HHS Public Access

Author manuscript

Am J Sports Med. Author manuscript; available in PMC 2023 July 01.

Published in final edited form as:

Am J Sports Med. 2022 July ; 50(9): 2410–2416. doi:10.1177/03635465221099456.

Changes in Bone Mineral Density of the Femur and Tibia Before Injury to 2 Years After Anterior Cruciate Ligament Reconstruction in Division I Collegiate Athletes

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Abstract

Background: Osteoarthritis (OA) is a significant long-term concern following anterior cruciate ligament reconstruction (ACLR). Low bone mineral density (BMD), particularly of the subchondral region, has been associated with the development of OA and is evident at the knee in individuals long after ACLR. It is unknown if persistent BMD deficits are present in high-level collegiate athletes.

Hypothesis/Purpose: Evaluate bilateral changes in BMD of the femur and tibia from preinjury to 24 months post-ACLR in collegiate athletes. We hypothesized that BMD of both the distal femur and proximal tibia would be significantly reduced within the surgical limb initially post-operatively, but return to preinjury levels by 24 months post-ACLR.

Study Design: Analysis of routinely collected athletic performance data; Level of Evidence, 3.

Methods: Thirty-three Division I collegiate athletes were identified between 2010 and 2021 (13 female) who had total body dual-energy x-ray absorptiometry (DXA) scans acquired prior to sustaining an ACL injury. DXA scans were repeated at 6, 12, and 24 months (6M, 12M, 24M) post-ACLR. Linear mixed effects models assessed differences in BMD of 5%, 15%, and 50% of femur length (F_5, F_{15}, F_{50}) and 5%, 15%, and 50% of tibia length (T_5, T_{15}, T_{50}) between post-ACLR time-points and preinjury within each limb, reported as Tukey-adjusted p-values.

Results: Compared to preinjury, BMD at F_5 of the surgical limb was reduced 0.15 (0.02) g/cm^2 at 6M (p-value < 0.001). BMD at F_{15} of the surgical limb was reduced 0.06 (0.01), 0.09 (0.01), 0.09 (0.01) g/cm^2 at 6M, 12M, and 24M, respectively (all p-values < 0.001). BMD at T_5 of the non-surgical limb was reduced 0.07 (0.02) g/cm^2 at 12M (p-value = 0.02) and 0.10 (0.02) g/cm^2 at

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24M (p-value = 0.001). BMD at T_{15} of the surgical limb was reduced 0.07 (0.01) g/cm^2 at 6M and 0.08 (0.02) g/cm^2 at 12M (p-values < 0.001).

Conclusion: BMD deficits of the surgical limb F_{15} region persisted out to 24M (−7.1%) post-ACLR compared to preinjury in collegiate athletes. The surgical limb F_5 and T_{15} regions BMD were reduced at 6M and 12M, but not at 24M compared to preinjury levels. For the non-surgical limb, no significant differences were detected except for the T_5 region at 12M (−5.1%) and 24M (−7.2%). The BMD at the F_{50} and T_{50} regions of both limbs were not significantly different than preinjury levels at any time post-ACLR.

Clinical Relevance: Following ACLR, long-term deficits in femoral BMD may be related to the early onset and progression of OA and should be further explored.

Keywords

ACL; Imaging; Bone; Knee

Introduction

Poor long-term health outcomes are a significant concern following anterior cruciate ligament reconstruction (ACLR). Individuals who have suffered an anterior cruciate ligament (ACL) injury are more likely to demonstrate decreased quality of life,[12] increased body mass index,[47] increased prevalence[4,5,39] and earlier onset of osteoarthritis (OA),[18] and higher rates of future orthopedic surgeries.[48] Up to 50-90% of individuals following ACLR demonstrate signs of OA later in life compared to 12% in the general population,[15,29,46] and the prevalence of total knee arthroplasty (TKA) is increased, especially at younger ages.[1,35,40] Reduced subchondral bone mineral density (BMD), particularly surrounding the knee, has been associated with the development of OA in the general population.[3] Therefore, bone loss following ACLR may be an important metric to consider as a precursor to the development of OA in these individuals.[4,5,39] Moreover, it is plausible that such bone loss increases periprosthetic fracture risk following TKA.[23]

Lower extremity BMD deficits have been observed in both the short- (less than 1 year)[10,26,30,34] and long-term (10-11 years) following ACLR.[21] One systematic review of 10 studies found significant BMD deficits at the proximal tibia, distal femur, patella, proximal femur or hip region, and calcaneus of the involved limb following ACLR.[36] More recently, longitudinal studies found significant reductions in BMD compared to pre-surgery at the distal femur and proximal tibia, which persisted 2 years post-operative.[33,34] Despite being large longitudinal studies, the populations varied in physical activity levels and the findings may not generalize to high-level athletes.

To date, no studies have investigated changes in BMD following ACLR in collegiate athletes. Collegiate athletes are consistently exposed to high levels of physical activity year round, providing an excellent stimulus for bone development. In fact, healthy collegiate athletes exhibit BMD levels significantly higher than the general population norms.[41] It has been postulated that reduced physical activity and bone loading following ACLR may, in part, lead to the observed reductions in BMD.[21] Athletes who undergo ACLR and return to collegiate athletics are typically exposed to the same training frequency and magnitudes that they were prior to injury, which in turn, should help to restore lower extremity BMD levels post-operatively.

Therefore, the purpose of this study was to evaluate bilateral changes in BMD of the distal femur and proximal tibia from preinjury to 24 months post-ACLR in collegiate athletes. We hypothesized that BMD of both the distal femur and proximal tibia would be significantly reduced within the surgical limb compared to preinjury values throughout the first year post-ACLR, but would be restored to preinjury levels by 24 months. Additionally, we hypothesized that no differences would be detected within the non-surgical limb at any time point following ACLR.

Methods

Participants

Performance and healthcare data from NCAA Division I collegiate athletes over ten years (2010-2021) were obtained via records review from the University of Wisconsin-Madison Badger Athletic Performance database. The University's Health Sciences Institutional Review Board approved this records review of routinely, prospectively collected data. To be included, athletes must have met all of the following criteria: 1) underwent an ACLR during the study period; 2) had no history of prior ACL injury; 3) had both a healthy, preinjury dual-energy x-ray absorptiometry (DXA) scan and at least one post-operative DXA scan near the time points of interest (6, 12, and 24 months post-ACLR); 4) had no lower extremity surgeries 12 months prior to the preinjury DXA scan; and 5) had no internal hardware beyond common ACLR fixation hardware. For athletes that sustained a second ACL injury, only scans prior to the second injury were included in this analysis. Although post-operative rehabilitation was not standardized, the majority of athletes completed rehabilitation at the same facility under similar post-operative rehabilitation protocols.

Data Collection

As part of the University Athletics' standard performance testing protocol, DXA scans were acquired each pre-season on all collegiate athletes. For athletes following ACLR, a standard post-operative testing protocol was followed in which total body DXA scans were obtained at 6, 12, and 24 months following surgery. All BMD measures were obtained from whole-body DXA scans using a GE Healthcare Lunar iDXA densitometer and analyzed using enCORE software V.14.1 (Madison, WI, USA). International Society for Clinical Densitometry (ISCD)–certified technologists obtained and analyzed all total body scans, using standard clinical operating procedures.[27,38] A physician with expertise in BMD assessments and extensive total body DXA experience reviewed all scans to validate correct acquisition and analysis.[27]

Data Analysis

Lower extremity BMDs were acquired using custom 2 cm tall regions of interest (ROIs) spanning the entire width of the respective lower extremity. ROIs were placed at 5%, 15%, and 50% of femur (F_5, F_{15}, F_{50}) and tibia (T_5, T_{15}, T_{50}) length measured from the knee joint (Figure 1). Femur length was defined as the distance from the most superior aspect of the greater trochanter to the center of the intercondylar notch. Tibia length was defined as the distance from the most superior aspect of the intercondylar eminence to the most distal aspect of the medial malleolus. Manual analysis of the DXA scans were performed by four individuals, all of whom were trained using the same standardized protocol and demonstrated excellent inter-rater reliability (Intraclass correlation coefficients = 0.97 to 0.99, Supplemental Table 1). BMD values (g/cm^2) were recorded for each ROI for both the surgical and non-surgical limb at each time point of interest (preinjury, 6, 12, and 24 months), and subsequently used in the statistical analyses.

Statistical Methods

Standard descriptive statistics (mean and standard deviation [SD] for continuous variables, frequency and percentage for categorical variables) were used to describe the study sample. Linear mixed effects models were constructed to assess the influence of time post-operatively, limb, and a time-limb interaction effect on each BMD ROI. Athlete and limb were assigned as random effects to account for the correlation among repeated time points and limbs. Meaningful pairwise interactions between preinjury and postoperative time points for the surgical and nonsurgical limbs were assessed. Least-square mean differences and their associated standard errors were reported alongside Tukey-adjusted p-values to account for multiple comparisons. Analyses were conducted using the R Statistical language (version 4.0.5; R Core Team, 2021).

Results

Following the records extraction process, 33 athletes were identified for inclusion in the final dataset (Figure 2), with 33, 31, 28, and 16 DXA scans included at preinjury, 6 months, 12 months, and 24 months, respectively. Athlete demographics, including: age, sex, anthropometrics, graft type, concomitant procedures, and sport are reported in Table 1.

Femur

A significant time-limb interaction was detected for BMD at F_5 and F_{15} (both p-values < 0.001), but not for BMD at F_{50} (p-value = 0.72). Fixed effect estimates from each linear mixed effect model can be found in Supplemental Table 2. Compared to preinjury, BMD at F_5 of the surgical limb was reduced 0.15 (0.02) g/cm^2 at 6-months (p-value < 0.001, Figure 3, Table 2). Compared to preinjury, BMD at F_{15} of the surgical limb was reduced 0.06 (0.01), 0.09 (0.01), 0.09 (0.01) g/cm^2 at 6, 12, and 24-months, respectively (all p-values < 0.001, Figure 3, Table 2). A significant main effect of time was observed for F_{50} (p = 0.02), but this was not significant for a specific time point compared to preinjury (p = 0.08 at 24-months).

Tibia

A significant time-limb interaction was detected for BMD at T_5 and T_{15} (both p-values < 0.001), but not for BMD at T_{50} (p-value = 0.69). Fixed effect estimates from each tibia linear mixed effect model can be found in Supplemental Table 3. Compared to preinjury, BMD at T_5 of the non-surgical limb was reduced 0.07 (0.02) g/cm^2 at 12-months (p-value =

0.02) and 0.10 (0.02) g/cm^2 at 24-months (p-value = 0.001, Figure 3, Table 2). Compared to preinjury, BMD at T_{15} of the surgical limb was reduced 0.07 (0.01) g/cm^2 at 6-months and 0.08 (0.02) g/cm^2 at 12-months (p-values < 0.001, Figure 3, Table 2).

Discussion

This study aimed to characterize changes in lower extremity BMD from preinjury to 24 months following ACLR in division I collegiate athletes. Contrary to our primary hypothesis, the F_{15} ROI demonstrated a significant reduction in BMD from the preinjury state that persisted to 24 months (−7.1%). However, the F_5 and T_{15} ROIs of the surgical limb changed as hypothesized, demonstrating significantly reduced BMD at 6 and 12 months post-ACLR, which was no longer statistically different at 24 months compared to preinjury levels. Additionally, the T_5 ROI did not significantly change from preinjury levels in the surgical limb at any time point. Contrary to our secondary hypothesis, a significant decrease in BMD was observed at the T_5 ROI of the non-surgical limb (−7.2%). No other changes in the non-surgical limb were observed.

Interestingly, BMD deficits in the surgical limb were present in the distal femur (both F_5 and F_{15}) and the proximal tibia (T_{15}), but not in the mid shaft regions (F_{50} and T_{50}) or most proximal tibia region (T_5). This may be partially explained by the fact that the distal femur and proximal tibia regions contain greater levels of trabecular bone, which experiences a higher rate of bone turnover.[6] Recovery of local BMD takes roughly 4 times longer than the period of disuse based on animal models.[2,43] Additionally, to maintain bone density, weight-bearing bones require a stimulus that exceeds the bones' strain thresholds which in turn produces an osteogenic response. The strain threshold appears to be site-specific, varying between bones and location within a given bone.[13,16] Strain thresholds tend to be greatest in regions with the greatest mechanical stimuli.[16] In weight-bearing bones strain threshold and disuse-related bone loss tend to be greatest distally, where locomotor forces tend to be highest.[9,13,16] Therefore, differences in BMD observed across sites could be due, in part, to altered movement mechanics such as reduced knee flexion angles and extensor moments during walking,[8,11,44] running,[22,37] jumping,[24,25] and change of direction tasks,[31] as well as reduced quadriceps strength.[28] Site specific loss in BMD is multifactorial, likely being influenced by the initial injury, subsequent surgical procedure, local inflammation, period of immobilization, and disuse of the involved lower extremity.[14,17,20,26,33] The combination of reduced lower extremity loading, altered movement mechanics, and quadriceps dysfunction following ACLR likely has an impact on bone health, as bone is particularly responsive to changes in loading.[6,13]

Unexpectedly, a significant decrease in the non-surgical proximal tibia BMD ROI (T_5) was observed and persisted to 24 months post-ACLR. We have no explanation for this observation. Previous literature provides conflicting evidence regarding the impact ACLR has on BMD of the non-surgical tibia.[26,33,49] Van Meer et al. observed a slight (3%) but significant reduction in BMD of the proximal tibia of the uninjured limb in 141 patients from three hospitals in the Netherlands that persisted to 24 months after ACL injury.[33] We observed a larger (7.2%) reduction in the proximal tibia BMD of the non-surgical limb at 24 months. This discrepancy may be due to difference in the population, sample size, scan acquisition methods, surgical and rehabilitation management, reduction in physical activity post-operatively, or it may simply be an incidental finding. As this study is more exploratory in nature, future studies aimed at exploring BMD changes in the non-surgical limb are needed to confirm these findings.

This is the first study to our knowledge that highlights changes in lower extremity BMD of elite collegiate athletes following ACLR compared to the preinjury state. Prior literature has consisted of more heterogeneous samples with varying ages and levels of sports participation.[33,34,36] The cohort in this study received frequent and unrestricted access to sports medicine facilities and rehabilitation. Most athletes (85%) in this cohort returned to sport. As such, this creates a homogenous group with significant exposure to both high frequency and magnitudes of loading as part of training and competition. Despite this environment for recovery following ACLR, athletes demonstrated significant reductions in BMD out to 24 months, over a year beyond when most returned to sport.

These persistent deficits in BMD observed are concerning. BMD loss early in life may predispose athletes to future bone and joint pathology such as OA and fracture. OA is a well-known long-term risk following ACLR, which can progress to the need for TKA. Individuals with a history of ACLR are at a greater risk of undergoing TKA compared to the general population and at an earlier age.[1,35] As the long-term risk for OA is high in individuals who have undergone ACLR, restoring BMD may be an important factor to consider. Moreover, reduced BMD has been associated with increased risk of fracture,[19,32] and cases of distal femur fractures following ACLR have been reported.[7,42,45] If the reduced BMD observed persists later in life, surgical complications such as periprosthetic fractures may be a significant concern in those with a history of ACLR, which has been reported in a male that was 8 years post-TKA and 25 years post-ACLR.[23]

Our findings are limited by the specific nature of DXA, which provides a 2-D assessment of bone. DXA scans measure summative bone mass in a given area, and cannot differentiate between trabecular and cortical bone. BMD values for this study were acquired using full body DXA scans, which may not provide as precise estimates of local BMD as site-specific scans; however, to the authors' knowledge, there is no published literature comparing full body to site specific scans at the knee. Moreover, we were unable to isolate only the tibia in the ROIs of the lower shank. As such, the tibia ROIs represent a cumulative BMD across both the tibia and the fibula. Similarly, the patella overlies the distal femur, providing a cumulative value for the two bones in the involved ROIs. A section of the patella falls within the F_5 ROI, but does not extend into the F_{15} ROI. Interestingly, the F_5 ROI had a significant drop in BMD at 6 months but restored to preinjury levels by 24 months post-ACLR. A portion of the patella is harvested for the bone-patellar tendon-bone (BPTB) graft during ACLR (91% of the sample). Therefore, the initial deficits and subsequent recovery in BMD at the F_5 ROI may be related to the defect left from harvesting the graft and reconstitution of this defect, respectively. As the patella is a non-weight bearing joint, is disrupted when harvesting a BPTB graft, and receives its mechanical loading primarily from the quadriceps, it may be an important bone to isolate in future studies as quadriceps dysfunction is the norm following ACLR.[28] Additionally, as most athletes included in this study underwent ACLR with a BPTB graft, findings may not generalize to other graft types. It is important to note that athletes activity levels were not controlled for and not all athletes underwent testing at every time point. Due to fewer collections at 24-months, a lack of significant difference from preinjury may not reflect true recovery of BMD, but may be due to reduced statistical power at that time. Linear mixed effects models were used to account for missing data. Further, findings did not change when only athletes with 24-month collections were included in the analysis.

In conclusion, NCAA Division I collegiate athletes demonstrated focal BMD deficits to the distal femur (F_{15}) of the surgical limb that persisted to 24 months following ACLR compared to preinjury scans. Deficits in BMD were also observed in the proximal tibia (T_5) of the non-surgical limb. All other regions of both the surgical and non-surgical limb remained at preinjury levels or returned to preinjury levels by 24 months post-ACLR.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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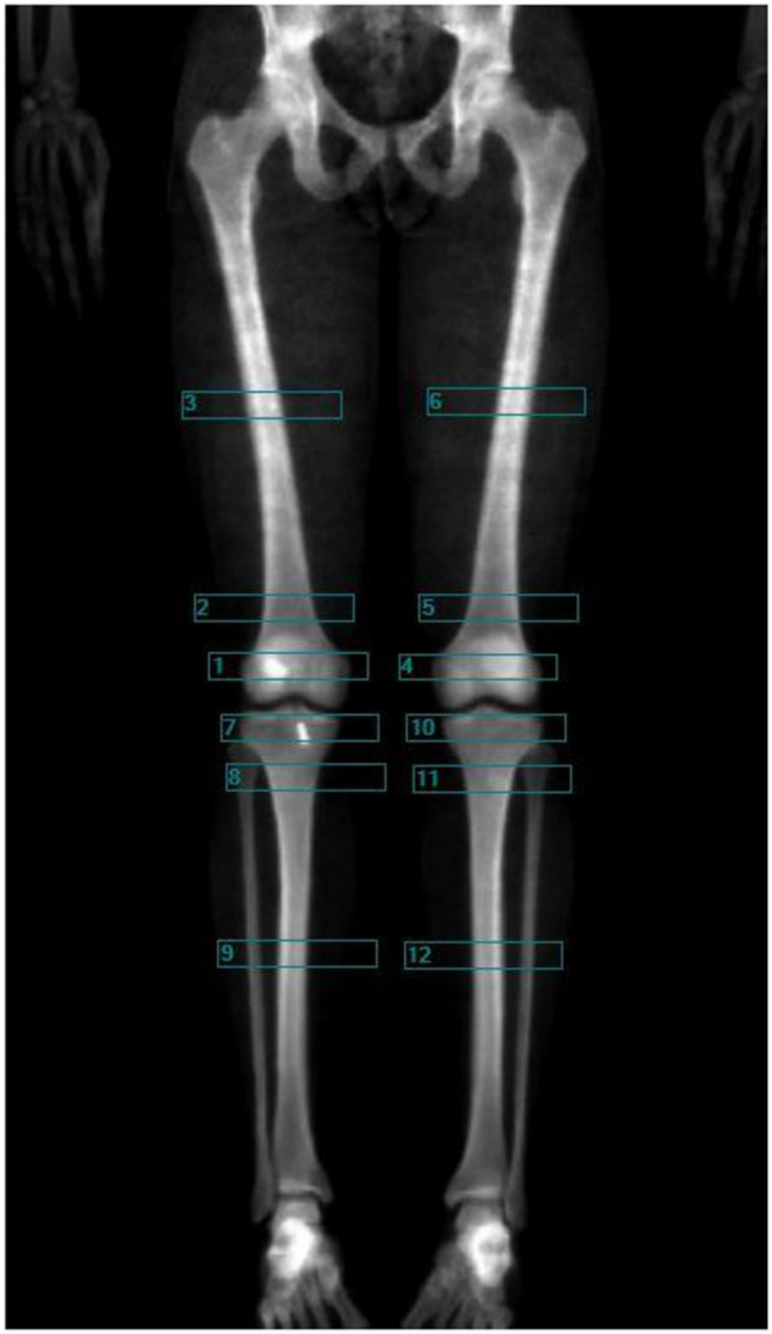

Figure 1.
Representative image of a dual-energy x-ray absorptiometry (DXA) scan with the custom regions of interest (ROI) applied. ROIs were 2 cm tall and a width that spanned the respective lower extremity. ROIs were placed at 5% (box 1 and 4), 15% (box 2 and 5), and 50% (box 3 and 6) of femur length, measured from the distal femur, and at 5% (box 7 and 10), 15% (box 8 and 11), and 50% (box 9 and 12) of tibia length, measured from the proximal tibia. Bone mineral densities (BMD) in g/cm^2 were extracted from each ROI for analysis.

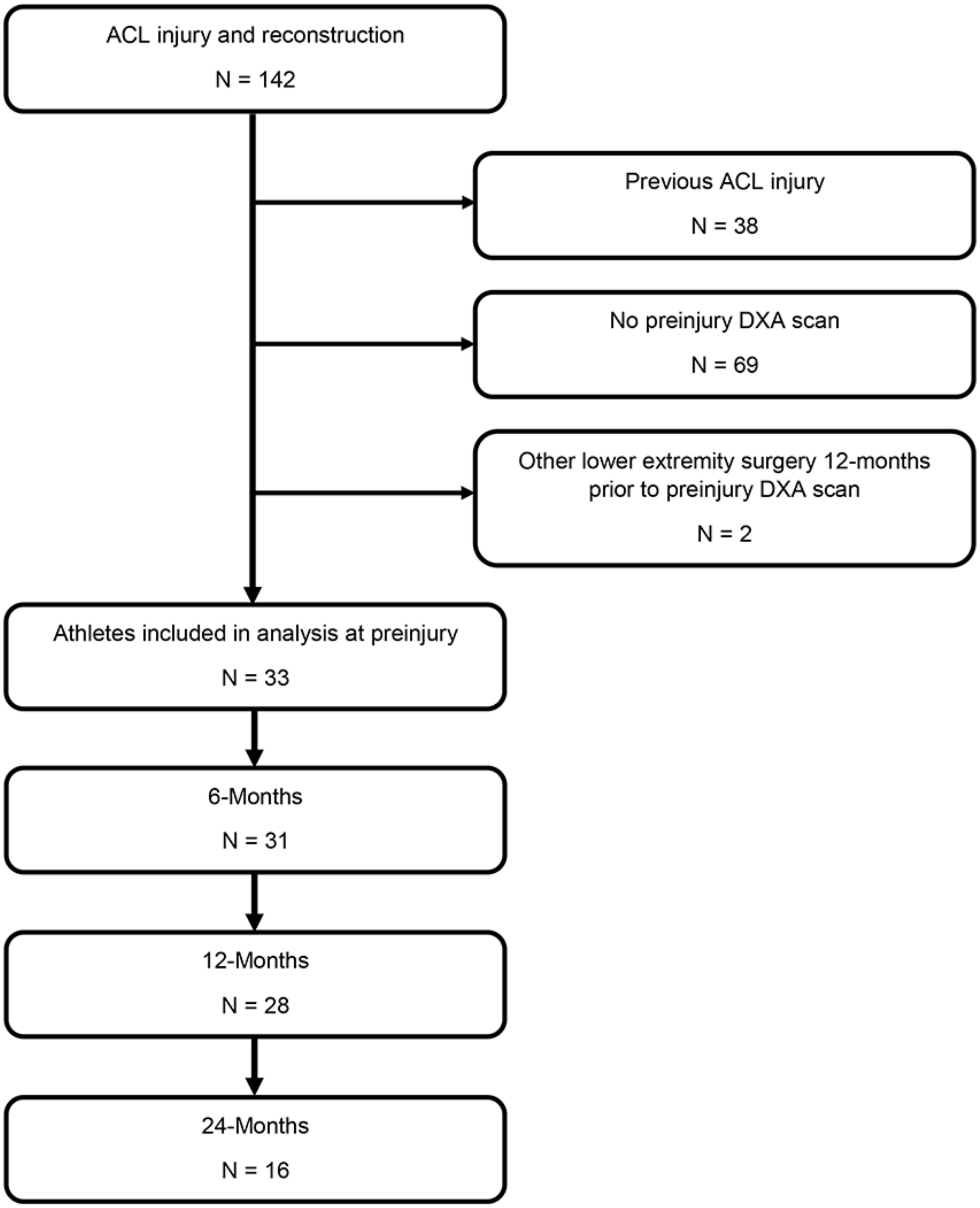

Figure 2.
Records extraction process. All athletes included in the analysis had dual-energy x-ray absorptiometry (DXA) scans from preinjury and at least one post-operative time point. ACL, anterior cruciate ligament.

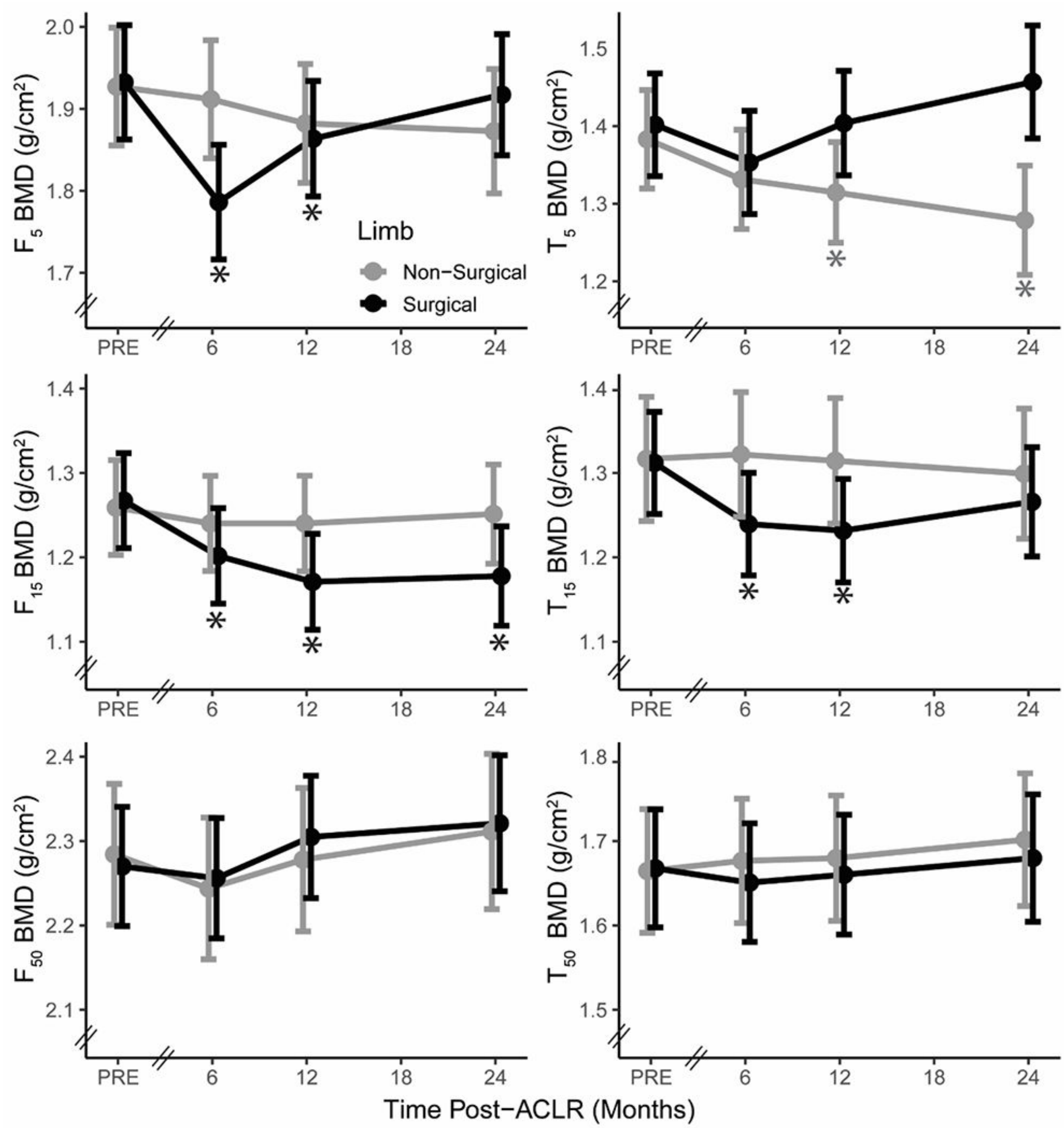

Figure 3.

Least-square mean values of bone mineral density (BMD) at 5% (F_5), 15% (F_{15}), and 50% (F_{50}) of femur length and 5% (T_5), 15% (T_{15}), and 50% (T_{50}) of tibia length from preinjury (PRE) to 24-months post-anterior cruciate ligament reconstruction (ACLR) within the surgical (black) and non-surgical limb (grey). Error bars depict the 95% confidence interval of the least-square mean. The axis break between preinjury and 6-months demonstrates that the time interval between preinjury and 6-months varies between participants. * Significant within-limb difference from preinjury $p < 0.002$.

Table 1.

Summary of participant information.

Participant Information (N = 33)[a]	Values
Age, y[*]	21.2 (1.2)
Body Mass, kg[*]	88.4 (20.1)
Height, cm[*]	194.9 (44.3)
Body Mass Index, kg/m^2[*]	26.8 (4.2)
Females, n (% of total participants)	13 (39%)
Graft type, n (% of total participants)	
Bone-patellar-tendon-bone	30 (91%)
Hamstring tendon	2 (6%)
Quadriceps tendon	1 (3%)
Concomitant procedures, n (% of total participants)	
Meniscectomy	10 (30%)
Meniscal repair	10 (30%)
MPFL reconstruction	2 (6%)
Time between DXA scan and ACLR, mo	
Preinjury	3.0 (2.0)
6-month	6.1 (0.7)
12-month	12.1 (1.2)
24-month	24.4 (2.9)
Participants at each time, n (% of total participants)	
Preinjury	33 (100)
6-month	31 (94)
12-month	28 (85)
24-month	16 (48)

[a]Values are presented as mean (SD) unless otherwise indicated.

[*]Based on 6-month post-operative assessment.

DXA, dual-energy X-ray absorptiometry, ACLR, anterior cruciate ligament reconstruction. MPFL, medial patellar femoral ligament.

Table 2.

Least-square means, standard errors (SE), mean differences from preinjury, and Tukey-adjusted p-values for surgical and non-surgical limb bone mineral density (BMD) regions of interest (ROI) at all time-points. A negative value notes a deficit in the post-operative BMD compared to preinjury.

BMD ROI	Limb	Preinjury	6-Months Post-ACLR			12-Months Post-ACLR			24-Months Post-ACLR		
		Mean (SE)	Mean (SE)	Mean Difference from Preinjury (SE) [% Change]	p-value	Mean (SE)	Mean Difference from Preinjury (SE) [% Change]	p-value	Mean (SE)	Mean Difference from Preinjury (SE) [% Change]	p-value
5% femur length (g/cm^2)	Surgical	1.94 (0.04)	1.79 (0.04)	−0.15 (0.02) [−7.7%]	<0.001	1.87 (0.04)	−0.07 (0.02) [−3.6%]	0.002	1.92 (0.04)	−0.02 (0.02) [−1.0%]	0.97
	Non-Surgical	1.94 (0.04)	1.92 (0.04)	−0.02 (0.02) [−1.0%]	0.98	1.89 (0.04)	−0.05 (0.02) [−2.6%]	0.18	1.89 (0.04)	−0.05 (0.02) [−2.6%]	0.33
15% femur length (g/cm^2)	Surgical	1.26 (0.03)	1.20 (0.03)	−0.06 (0.01) [−4.8%]	<0.001	1.17 (0.03)	−0.09 (0.01) [−7.1%]	<0.001	1.17 (0.03)	−0.09 (0.01) [−7.1%]	<0.001
	Non-Surgical	1.26 (0.03)	1.24 (0.03)	−0.02 (0.01) [−1.6%]	0.71	1.24 (0.03)	−0.02 (0.01) [−1.6%]	0.74	1.25 (0.03)	−0.01 (0.01) [−0.8%]	0.99
50% femur length (g/cm^2)	Surgical	2.27 (0.04)	2.26 (0.04)	−0.01 (0.02) [−0.4%]	0.99	2.31 (0.04)	0.04 (0.03) [1.8%]	0.87	2.32 (0.04)	0.05 (0.02) [2.2%]	0.84
	Non-Surgical	2.28 (0.04)	2.24 (0.04)	−0.04 (0.02) [−1.8%]	0.73	2.28 (0.04)	0.00 (0.02) [0.0%]	0.99	2.32 (0.05)	0.04 (0.02) [1.8%]	0.97
5% tibia length (g/cm^2)	Surgical	1.40 (0.03)	1.35 (0.03)	−0.05 (0.02) [−3.6%]	0.20	1.40 (0.03)	0.00 (0.02) [0.0%]	0.99	1.46 (0.04)	0.06 (0.02) [4.3%]	0.34
	Non-Surgical	1.38 (0.03)	1.33 (0.14)	−0.05 (0.02) [−3.6%]	0.14	1.31 (0.03)	−0.07 (0.02) [−5.1%]	0.02	1.28 (0.04)	−0.10 (0.02) [−7.2%]	0.001
15% tibia length (g/cm^2)	Surgical	1.31 (0.03)	1.24 (0.03)	−0.07 (0.01) [−5.3%]	<0.001	1.23 (0.03)	−0.08 (0.02) [−6.1%]	<0.001	1.26 (0.03)	−0.05 (0.02) [−3.8%]	0.21
	Non-Surgical	1.31 (0.04)	1.32 (0.04)	0.01 (0.01) [0.8%]	0.99	1.31 (0.04)	0.00 (0.02) [0.0%]	0.99	1.30 (0.04)	−0.01 (0.02) [−0.8%]	0.98
50% tibia length (g/cm^2)	Surgical	1.66 (0.03)	1.65 (0.30)	−0.01 (0.01) [−0.6%]	0.98	1.66 (0.03)	0.00 (0.01) [0.0%]	0.99	1.68 (0.03)	0.02 (0.02) [1.2%]	0.99
	Non-Surgical	1.66 (0.04)	1.67 (0.04)	0.01 (0.02) [0.6%]	0.99	1.68 (0.04)	0.02 (0.01) [1.2%]	0.99	1.70 (0.04)	0.04 (0.02) [2.4%]	0.75

ACLR, anterior cruciate ligament reconstruction