Osteoporosis International (2019) 30:1573–1580
https://doi.org/10.1007/s00198-019-05001-x

ORIGINAL ARTICLE

A case-control pilot study of stress fracture in adolescent girls: the discriminative ability of two imaging technologies to classify at-risk athletes

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Received: 6 December 2018 / Accepted: 22 April 2019 / Published online: 29 May 2019

Abstract

Summary Since stress fractures are common among adolescent athletes, it is important to identify bone assessment tools that accurately identify risk. We investigated the discriminative ability of two imaging technologies to classify at-risk athletes. Findings suggested that peripheral quantitative computed tomography (pQCT) has the ability to distinguish differences in bone structure in injured vs. uninjured limbs.

Introduction Given the high stress fracture (SFX) prevalence among adolescent girls, an understanding of the most informative assessment tools to identify SFX risks are required. We investigated the discriminative ability of pQCT vs. dual-energy X-ray absorptiometry (DXA) to classify athletes with or without SFX.

Methods Twelve adolescent athletes diagnosed with a lower-extremity SFX were compared with 12 matched controls. DXA measured areal bone mineral density (aBMD) and content of the total body, and lumbar spine. Bilateral tibiae were assessed with pQCT. At the metaphysis (3%), total density (ToD), trabecular density (TrD), trabecular area (TrA), and estimated bone strength in compression (BSIc), and at the diaphysis (38% and 66%), total bone area (ToA), cortical density (CoD), cortical area (CoA), estimated bone strength in torsion (SSIp), and peri- and endocortical and muscle area (MuA) were obtained. Cortical bone mass/density around the center of mass and marrow density (estimate of adiposity) were calculated using ImageJ software. General estimated equations adjusting for multiple comparisons (Holm-Bonferroni method) were used to compare means between (1) injured limb of the case athletes vs. uninjured limb of the control athletes and (2) uninjured limb of the case athletes vs. uninjured limbs of the controls and injured vs. uninjured limb of case athletes with a SFX.

Results aBMD and content showed no significant differences between cases and controls. When comparing the injured vs. uninjured leg in the case athletes by pQCT at the 3% tibia, unadjusted TrD, total density, and BSIc were significantly lower ($p < 0.05$) in the injured vs. uninjured leg. Marrow density at the 66% site was 1% ($p < 0.05$) lower in the injured vs. uninjured leg.

Conclusions These preliminary data in athletes with SFX suggest that pQCT has the ability to distinguish differences in bone structure in injured vs. uninjured limbs. No discriminative bone parameter classifications were identified between adolescent athletes with or without SFX.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00198-019-05001-x) contains supplementary material, which is available to authorized users.

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Keywords Stress fracture · Females · Bone mineral density · Trabecular density · Marrow density

Introduction

Stress fractures (SFX) are the most common overuse injury in athletes; they are painful and disabling and can interrupt training and prematurely end sporting careers [1, 2]. SFX often occur when microdamage caused by repetitive mechanical loading exceeds the biological capacity of the bone. The occurrence of SFX during adolescence, an important period for peak bone accrual, is an important issue, with 3.9% of adolescent girls reporting at least one SFX [3]. Despite the growing concern of suboptimal bone health in adolescent athlete girls, few studies have fully explained the risk factors for SFX in this population [3, 4].

It is well established that the adolescent years are critical for the acquisition of peak bone mass. However, determining the underlying cause of a SFX can be difficult as many teenagers do not present with known risk factors [4]. The female athlete triad [low bone mineral density (BMD), low energy availability, and menstrual dysfunction], recently re-termed relative energy deficiency-sport (RED-S), biomechanics, and compulsive exercise are known contributors to SFX [3]. Previous studies have yielded conflicting findings. For example, low BMD has been associated with SFX in some [5], but not all [1, 6, 7], studies. To our knowledge, there are limited case control studies conducted at the onset of SFX diagnosis to determine the role that bone mass and structure may play in the etiology of SFX in adolescent athletic girls.

BMD is typically evaluated clinically in athletes using dual-energy x-ray absorptiometry (DXA). However, this technique may be less sensitive as a screening tool in detecting the risk of SFX as rapid changes in skeletal dimensions occur during adolescence. Currently, there is limited evidence to support an association between lower BMD and increased risk for SFX among athletes [5, 8, 9], with some [1, 10–12], but not all, studies [6, 7, 13, 14] reporting lower BMD in athletes who sustain a SFX injury compared to those without. The lack of concordance among prior findings may be explained in part by the fact that athletes often present with BMD values approximately 10% higher than their non-active counterparts due to the increased skeletal loading [15, 16]. For that reason, athletes who present with a SFX may not be diagnosed clinically with low bone density although their bone structure may be compromised [5]. In a recent 12-month study by Duckham and colleagues, it was reported that female athletes who sustained a SFX did not exhibit the previously identified risk factors and in particular, DXA assessed BMD was not significantly different between athletes with and without SFX [7]. Given the SFX prevalence in adolescent girls, it is imperative to investigate the best predictive tools for this patient group. The structural features captured by peripheral quantitative computed tomography (pQCT) could offer important information for the prevention and clinical monitoring of SFX since pQCT provides additional information on bone size, structure, and cross-sectional geometry, potentially affording an enhanced understanding of SFX injury [17, 18] However, currently, it remains unknown whether a clinical pQCT evaluation is warranted in adolescent athletes at potential risk for SFX as a preventative clinical monitoring tool.

The purpose of this study was to investigate the discriminative ability of two imaging technologies, pQCT and DXA, to classify adolescent athletes with and without stress fracture. Three hypotheses were tested at each skeletal location to determine the discriminative ability of the two imaging techniques to identify stress fracture injuries: (1) injured vs. uninjured leg of case athlete, (2) injured leg of case athletes vs. uninjured legs of controls, and (3) uninjured leg of case athletes vs. that of controls.

Methods

Study design

A case-control design was used to assess the discriminative ability of pQCT versus DXA to classify athletes with and without a stress fracture injury. All bone measurements were assessed within 6 weeks of a clinically diagnosed stress fracture using both DXA and pQCT. Questionnaires were used to determine menstrual function, dietary intake, and training volume. Institutional Review Board approval was obtained at Rhode Island Hospital. Written informed assent/consent was obtained for all participants.

Participants

Twelve adolescent female athletes, aged 12–17 years, with a lower extremity SFX, and 12 controls matched for age, race, sport, training, and age or years since menarche, were recruited through the Divisions of Sports Medicine and Adolescent Medicine at Rhode Island Hospital in Providence, RI, registered sports clubs within Providence, via letters, posters, and word of mouth. SFX case athletes were required to have a radiographically (via computed tomography, magnetic resonance imaging, or radiography) confirmed stress injury of the lower extremity (tibia, fibula, metatarsal, or malleolus) within the previous 6 weeks, were post-menarchal, and involved in weight-bearing sports. Control athletes were required to be uninjured, with no stress fracture sustained during the previous 12 months and actively engaged in normal

training. Controls were screened to exclude any athlete who had recently been exposed to high levels of radiation. SFX case and control athletes were excluded if pregnant, suffering from chronic conditions such as anorexia nervosa, if using oral contraception, or taking other medications known to affect bone.

Bone parameters

Dual energy X-ray absorptiometry

DXA was used to measure areal BMD and content (BMC) of the total body, and lumbar spine (2009 Hologic Discovery W QDR series, software V23.1). Areal BMD Z-scores were calculated using pediatric software, according to age, sex, and ethnicity. Coefficient of variation (CV) for all bone outcomes in our laboratory ranged from 0.5 to < 1%.

Peripheral quantitative computed tomography

Bone structural and density parameters, estimates of bone strength, and regional body composition of bilateral lower extremities were measured using peripheral quantitative computed tomography (pQCT) (XCT 3000, Stratec Medical, Pforzheim). Scout scans were performed over the ankle joint, with the scanner reference line positioned at the most proximal aspect of the endplate of the distal tibia. For all athletes, cross-sectional images were acquired proximal to the reference line: 3%, 38%, and 66% of the tibial length, with tibial length measured from the distal end of the medial malleolus to the superior aspect of the medial tibial epicondyle. Scanning parameters included 2.3-mm slice thickness, 0.4-mm pixel size, and 20-mm/s scanning speed. The manufacturer's software (Stratec Medical, Pforzheim, Germany, version 6.2), in conjunction with edge detection and thresholding steps, was used to acquire structural and densitometric parameters of bone and muscle. At the metaphysis (3%), using a thresholding at 169 mg/cm^3, total density (ToD, mg/cm^3), trabecular density (TrD, mg/cm^3) was derived. To estimate bone strength in compression, a bone strength index (BSIc, mg^2/mm^4) was calculated by multiplying ToA by ToD squared (BSIc = ToA xToD^2) [19]. At the diaphysis (38% and 66%), the periosteal surface of the tibia was found, using thresholding at 280 mg/cm3 from which total bone area (ToA, mm^2) was calculated. Cortical bone was selected by thresholding at 710 mg/cm^3, from which cortical density (CoD, mg/cm^3), cortical area (CoA, mm^2), and peri- and endocortical circumferences were derived. Estimated bone strength in torsion (SSIp, mm^3) was calculated to estimate diaphyseal bone resistance in bending and torsion (Schoenau 2001). Muscle area (MuA, mm^2) was assessed from the shaft sites. Muscle tissue was defined as voxels with a density greater than 40 mg/cm^3 (differentiating muscle from subcutaneous fat) and less than 280 mg/cm^3 (differentiating muscle from bone). The manufacturer's phantom was scanned daily for quality assurance (average CV 0.2–0.6%).

Polar cortical bone mass (mg) and radial vBMD (mg/cm^3) distribution at the 38% and 66% tibia cortex were calculated using ImageJ as previously described [20]. In brief, a threshold of 710 mg/cm3 with a 3 × 3 median filtering of the image was used to distinguish the cortical bone from the surrounding soft tissue and bone marrow. The outermost and innermost layers of the cortical pixels were excluded to eliminate partial volume effects from the analysis. Dividing the tibia cortex into six equal 60-degree sectors led to derivation of the polar bone mineral mass distribution.

Marrow density (MaD) was analyzed as a surrogate of marrow adiposity at the 38% and 66% tibia. The analysis was conducted using Java software as described previously [21] by separating the marrow fat from bone using a threshold of 80 mg/cm^3. Marrow density has been calculated to vary from 0.92 g/cm^3 to 1.08 g/cm^3 based on the chemical composition derived from human tissue. Therefore, the higher the MaD, the lower the fraction of marrow fat and adiposity.

Questionnaires

Questionnaires were completed to assess SFX history, history of menstrual dysfunction, age at menarche, training history, and current intakes of calcium- and vitamin D-rich food. SFX history was defined as a fracture/reaction clinically diagnosed by a physician and confirmed by radiography (X-ray, CT or MRI). For each SFX reported, the athlete recorded the time since the SFX (year), the anatomical location, and method of diagnosis. Menstrual function history in the proceeding 12 months was classified as amenorrheic ($\leq$ 3 menses per year), oligomenorrheic (4–9 periods per year), or eumenorrheic ($\geq$ 10 periods per year) [22]. Athletes also reported the years since their first menstrual period. Calcium intake was assessed through questionnaire. Athletes were asked if they consumed calcium-rich foods, such as milk, yogurt, and cheese, and the amount of each calcium-rich food they consumed (cups) per day. Athletes were also asked to report the number of glasses of soda they consumed during the past week. Dietary supplements containing calcium and vitamin D and multivitamin use were recorded. Training history was quantified by asking athletes to record the primary type of sport participated and the average hours per week of training for the sport.

Anthropometric measures

Height (cm) and weight (kg) were measured prior to the bone measurements using standard protocols, via a stadiometer and digital scales, respectively, and body mass index (BMI) was calculated using the following equation: BMI = weight (kg)/height (m)^2 and reported as BMI for age-percentile. Body composition (mass of fat, lean and bone) was assessed from the total body DXA scan.

Statistical analysis

Statistical analyses were performed using SAS (SAS Institute, Inc., Cary NC). Differences in anthropometric characteristics, nutritional data, and training volume were compared between groups using independent *t* tests. General estimated equations (GEE) for lognormal distributed data were used to model skeletal outcomes from DXA and pQCT tibial data in both legs of injured and uninjured female athletes. Adjustments for multiple comparisons were made using the Holm-Bonferroni method. All within-subjects locations were nested within athletes using a residual variance approach. Three hypotheses were tested at each location: (1) injured leg of case athletes vs. uninjured legs of controls, (2) uninjured leg of case athletes vs. uninjured legs of controls, and (3) injured vs. uninjured leg of case athlete. Alpha was maintained at 0.05 after correcting for the multiple comparisons across models using the Holm test. Model parameters were back translated to geometric means and 95% confidence intervals.

Results

In the 12 case athletes, SFX were diagnosed at the tibia ($n = 5$), metatarsals ($n = 5$), and fibula ($n = 2$). The characteristics of adolescent athletes according to SFX groups are shown in Table 1. However, 3 out of the 12 SFX cases reported a history of menstrual dysfunction compared to none of the control athletes (25% vs 0%) and the time since menarche was not significantly different between cases (2.2 ± 1.3 years) and controls (2.1 ± 1.2 years). There were no significant differences in BMI for age percentiles, menarchal age, and dietary supplementation or intake (Table 1). SFX athletes presented with 14% lower (CI − 46, 34) lean mass, 5% (− 29, 27) lower fat mass, and 7% (− 23, 13) lower % body fat than controls; however, these differences were not statistically significant ($p > 0.05$).

Comparisons between SFX case and control athletes

DXA-derived bone outcomes indicated that SFX athletes had 2% (CI − 4, 9) higher total body and 3% (− 7, 13) higher lumbar spine BMD and 3% (− 9, 18) higher total body and 3% (− 11, 21) higher lumbar spine BMC when compared to control subjects, although these differences were not significantly different after controlling for multiple comparisons ($p > 0.05$).

Similar to the findings from bone outcomes generated by DXA, the GEE revealed no significant differences in bone outcomes generated by pQCT at the 3%, 38%, and 66% tibia shaft when comparing: (1) injured leg of case athletes vs. uninjured legs of controls and (2) uninjured leg of case athletes vs. that of controls (Table 2). There were no other significant differences in bone outcomes between groups.

Injured verse uninjured leg in case athletes

At the distal (3%) tibia, when comparing injured vs. uninjured legs in the case athletes, the GEE revealed a significantly lower TrD (4%), ToD (7%), and BSIc (9%) in the injured compared to the uninjured leg (Table 2). However, once controlling for multiple comparisons, only a trend $p < 0.1$ persisted for these bone parameters. In addition, adjusted MaD at the 66%, but not 38% site, was significantly lower in the injured compared to uninjured leg, with no significant differences between cases and controls (Fig. 1). There were no other significant differences in bone outcomes between the injured vs uninjured leg in SFX athletes.

Discussion

To our knowledge, this pilot study is the first to identify the discriminative ability of pQCT versus DXA generated bone outcomes to classify athletes with and without a SFX. The primary findings from this study are that when comparing bone parameters obtained by pQCT in SFX case athletes alone, these athletes appear to have lower bone marrow density (an estimate of adiposity) at the 66% site of the fractured limb (vs. the uninjured limb), although the fractured limb was not significantly different from control athletes. However, other bone parameters, including pQCT and BMD, generated measures of BMD showed no differences among adolescent athletes with and without a SFX injury, replicating findings from previous retro- and prospective studies [1, 6, 7]. Similarly, there were no significant differences in bone structural parameters between groups when assessed by pQCT.

As a tool to discriminate bone measures that would identify athletes at increased risk for SFX injury, our findings suggest DXA measures alone to be inadequate. Furthermore, bone mass measured by DXA in this current study was clinically normal for both case (z-scores 0.4 and 0.9 for total body and lumbar spine respectively) and control (z-scores 0.7 and 1.1 for total body and lumbar spine respectively) athletes. In this case control study, we have shown that at-risk athletes may have more pronounced differences in bone structure versus BMD between limbs. Bilateral assessments throughout the competitive season could potentially identify those athletes at increased risk for SFX. However, larger studies will be needed to verify these findings.

We postulate that lower marrow density in the injured limb of case athletes may indicate higher rates of bone turnover that promote skeletal healing [21]. The bone marrow cavity contains fat, which may modulate bone remodeling, although the metabolic function of marrow fat remains under investigation [23]. Mesenchymal stem cells within bone marrow differentiate to become adipocytes or osteoblasts. Adipocytes secrete cytokines and adipokines that may stimulate or inhibit

Table 1 Physical characteristics of stress fracture (SFX) cases and control athletes

	SFX Cases ($N = 12$)	Controls ($N = 12$)
Physical characteristics		
Age (year)	15.2 (1.7)	14.7 (1.4)
Body mass (kg)	58.8 (11.2)	56.6 (7.3)
Height (cm)	166.1 (8.2)	164.0(5.2)
BMI (kg/m^2)	21.8 (2.9)	21.1 (3.1)
BMI (z-score)	0.17 (0.7)	0.16 (1.1)
BMI (percentile-age)	54.7 (19.8)	57.7 (27.7)
Training		
Weekly training duration (hr)	11 (4)	11 (6)
History of past stress fracture [n (%)]	12 (100%)*	3 (25%)
Menstrual function		
Years since menarche	2.2 (1.3)	2.1 (1.2)
Current oligo/amenorrhea [n (%)]	3 (25%)	0 (0%)
Use of dietary supplements		
Calcium [n (%)]	3 (25%)	0 (0%)
Vitamin D [n (%)]	3 (25%)	0 (0%)
Multivitamins [n (%)]	3 (25%)	3 (25%)
Daily dietary intake		
Calcium [milk cups (SD)]	2.1 (1.4)	1.7 (1.6)
Calcium [cheese cups (SD)]	1.1 (0.8)	0.9 (0.5)
Calcium [yogurt cups (SD)]	0.9 (0.2)	0.9 (0.2)
Soda [glasses 8oz (SD)]	2.0 (1.8)	2.7 (2.3)

Independent *t* tests used to report comparison of means and standard deviation between group characteristics. For dietary intake: mean number of servings and the standard deviation (in parentheses).

*$p < 0.05$ comparing stress fracture case to control athletes

adjacent osteoblasts. The relationship of marrow adipose tissue to fat depots in other parts of the body is complex and may play a distinct role in metabolic homeostasis, hematopoiesis, and osteogenesis [24]. States of malnutrition, as can occur with high prevalence in elite female athletes, has been shown to increase marrow adiposity accompanying the loss of subcutaneous adipose tissue, and there is an inverse association between marrow fat and areal BMD measures in adults with restrictive eating disorders [25, 26]. In adolescents and young women with anorexia nervosa, increased marrow fat has been documented to be present in the peripheral skeleton [27], as well as lumbar spine [25]. Emerging data regarding bone-fat interactions suggest that identified novel molecules could serve as targets to enhance bone formation and lead to strategies to prevent bone loss and fractures [24]. Imaging findings as observed in the current study could serve as important outcomes for monitoring.

Limitations bear acknowledgment and discussion and should be addressed to confirm conclusions. The sample size was small, but SFX cases were matched carefully to control athletes and athletes were assessed within 6 weeks of SFX diagnosis. Although the SFX cases in this study were matched for both age and age at menarche, we were not able to control the location of the SFX diagnosis. The baseline assessments on average were taken 6 weeks following a positive diagnosis of SFX; however, there was no indication as to the length of time for which pain persisted prior to the medical intervention. Therefore, some bone remodeling may have occurred prior to the assessment and would have been undetected by this study. Past research in the recovery of fractures and musculoskeletal injury have identified that bone remodeling in limbs can be determined by the location of the injury, with the greatest bone remodeling occurring more proximal to the injury site [28, 29]. The present study, therefore, may have reduced the ability to detect differences in bone mass and structure due to the differing locations of SFX. Similarly, the anatomical sites at which bone mass and structure were measured using DXA and pQCT may not have detected the potential bone differences proximal to the SFX. Therefore, in future studies, the location of the SFX should be kept constant and measurements include sites proximal to the injury. Secondly, we only asked athletes to recall their intake of calcium and soda which are known nutrients which influence bone health, and therefore, we are unable to determine if the macro and micronutrient breakdown of these athletes energy intake were influencing the bone health in the athletes with a stress fracture. Furthermore, we did not obtain information on the vitamin D status of these athletes, which may have increased the risk

Table 2 General estimated equation (GEE) comparisons of bone parameters across the tibia shaft (3, 38, and 66%) measured with pQCT between athletes with a stress fracture (SFX) injury and matched controls

	Control vs. SFX un-injured limb	SFX injured limb vs. control	SFX limb vs. non-SFX limb
Tibia 3%			
ToA (mm^2)	3 (− 14, 9)	3 (− 9, 17)	6 (− 2, 14)
ToD (mg/cm^3)	− 3 (− 6, 12)	− 5 (− 13, 3)	− 7 (− 13, − 1)*
TrA (mm^2)	− 4 (− 17, 11)	4 (− 9, 21)	9 (− 1, 21)
TrD (mg/cm^3)	− 1 (− 8, 6)	− 4 (− 11, 4)	− 4 (− 6, − 1)*
BSI (mg^2/mm^4)	3 (− 15, 26)	− 6 (− 22, 13)	− 9 (− 17, 0)*
Tibia 38% characteristics			
Muscle CSA (cm^2)	8 (− 5, 21)	7 (− 3, 19)	0 (− 4, 4)
Marrow Density (g/cm^3)	0 (− 1, 1)	0 (− 2, 1)	0 (− 1, 0)
Tibia 38% bone parameters			
ToA (mm^3)	1 (− 8, 9)	0 (− 7, 8)	0 (− 2, 3)
CoA (mm^3)	2 (− 8, 12)	2 (− 7, 12)	0 (− 2, 2)
CoD (mg/cm^3)	1 (− 2, 5)	0 (− 2, 3)	− 1 (− 2, 0)
SSIp (mm^3)	1 (− 1, 16)	1 (− 11, 15)	0 (− 3, 5)
Pericortical	0 (− 4, 4)	0 (− 4, 4)	0 (− 1, 1)
Endocortical	− 2 (− 9, 5)	− 2 (− 9, 6)	0 (− 3, 4)
Cortical distribution 38%			
S1: posterior Lateral (mg)	− 2 (− 18, 18)	− 2 (− 12, 20)	4 (− 4, 12)
S2: Lateral (mg)	8 (− 5, 23)	6 (− 7, 20)	− 2 (− 6, 2)
S3: anterior-lateral (mg)	− 7 (− 20, 8)	− 7 (− 18, 6)	0 (− 7, 7)
S4: anterior-medial (mg)	6 (− 8, 20)	8 (− 6, 24)	2 (− 4, 9)
S5: medial (mg)	1 (− 13, 17)	3 (− 8, 17)	3 (− 1, 6)
S6: posterior-medial (mg)	1 (− 13, 17)	− 2 (− 15, 14)	− 3 (− 9, 3)
Tibia 66% characteristics			
Muscle CSA (cm^2)	8 (− 2, 19)	8 (− 1, 17)	0 (− 6, 5)
Marrow Density (g/cm^3)	0 (− 1, 1)	0 (− 3, 1)	− 1 (− 2, 0) **
Tibia 66% bone parameters			
ToA (mm^3)	0 (− 11,13)	2 (− 9, 13)	1 (− 2, 5)
CoA (mm^3)	2 (− 7, 12)	2 (− 10, 17)	− 1 (− 6, 4)
CoD (mg/cm^3)	1 (− 1, 4)	0 (− 8, 10)	1 (− 5, 2)
SSIp (mm^3)	2 (− 13, 19)	1 (− 12, 16)	− 1 (− 4, 2)
Pericortical	0 (− 6, 4)	0 (− 4, 6)	0 (− 1, 3)
Endocortical	1 (− 9, 9)	− 1 (− 8, 10)	2 (− 3, 7)
Cortical distribution 66%			
S1: posterior Lateral (mg)	− 4 (− 19, 14)	0 (− 14, 15)	3 (− 3, 10)
S2: Lateral (mg)	9 (− 4, 24)	8 (− 3, 22)	− 1 (− 6, 5)
S3: anterior-lateral (mg)	− 4 (− 16, 8)	− 7 (− 16, 4)	− 2 (− 9, 6)
S4: anterior-medial (mg)	1 (− 14, 19)	0 (− 15, 16)	− 1 (− 5, 4)
S5: medial (mg)	8 (− 5, 23)	7 (− 5, 21)	− 1 (− 7, 5)
S6: posterior-medial (mg)	− 3 (− 14, 11)	− 9 (− 19, 4)	− 6 (− 12, 0)

Values represent the proportion (%) of the difference between the geometric mean (95% confidence interval). Testing three comparisons (1) injured leg of case athletes vs. uninjured legs of controls, (2) uninjured leg of case athletes vs. uninjured legs of controls, and (3) injured vs. uninjured leg of case athlete

*$p < 0.05$ unadjusted for Holm; **$p < 0.05$ adjusted for Holm multiple comparisons

for SFX injury. Finally, the study design was cross-sectional and some of the data was obtained by self-report, which has inherent limitations.

In conclusion, athletes with SFX appear to have a lower TrD, ToD, BSIc, and marrow density (estimate of adiposity) in the fractured vs. uninjured limb, although these

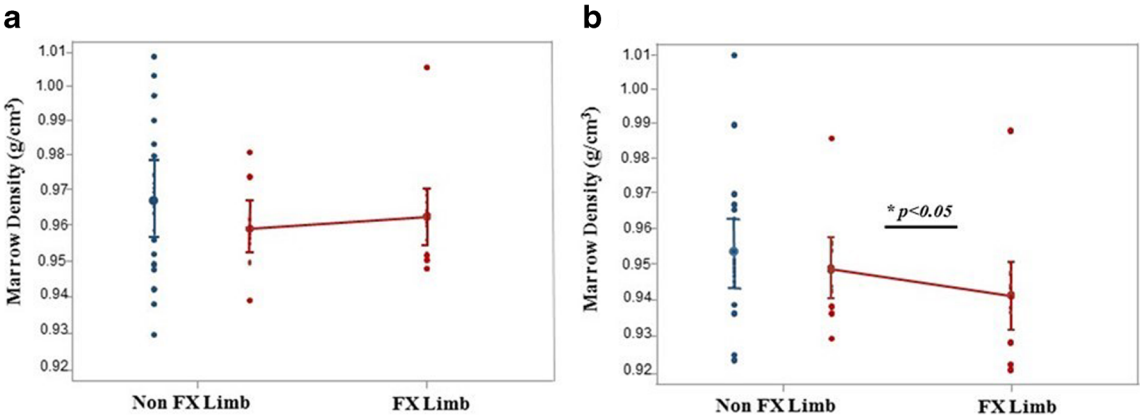

Fig. 1 General estimated equation of marrow density at: a. the 38 and b. 66% tibia as a function of the non-stress fractured (SFX) limb of the athlete compared with the athletes SFX limb and control athlete. Control athletes are represented with blue lines and dots and FX case athletes are represented with red lines and dots. *p<0.05 adjusted for Holm

findings were not significantly different from healthy controls. We postulate that the reduced marrow adiposity in the injured limb of case athletes may indicate higher rates of bone turnover that promotes skeletal healing [21]. In addition, athletes with a SFX injury did not present with clinically low bone mass or structure. In future evaluations of athletes at risk of SFX injury, it would be informative to focus on bilateral differences in athletes rather than solely on low bone mass and structure. Future studies are needed to understand more fully the risk factors for SFX in adolescent athletes and when a pQCT evaluation is warranted.

Acknowledgments The authors thank Valerie Marsocci, RT and Nicole DaSilva, RT, CNMT for their excellent technical assistance, Dr. Sara Vogrin affiliated with the Australian Institute for Musculoskeletal Sciences (AIMSS) for biostatistical advice, and our patients and their families for their participation.

Disclosure of funding This study was funded by the Brown University Department of Orthopedics.

Compliance with ethical standards

Institutional Review Board approval was obtained at Rhode Island Hospital. Written informed assent/consent was obtained for all participants.

Conflicts of interest None.

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