



Multivariable analysis of anatomic risk factors for anterior cruciate ligament injury in active individuals

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Abstract

Objective The aim of the present study was to compare the morphometric differences between patients with or without anterior cruciate ligament (ACL) injury, and identify the anatomic risk factors associated with ACL injury in active individuals.

Methods The knee joint magnetic resonance images (MRI) of 100 subjects were included in this study. Data from the ACL-injured group (50 patients) and matched controls (50 subjects) were obtained from the same hospital. These data were analyzed by univariable analysis or multivariable conditional logistic regression analysis to examine the effects of the following variables on the risk of suffering ACL injury for the first time: TT-TG distance, medial and lateral tibial slope, intercondylar notch width and depth, femur condylar width, lateral femoral condylar depth, notch width index (NWI), notch shape index (NSI), notch depth index (NDI), and cross-sectional area (CSA).

Results In the univariable analysis, the ACL-injured group had a larger TT-TG distance, increased medial and lateral tibial slope, narrower intercondylar notch width, deeper lateral femoral condylar depth, lesser NWI and NSI, and CSA when compared with the control group ($P < 0.05$). However, there were no significant between-group differences in intercondylar notch depth ($P = 0.174$), femur condylar width ($P = 0.797$), and NDI ($P = 0.436$). The multivariable analysis revealed that TT-TG distance [odds ratio (OR) = 1.37, 95% CI = 1.04–1.81, $P = 0.028$], medial tibial slope (OR = 1.30, 95% CI = 1.02–1.66, $P = 0.036$) and NWI (OR = 0.46, 95% CI = 0.24–0.91, $P = 0.025$) had significant multivariable associations with the sole independent risk of ACL injury.

Conclusion Larger TT-TG distance, increased MTS, and lesser NWI are independent anatomic risk factors for active individuals with ACL injury.

Level of evidence Case-control study; Level of Evidence, III.

Keywords Anterior cruciate ligament injury · Tibial plateau · TT-TG distance · MRI · Risk factors

Xianyue Shen and Jianlin Xiao contributed equally to this study.

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Introduction

With the increasing popularity of sports, injuries to the knee joint are common [1]. The most common ligament injury around the knee is anterior cruciate ligament (ACL) injury due to its unique anatomical structure and function [1–3]. The incidence of ACL injury in the general population is approximately 8.1/10,000 in USA, and this incidence becomes higher among active individuals [4, 5]. ACL rupture is regarded as a severe injury in active individuals, which contributes to meniscal and articular cartilage degeneration and turns out to be an increased risk of the onset and progression of osteoarthritis [6–9], leading to a series of clinical sequelae and high economic expenses [10–12]. Thus, preventive programs are essential for minimizing ACL

injuries, and the precondition for primary prevention is a thorough understanding for these anatomic risk factors.

Although the cause of disparity in ACL injury remains elusive, extrinsic and intrinsic factors of the knee joint have been considered to be relevant, as shown in the extant of researches [13–23]. The tibial slope [15, 16, 18, 20], notch width [13, 20], notch shape [14, 21], and notch width index [14, 17, 22] are some of the anatomic variables used to predispose an individual to ACL injury, as well as tibial tubercle–trochlear groove (TT-TG) distance [19].

Nevertheless, the role of the tibial slope, intercondylar notch width, and TT-TG distance remains controversial [24, 25], and the mechanism of ACL injury has not been well clarified at present. Furthermore, there are limited existing studies available for the combined influence of multiple anatomic risk factors on ACL injury in active individuals [20]. Given the potentially important correlation between ACL injury and morphometric features in knee, the aim of the present study was to measure morphometric parameters using magnetic resonance imaging (MRI) and determine the potential anatomic risk factors associated with ACL injury. Furthermore, the morphometric differences between patients with or without ACL injury were compared, and the anatomic risk factors determined by multivariable analysis in active individuals were discussed. We hypothesized that patients with ACL injury have specific anatomic characteristics, which can predispose to ACL injury.

Materials and methods

Patients

The present retrospective study was approved by the Institutional Review Board, Ethics Committee of China-Japan Union Hospital (IRB NO:2016-nsfc028). All patients provided a signed informed consent prior to undergoing the MRI examination. The present retrospective study was performed to identify anatomic risk factors associated with ACL injury in active individuals, who are at the greatest risk of suffering their first noncontact ACL injury when they are engaged in daily sports [15]. Patients with ACL injury, who underwent ACL reconstruction at our hospital between October 2015 and October 2017, were examined. Eligibility criteria were: age within 20–45 years, suffering from the initial ACL injury, no history of other knee injuries, and no evidence of displaced fractures altering the osseous morphology. Exclusion criteria were as follows: a history of operation, trauma and high energy violence injury around the knee joint, advanced degenerative changes, evidences of other ligament injury, and cases with substandard MRI scans. The flow of patient selection is shown in Fig. 1. Out of an initial cohort of 178 cases, after screening, a total of

50 patients (30 males and 20 females), who were diagnosed with ACL injury based on the MRI performed by an experienced orthopaedic surgeon (JLX), were recruited into the present study. The diagnosis was confirmed by knee arthroscopy by an orthopaedic surgeon (JLZ). In addition, 50 normal cases (38 males and 12 females), who were matched by age, height, weight, and level of exercise, and had knee MRIs available for review, were assigned as the control group for comparison. Demographic data for the subjects are shown in Table 1.

Image processing

All eligible participants were required to undergo MRI of the selected knee for review in the clinical imaging system using a Phillips 3.0-T MRI scanner. These patients were placed in the supine position with the injured knee in 15° flexion. The scan sequence was acquired using the following parameters: proton fast spin echo with fat saturation (PD-TSE-FS-TRA) in axial, TR 2886 ms, TE 25 ms, 160 mm FOV, layer thickness of 3 mm. SE-T1W1 sequence in coronal plane, TR 520 ms, TE 20 ms, FOV 160 mm, and layer thickness of 3 mm.

Data acquisition and outcome parameters

All scan data were extracted, deposited to a personal computer in DICOM format, and exported to Mimics 17.0 (Materialise, Belgium) for gauging parameters. TT-TG measurements were performed on the axial images described by Schoettle et al. [26] (Fig. 2). First, the most posterior point of the medial and lateral condyle of the femur was defined as the reference line. Second, a line perpendicular to the reference line was drawn through the deepest bony point of the trochlear groove. Third, a second line perpendicular to the reference line was drawn through the most anterior point of the tibial tuberosity on the axial section, showing the most anterior point of the tuberosity. The TT-TG distance was defined as the distance between these two perpendicular lines. Femoral condylar width (W) was expressed as a line through the popliteal groove parallel to the reference line. The intercondylar notch depth (D) was defined as the maximum height of the notch. The intercondylar notch width (N) was defined as the length of a line parallel to the reference line at the upper two-thirds of D. The maximum height of the lateral femoral condyle was expressed as the femoral condylar depth (CD). Intercondylar NWI was defined as the ratio of the intercondylar notch width to the femoral condylar width. The NSI was calculated by dividing the intercondylar notch width by the intercondylar notch depth. The NDI was defined as the ratio of the intercondylar notch depth to the lateral femur CD. The CSA of the femoral intercondylar notch was defined as the intercondylar notch

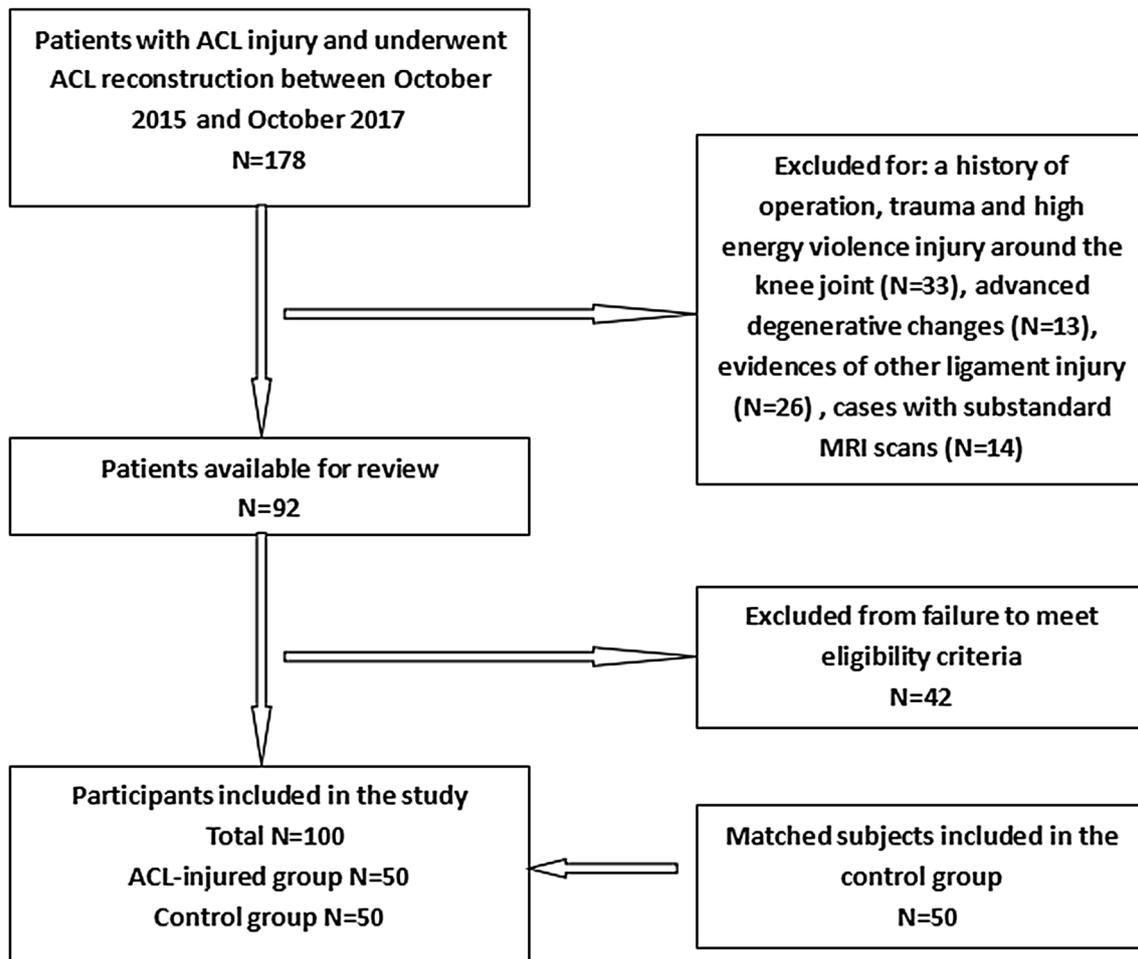


Fig. 1 Flowchart showing selection of patients for this study

Table 1 Comparison of demographic characteristics between the ACL-injured group and control group

Variable	ACL-injured group (n = 50)	Control group (n = 50)	P value
Age, year	28.5 ± 6.3	27.0 ± 4.7	0.180
Height, cm	172 ± 7.5	170 ± 8.0	0.344
Weight, kg	70.0 ± 10.6	67.5 ± 14.3	0.396
BMI, kg/m ²	23.5 ± 2.6	23.0 ± 3.3	0.444

Data are presented as mean and standard deviation

width multiplied by the intercondylar notch depth (Fig. 3). In order to measure the tibial slope on the sagittal MRI cut, the central sagittal image of the knee was distinguished, including the posterior cruciate ligament, intercondylar eminence, and anterior and posterior tibial cortices that appeared in a concave shape. Then, the longitudinal axis of the tibia was determined by drawing a line through the center of two best-fit circles in the proximal part of the tibia, and the tibial

slope was defined using the angle between the longitudinal axis of the tibia and tangent to the tibial plateau [27] (Fig. 4).

Statistical methods

The mean and standard deviation were calculated for continuous variables, and a descriptive analysis for the study population was conducted. A paired-samples *t* test was used to determine the age, height, weight, and BMI difference between two groups. In order to assess the association between anatomic risk factors and ACL injury, independent Student's *t* test was used for the univariable analysis. Variables with a *P* value of <0.10 in the univariable analysis were considered for the multivariable analysis [28]. Multivariable logistic regression analysis was used for the multivariable analysis. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were presented with the respective *P* values. All statistical analyses were conducted using SPSS version 21.0 software (SPSS, Chicago, IL, USA). *P* < 0.05 was considered statistically significant.

Fig. 2 Measurement of the TT-TG distance. The perpendicular distance between lines a and b represent the TT-TG distance

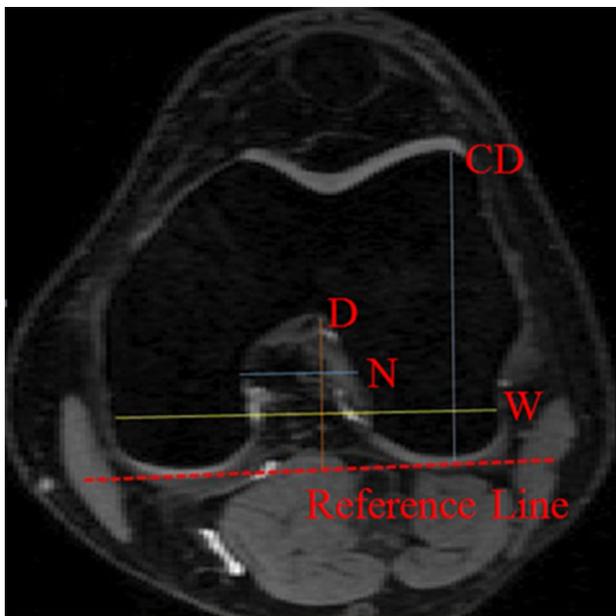
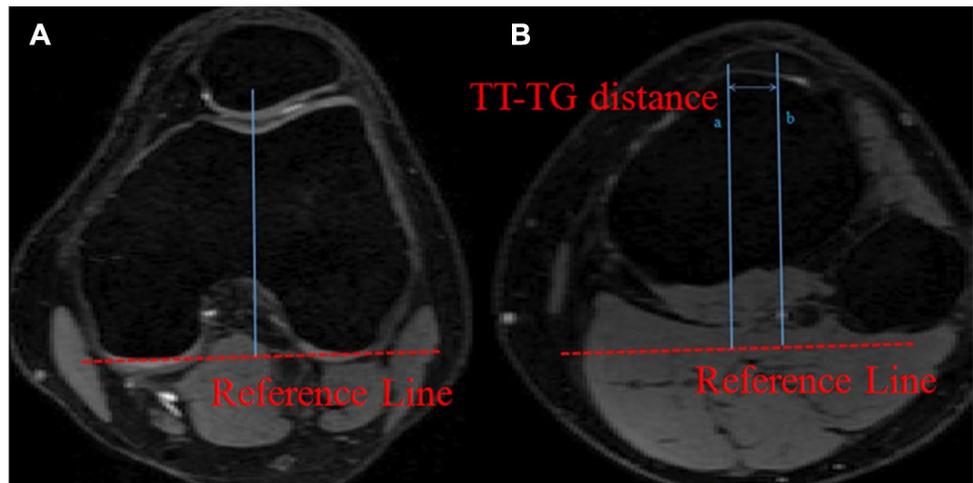


Fig. 3 Measurement of the intercondylar notch in an axial image. *W* The femoral condylar width, *N* The intercondylar notch width, *D* The intercondylar notch depth, *CD* The lateral femoral condylar depth; Red dotted line: Reference line

In order to assess for intraobserver variations, all parameters were measured repeatedly by one observer a month later. In order to assess for interobserver reliability, two independent blinded observers remeasured the subjects. The intraclass correlation coefficient (ICC) for intra- and interobserver reliability was evaluated by a one-way random effects model to assess the reproducibility of each researcher and the overall agreement among the researchers for each parameter. A post hoc power calculation was performed for eliminating type II error through statistical power analyses using G-Power 3.1 [29].

Results

As shown in Table 1, there were 50 subjects in the control group and 50 subjects in the ACL-injured group. No significant differences were observed in the demographic characteristics between these two groups ($P > 0.05$, Table 1).

The univariable analysis of the data demonstrated that larger TT-TG distance, increased MTS, increased LTS, narrower intercondylar notch width, and deeper lateral femoral condylar depth were significantly associated with ACL injury risk (Table 2). In addition, subjects in the ACL-injured group had a significantly smaller NWI, NSI, and CSA, when compared with the control group (Table 2). However, intercondylar notch depth, femur condylar width, and NDI were not significantly different between these two groups (Table 2). Intraclass correlation coefficient results of the intraobserver and interobserver reliabilities were in the excellent range (Table 3). Post hoc power analysis revealed a power of > 0.80 for detecting a significant difference between the ACL-injured group and control group, except for TT-TG distance (0.73) and lateral femoral condylar depth (0.67).

Variables with a P value of < 0.10 in the univariable analysis were finally included in the multivariable logistic regression analysis. The multivariable analysis revealed that TT-TG distance (OR = 1.37, 95% CI = 1.04–1.81, $P = 0.028$), MTS (OR = 1.30, 95% CI = 1.02–1.66, $P = 0.036$), and NWI (OR = 0.46, 95% CI = 0.24–0.91, $P = 0.025$) had significant associations with the sole independent risk of ACL injury (Table 4).

Discussion

The principal finding of the present study was the diverse combination of anatomic risk factors that can predispose to ACL injury in active individuals. According to the

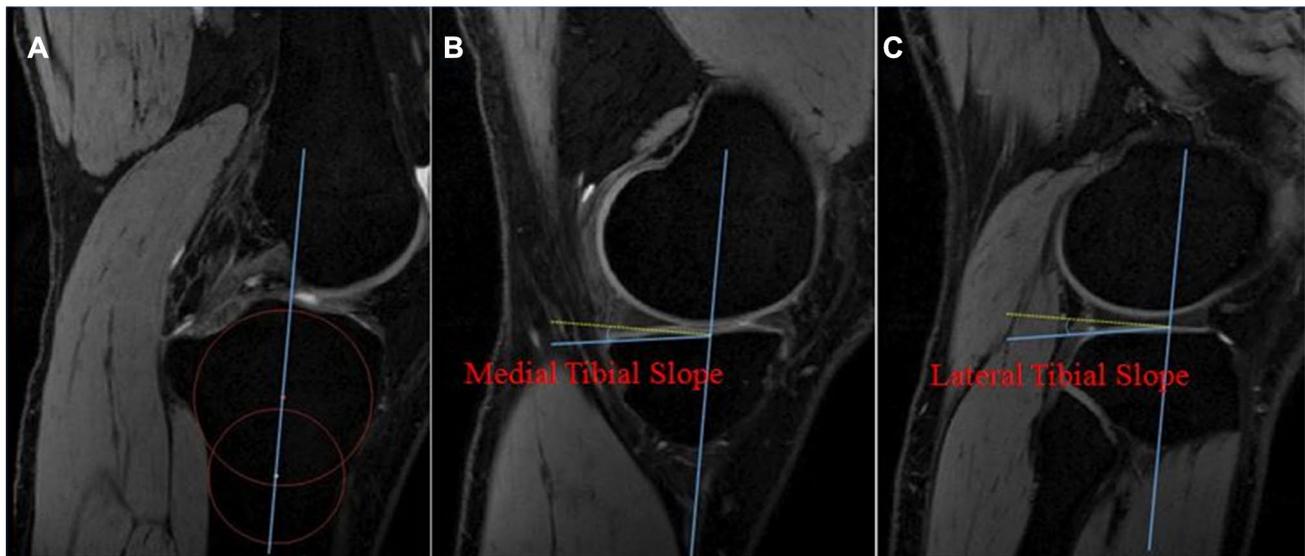


Fig. 4 Measurement of the tibial slope. **a** The longitudinal tibial axis was defined as the connecting line through the centers of the two best-fit circles to the proximal part of the tibia. **b** The slope of the lateral tibial plateau was measured in the midcondylar plane, and was defined as the angle between the line fitting the lateral tibial plateau

and the longitudinal tibial axis. **c** The slope of the medial tibial plateau was measured in the midcondylar plane and was defined as the angle between the line fitting the medial tibial plateau and the longitudinal tibial axis

Table 2 Univariable association between measurements of osseous morphologic characteristics and risk of ACL injury

Variable	Total	ACL-injured group	Control group	<i>P</i> value
TT-TG distance, mm	9.63 ± 2.05	10.08 ± 1.71	9.17 ± 2.26	0.025*
Medial tibial slope, degree	6.05 ± 2.43	6.88 ± 2.47	5.22 ± 2.11	<0.001*
Lateral tibial slope, degree	7.30 ± 2.45	8.06 ± 2.38	6.54 ± 2.30	0.002*
The intercondylar notch width, mm	20.87 ± 2.20	19.93 ± 1.58	21.81 ± 2.35	<0.001*
The intercondylar notch depth, mm	29.89 ± 2.43	30.23 ± 2.38	29.56 ± 2.46	0.174
The femur condylar width, mm	72.67 ± 5.16	72.54 ± 4.80	72.80 ± 5.55	0.797
The lateral femoral condylar depth, mm	57.74 ± 5.62	58.91 ± 6.56	56.58 ± 4.24	0.038*
Notch width index (NWI)	0.29 ± 0.05	0.28 ± 0.02	0.30 ± 0.03	<0.001*
Notch shape index (NSI)	0.70 ± 0.09	0.66 ± 0.07	0.74 ± 0.08	<0.001*
Notch depth index (NDI)	0.52 ± 0.04	0.52 ± 0.05	0.52 ± 0.04	0.436
Cross-sectional area (CSA), mm ²	624.76 ± 89.94	602.62 ± 69.72	646.89 ± 102.38	0.013*

Data are presented as mean and standard deviation. *Represents $P < 0.05$

Table 3 Intraobserver and Interobserver reliability for all osseous morphologic characteristic measurements

Variable	Intraobserver intraclass correlation coefficient	Interobserver intraclass correlation coefficient
TT-TG distance	0.947 (0.892–0.974)	0.972 (0.943–0.987)
Medial tibial slope	0.986 (0.970–0.993)	0.921 (0.843–0.962)
Lateral tibial slope	0.994 (0.987–0.997)	0.959 (0.917–0.980)
The intercondylar notch width	0.820 (0.658–0.910)	0.971 (0.940–0.986)
The intercondylar notch depth	0.955 (0.909 to 0.978)	0.864 (0.737–0.933)
The femur condylar width	0.988 (0.975 to 0.994)	0.966 (0.931–0.984)
The lateral femoral condylar depth	0.975 (0.948 to 0.985)	0.789 (0.606–0.893)

Data are presented as intraclass correlation coefficients, with 95% confidence interval in parentheses

Table 4 Multivariable association between measurements of osseous morphologic characteristics and risk of ACL injury

Variable	<i>P</i> value	Odds ratio	95% CI	Coefficient
TT-TG distance, mm	0.028*	1.368	1.035–1.808	0.313
Medial tibial slope, degree	0.036*	1.300	1.017–1.662	0.263
Lateral tibial slope, degree	0.180	1.173	0.929–1.482	0.160
The intercondylar notch width, mm	0.700	1228.377	0–6,251,132	7.113
The lateral femoral condylar depth, mm	0.696	1.002	0.990–1.015	0.002
Notch width index (NWI)	0.025*	0.464	0.237–0.909	-0.768
Notch shape index (NSI)	0.173	1.122	0.951–1.324	0.115
Cross-sectional area (CSA), mm ²	0.096	1.152	0.975–1.361	0.141

*Represents $P < 0.05$

univariable analysis, larger TT-TG distance, increased MTS and LTS, smaller intercondylar notch width, deeper lateral femoral condylar depth, lesser NWI and NSI, and CSA were associated with ACL injury. Moreover, the important independent factors were identified in the multivariable analysis. We found that larger TT-TG distance, increased MTS, and lesser NWI had significant associations with the independent risk of ACL injury.

Interestingly, the significant association of larger TT-TG distance with ACL injury was basically consistent with the previous literature [19]. Saper et al. was the first to explore the relationship between TT-TG distance and ACL injury and found that TT-TG distance in noncontact ACL tears was statistically larger than controls in adolescents and young adults [19]. Unlike the study conducted by Saper et al., the present study comprehensively revealed that TT-TG distance was independently associated with ACL injury through multivariable regression analysis. A possible explanation for the increased risk is that TT-TG distance may influence the rotation degree of the knee during pivoting moment. It is well known that TT-TG distance represents the rotation angle between the femur and tibia of the knee, and tibial tubercle is located on the lateral side of the trochlear groove under normal circumstances [30]. The larger TT-TG distance, indicating the tibia is more externally rotated relative to femur [31, 32], would be contributed to greater stress of the posterolateral bundle and greater force of the anterior shear on the tibia, thereby resulting in ACL damage [33, 34]. In contrast, the tibia became an internal rotation relative to the femur with the loss of limited rotation mechanism after ACL tears [31], resulting in the reduction in TT-TG value. However, the present results revealed that TT-TG distance in the ACL-injured group was 0.91 mm larger than the control group. Therefore, we believe that this difference is of greater significance prior to the ACL injury, which may help the surgeon alert those people with a larger TT-TG distance to take appropriate steps in sports and avoid suffering from ACL injury. Future studies are needed to prospectively explore changes in TT-TG distance before and after ACL injury of the same knee.

Although these series of studies identified the tibial slope to be associated with ACL injury [15, 16, 18, 20], no unanimous conclusion could be drawn. Beynnon et al. concluded that the increased posterior–inferior directed slope of the lateral tibial plateau shows that there is increased risk of noncontact ACL trauma in females. Furthermore, Dare et al. found that pediatric patients with increased posterior tibial slope had an increased risk of sustaining ACL tears. However, the study conducted by Blanke et al. demonstrated that neither LTS, nor MTS was associated with the risk of ACL tear during noncontact injury among the recreational alpine. Moreover, the study conducted by Hashemi et al. [35], indicated that increased MTS and LTS were associated with increased risk of ACL injury. Even Jaecker et al. [36] concluded that increased LTS and MTS are independent risk factors for graft failure following ACL reconstruction. Due to different inclusion criteria and participants with different levels of exercise, we came to a different conclusion from Blanke et al. [37]. The results of the present study revealed that MTS and LTS were the predisposing causes of ACL injury. This was consistent with the in-depth study conducted by Rahnemai-Azar et al., which revealed that the role of MTS was the only independent predictor of ACL injury by multivariable regression analysis. This was because the medial tibial slope has a closer approximation to the tibial AM bundle insertion site, thereby increasing its influence on the anterior–posterior translation, when compared to the lateral tibial slope. Furthermore, this indicates that LTS might be a confounding factor for ACL injury. This geometric difference may be important to consider when assessing the risk of knee injury and the design and success of ACL reconstruction. However, more biomechanical or kinematic evaluation of MTS should be added to describe the correlation between MTS and postoperative effect and surgical choice.

The role of the narrower intercondylar notch in ACL injury remains controversial [17, 18, 38–42]. Various studies of NWI on MRI have been conducted, which were helpful to the judgment of intercondylar notch stenosis [38–40]. And some of these studies confirmed that the value of NWI in ACL injury is smaller than that in healthy populations [17,

38–40]. The study conducted by Sonnery-Cottet et al. found that patients with a ruptured ACL had significantly increased narrow NWI. Furthermore, Zeng et al. suggested that narrow intercondylar notch dimensions may put the ACL at risk for injury based on a meta-analysis. Interestingly, the study conducted by Comerford et al. revealed that canines with a narrow intercondylar notch had high risk of ACL injury. The present study was consistent with previous studies, and progressively revealed that NWI was another independent risk factor for ACL injury in active individuals. This mechanism may contribute to ACL injury due to ACL impingement or the correspondingly smaller size of ACL. On the contrary, some other studies did not find any relationship between narrow intercondylar notch dimensions and increased risk of ACL injury [14, 18]. For instance, Al-saeed et al. concluded that there was no correlation between low NWI and the presence of ACL tears. And we found that average values of NWI in both injured and controls presented here were higher than those reported by Al-saeed et al. In our study, we found the average NWI among ACL-injured group was 0.28, which was confirmed to be accurate when compared to a study done by Dienst et al. [43]. This difference may be caused by different imaging techniques and different knee flexion angle. Further investigations are required to identify the relationship of ACL injury with NWI and establish MRI-based baseline values for NWI on larger and different population groups.

Several limitations involved in the present study should be considered. First, the present study was a single-center retrospective study and the sample size was relatively small. Despite this, the results of statistical analysis indicated reliable reproducibility. Second, the present study only assessed for several anatomic risk factors, which were considered as the most relevant risk factors for ACL injury based on previous literature. And we think this may help us to draw accurate conclusions. Furthermore, ACL injury risk is likely to be correlated to external conditions, such as neuromuscular characteristics, which could not be controlled in this investigation. Despite these limitations, our data confirmed that patients with ACL injury would have statistical difference in anatomic characteristics and we hope that the findings of this study will be helpful for guiding clinical diagnosis and treatment of ACL injury.

Conclusion

The present study demonstrates that larger TT-TG distance, increased MTS, and lesser NWI can be regarded as independent factors for active individuals with ACL injury. Multivariable analysis revealed that LTS, intercondylar notch width, lateral femoral condylar depth, NSI, and CSA were not associated with ACL injury. This information might

help physician to identify individuals who are at high risk of suffering ACL injury and provide targeted intervention programs to prevent ACL injuries. Future prospective work should take these factors into account to verify our findings.

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Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

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