Original Article

Quantitative ultrasound densitometry of the calcaneus in acute and chronic anterior cruciate ligament deficiency

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Abstract

Purpose: To evaluate the effect of acute and chronic knee instability secondary to anterior cruciate ligament (ACL) deficiency on the ultrasound-measured density and bone quality of the calcaneus, implementing quantitative ultrasound densitometry. **Methods:** Bilateral measurements of the speed of sound (SOS) and broadband ultrasound attenuation (BUA) of the calcaneus were performed on a cohort of 97 male patients with acute (n=38) or chronic (n=57) unilateral ACL deficiency. **Results:** In the acute ACL tear group, BUA was 56.181±3.731 dB/MHz on the affected extremity calcaneus and 57.030±6.564 dB/MHz on the uninjured side, whilst the SOS was 1577.265±14.04 m/sec and 1584.675±11.484 m/sec respectively. The difference between the two sides was not significant. In the chronic ACL deficiency group, however, there was significant difference between both calcanei for both BUA ($p<0.01$) and SOS ($p<0.001$). BUA was 47.307±3.786 dB/MHz on the affected extremity calcaneus and 59.011±3.64 dB/MHz on the uninjured extremity calcaneus, whilst the SOS was 1457.873±9.467 m/sec and 1579.413±8.404 m/sec respectively. **Conclusion:** Chronic ACL deficiency adversely affects the structural properties and the bone quality of the calcaneus. **Level of evidence:** Level II, prospective comparative study.

Keywords: Anterior Cruciate Ligament Deficiency, Bone Mineral Density, BUA, Calcaneus, SOS, Quantitative Ultrasound

Introduction

Anterior cruciate ligament tear (ACL) is a relatively common yet serious knee injury, and is more prevalent in young, athletic individuals[1]. Traumatic ACL injuries have local and systemic consequences, affecting bone metabolism not only around the knee but also at distant bone locations. Following an ACL injury, sarcopenia gradually occurs in the quadriceps and hamstring muscles[2-5] as well as osteopenia around the knee[6-17] or at distal sites[10,14,18], which can develop quickly in animals and humans. Considerable post-traumatic osteopenia occurs soon after the ACL injury or reconstruction and does not completely recover[5,8,9,16,19-21], or the loss is only partially reversible[10,17].

The loss of knee stability, the altered joint loading environment and knee kinematics, and the osteopenia in the cancellous bone induce loss of anatomical and functional integrity in the tissues in and around the knee joint, eventually leading to loss of function and knee osteoarthritis in animal models and humans[2,19,20-24]. ACL tears are also associated with concomitant menisci tears and cartilage degeneration and can lead to secondary osteoarthritis, regardless of surgical or conservative treatment[23,24].

Following ACL injury or experimental ACL transection, several methods have been employed for the measurement of bone density changes around the knee joint and at distant sites, including quantitative computed tomography (QCT)[21,23], dual energy X-ray absorptiometry (DEXA)[5,9,25], dual-energy photon absorptiometry (DPA),6 and quantitative computed tomography (pQCT)[12,15].

The authors have no conflict of interest.

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ACL deficiency	n	Age (SD) years	Knee Side		Height (SD) cm	Weight (SD) kg	BMI (SD) (kg/m^2)	Time since injury (SD) days	Lysholm Score	Tegner Score
			Left	Right						
Acute	38	22.96 (4.26)	17	21	174.82 (7.35)	71.33 (12.19)	22,72 (3,01)	11.2 (6.1)	100	6.8 1.1
Chronic	59	24.85 (5.53)	26	33	176.71 (9.71)	75.98 (7.55)	23,98 (3,81)	457.63 (129.44)	51 35	4.3 1.2

Table 1. Demographic data of the patients included in the study. Mean values of the various parameters are presented with the standard deviation in brackets. There was no statistical significance between the patients with acute or chronic ACL-deficiency.

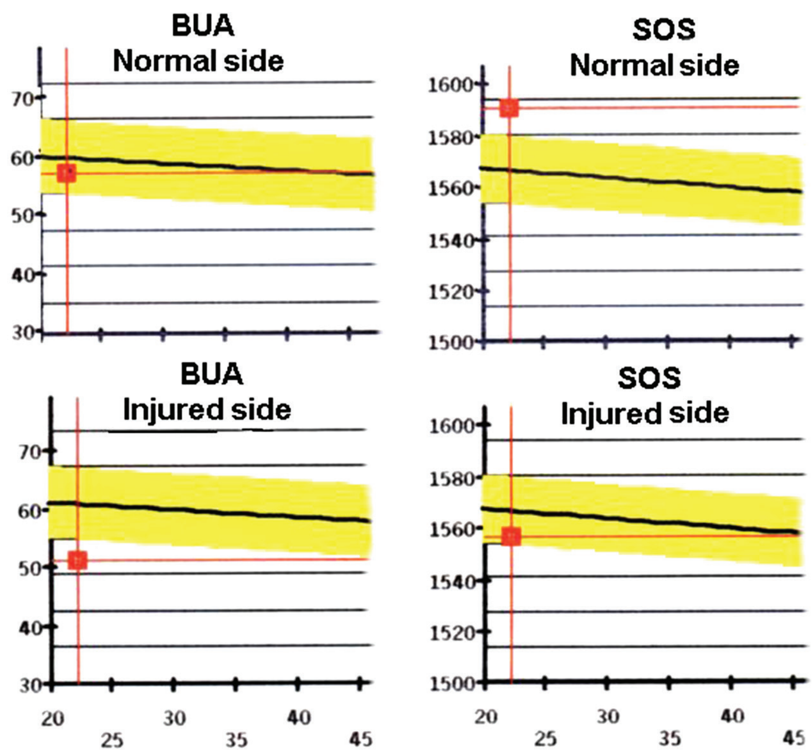

Figure 1. In a 25 year-old patient with chronic unilateral ACL deficiency the values of the QUS parameters, BUA and SOS, are decreased in the injured-side calcaneus compared to the uninjured side.

Calcaneal quantitative ultrasound densitometry (QUS) is a non-invasive, radiation-free method that relies on the interaction of the acoustical ultrasound wave with the material as it travels through the calcaneus bone structure[26,27]. As such, it is a potentially useful evaluation tool for the assessment of osteoporosis[28]. Thus far, however, QUS has not been used to evaluate the bone status of patients with ACL injuries.

The purpose of this paper is to implement QUS to evaluate the calcaneus bone properties in patients with acute and chronic ACL deficiency. The null hypothesis is that that there is no difference in the acoustic properties between both calcanei in both acute and chronic ACL injuries.

Patients - Methods

In this prospective, comparative study, 97 healthy male patients with unilateral acute ACL injury or chronic ACL deficiency were included. The contralateral limb was normal in all patients with no history of injury, immobilization, or operations. Patients with bilateral ACL tears were excluded. The rupture was acute (less than 3 weeks) in 38 patients, and chronic (longer than 12 months) in 59 patients. All patients with chronic ACL injury had symptomatic knee instability and were evaluated prior to ACL reconstruction. The Lysholm and Tegner scores were recorded for all patients, and the study was approved by the Institutional Ethics and Research Board.

ACL deficiency	n	BUA (SD) (db/MHz)			SOS (SD) (m/s)		
		Injured side	Normal side	p	Injured side	Normal side	p
Acute	38	56.181 (3.731)	57.030 (6.564)	n.s	1577.265 (14.04)	1584.675 (11.484)	n.s.
Chronic	59	47.307 (3.786)	59.011 (3.64)	<0.01	1457.873 (9.467)	1579.413 (8.404)	<0.001

Table 2. QUS measurements in the acute and chronic ACL-deficient patients. Mean values of the various parameters are presented with the standard deviation in brackets. BUA, Broadband ultrasound attenuation, SOS, Speed of sound, p, statistical significance, n.s., statistically non significant.

Bilateral calcaneus measurements of two acoustic parameters were performed, i.e., the speed of sound (SOS) in m/sec and broadband ultrasound attenuation (BUA) in dB/MHz using the DTU-one device (Osteometer MediTech, Rodovre, Denmark). The foot was immersed in a water tank with a constant water temperature of 35°C. A pre-determined, standardised area of 60x80 mm on the calcaneus was scanned and, using high definition images (pixel size 0.01 mm^2), the region of interest (ROI) was selected at the area of minimum local ultrasound absorption[29]. The ROI automatically selected by the software was circular with a diameter of 4.8 mm. BUA was calculated from the ultrasound attenuation curve in relation to the frequency of the emitted ultrasounds, ranging between 0.2 and 0.6 MHz. All measurements were performed within a 12-month period by the same technician.

Precision of QUS parameters

The short-term precision of the QUS variables was examined using double measurements obtained in all subjects with re-positioning of the feet as the root mean-square coefficient of variation (RMS-%CV) according to the following formula[27]:

RMS-%CV= $\sqrt{\sum CVi2/n} x\ 100$ (CV: coefficient of variation).

Statistical analysis

Sample size calculation was performed to provide the number of individuals necessary to detect a difference. The power was set to 90% with α=0.05 and β=0.10 and a sample size of k=12 individuals was calculated.

For statistical analyses, SPSS software, version 25.0 (SPSS Inc., Chicago, IL, USA) was employed. Paired and unpaired Student's t-test and Chi square tests were used to compare continuous and dichotomous variables. The level of significance was set at p=0.05.

Results

The short-term precision of QUS variables expressed as RMS-CV% was for BUA and SOS for the right calcaneus 2.97 and 0.25 and, for the left heel, 3.25 and 0.26 respectively.

The demographic data of the patients are presented in Table 1. There was no difference between the groups in age, height, weight, BMI, and side of ACL injury. The rupture was acute in 38 patients (mean age 22.96±4.26 years), and chronic in 59 patients (mean age 24.85±5.53 years). The time since injury was 11.2±6.1 days in the acute injury group, and 457.63±129.44 days in the chronic injury group. The functional performance of the knee in the chronic ACL injury group before ACL reconstruction as expressed by the mean Lysholm score and the Tegner activity scale score in the acute injury group was 100 and 6.8±1.1 respectively, and 51±35 and 4.3±1.2 respectively in the chronic ACL deficiency group. Both Lysholm and Tegner scores were significantly lower in the chronic ACL deficiency group ($p<0.001$ and $p<0.05$ respectively).

In the acute ACL tear group, BUA on the affected extremity calcaneus was 56.181±3.731 dB/MHz and, on the uninjured side, 57.030±6.564 dB/MHz, whilst the SOS was 1577.265±14.04 m/sec and 1584.675±11.484 m/sec respectively. In the chronic ACL deficiency group, BUA on the affected extremity calcaneus was 47.307±3.786 dB/MHz and, on the uninjured extremity, 59.011±3.64 dB/MHz, whilst the SOS was 1503.873±9.467 m/sec and 1579.413±8.404 m/sec respectively (Table 2). In the acute ACL rupture group, no significant difference was noted between the two sides ($p>0.10$), whilst a statistically significant difference was noted for both BUA ($p<0.01$) and SOS ($p<0.001$) in the group of patients with chronic ACL deficiency. No difference was found between the non-affected side in the chronic group and both calcanei in the acute ACL tear group ($p>0.05$). Figure 1 depicts the measurements in a patient with chronic knee instability secondary to a chronic ACL tear.

Discussion

In the present study, it has been shown that chronic, as opposed to acute, ACL deficiency is associated with significant alteration in the QUS properties of the ipsilateral calcaneus compared to the contralateral side. The null hypothesis is therefore rejected in patients with chronic ACL deficiency but not in patients with an acute ACL tear.

ACL tears lead to increased laxity, proprioception deficit, decreased muscle strength, sarcopenia and osteopenia and, eventually, osteoarthritis[2-9,23,24,30]. Weakness and functional deficits may be permanent and persist even after ACL reconstruction[3,31].

Bone Mineral Density (BMD) loss following ACL injury or reconstruction can occur at various sites along the involved lower extremity, as well as the proximal[14] and distal femur[25], the proximal tibia[25], the patella[25], the calcaneus[6,8] or the hip[10,14,18], although the latter finding has not been confirmed by other studies[7,9,19].

Several authors have performed BMD measurements on human patients after ACL injury or reconstruction[5,9,16,18-21]. Early decrease and anatomical heterogeneity of the bone mineral density (BMD) in the ACL deficient knee has been reported both in animals and humans[2,6,8,15,21,22]. Bone loss is primarily to be expected around the knee[7,9,10,16,19,25], and lower BMD may persist even after ACL reconstruction[6,8,11,15,17,18,19]. Periarticular bone mineral loss in ACL-deficient knees tends to be localised[25] and not uniform.

BMD loss has not been reported in all studies. Takata et al.[5] reported significant reduction in the lean mass and bone mineral content (BMC) of the involved lower extremity in a series of patients with unilateral chronic ACL deficiency, as well as a decrease in the isometric and isokinetic muscle strength and an increase in the fat mass, but the BMD was not significantly reduced[5].

Bone loss following ACL injury may be prolonged. In a case study, DEXA was used to determine the effects of one year of strenuous training and subsequent ACL rupture on the BMD of the spine and extremities. Soon after the injury, BMD of the injured extremity declined 20%, one year later the function of the knee recovered but the BMD was still 10% lower than baseline. After 2 further years, it still had not recovered completely[7].

In another study with a 5-year follow up after ACL reconstruction using hamstring tendons, patients of both sexes showed significant bone mineral area (BMA) decrease in both calcanei and both hips[18] despite the increase in their activity levels.

Surgical ACL reconstruction with extended non-weight bearing leads to considerable bone loss in the affected knee[6,9,17]. A study using peripheral quantitative computed tomography (pQCT) in patients with ACL reconstruction showed that, despite recovery of the muscle strength, significant side-to-side differences in BMC were found in the trabecular compartment in the femoral and tibial epiphysis[15]. Another prospective study using pQCT in patients with ACL reconstruction showed significant decrease in the vBMD in the proximal tibia of the operated leg as soon as 3 months after the operation, and the decrease remained below baseline for 12 months after surgery (total -8%, cortical -5%, and trabecular -11%)[12]. In this study, there was no significant vBMD reduction in the non-injured leg.

Evaluation of the calcaneus BMD[6,7,9,11,17-19] or BMA[6,7] using DXA[6,7,9,19] or dual-photon absorptiometry DPA[17] after ACL injury and reconstruction has been reported in various studies. Calcaneus BMD decrease prior to reconstruction of chronic ACL tears was shown in several[6,8] but not always similar studies[7,9,17,19]. In a prospective study of 18 patients who underwent ACL reconstruction, there was no BMD change in the calcaneus or the contralateral leg, although significant BMD reduction in the proximal tibia was noticed[17]. Conversely, in another study[6], ACL reconstruction in a group of patients with chronic instability was followed by 16% and 17% decrease in the BMA of the calcaneus on both the injured and the non-injured side. BMA was lower on the injured side than on the non-injured side[6].

In animal studies, it has been reported that ACL transection leads to the rapid loss of trabecular bone in injured knees compared to uninjured knees, followed by a partial recovery of trabecular bone to a new steady state[20,22,32]. Trabecular bone loss is also observed at distant skeletal sites[33]. Administration of local[34] or systemic[35] bisphosphonate antiresorptive therapy increases the periarticular knee bone density in normal animals and prevents the anticipated trabecular bone loss in animals with ACL transection.

Quantitative ultrasound (QUS) measurements have been introduced as an alternative method for assessing mechanical and architectural properties in bone other than bone density, and is complementary to other absorptiometric techniques. QUS is fast and simple to perform, inexpensive, portable, non-invasive, free of ionising radiation, and is a valid technique in the non-destructive evaluation of the elastic and mechanical properties of bone tissue in vitro in addition to that provided by density measurements[27,36].

BUA derived from the slope of the curve of attenuation plotted against frequency is a measure of the loss of energy, or attenuation, of sound as it passes through bone and reported in decibels per megahertz (dB/MHz). The higher these values, the higher the bone density. BUA is determined not only by bone density, but also by trabecular quality, spacing, and orientation[37]. BUA, therefore, is not a direct measure of bone mass, and cannot be seen as a surrogate measure for BMD. Histomorphometric studies suggest that calcaneal BUA is an indicator of microarchitectural parameters, such as trabecular separation and connectivity[26]. SOS has a quantitative relationship to the stiffness and mass density of bone[29]. In cadaveric biomechanical studies, it has been shown that QUS measures predict in vitro failure loads of the proximal femur as strongly as femoral neck and lumbar spine BMD[38].

The calcaneus is a preferred measurement site for commercial ultrasound devices since it is composed mainly of weight bearing cancellous bone, and its mediolateral surfaces are reasonably flat and parallel and lie immediately under the skin. BMD of the calcaneus shows high correlation with QUS parameters when the site of measurement is matched[27]. Nevertheless, calcaneal QUS is a potentially useful pre-screen tool for osteoporosis despite there being no consensus of device, measurement variable, normal values or cut-off point[28].

Osteopenia following ACL injury or reconstruction could be due to several mechanisms: i) immobilisation and loss of function, ii) reduced activity and bone loading[6,9,17], iii) muscle atrophy, iv) harvesting of autologous tendon grafts with inability of the muscles to exert their action on the bone, v) increased laxity, altered kinematics and gait adaptation, vi) increased local blood flow and bone turnover, especially on the cancellous bone[21], vi) overloading of the un-injured limb, and vii) surgically removed bone from tunnel drilling.

Limitations

The study has several limitations. Only male patients who were ACL deficiency non-copers presenting symptomatic knee instability were included in study because, firstly, there is a greater number of males in our practice and, secondly, to avoid the confounding effect of osteopenia or secondary amenorrhea, which are more commonly found in female athletes. Inclusion of patients with compensated instability would offer the opportunity to compare copers and non-copers. Additionally, the study was a cross-sectional cohort study and not a prospective follow-up study, thus the dynamics of the QUS variables over time could not be described. Ultrasound instruments used for the measurement of bone properties present significant differences in their design, calibration method and analysis software, thus considerable variation exists with no absolute standard for QUS measurement[29]. Another major limitation is that the status of cartilage and menisci, which may effect the development of later osteopenia, was not taken into account, but all chronic patients had symptomatic instability and were evaluated prior to ACL reconstruction. Finally, the lack of similar QUS studies in ACL deficient patients rendered any comparison impossible.

Conclusion

This study has shown that in patients with chronic unilateral knee instability secondary to an ACL tear, reduction in the BUA and SOS is evident on the injured side calcaneus compared with the uninjured contralateral side. QUS may be useful to monitor the impact of the ACL injury on the properties of the calcaneus.

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