Smaller anterior cruciate ligament diameter is a predictor of subjects prone to ligament injuries: An ultrasound study

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Aims and objectives

Anterior cruciate ligament (ACL) is the most commonly injured knee ligament in athletes and can cause significant morbidity in all age groups. ACL injuries can be particularly devastating to young athletes. Although numerous procedures have been devised to treat ACL tears, they have limited cure rates. Therefore, it is essential to find techniques or processes to foresee the risk of injury to ACL to adopt appropriate preventive measures.

Approximately three-fourths of mechanical injuries of ACL are noncontact type, suggesting that early recognition of this risk may help in the prevention of injury [1].

Since physical attributes of every single fibril constituting the ACL and other ligaments of a person are identical [2] and that mean fibril diameter is uniform across sexes [3], a thinner ACL may just have less number of fibrils, resulting in inferior strength [4].

A 2009 study reports that magnetic resonance imaging (MRI) measured smaller ACL volume correlates with ACL injury when weight, height, gender, and age are kept almost constant [4]. However it is debatable, whether performing an MRI of the knee in an athlete without symptoms is justifiable [5]. Surprisingly there are a very few studies directly or indirectly examining the ACL by ultrasound despite it being an ideal screening examination to assess the size of a normal ACL [6-9].

Hence this study was designed to:

1. Evaluate usefulness of ultrasound in measuring diameter of normal ACL

2. Test if there exists a relationship between smaller ACL diameter and ACL injury, by measuring the ACL diameter in contralateral knees of ACL injured subjects and comparing them to ACL size in weight, height, gender, and age matched controls.

3. Assess agreement between two radiologists in measuring ACL diameter in cases and matched controls.
Methods and materials

Subject population:

First 25 subjects undergoing knee MRI at our hospital who satisfied the following inclusion criteria were prospectively studied:

a) Subjects in whom ACL injury has been diagnosed on MRI
b) It is a self-reported non-contact ACL injury
c) Those who are willing to participate in the study and
d) Those who sign our institutional review board-approved informed consent.

Following exclusion criteria were used:

a) History of trauma to the soft tissue of the lower extremity requiring surgical repair/reconstruction (excluding ACL tears)
b) Meniscectomy of greater than one-fourth of the meniscus and
c) Fracture of lower extremity bones requiring internal fixation.

Also, another 25 control subjects with normal or non-injured ACL who match the above selected subjects in gender, age, weight, height, and ethnicity were invited to participate in the study.

Static and dynamic ultrasound study of the normal knees of all 50 subjects was performed to measure maximum diameter of ACL near tibial insertion site.

The sonographer was blinded as to the status of the subject being examined. Agreement between the sonographers was studied. In addition to the main objectives, correlation between diameter of ACL and weight, height, and age of the subject was also studied. We did one to one matching between the injured subjects and the matched controls for height, weight, gender and ethnicity and achieved similar mean between groups for age. Each injured subject and the matched control had the same gender and ethnicity. The control subjects were chosen in such a way that the disparity between heights of each and every ACL-injured subject and the matched control was less than 5 centimeters and the disparity between weights of each and every ACL-injured subject and the matched
control was less than 3 kilograms. The average difference between the heights of control and injured subjects was within 1 cm (170.7 cm vs 171.2 cm) and the average difference between the weights of control and injured subjects was within 1.5 kg (78.7 kg vs 80.2 kg). No statistically significant disparity was observed amongst the ACL-injured and control groups for age (P=0.890), height (P=0.768), weight (P=0.685), and gender (P=1.00) based on statistical analysis using an unpaired Student t test and Chi-square tests [Table 1 on page 6].

The study was approved by our institutional research ethics committee.

Ultrasound-Based Diameter Calculation

Only tibial part of ACL could be examined by ultrasound. Maximum diameter of ACL near tibial insertion site was measured by static and dynamic ultrasound (Siemens, Munich, Germany) study using high frequency (7-9 MHz) linear transducer with the subject’s knee in 90 degree flexion in supine position. While examining the ACLs, we asked the subjects to internally or externally rotate their leg to perform the dynamic ultrasound examination. The linear high frequency ultrasound probe was placed on the subject’s skin inferior to patella such that its long axis is parallel to that of the ACL. This was achieved by rotating the superior part of the probe externally by 30 degrees [Fig. 1 on page 6]. The ACL was visualized as a thick linear hypoechoic band like structure inserted approximately 11 mm caudal to the tibial plateau and intercondylar eminence [Fig. 1 on page 6]. The maximum diameter of ACL near tibial insertion site was measured for 25 opposite, normal or unaffected knees of persons who suffered noncontact injury to ACL and for 25 controls matched for weight, height, gender, and age. Each ACL was measured separately by two radiologists who were blinded to the status of the subject (injured or control group). Interobserver variation was calculated. Average of the two measurements was considered for statistical analysis. We applied stepwise multiple regression to the statistical data to assess the disparity in the diameter of ACL between injured and control groups. During this analysis weight, height, age, and gender were deemed to be potential covariates.

Validation of Ultrasound-Based Diameter Calculation

MRI is considered a gold standard for in vivo ACL diameter measurement. We used MRI studies of 10 knees of 10 control subjects for validating the ultrasound-based ACL diameter (near tibial insertion site) measurement performed in this study. MRI examinations were performed using a GE Signa 1.5T system. Sagittal 3D-SPGR MRI images with voxel size of 0.055 x 0.055 x 0.15 cm were obtained. The MRI examination was performed on one randomly chosen knee of each of the control subjects. The
subject was placed in supine position with knee in 90 degree flexion to mimic the position during ultrasound study. Maximum antero-posterior diameter of each ACL (near tibial insertion site) was measured by two radiologists independently. Interobserver variation was measured. Average of the two measurements was compared with average of maximum ACL diameter estimated by ultrasound.

Sample size

No similar studies in literature.

No formal sample size calculation.

Total of 50 subjects/knees

- 25 ACL-injured subjects
- 25 non-injured matched controls.

Statistical analysis

- Descriptive statistics.
- Chi-square test/Fisher's exact test.
- Unpaired t-test/Mann Whitney U test.
- Paired t-test.
- Intra-class correlation coefficient (ICC).
- Bland-Altman plots.
- Pearson's correlation coefficients.
- Stepwise multiple regression.
- PASW Statistics (v19.0, SPSS Inc.)
Fig. 1: (A, B, C and D): Position of the patient and the ultrasound probe during ultrasound examination of anterior cruciate ligament (ACL) is shown in 1A. MRI image of knee in 90-degree flexion is shown in 1B. The red rectangle denotes area of the image rotated and presented in 1D to match the morphology as seen in ultrasound image (1C). White arrowheads in 1C demonstrate normal ACL. P-denotes patella and T-denotes tibia.

<table>
<thead>
<tr>
<th></th>
<th><strong>ACL Injured</strong> (N= 25)</th>
<th><strong>Control</strong> (N= 25)</th>
<th><strong>P-value</strong>*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>33.52 ± 12.22</td>
<td>33.92 ± 7.64</td>
<td>0.890</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>170.7 + 6.37</td>
<td>171.2 + 5.53</td>
<td>0.768</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>78.68 + 12.50</td>
<td>80.16 + 13.15</td>
<td>0.685</td>
</tr>
<tr>
<td>BMI</td>
<td>26.98 + 3.77</td>
<td>27.45 + 5.10</td>
<td>0.711</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>24 (96%)</td>
<td>24 (96%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Female</td>
<td>1 (4%)</td>
<td>1 (4%)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arab</td>
<td>18 (72%)</td>
<td>18 (72%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Non-Arab Asian</td>
<td>6 (24%)</td>
<td>6 (24%)</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>1 (4%)</td>
<td>1 (4%)</td>
<td></td>
</tr>
<tr>
<td>ACL Injury</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Injury</td>
<td>--</td>
<td>25 (100%)</td>
<td>--</td>
</tr>
<tr>
<td>Non-contact injury</td>
<td>25 (100%)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Type of ACL Injury</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete Thickness</td>
<td>17 (68%)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Partial Thickness</td>
<td>8 (32%)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>ACL Injury side</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>10 (40%)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Left</td>
<td>15 (60%)</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

P-value computed using Chi-square and unpaired t test.
Quantitative variable values were presented in mean ± SD.

**Table 1:** Demographic, anthropometric and clinical characteristics among cases and controls

Fig. 2: Plot showing mean ACL diameter (cm) in controls and injured cases in relation to body weight (kg).

Results

No significant difference was observed amongst the ACL-injured and control groups for age (P=0.890), height (P=0.768), weight (P=0.685), and gender (P=1.00) using an unpaired Student t test and Chi-square tests [ Table 1 on page 10 ]. The control group was adequately matched to the injured group.

Contralateral ACL maximum diameter (near tibial insertion site) for ACL-injured subjects was significantly less than that for non-injured matched control subjects (0.62 ± 0.07 vs 0.81 ± 0.06 cm; P<0.0001).

Stepwise regression analysis showed that body weight was a significant predictor (R=0.357; P=0.016), while height, age, and gender were insignificantly associated with ACL diameter. The mean diameter of the contralateral ACL near tibial insertion site for the injured group was 0.19 cm less than that for a control subject having similar weight (P<0.0001). The 95% confidence interval (CI) of the mean difference was 1.5 to 2.3 [ Table 2 on page 10 and Fig. 2 on page 11 ]. The ACL diameter of all 25 subjects in the ACL-injured group was smaller than their matched controls, and just 6 subjects had lower body weight. For the mean body weight of 78.5 kg for the studied population the ACL-injured group had a mean contralateral ACL maximum diameter (near tibial insertion site) of 0.62 cm, while the control group had a mean diameter (maximum) of 0.81 cm.

The consensus amongst the two recurring measures during validation with MRI measurements demonstrated a very strong agreement (intraclass correlation of 0.87; 95% CI: 0.50 to 0.97) [ Fig. 3 on page 12 ]. The regression analysis amongst the MRI-measured diameter and the ultrasound-measured diameter revealed a correlation of 0.070, a slope of 0.052, and a constant offset of 0.041 cm. The regression line was almost similar to y = x (slope P=0.05; intercept P=0.051). We also compared the results of measurements by two radiologists (raters) by conducting an inter-rater accuracy test. The intraclass correlation coefficient for these 2 radiologists was 0.93 (95% CI: 0.88 to 0.96), indicating a very strong agreement. The limits of the [ Fig. 2 on page 11 ] show a comparison of ultrasound ACL diameter measured by radiologist 1 and radiologist 2 [ Fig. 4 on page 13 ]. Here the mean difference was -0.01 with 95% CI -0.03 to 0.01. Thus radiologist 1 tends to give a lower reading, ranging from -0.03 and 0.01. Despite this, the limits of disagreement are considerably low (high agreement) and hence both radiologists provide similar values measuring ultrasound ACL diameter. Similarly strong agreement was observed when analyzed separately for ACL-injured and control group subjects [ Fig. 5 on page 14 and Fig. 6 on page 15 ]. Finally, the investigation of variance showed a mean systematic difference of 0.3 cm between the 2 radiologists.
Table 1: Demographic, anthropometric and clinical characteristics among cases and controls

<table>
<thead>
<tr>
<th></th>
<th>ACL Injured (mean ±SD) (N= 25)</th>
<th>Control (mean ±SD) (N= 25)</th>
<th>Mean Difference (95% CI)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound ACL diameter (cm) measurements by Radiologist 1</td>
<td>0.61 ± 0.06</td>
<td>0.80 ± 0.07</td>
<td>-0.19 (-0.23 to -0.16)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ultrasound ACL diameter (cm) measurements by Radiologist 2</td>
<td>0.62 ± 0.09</td>
<td>0.81 ± 0.07</td>
<td>-0.18 (-0.23 to -0.14)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean Ultrasound ACL diameter (cm) measurements by both radiologists</td>
<td>0.62 ± 0.07</td>
<td>0.81 ± 0.06</td>
<td>-0.19 (-0.23 to -0.15)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ACL Diameter (MRI vs US) (cm) measurements in 10 controls by Radiologist 1</td>
<td>0.84 ± 0.05 vs 0.80 ± 0.06</td>
<td></td>
<td>-0.04 (-0.07 to -0.00)</td>
<td>0.06†</td>
</tr>
<tr>
<td>MRI ACL diameter (MRI vs US) (cm) measurements in 10 controls by Radiologist 2</td>
<td>0.81 ± 0.06 vs 0.79 ± 0.08</td>
<td></td>
<td>-0.19 (-0.06 to -0.03)</td>
<td>0.449†</td>
</tr>
</tbody>
</table>

**Abbreviation:** CI, Confidence interval

*P-value computed using unpaired t test.
† Paired t test

**Table 2:** ACL diameter measurements between Injured and control subjects

Fig. 2: Plot showing mean ACL diameter (cm) in controls and injured cases in relation to body weight (kg).

Fig. 3: Bland Altman Plot: MRI based ACL diameter (cm) measurements in controls by two Radiologists.

Fig. 4: Bland Altman Plot: Ultrasound based ACL diameter (cm) measurements by two Radiologists.

Fig. 5: Bland Altman Plot: Ultrasound based ACL diameter (cm) measurements in injured cases by two Radiologists.

Fig. 6: Bland Altman Plot: Ultrasound based ACL diameter (cm) measurements in controls by two Radiologists.

Conclusion

• Ultrasound is useful in measuring diameter of normal ACL and it can be an ideal screening tool in detecting aspiring athletes at increased risk of ACL injury.
• Smaller ACL diameter predisposes to ACL injury.
• ACL diameter is significantly proportional to body weight and not significantly associated to height, gender, and age.
• Strong agreement between radiologists in measuring ACL diameter in cases and matched controls by ultrasound and by MRI.

Practical implications of study findings

Screening of athletes to identify potential risk factors predisposing to ACL injury has obvious advantages. Our study identifies diameter (size) of ACL as one such important potential risk factor. Subjects with thinner ACL could negate this risk by undertaking special neuromuscular exercises targeted to decrease the knee loading [2, 10, 11]. Improving the strength of the adjacent muscles and making them function as ACL agonists can significantly decrease the biomechanical loading of ACL, thus decreasing the injury risk [4]. Specific exercise routines that induce ACL hypertrophy may be developed for subjects at risk of ACL injury, especially adolescents. Few molecules inducing proliferation of ACL cells have been identified [4]. More such highly effective molecules may be identified.

Why ultrasound of ACL?

MRI is more accurate in assessing ACL size than ultrasound; however, using MRI of knee to screen a large number of aspiring athletes can be extremely expensive and time consuming and can significantly overburden the already strained healthcare resources. It is thus debatable whether performing an MRI of the knee in an aspiring athlete without symptoms is justifiable [5]. Ultrasound is a promising modality that can be used as an excellent screening test to detect subjects especially aspiring athletes prone to ACL injury. Ultrasound can be an ideal screening examination to assess the size of a normal ACL due to its wide availability and short completion time and also due to its economical and nonionizing radiation nature [6-9].

Limitations of study
Major limitations of our study include **ACL diameter as the measured criteria to determine ACL size and evaluation of only tibial aspect of the ACL by ultrasonography.** Since stress in a ligamentous tissue is a product of force divided by cross-sectional area (CSA), minimum CSA would be an excellent measure compared to diameter in assessing ACL size. Measuring cross-sectional area of ACL by ultrasound would require further studies and may be difficult due to inability to clearly separate ACL from adjacent soft tissue. Volume would also be a very good criterion to assess ACL size; however, it is not possible to measure ACL volume by ultrasound. If the ACL is assumed to have a fairly regular and characteristic shape and aspect ratio (CSA/length), the diameter should be an appropriate surrogate measure for CSA [4]. It is possible to examine only the tibial part of ACL by ultrasound and not the whole ACL. Sometimes it may be difficult to distinguish ACL from surrounding tissue on ultrasound. This can be minimized by using dynamic ultrasound. **Utilizing the unaffected ACL from opposite extremity to represent the diameter of the torn ACL, which cannot be measured after injury, is also a limitation of the study.** However, Jamison et al. in 2009 compared the bilateral knee ACL sizes using MRI in healthy subjects and concluded that no remarkable disparity is present between normal unaffected ACLs in the same individual [12], thus demonstrating that the contralateral ACL is a suitable substitute for the torn ACL for diameter or size measurements.

The ACL diameters computed by us are within the range of previously published data (0.83 ± 0.146 cm) [6]. **The ACL injury mechanisms that our study depended on were self-reported. Our study did not take into account the levels of physical activity of the subjects,** which may alter the tensile and other mechanical properties of the ACL [4, 13]. It is possible that professional sportspersons may have stronger and firmer ligaments than recreational sportspersons or nonathletes because of recurrent loading of the ligaments [4]. However, to our knowledge, no published data is available to support this hypothesis [4]. Our study **assumes matching past physical activity level between control and ACL-injured subjects** [10]. Our study also **assumes matching ACL injury risk due to extrinsic and intrinsic factors other than ACL diameter between control and ACL-injured subjects** [4]. In the future, it is possible that the subjects from the control group may also suffer an injury of the ACL [4]. We tried to control this variable to a significant extent by matching the ages of these two groups; however, disparity in the levels of physical activity affecting both past and future likelihood of an ACL injury remains a shortcoming [4].

**Additional research studies** are needed to validate the differences that we observed amongst control and ACL-injured subjects.

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Major parts of this poster presentation are derived from an original research article already **accepted for publication** and having the same title and the same authors [14].

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