Original Article

Greater subchondral vBMD at the tibia is observed between 1 and 5 years of anterior cruciate ligament injury

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Abstract

Objectives: This study aimed to determine if differences exist in tibial subchondral bone and muscle imbalances between individuals with and without an Anterior Cruciate Ligament (ACL) repair within the past 1 to 5 years (median 3 years). **Methods**: Fifteen individuals (ages 18-23 years) that had a unilateral ACL repair with no contralateral knee injuries and 15 age- and sex-matched controls (no prior knee injuries) were recruited to participate. Subchondral bone was measured using peripheral quantitative computed tomography (pQCT) distal to the tibial plateau. Muscle force, power, and force efficiency were measured using single leg jumps performed on a force platform. **Results**: Within subject analysis showed a greater subchondral vBMD in the injured versus uninjured legs of cases (278 ± 11 mg/cm^3 and 258 ± 6 mg/cm^3, respectively, mean±SD, p=0.01). Subchondral vBMD was greater on the injured leg of cases than controls (267 ± 8 mg/cm^3 and 237 ± 8 mg/cm^3, respectively, marginal mean±SE, p=0.01). No differences were observed between cases and controls for muscle force, power, or force efficiency. **Conclusions**: Greater subchondral bone mineral density was observed in participants between 1- and 5-years post-op. Given the results of this study and the known long-term effects of ACL injuries, future research must continue to focus on the prevention of these injuries.

Keywords: ACL, Knee, Osteoarthritis, pQCT, Subchondral

Introduction

Injuries to the lower extremity are the most common injuries experienced by physically active individuals with the most common being hip, knee and ankle osteoarthritis, ankle sprains, chronic joint instability, and structural injuries to the knee[1-4]. Anterior cruciate ligament (ACL) injuries are of particular interest because of their relatively high prevalence the potential long term negative consequences of these injuries. One of these consequences is the increased risk of osteoarthritis (OA) as illustrated by a previous study showing that 41 percent of athletes who suffered an ACL injury had a clinically diagnosed case of OA at 14 years follow-up while only 4 percent of uninjured knees had an OA diagnosis[5]. Another study reported that between 12 and 14 years follow-up, knees with a history of ACL injury made up 57 percent of OA cases while only 18 percent of cases were in a patients non-injured leg[6]. Furthermore, a recent meta-analysis reported a relative risk of 3.6 for developing OA after an ACL reconstruction[7]. These data are particularly troubling given that approximately 100,000 ACL injuries occur in the United States each year with the number of ACL reconstruction performed in the United States range from 100,000 to 300,000 operations annually with a total annual monetary cost of over 600 million dollars[8-11].

Subchondral bone, which lies directly beneath the articular cartilage of the knee is an area that may be affected by injury to the ACL and has also shown to be different in persons with OA. A previous investigation using peripheral quantitative computed tomography (pQCT) to measure subchondral bone revealed differences in the subchondral bone of individuals with an without OA[12]. Another study utilizing pQCT reported greater vBMD in the daughters and grandchildren of individuals with OA compared with controls[13]. The results of this study are consistent with previous findings that

Table 1. Participant characteristics by cases and controls.

	Cases	Controls	p-value
[1]Age (years)	20 [19-23]	20 [18-23]	0.936*
Height (cm)	172.0±6.0	172.5±10.5	0.858*
Weight (kg)	73.9±15.5	72.2±14.4	0.754*
BMI (kg/m^2)	24.8±3.8	24.1±3.8	0.632*
Gender (% female)	79	86	0.622[#]
[1]Time Since Surgery (years)	3 [1-5]	NA	NA
Meniscus Injuries (%)	27	0	NA
Graft Type (% autograft)	93	NA	NA
[1]Age and time since surgery are given as median [range]. *p-value from Student's t-test. #p-value from Pearson chi^2.			

areal bone density (aBMD) of the femoral neck and lumbar spine is greater in individuals with hip or knee arthroplasty resulting from OA and similar findings were reported in the offspring of these individuals[14]. These relationships may be partially explained by biomechanical modeling studies that have identified subchondral aBMD at the knee as a significant predictor of theoretical loads generated at the knee in children[15]. Increased loads at the knee may lead to microdamage of the articular cartilage which may result in the development of osteoarthritis later in life.

Injuries to the anterior cruciate ligament are highly prevalent in physically active, athletic, and military populations. The deleterious long-term consequences of these injuries is well documented but not well understood. The present study had two specific aims: 1) To determine whether changes in subchondral bone are observed following injury and subsequent repair of the ACL. 2) To determine if graft type or muscle function affect any changes that are occurring. We hypothesized that subchondral vBMD would be greater in participants with a history of ACL injury and that this difference would be isolated to the affected knee.

Materials and Methods

Participants

Participant characteristics are given in Table 1. Fifteen college-aged participants with a history of an acute ACL tear and subsequent reconstruction performed greater than 1 year prior and less than 5 years prior to testing were recruited to participate in this study. Additionally, 15 age- and sex-matched controls with no prior history of knee injuries were recruited. The original study was approved by the South Dakota State University Human Subjects Committee and written informed consent was obtained from all participants prior to the collection of any data.

Questionnaires and Medical Records

General health history questionnaires, in addition to orthopedic questionnaires were administrated during the one-hour study visit. These questionnaires were used to determine whether a participant had any additional health factors that could have potentially affected subchondral bone. Each participant signed a release of medical records form for the individual facility that performed their surgery to confirm the presence of an ACL tear and determine if any other underlying injuries such as an articular cartilage injury were present that could affect the study outcomes.

Anthropometrics

Height without shoes was measured using a portable stadiometer (Seca, Chino, CA). Height was measured in duplicate and if the measurements differed by more than 0.5 cm the measurements were repeated. Weight with light clothing was measured in duplicate on a digital scale (Seca, Model 770). Measurements were made to the nearest 0.5 cm for height and the nearest 0.1 kg for weight.

Mechanography

Ground reaction force and movement efficiency was measured using a Leonoardo Mechanograph (NovoTec Medical, Carmel, CA). The first test consisted of the participant standing on the force platform and performing a two-legged countermovement jump. This was repeated three times and the highest measurement from the three jumps was used. Additionally, each participant performed a maximal one-legged jump. This test was performed bilaterally with the participant repeating the test three times per leg. The results from these tests were used as a measurement of muscle function and were used as an outcome variable to determine if muscle function and side-to-side leg differences are similar or not between participants with and without a history of ACL injuries.

Subchondral vBMD

Subchondral vBMD was measured by pQCT using an XCT 3000 (Stratec, Pforzheim, Germany) with XCT 6.0 B software (Stratec, Pforzheim, Germany). A scout scan of the
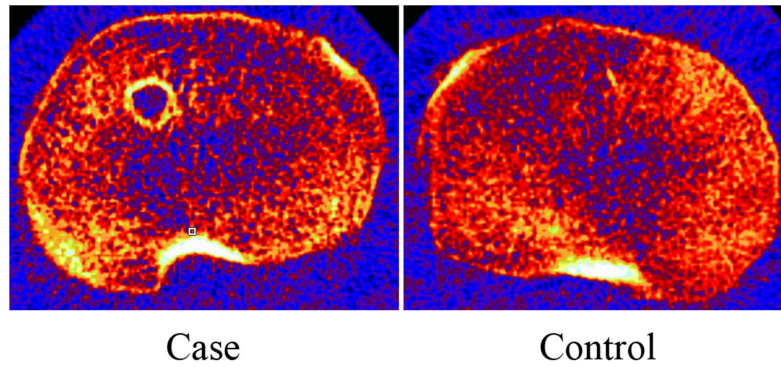
Figure 1. Sample pQCT images obtained from a case participant within the study sample. These are sample images to illustrate how data was collected and are not used for comparison purposes.

Table 2. Subchondral bone and mechanography measurements between cases and controls.

	Case	Control	p-value
pQCT Measurements			
Bone Mineral Content (mg)[1]	777.0±22.5	711.4±23.3	0.05
Subchondral vBMD (mg/cm^3)[1]	267.3±7.7	236.6±7.9	0.01
Periosteal Circumference (mm)[1]	190.4±1.9	193.9±2.0	0.2
Mechanography Measurements[3]			
Jump Force (N/kg)[2]	23.2±0.6	21.8±0.6	0.09
Jump Power (W/kg)[2]	46.9±1.6	45.0±1.7	0.4
Force Effeciency (%)[2]	105.0±3.5	103.1±3.4	0.7
p-values are from linear contrasts of marginal means. [1]Data are marginal means±SE adjusted for height, weight, and sex. [2]Data are marginal means±SE adjusted for sex. [3]Data are from the 2-legged counter-movement jump.			

tibiofemoral joint was performed, after which a reference line was placed on the proximal medial and proximal lateral tibial plateaus. An image was then taken at 2mm distal to the reference line representing a location immediately beneath the cortical shell of the tibial plateau. Scan settings included a voxel size of 0.5 mm and a scan speed 30 mm/s. Analysis settings were as follows: contour mode set to 2, peel mode set to 2, trabecular bone threshold was set to 400 mg/cm^3 and cortical bone threshold was set to 710 mg/cm^3. All measurements were taken by a single technician who has completed a reliability study yielding a percent CV less than one percent for vBMD between scans. Sample images are shown in Figure 1.

Statistical Analysis

Participant characteristics were compared between cases and controls using a student's t-test for continuous variables and a Pearson's Chi^2 test for categorical variables. Within subject analysis of BMC, subchondral vBMD, periosteal circumference, jump force, relative jump power, and force efficiency was performed using paired t-tests to compare outcome variables between the injured and uninjured legs of cases and left and right legs of controls. Ordinary least squares regression was used to determine the effect of ACL injury (cases vs controls) on dependent variables while adjusting for covariates. Dependent variables included BMC, subchondral vBMD, periosteal circumference, jump force, relative jump power, and force efficiency. Independent variables for vBMD models included group, time since surgery, and jump force and covariates included height, weight, and sex. For models testing jump force, jump power, and force efficiency, time since surgery was tested as an independent variable and sex was included as a covariate. For each model, marginal means for cases and controls were calculated from regression models and compared using linear contrasts. Data were analyzed using Stata version 17 (StataCorp. 2021. *Stata Statistical Software: Release 17*. College Station, TX: StataCorp LP).

Results

Subchondral Bone Measurements

Within subject analysis showed a greater subchondral vBMD in the injured compared to the uninjured legs of participants with a history of ACL injury (278±11 mg/cm^3 and 258±6 mg/cm^3, respectively, p=0.01). BMC was not different between the injured and uninjured legs of cases (780±45 mg and 768±34 mg, respectively, p=0.8) nor was periosteal circumference (190±3 mm and 189±3 mm, respectively, p=0.9). The within subject differences in vBMD observed in the participants with a history of ACL injury were not observed in the control group (238±9 mg/cm^3 and 230±10 mg/cm^3, p=0.4). Similarly, BMC was not different between legs of controls (708±39 mg and 722±38 mg, p=0.8) nor was periosteal circumference (194±4 mm and 197±5 mm, p=0.7).

Analysis comparing cases and controls showed subchondral vBMD and BMC of the injured leg was greater in cases verses controls with no difference in periosteal circumference observed (Table 2). In comparison, subchondral vBMD of the uninjured leg was not different between cases and controls (258±6 mg/cm^3 and 230±10 mg/cm^3, respectively, p=0.21) nor was BMC different between cases and controls (766±20 mg and 724±22 mg, respectively, p=0.17). Periosteal circumference was not different between cases and controls in the uninjured leg (190±2 mm and 197±2 mm, respectively, p=0.07).

Mechanography

Jump force relative to body weight showed no significant difference between injured and uninjured legs in cases (18.4±1.9 and 18.1±2.1 N/kg, respectively, p=0.3) or between legs (18.6±2.4 and 18.9±2.2 N/kg, respectively, p=0.5) in the control group. Relative jump power also showed no significant difference between injured and uninjured legs in cases (29.6±9.4 and 27.6±6.2 W/kg, respectively, p=02.) or between legs (27.8±5.9 and 27.8±6.3 W/kg, respectively, p=0.9 in the control group. No differences in force efficiency were observed between legs injured and uninjured legs in cases (80.4±17.0 and 74.4±9.3%, respectively, p=0.1) or between legs in controls (76.9±9.7 and 78.7±13.8%, respectively, p=0.5). Double legged relative jump force, relative jump power, and force efficiency also showed no significant difference between case and control groups (Table 2).

Additional statistical analysis showed that time since surgery was not a significant predictor of any outcomes. Neither jump force, power or efficiency predicted any differences or changes in subchondral bone. Fourteen out of fifteen subjects utilized an autograft for their reconstruction. The impact of graft-type on subchondral bone was unable to be investigated over the course of this study.

Discussion

The purpose of this present study was to determine whether ACL rupture and reconstruction would lead to any significant difference in subchondral bone density, BMC or periosteal circumference in a repaired knee within 1 to 5 years post-surgical repair. We hypothesized that significantly greater subchondral bone mineral density would be seen in cases compared to controls within 1-5 years following the ACL injury and reconstruction.

The current literature[16-19] provides an array of controversial findings when examining changes to bone mineral density following ACL rupture and subsequent repair. A matched case-control study by Zerahn et al. reported significantly reductions bone mineral density and Z-scores in the proximal tibia of the operated leg during the first year following surgery[16]. Z-Score and bone mineral density values did return to baseline values in the operated knee in all regions of interest (ROIs) except the lateral side of the proximal tibia, which still showed a decrease in BMD 24 months post operation[16]. These findings led Zerahn to conclude that a decline in BMD after ACL reconstruction may be associated with the surgical intervention[16]. Similarly, A 2013 study by van Meer et al. evaluated 90 subjects who underwent ACL reconstruction, utilizing DXA scans to assess the subchondral vBMD of the tibia. After evaluating subjects at baseline, 1- and 2-years post-surgery, and using a linear regression analyses, van Meer et al. concluded that vBMD was significantly lower at the 1-year follow up in all ROIs of the tibia when compared to baseline values[17]. At the 2-year follow-up, vBMD had significantly increased but had not yet recover to baseline levels[17]. When compared to the contralateral knee all vBMD findings, in all ROIs of the tibia in the injured knee, were significantly lower (P value <0.008) at all time points[17]. Additionally, Mundermann et al. utilized pQCT and performed a 1 year follow up on ACL-reconstructed knees[18]. They found that by 3 months post-operation vBMD had significantly decreased from baseline values and remained reduced until 12 months following ACL Surgery[18]. With the majority of studies only evaluating 1-2 year post-surgery, Kroker et al. explored the vBMD of subject who were 5-years post ACL reconstruction. In that study, little variability in tibial, subchondral vBMD between ACLR and contralateral knees was observed, with only the medial tibial compartment showing a slight significant increase (p=0.016). Conversely, the results of the present study demonstrated that subchondral bone density significantly greater in cases compared to control groups (p=0.01). One explanation for the greater vBMD observed in the present study when comparing the earlier studies that showed a decrease in BMD following ACL reconstruction could be the time since surgery. The previously mentioned study by van Meer et al. showed that by 2 years follow-up vBMD was increasing but not yet to baseline. The present study had a median follow-up period of 3 years, and this longer time-

period may explain the differences. It may be possible that an early decrease in vBMD following surgery is followed by an increase as the time since surgery grows longer. The specific mechanisms causing these density changes are complex and are still being intensely evaluated by the current literature.

Additionally, we hypothesized that differences in muscle function between the operated and contralateral limbs of subjects may exist 1-5 years post-surgery. Such a hypothesis was based on the current literature[20-25], which indicates that subjects could see quadriceps strength and functional deficits as far out as 28 months post ACLR. Curran et al. found that when looking at 20 patients (12 female, 8 male, age=21.40±5.60 years) who returned to sport activity 6-months post ACLR, strength and biomechanical values were less than 80% symmetrical[21]. A similar study by Kobayashi et al. found similar results, noting that quadriceps strength could take up to 24 months to achieve the 90% symmetry with the uninvolved limbs[25]. Additional studies have reported lower force production and lower performance on functional assessments in observed at 18 months post-surgery[23,24]. While the results of the current study did not show any strength differences between the subjects involved, contralateral or control limbs, it's important to note that isokinetic testing was not performed in the present study, and all jump force and power measurements were gathered between 1 and 5 years (median 3 years) post-ACLR which is beyond what was observed in the previous studies and may explain the differences in the results.

Limitations

The present study had a very small sample size, making these results difficult to generalize. Future studies could build upon these results by looking to increase study recruitment and participation. Further limitations include the lack of available pre-injury data for the case group. Additionally, no baseline vBMD values were able to be obtained from case-patient's immediately following surgery. Future studies should look to investigate the reported decrease in vBMD 1 to 2 years following ACLR. These decreases have been reported in many, well-designed research studies and further investigation should be done to assess whether these vBMD decreases rebound into the increases seen in this current study. During this literature search it was clear that there is a limited number of research studies investigating subchondral bone density and quadriceps strength 5-10 years post-ACLR. Further evidence investigating the effects of ACL rupture and repair on bone mineral density 5-10 years post-surgical intervention is critical to OA research and prevention.

Additional limitations to this study include the possibility for control subjects to have experienced previous knee trauma that was not reported in pre-study participation screening. A small number of self-reported meniscus tears were also disclosed by case subjects. During this study we were not able to investigate the effect of graft type on any changes to subchondral bone density. While investigating changes in force and power production, this present study

only used a Leonardo Mechanograph to assess ground reaction forces and movement efficiency. Future studies should look at including isokinetic strength values as these measurements are the gold-standard. EMG could be included in future studies to provide an additional variable for analysis. Lastly, join alignment and stability were not measured in either control or case groups and is a value that could be included in future research.

Conclusion

This study aimed to determine whether ACL rupture and reconstruction would lead to any significant changes in subchondral bone density, in a surgically repaired knee, within 1-5 years post intervention. The results of this study did confirm the established hypothesis that case subjects would demonstrate greater subchondral bone density when compared to control subjects and uninjured limbs. Based on the results of this present study, we conclude that significant differences in subchondral bone density can be observed 1-5 years following ACLR, in the patient's reconstructed knees. These findings confirm suspicions that the rupturing force of the ACL injury, the surgical repair intervention, and the recovery process could also contribute to changes in subchondral bone density and the risk of OA. While these results were found to be significant, further research should be conducted to substantiate these findings.

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