia}MCH$ (OR = 0.44 per mm increase; *P* = .019), and the notch width at the anterior outlet, NW_O (OR = 0.688 per mm increase; *P* = .0004), were jointly associated with risk of suffering an ACL injury (Table 3). Similar relationships were found when this model was applied to the females as a separate group, but the odds ratio for $L_{at}T_{ibia}MCH$ was not statistically significant (OR = 0.37; *P* = .057). When the combined sex model was applied to the males as a group, only the notch width at the anterior outlet, NW_O, displayed a similar association with risk of ACL injury (OR = 0.727 per mm increase; *P* = .036).

TABLE 3
Best-Fit Multivariate Risk Model for Combined Male and Female Data[a]

	Males and Females Combined		Males		Females	
Variable (Unit Change)	Odds Ratio (95% CI)	*P* Value	Odds Ratio (95% CI)	*P* Value	Odds Ratio (95% CI)	*P* Value
$L_{at}MCS$ (per degree)	1.216 (1.088-1.359)	**.001**	1.023 (0.842-1.244)	.816	1.325 (1.123-1.564)	**.001**
$L_{at}MCH$ (per mm)	0.44 (0.221-0.874)	**.019**	0.493 (0.181-1.337)	.165	0.374 (0.136-1.03)	.057
NW_O (per mm)	0.688 (0.559-0.847)	**.0004**	0.727 (0.539-0.979)	**.036**	0.649 (0.483-0.872)	**.004**

[a]Multivariate conditional regression was performed using the uninjured knee of anterior cruciate ligament–injured subjects and the corresponding knee of control subjects. Also presented are the results when the model based on combined data were applied to males and females separately. Odds ratios and associated 95% CIs describe the effects of each variable on risk of an ACL injury. Significant associations are in boldface. $L_{at}MCH$, lateral compartment meniscus-cartilage height; $L_{at}MCS$, lateral compartment middle region articular cartilage slope; NW_O, femoral intercondylar notch width at the anterior outlet.

The variables in the risk models for males and females as separate and combined groups retained the same relationships with ACL injury risk after inclusion of subject body weight and the rotational position of the superior-inferior–directed axis of the tibia relative to the femur during MRI data acquisition as covariates. This finding indicated that each measurement was independently associated with the risk of sustaining an ACL injury and not influenced by variations in body weight or rotational position of the tibia relative to the femur during acquisition of MRI data. Additionally, these covariates were not found to be significantly associated with the risk of suffering an ACL injury when included in the multivariate models.

DISCUSSION

The findings from this comprehensive multivariate analyses lead us to confirm our hypothesis that combinations of knee geometry measurements are more highly associated with risk of suffering a noncontact ACL injury than individual measurements. These findings also demonstrate that the MRI-based risk models for males and females involve different anatomic structures, supporting the hypothesis that the anatomic features of the knee that are most associated with risk of sustaining an ACL injury differ between males and females. For females, a smaller femoral intercondylar notch width combined with an increased posterior-inferior–directed slope of the tibial lateral compartment articular cartilage surface conferred the greatest risk (OR = 1.5 and 1.32 per mm decrease and degree increase, respectively). Thus, a female athlete who differs by both these amounts from the mean values for her peers on both variables has double the risk of sustaining an ACL injury (1.50 × 1.32 = 1.98). For males, the combined effects of smaller ACL volume and smaller wedge angle of the lateral posterior meniscal horn measured relative to bone were most highly associated with risk of suffering ACL injury (OR = 1.43 and 1.23 per 0.1 cm^3 and 1.0° decrease, respectively). Consequently, a male athlete who has these decreased amounts of both ACL volume and wedge angle of the posterior meniscal horn relative to the mean values of his peers has about 1.76 times the risk of suffering an ACL injury (OR = 1.43 × 1.23 = 1.76).

The different anatomic structures associated with ACL injury risk suggest that the mechanisms for an ACL injury may be different between the sexes. This indicates that different screening methods for identifying those at increased risk for suffering an ACL injury may need to be developed for males and females. Recent work has found current screening protocols are not cost-effective at identifying individuals at high risk for ACL injury so intervention programs can be targeted at them to reduce the incidence of ACL injury.[36] Development of sex-specific screening methods could increase the sensitivity and specificity of such tools and allow for a more efficient expenditure of resources on injury prevention strategies. Currently, the cost and time involved with acquisition of MRI of the knee and measurement of geometric characteristics associated with increased risk of ACL injury make it impractical to use as a large-scale screening tool. However, it is anticipated that the expenses associated with MRI acquisition will decrease over time and new imaging techniques will be developed that are cost-effective to use as screening tools. Correspondingly, automated methods for quantifying these measurements should be developed for application in clinical settings. Alternatively, it may be that certain aspects of knee geometry that are associated with increased risk of ACL injury are also related to other measurements that can easily be made in a clinical setting, such as laxity and stiffness of the knee joint. This should be the focus of future research. Although knee anatomy is a nonmodifiable risk factor, those at increased risk could benefit from intervention programs that focus on modifiable factors, such as landing biomechanics, neuromuscular training, balance training, and improvements in playing surfaces and footwear.

The differing risk models also provide new insight into how the mechanism of ACL injury may differ between the sexes. Females have been observed to suffer noncontact ACL injuries with their knee flexed between approximately 15° and 27°.[17] In this range of knee flexion, the center of the tibiofemoral contact region in the lateral compartment is located in the center of the cartilage surface in the mediolateral direction,[18] which is also the location of the cartilage slope measurement. Additionally, although mechanisms of axial tibial compression combined with knee valgus loading and internal tibial rotation have been reported to produce high tensile strains and ACL rupture,[21,24] ACL impingement against the femoral intercondylar notch has been reported to occur during common noncontact injury mechanisms such as those that involve external rotation and abduction of the tibia relative to the femur with the knee in a flexed position (30° of flexion and beyond).[12,25] The stronger relationship between the femoral intercondylar notch size and the risk of suffering an ACL injury in females may be further indicative of this specific mechanism. Consistent with previous reports,[1,6] female participants in the current study displayed a weaker correlation, compared with male participants, between the size of the ACL and the size of the intercondylar notch in which it resides. Such findings, along with inherently greater passive knee internal-external rotation of the tibia relative to the femur in females[25] may further support the potential for ACL impingement as an injury mechanism. As previously theorized by Simon et al,[27] an increased posterior-inferior–directed slope of the middle articular region of the lateral tibial plateau could correlate with an increased internal tibial torque about its long axis and a decreased femoral intercondylar notch width could act to increase the magnitude of impingement between the notch and ACL. It may be that ACL injuries in females more commonly occur as a result of multidirectional loading of the ligament.

Noncontact ACL injuries in male subjects tend to occur with the knee closer to full extension, from 9° to 19° of flexion.[17] The menisci have been shown to transmit loads when the knee is near full extension, particularly when transitioning from nonweightbearing to weightbearing conditions.[41] A common mechanism for ACL injury involves transition of the knee from unloaded to loaded conditions, which occurs when landing from a jump or during plant and cut maneuvers.[4,26] With the ACL-injured knee closer to full extension in males combined with the observation that both compartments of the tibia experience contact stress, it is fitting that measurements of the lateral compartment meniscus are associated with the risk of suffering an ACL injury in males. Although few studies have investigated the relationship between geometry of the meniscus and the biomechanical function of the knee and ACL, when the knee is subjected to anterior-posterior loading, both tibial displacement and ACL strain reportedly increase after meniscectomy.[32] In addition, the primary function of the meniscus is to distribute and transmit the intersegmental compressive loads between the tibia and femur.[22] When transmitting a compression force from the femur to the tibia, the geometry of the posterior aspect of the menisci could influence the magnitude of the anterior-directed shear force that acts on the tibia. A decrease in the lateral compartment posterior meniscus wedge angle may be associated with a decrease in the resistance to anterior-directed shear force that acts on the tibia and a corresponding increase in anterior translation of the tibia relative to the femur. In addition, peak ACL force and strain values occur with the knee closer to extension.[11,20] Since the ACL volume is associated with its structural properties,[15] it was expected to be more highly associated with the risk of suffering an ACL injury in males. It may be that injury to the ACL in males occurs more commonly as a result of unidirectional tensile loading to failure.

Two studies have investigated the combined effect that multiple structures of the knee have on the risk of suffering an ACL injury. Simon et al[27] identified the width of the femoral intercondylar notch at its anterior outlet as most predictive of ACL injury risk and the volume of the ACL and the slope of the lateral tibial plateau subchondral bone did not improve prediction of injury when added to their multivariate discriminant analysis. Our current study confirms a portion of these findings. While the femoral notch width is a similar finding for female subjects, the posterior-directed slope of lateral compartment articular cartilage surface, rather than the subchondral bone surface, combined to better predict the risk of noncontact ACL injury in female subjects. Sonnery-Cottet et al[31] investigated the size of the femoral notch and the posterior-inferior–directed slope of the tibial plateau subchondral bone in an analysis of combined data from male and female subjects using multivariate logistic regression. The control data were obtained from subjects with a symptomatic knee produced by a condition other than an ACL injury, and it is unknown how this may have affected the geometry of the knee. Our current study supports these findings in part and only for females, with the tibial plateau slope of the lateral compartment articular cartilage surface, rather than the slope of the medial compartment underlying subchondral bone, and the notch width providing the most information on the risk of ACL injury. The use of sex-specific versus combined male and female analysis, along with investigation of the articular surface geometry in addition to that of the subchondral bone, could explain the contrasting outcomes between the studies. Aside from the addition of the lateral compartment posterior meniscus height, our combined male and female model was similar to the separate model for females, which included the femoral notch width at the anterior outlet and lateral compartment articular cartilage slope. This could be attributed to females making up two-thirds of our combined population. The combined model provided a poor fit to the data from just the males, further demonstrating that separate models for predicting ACL injury risk are needed for males and females.

The advance made by our study was its comprehensive analysis of the structures that make up the overall geometry of the knee. Our previous reports focused on the investigation of anatomic risk factors for ACL injury to replicate or build on what was known in the literature,[2,42] introduced new measurements of knee geometry, and established how they were related to the risk of suffering noncontact ACL injury.[3,34,35] Univariate and multivariate analyses were conducted within related measurements of knee joint geometry to strengthen the understanding of the risk association with each measurement. The current report investigated the group of measurements of knee geometry that were each strongly associated with risk and included them in multivariate analyses to establish the specific combination of measurements that had the strongest association with risk for males and females. The results indicated that the relationships between combined measurements of knee geometry and risk of sustaining an ACL injury were stronger than when each variable was analyzed univariately. This resulted in a comprehensive understanding of how each risk factor is related to noncontact ACL injury.

Additional advances of the current study include its rigorous study design and standardized methodology that included 3-dimensional coordinate systems that were located in the tibia and femur, which provided reliable and reproducible outcome measurements. From the respective reliability studies for the 4 measurements in the male and female multivariate models, conducted before data collection, the intraobserver ICCs, and estimated measurement trial error, respectively, include the following: middle cartilage slope, 0.96 and 0.53°; notch outlet width, 0.85 and 0.96 mm; ACL volume, 0.92 and 0.70 mm3; and lateral compartment meniscus-bone angle, 0.75 and 3.28°. Another important advance was the central focus on subjects who suffered their first noncontact ACL injury and the use of control subjects with normal knees who were selected from the same team in an effort to match on level of play, subject sex, and environmental risk factors such as the playing surface and exposure to sport. With the design used in this study, the odds ratios calculated to describe the association between geometric measurement of knee morphologic characteristics and the risk of suffering an ACL injury are mathematically comparable with the relative risk estimates that would be obtained using a complete longitudinal study design, where each individual in a cohort is followed over time and the data are used in a Cox regression analysis to model time to injury.[5]

This study had potential limitations. Although subjects were recruited longitudinally, MRI data were acquired after the ACL injuries occurred. If a completely prospective approach were used in which MRI data were obtained before ACL injury, it would have been necessary to perform MRIs on over 8000 subjects to obtain data on the same number of ACL-injured subjects who were the focus of the current study.[28] This is simply not feasible considering the cost and time associated with MRI acquisition and analysis of such a large sample. To avoid the potential for the ACL injury to modify knee geometry, the measurements obtained from the contralateral uninjured limb were used as a surrogate measure for the injured knee before the injury. This approach was validated by confirming that each of the geometric measures displayed symmetry between the uninjured knees of control subjects.[2,34,35,42] Although the potential exists for cartilage and meniscus morphologic characteristics of ACL-injured subjects and control subjects to be influenced by different levels of activity before MRI acquisition,[22] this was not considered to be substantial. Studies have reported minimal deformations of articular cartilage under different types of loading conditions,[7,9] including only a 7% decrease in overall cartilage volume after repeated high-impact loading[9] and a 2.7% decrease in cartilage thickness after 45 minutes of static loading.[7] Additionally, limb alignment in the MRI scanner was standardized using traditional placement of subjects in the scanner in the supine position with their legs extended. Before data acquisition, the sagittal planes of the MRI were oriented to evenly bisect the femoral condyles, which did not account for the orientation of the tibia relative to the femur in the scanner. The previously described tibial coordinate system[3] was used as a standardized reference for measurements of the tibial plateau subchondral bone and articular cartilage surface as well as the meniscus. The rotational position of the long axis of the tibia relative to the long axis of the femur during MRI acquisition was considered as a covariate in the comprehensive multivariate models. Although both knees of ACL-injured subjects had a bias for the tibia to display greater internal rotation relative the femur, when compared with the control subjects, adjustment for rotational orientation did not have a significant effect on the outcome of the analysis.

Another limitation is that while stepwise regression procedures identify models that maximize the fit to the data from which they are derived, they can overestimate associations with risk and may not perform as well with other datasets. We tried to mitigate some of the weaknesses of stepwise regression by performing initial multivariate analyses on small subsets of related variables and only selected those that were independently associated with ACL injury risk for inclusion in the stepwise analysis. As with all statistical modeling, application to an independent dataset is needed to assess the validity of our results.

Lastly, the difference in sample size between males and females may have influenced the different associations between measurement of knee geometry and risk of ACL injury observed for males and females. Some measurements associated with ACL injury risk in females, such as the posterior-inferior–directed slope of the middle region of the lateral tibial plateau articular cartilage, displayed no relationship with the risk of suffering an ACL injury in males. With odds ratios and confidence intervals close to and evenly spanning 1, it is unlikely that significant associations with risk would be found for males even if a larger sample size were used. In contrast, measurements such as the height of the lateral compartment posterior meniscus did display potential for a relationship with risk. A larger sample size in the male subgroup may therefore have revealed additional associations between knee structure and risk of injury. The associations identified with our smaller sample size of males that were not found in the females strengthen the conclusion that they are more highly related to ACL injury risk in males.

In conclusion, the comprehensive analysis of anatomic measurements of knee geometry revealed different combinations of 2 separate measurements were associated with the risk of suffering a noncontact ACL injury for males and females. In males, the size of the ACL and geometry of the posterior horn of the lateral meniscus combined to best predict risk of ACL injury. In females, the size of the femoral notch and slope of the articular cartilage surface of the lateral compartment combined to best predict risk.

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FOOTNOTES

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REFERENCES

1. Anderson AF, Dome DC, Gautam S, Awh MH, Rennirt GW. Correlation of anthropometric measurements, strength, anterior cruciate ligament size, and intercondylar notch characteristics to sex differences in anterior cruciate ligament tear rates. Am J Sports Med. 2001;29(1):58-66.

2. Beynnon BD, Hall JS, Sturnick DR, et al. Increased slope of the lateral tibial plateau subchondral bone is associated with greater risk of noncontact ACL injury in females but not in males: a prospective cohort study with a nested, matched case-control analysis. Am J Sports Med. 2014;42(5):1039-1048.

3. Beynnon BD, Vacek PM, Sturnick DR, et al. Geometric profile of the tibial plateau cartilage surface is associated with the risk of non-contact anterior cruciate ligament injury. J Orthop Res. 2014;32(1):61-68.

4. Boden BP, Dean GS, Feagin JA Jr, Garrett WE Jr. Mechanisms of anterior cruciate ligament injury. Orthopedics. 2000;23(6):573-578.

5. Breslow NE, Lubin JH, Marek P, Langholz B. Multiplicative models and cohort analysis. J Am Statistical Assoc. 1983;78(381):1-12.

6. Chandrashekar N, Slauterbeck J, Hashemi J. Sex-based differences in the anthropometric characteristics of the anterior cruciate ligament and its relation to intercondylar notch geometry: a cadaveric study. Am J Sports Med. 2005;33(10):1492-1498.

7. Cotofana S, Eckstein F, Wirth W, et al. In vivo measures of cartilage deformation: patterns in healthy and osteoarthritic female knees using 3T MR imaging. Eur Radiol. 2011;21(6):1127-1135.

8. Dienst M, Schneider G, Altmeyer K, et al. Correlation of intercondylar notch cross sections to the ACL size: a high resolution MR tomographic in vivo analysis. Arch Orthop Trauma Surg. 2007;127(4):253-260.

9. Eckstein F, Lemberger B, Gratzke C, et al. In vivo cartilage deformation after different types of activity and its dependence on physical training status. Ann Rheum Dis. 2005;64(2):291-295.

10. Frobell RB, Roos HP, Roos EM, Roemer FW, Ranstam J, Lohmander LS. Treatment for acute anterior cruciate ligament tear: five year outcome of randomised trial. BMJ. 2013;346:232.

11. Fujiya H, Kousa P, Fleming BC, Churchill DL, Beynnon BD. Effect of muscle loads and torque applied to the tibia on the strain behavior of the anterior cruciate ligament: an in vitro investigation. Clin Biomech (Bristol, Avon). 2011;26(10):1005-1011.

12. Fung DT, Zhang LQ. Modeling of ACL impingement against the intercondylar notch. Clin Biomech (Bristol, Avon). 2003;18(10):933-941.

13. Goetschius J, Smith HC, Vacek PM, et al. Application of a clinic-based algorithm as a tool to identify female athletes at risk for anterior cruciate ligament injury: a prospective cohort study with a nested, matched case-control analysis. Am J Sports Med. 2012;40(9):1978-1984.

14. Hashemi J, Chandrashekar N, Mansouri H, et al. Shallow medial tibial plateau and steep medial and lateral tibial slopes: new risk factors for anterior cruciate ligament injuries. Am J Sports Med. 2010;38(1):54-62.

15. Hashemi J, Mansouri H, Chandrashekar N, Slauterbeck JR, Hardy DM, Beynnon BD. Age, sex, body anthropometry, and ACL size predict the structural properties of the human anterior cruciate ligament. J Orthop Res. 2011;29(7):993-1001.

16. Hohmann E, Bryant A, Reaburn P, Tetsworth K. Is there a correlation between posterior tibial slope and non-contact anterior cruciate ligament injuries? Knee Surg Sports Traumatol Arthrosc. 2011;19(suppl 1):S109-S114.

17. Krosshaug T, Nakamae A, Boden BP, et al. Mechanisms of anterior cruciate ligament injury in basketball: video analysis of 39 cases. Am J Sports Med. 2007;35(3):359-367.

18. Li G, DeFrate LE, Park SE, Gill TJ, Rubash HE. In vivo articular cartilage contact kinematics of the knee: an investigation using dual-orthogonal fluoroscopy and magnetic resonance image-based computer models. Am J Sports Med. 2005;33(1):102-107.

19. Lohmander LS, Englund PM, Dahl LL, Roos EM. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. Am J Sports Med. 2007;35(10):1756-1769.

20. Markolf KL, O'Neill G, Jackson SR, McAllister DR. Effects of applied quadriceps and hamstrings muscle loads on forces in the anterior and posterior cruciate ligaments. Am J Sports Med. 2004;32(5):1144-1149.

21. Meyer EG, Haut RC. Anterior cruciate ligament injury induced by internal tibial torsion or tibiofemoral compression. J Biomech. 2008;41(16):3377-3383.

22. Mow VC, Gu WY, Chen FH. Structure and function of articular cartilage and meniscus. In: Mow VC, Huiskes R , eds. Basic Orthopaedic Biomechanics and Mechano-Biology. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:181-258.

23. Murshed KA, Cicekcibasi AE, Karabacakoglu A, Seker M, Ziylan T. Distal femur morphometry: a gender and bilateral comparative study using magnetic resonance imaging. Surg Radiol Anat. 2005;27(2):108-112.

24. Oh YK, Kreinbrink JL, Wojtys EM, Ashton-Miller JA. Effect of axial tibial torque direction on ACL relative strain and strain rate in an in vitro simulated pivot landing. J Orthop Res. 2012;30(4):528-534.

25. Park HS, Ahn C, Fung DT, Ren Y, Zhang LQ. A knee-specific finite element analysis of the human anterior cruciate ligament impingement against the femoral intercondylar notch. J Biomech. 2010;43(10):2039-2042.

26. Shimokochi Y, Shultz SJ. Mechanisms of noncontact anterior cruciate ligament injury. J Athl Train. 2008;43(4):396-408.

27. Simon RA, Everhart JS, Nagaraja HN, Chaudhari AM. A case-control study of anterior cruciate ligament volume, tibial plateau slopes and intercondylar notch dimensions in ACL-injured knees. J Biomech. 2010;43(9):1702-1707.

28. Smith HC, Johnson RJ, Shultz SJ, et al. A prospective evaluation of the Landing Error Scoring System (LESS) as a screening tool for anterior cruciate ligament injury risk. Am J Sports Med. 2012;40(3):521-526.

29. Smith HC, Vacek P, Johnson RJ, et al. Risk factors for anterior cruciate ligament injury: a review of the literature—part 1: neuromuscular and anatomic risk. Sports Health. 2012;4(1):69-78.

30. Smith HC, Vacek P, Johnson RJ, et al. Risk factors for anterior cruciate ligament injury: a review of the literature-part 2: hormonal, genetic, cognitive function, previous injury, and extrinsic risk factors. Sports Health. 2012;4(2):155-161.

31. Sonnery-Cottet B, Archbold P, Cucurulo T, et al. The influence of the tibial slope and the size of the intercondylar notch on rupture of the anterior cruciate ligament. J Bone Joint Surg Br. 2011;93(11):1475-1478.

32. Spang JT, Dang AB, Mazzocca A, et al. The effect of medial meniscectomy and meniscal allograft transplantation on knee and anterior cruciate ligament biomechanics. Arthroscopy. 2010;26(2):192-201.

33. Stijak L, Herzog RF, Schai P. Is there an influence of the tibial slope of the lateral condyle on the ACL lesion? A case-control study. Knee Surg Sports Traumatol Arthrosc. 2008;16(2):112-117.

34. Sturnick DR, Argentieri EC, Vacek PM, et al. A decreased volume of the medial tibial spine is associated with an increased risk of suffering an anterior cruciate ligament injury for males but not females. J Orthop Res. 2014;32(11):1451-1457

35. Sturnick DR, Van Gorder R, Vacek PM, et al. Tibial articular cartilage and meniscus geometries combine to influence female risk of anterior cruciate ligament injury. J Orthop Res. 2014;32(11):1487-1494.

36. Swart E, Redler L, Fabricant PD, Mandelbaum BR, Ahmad CS, Wang YC. Prevention and screening programs for anterior cruciate ligament injuries in young athletes: a cost-effectiveness analysis. J Bone Joint Surg Am. 2014;96(9):705-711.

37. Todd MS, Lalliss S, Garcia E, DeBerardino TM, Cameron KL. The relationship between posterior tibial slope and anterior cruciate ligament injuries. Am J Sports Med. 2010;38(1):63-67.

38. Tourville TW, Johnson RJ, Slauterbeck JR, Naud S, Beynnon BD. Assessment of early tibiofemoral joint space width changes after anterior cruciate ligament injury and reconstruction: a matched case-control study. Am J Sports Med. 2013;41(4):769-778.

39. van Diek FM, Wolf MR, Murawski CD, van Eck CF, Fu FH. Knee morphology and risk factors for developing an anterior cruciate ligament rupture: an MRI comparison between ACL-ruptured and non-injured knees. Knee Surg Sports Traumatol Arthrosc. 2014;22(5):987-994.

40. Wahl CJ, Westermann RW, Blaisdell GY, Cizik AM. An association of lateral knee sagittal anatomic factors with non-contact ACL injury: sex or geometry? J Bone Joint Surg Am. 2012;94(3):217-226.

41. Walker PS, Erkman MJ. The role of the menisci in force transmission across the knee. Clin Orthop Relat Res. 1975;109:184-192.

42. Whitney DC, Sturnick DR, Vacek PM, et al. Relationship between the risk of suffering a first-time noncontact ACL injury and geometry of the femoral notch and ACL: a prospective cohort study with a nested case-control analysis. Am J Sports Med. 2014;42(8):1796-1805.