

An Investigation into the Association of Bone Characteristics and Body Composition with Stress Fracture in Athletes

Authors: Ian Varley^{1*}, Georgina Stebbings³, Alun G. Williams^{3,4}, Stephen Day⁵, Phil Hennis¹, Reece Scott¹, Neval Grazette¹, Adam J. Herbert²

Affiliations:

¹ *Department of Sport Science, Nottingham Trent University, Nottingham, UK*

² *Department of Sport and Exercise, Birmingham City University, Birmingham, UK*

³ *Department of Sport and Exercise Sciences, Manchester Metropolitan University, Manchester, UK*

⁴ *Institute of Sport, Exercise and Health, University College London, London, UK*

⁵ *University of Wolverhampton School of Medicine and Clinical Practice, Wolverhampton, UK*

*Corresponding author: Ian Varley

Email: Ian.Varley@ntu.ac.uk

Tel: +44 (0)115 8483542

Running title: Bone Characteristics, Body Composition and Stress Fracture Injury

Key Words: BMD, Body composition, Stress fracture

Abstract

Background: The aim of the study was to establish the bone and body composition characteristics of high-level athletes with and without a history of stress fracture injury.

Methods: 279 high-level athletes (212 men, 67 women) (age 28.0 ± 9.2 years; body mass 75.0 ± 17.4 kg; height 1.78 ± 0.10 m) and 112 non-athletic controls (60 women, 52 men) 36.2 ± 15.0 years; 70.9 ± 12.9 kg; 1.71 ± 0.10 m) were assessed by DXA to establish their bone mineral density and content, body fat and lean mass. Athletes completed a questionnaire detailing their stress fracture history.

Results: There were no differences in whole-body bone mineral density (men 1.41 ± 0.12 g/cm², women 1.19 ± 0.09 g/cm²), bone mineral content (men 3709 ± 626 g, women 2263 ± 290 g), body fat (men 16.3 ± 5.0 %, women 23.0 ± 4.6 %) and lean mass (men 65.4 ± 9.9 kg, women 38.7 ± 3.6 kg) between athletes with a history of stress fracture (34 men, 16 women) and those without (176 men, 40 women).

Conclusions: DXA derived bone and body composition characteristics were not independent risk factors for stress fracture injury in high-level athletes. This study in a large cohort of high-level athletes provides normative bone and body composition values that can be used as a benchmark for researchers and applied practitioners.

Introduction

Bone fractures can be broadly categorised as acute or stress related, and stress fracture injuries account for up to 20% of all clinically reported sports injuries [1-2]. The pathophysiology of stress fracture injury is multi-faceted, and associated with inadequacies in bone repair, with an inability to tolerate mechanical loading resulting in unrepaired micro-cracks and damage to bone micro-architecture [3-4]. For this reason, it is unsurprising that sports that have aspects of high magnitude and high frequency loading have a high incidence of stress fracture injury [2]. A greater understanding of the risk factors for stress fracture would aid practitioners in the prevention and rehabilitation of injury.

Currently, whole body dual-energy x-ray absorptiometry (DXA) measurements are used as a method to assess an individual's risk of stress fracture injury [5]. lower bone mineral density (BMD), bone mineral content (BMC) and reduced bone structural properties have been associated with stress fracture risk in some athletic population (cricketers (lumbar spine BMD,[6]), runners (tibial strength, [7]; hip BMD, [8]), triathletes (tibial cortex; [9]) and female athletes (trabecular BMD;[10]), but not in others (endurance athletes (triathletes and runners- whole body, lumbar spine and hip) [11] and runners (whole body, lumbar spine, hip, radius) [12-13]. The contrasting findings may be accounted for by the sport participated in, the likely difference in the pathophysiology of injury caused by the differing activity status of the participants (amateur and elite populations) in the aforementioned studies and the difference in the anatomical scan site. Although, possibly the most important factor explaining the variation is likely due to the relatively low number of stress fracture cases (median 19, range 2-42) limiting the power to detect differences between groups.

Associations between stress fracture injury incidence and body composition have also been studied due to the interaction between adipose tissue [14] and skeletal muscle [15] with bone. The association between adipose tissue and bone health is thought to be due to adipocytes elevating cytokines and causing a downstream increase in bone resorption [16-17]. Meanwhile, muscle forces are implicated with the governance of bone health due to the mechanical loading which muscle exerts on the bone and crosstalk between muscle- and bone-derived soluble factors [18]. However, the relationships between body fat, muscle mass and bone are far from established. Low body fat has previously been shown to be positively [19], negatively [19] and not associated [20] with stress fracture injury risk. Similarly, contrasting findings have been reported relating to the association between muscle mass/strength and stress fracture injury risk. Studies have reported that lower muscle strength is associated with increased stress fracture injury risk in athletes [7;10;20] and military recruits [21], while others have reported no association (athletes: [22-23]). The contrasting findings relating to body composition and stress fracture injury risk could be due to mechanical loading governing a large proportion of the bone's osteogenic response [24]. The loading was likely variable across previous

studies as some studied athletes with varying levels of ability [12-13] and others grouped participants regardless of the sport they participated in [24]. In addition, the majority of large-scale studies investigating body composition and stress fracture injury have been conducted in military personnel [21]. Due to the likely difference in the pathophysiology of injury between military recruits and elite athletes, it remains to be seen if the same risk factors are present in both professions.

Currently, the relationship between BMD, BMC and body composition with a history of stress fracture injury in high-level athletes is not well established. The establishment of sport-specific normative values for bone and body composition characteristics for high-level athletes with and without a history of stress fracture would aid researchers and applied clinicians when attempting to identify potential risk factors for stress fracture injury.

Therefore, the aims of the present study were to characterise the bone and body composition characteristics of high-level athletes with and without a history of stress fracture injury and compare those characteristics between athletes and non-athletes.

Materials and Methods

Participants.

A convenience sample of 279 high-level athletes (67 women, 212 men; age 28.0 ± 9.2 years; body mass 75.0 ± 17.4 kg; height 1.78 ± 0.10 m) consisting of 106 endurance runners (60 women, 46 men), 98 footballers (98 men), 38 rugby players (38 men), 20 cricketers (20 men) and 19 speed skaters (7 women, 12 men) were recruited from professional clubs and governing bodies, through previously established relationships with Manchester Metropolitan University or Nottingham Trent University or by word of mouth. 112 non-athletes (60 women, 52 men; 36.2 ± 15.0 years; 70.9 ± 12.9 kg; 1.71 ± 0.10 m) were recruited by mail-outs and word of mouth. Participants were deemed eligible for the study if they were aged 18 years or more, injury free, not currently taking any medication that influenced bone metabolism and had not received a joint replacement or prostheses. After reading the participant information sheet and having the opportunity to ask questions, participants provided informed consent, completed a pre-scan screening form (ensuring they met the inclusion criteria) and completed a health screen questionnaire. Forms were scrutinised by the lead investigator before the study commenced to confirm that participants met the inclusion/exclusion criteria. Runners were included if they had completed at least one official distance event ≥ 3000 m in a time faster than a predetermined threshold (Table 1). The predetermined threshold time for each distance was chosen to ensure all athletes placed in at least the top 600 in the UK rankings for a calendar year based on the years 2012-2017. Race PB time was verified by official race chip timings through individual race result websites, the power of 10 (<http://www.thepowerof10.info/>) and/or the International Association of Athletics Federations (IAAF) (<https://www.iaaf.org/home>). Athletes in other sports, that have less

objective criteria for elite performance, were included based on their professional employment status and the level of their sport in which they participate. The criteria for each sport are defined as follows: Football: professional players (English Premier League, Championship, League One, League Two); Rugby: professional players (English Premiership, Championship); Cricket: professional players (English County Championship Division One and Two), Speed Skating: International representation. Participants who did not compete in any sport with a major physical fitness component at regional, national or international level, were defined as non-athletes. The study conformed to Ionising Radiation (Medical Exposure) Regulations (IRR99) and was approved by the local Ethics Committee of Manchester Metropolitan University, Nottingham Trent University and the National Health Service Research Ethics Committee (Ref 15/EM/0037). The study was conducted ethically according to the principles of the World Medical Association Declaration of Helsinki.

Table 1 *****

Experimental design.

High-level athletes were tested for body composition and bone characteristics using DXA (iDXA, GE Healthcare, United Kingdom: Hologic Discovery W, Vertec Scientific Ltd, United Kingdom; r value of 0.854 between the two systems [25]). Each participant completed a statement of informed consent and a health status questionnaire. A fracture history questionnaire was also completed which contained questions on current sporting status (level of competition), stress fracture history and method of stress fracture confirmation [26]. The participants completed a hard copy of the questionnaire, which contained closed style questions and took 5-10 minutes to complete, prior to the commencement of the DXA scan. To be classified as a stress fracture case, participants self-reported the occurrence of a stress fracture confirmed by radiological scan (e.g., X-ray, MRI, CT). In the athlete group, 14 participants (endurance runners) were removed from the statistical analysis due to a lack of stress fracture history clarity (e.g. reports of stress reactions) and stress fracture symptoms without radiological confirmation. The non-stress fracture group was made up of athletes who had never had a stress fracture injury and had no reported history of stress fracture symptoms or radiological investigations suggestive of a stress fracture. Nine non-athletes were removed due to missing or incomplete DXA scan data.

Procedures.

Height (Stadiometer, Seca, Hamburg, Germany) and body mass (Seca, Birmingham, U.K.) were recorded with participants wearing minimal clothing. DXA scans assessed participant BMD, BMC, lean

mass and percentage body fat. Two manufacturer-trained operators performed all scans consistent with the manufacturer's guidelines. Calibration of the DXA was completed prior to scanning using a phantom of a known density. Participants were asked to wear minimal clothing or a cotton examination gown and remove any jewellery or metal prior to the scan to avoid measurement distortion. Participants fasted for at least 2 hours, emptied their bladder immediately before and were asked to be euhydrated prior to the scan. Participants were positioned supine on the DXA bed within the scanner range, with ankles and knees held in place by Velcro straps or medical tape to minimise unintended movements. The participants lay with arms by their sides and were asked to remain motionless for the duration of the scan. Whole-body scans lasted <10 min depending on the size of the participant. Subsequent segmental analysis for all scans were completed by the same trained operators. Coefficients of variation for the scanners used in the present study are 0.08–1.30% for BMD and 0.6% for fat mass [27-28].

The following measures were analysed: whole body lean mass and percentage body fat, whole body and legs BMD, whole body and legs BMC, T-score and Z-score. If any movement artefacts (inaccuracies in the measurement caused by motion) were present following the scan, the image was classified as invalid and a repeat measure was performed.

Statistical analysis.

All data are presented as mean \pm 1SD. Data were tested for normality using the Shapiro-Wilk test. Men and women were analysed separately. In athletes, independent sample T-tests were used to compare the means of the stress fracture cases to the non-stress fracture group (overall and sport specific). In a separate analysis, independent sample t-tests were used to compare athletes to non-athletes. The significance level was set at $P < 0.05$. In order to decrease the risk of a type I error, the Benjamini-Hochberg Procedure was applied with a false discovery rate value set at 5 percent [29]. All statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version 23.0 (SPSS, Inc., Chicago, IL, USA).

Results

Seventy-two stress fracture injuries were reported in 50 athletes (27 scanned using iDXA and 23 using Hologic Discovery W) (36 had 1 stress fracture, 9 had 2, 3 had 3, 1 had 4, 1 had 5). The location of stress fracture injuries are shown in Table 2.

Table 2 ****

Bone Characteristics

There were no differences in bone characteristics between athletes with and without a history of stress fracture injury for either men ($P \geq 0.15$) or women ($P \geq 0.09$) (Figure 1 and 2).

Male athletes had a greater whole-body BMD, BMC, T-score and Z-score compared to male non-athletes (Figure 1 and 2, Table 3a; $P \leq 0.03$), these differences were maintained following multiple comparison testing. There were no differences in bone characteristics between female athletes and female non-athletes (Table 3b; $P \geq 0.08$). When sub-categorised into specific sports, male endurance runners with a history of stress fracture had a greater T-score ($P = 0.04$) and Z-score ($P = 0.03$) than those without a stress fracture history (Table 4a), however no differences were shown following multiple comparison testing. For footballers, female endurance runners, rugby players and cricketers there were no differences in bone characteristics between athletes with and without a history of stress fracture injury ($P \geq 0.11$; Table 4a and 4b).

Body composition

There were no differences in body mass, BMI or body composition between athletes with and without a history of stress fracture injury for either men ($P \geq 0.47$) or women ($P \geq 0.19$) (Table 3a). Male athletes had ~6% lower body fat percentages than non-athletes ($P < 0.01$), while female athletes had lower body mass, percentage body fat and BMI than non-athletes (all $P < 0.01$) (Table 3b), these differences were maintained following multiple comparison testing.

Male endurance runners with a history of stress fracture injury were ~5 kg heavier than those without a history of stress fracture injury ($P < 0.01$; Table 4a), however no differences were shown following multiple comparison testing. There were no other sport-specific differences in body mass, BMI or body composition between athletes with and without stress fracture injury history ($P \geq 0.21$; Table 4a and 4b).

Figure 1 ****

Figure 2*****

Table 3a ****

Table 3b ****

Table 4a ****

Table 4b ****

Discussion

The present study is the largest known investigation assessing the bone and body composition characteristics of high-level athletes with and without a history of stress fracture injury. Overall, no differences were shown in the DXA derived bone or body composition characteristics of men or women athletes with a history of stress fracture injury and those who have never suffered a stress fracture injury. After adjusting for multiple comparisons, no sport specific differences between athletes with or without a history of stress fracture were shown. The study provides a valuable reference point of normative bone and body composition characteristics in high-level athletes with and without a history of stress fracture injury.

Bone characteristics

Overall, the present study showed no association between BMD and BMC with stress fracture injury history in high-level athletes. Previous studies have reported contrasting associations between BMD and stress fracture injury in athletes [11-13]. The reason for the contrasting findings may be due to several factors. Stress fracture injury susceptibility is multi-factorial and therefore BMD alone is not the only factor that contributes to increased risk of injury [3]. It could be suggested that a more holistic approach to the identification of those at risk of stress fracture injury is required, rather than relying on BMD measurements alone. This is exemplified in the current study, as the average T scores of athletes with and without stress fractures were higher than that considered to be a risk for adverse bone health, and no differences were present between the two groups

Previous studies in athletes assessing BMD and stress fracture injury have based their findings on a relatively low number of stress fracture cases (n = 2 [11]; n = 6 [6]; n = 20 [8]; n = 27 [13]), which be a reason for the variable results shown. As the present study contained 50 athletes with a history of stress fracture, the results provide more definitive data on the association between BMD and stress fracture and injury. The present study used a cohort of high-level athletes and used a quantifiable inclusion criterion (running personal best/professional athletes) to ensure the cohort was as homogenous as possible in terms of standard of competition and, accordingly, training practices required. Previous studies have based their inclusion criteria on distance covered per week (>20 miles; [13]) and collegiate athlete status [12], which could have led to a greater variability in competitive standard resulting in fluctuations in BMD of the athletes included compared to the present study. These factors ensure that the findings from the present study are reflective of the association between BMD and stress fracture injury in high-level athletes.

The bone characteristics of large populations of high-level athletes with and without a history of stress fracture injury are not commonly reported. The whole body BMD and BMC values shown for athletes

in the present study are comparable to values reported in previous studies involving high-level athletes that don't detail the stress fracture history of the participants (Men: BMD 1.25-1.41 g/cm²; BMC 3623-4185 g; [30-33]; Women: BMD 1.11-1.25 g/cm², BMC 2173-3047 g; [33-36]). This confirms that the cohort assessed in the present study is a representative sample of high-level athletes.

Body composition

Previous research has shown low body fat to be positively [19], negatively [19] and not associated [21] with stress fracture injury risk. Greater body mass caused by more body fat would potentially result in a higher mechanical load experienced by the bone when in weight-bearing locomotor activity, causing a net increase in bone formation [37]. Conversely, an increase in adipocytes as a result of a high percentage body fat could cause lipotoxicity in osteoblasts, leading to a decrease in bone formation [17]. The difficulty in separating these two seemingly opposing mechanisms could be the reason for the contrasting previous findings. In the current study, no association between percentage body fat and stress fracture injury was shown in the present study. Due to the relatively low percentage body fat of the athletes in the present study (Table 3a and 3b), lipotoxicity is highly unlikely. As no association was shown in the present study, it does not seem that percentage body fat alone is related to stress fracture history in high-level athletes.

The relationship between lean mass and stress fracture is unclear. No association between lean mass and stress fracture injury was observed in the present study. Previous studies have reported lower muscle strength associated with stress fracture injury [7; 10; 20; 22]. This has been attributed to muscle contractions inflict physical forces on bone causing a stimulation of the bone remodelling cycle [38]. Muscle hypertrophy and higher muscle mass also enhance physiological processes such as regenerative inflammation, insulin sensitising and endothelial function that result in osteogenesis [39]. However, resistance to stress fracture are multifactorial in nature, with mechanical loading [40], genetics [41], body fat [19], as well as muscle mass, all being suggested to influence stress fracture injury risk. No association between lean mass and stress fracture injury was shown in the present study, which is in agreement with previous studies [5; 18; 23]. As a hierarchy of influences on stress fracture risk are yet to be fully established [39], a variety of mechanisms are likely to be acting on a bone simultaneously. In order to fully elucidate the factors associated with stress fracture injury, further large-scale studies are required that examine a variety of risk factors.

Although no associations of bone and body composition characteristics with stress fracture injury were observed, it cannot be ruled out that these variables contribute to stress fracture incidence. A holistic approach, incorporating multiple risk factors, to identifying those at risk of stress fracture injury is encouraged due to the multifaceted nature of the injury [3]. The data presented in the current study provide researchers and applied practitioners with normative bone and body composition

characteristics for high-level athletes with and without a history of stress fracture injury from a range of sports. These data are valuable in the identification of 'normal' characteristics in athletes with and without stress fracture symptoms.

Athletes vs. Control

The male athlete group as a whole showed greater whole-body BMD, BMC, T-score, Z-score and less percentage body fat compared to the non-athlete group. These findings are unsurprising as long-term weight-bearing exercise has well established osteogenic effects in excess of non-weight-bearing activities [30-31]. The female athlete group there were no differences in bone characteristics of women athletes and non-athletes. This may be related to the women non-athletes having a 22% greater body mass than the athletes, which could have provided a greater mechanotransductive effect of habitual activity and an osteogenic response equivalent to that experienced by the lighter athletes undergoing heavy training.

Limitations

This cross-sectional study required participants to retrospectively report cases of stress fracture injury. This resulted in the time-point between stress fracture injury incidence and the athlete being assessed for bone and body composition characteristics being variable and, in some cases, separated by several years. In this time period bone and body composition characteristics could have increased or decreased from the values recorded at the time of the scan. However, to combat this problem a prospective longitudinal study regularly assessing bone and body composition characteristics and stress fracture status would be required. A study of this design would be prohibitively expensive and be exceedingly challenging to recruit the high number of athletes seen in the present study. Furthermore, although there was a difference between the age of the athletes and non-athletes in the present study, the majority of participants (>95%) were below the age at which BMD begins to significantly decline (> 50 years) and therefore any changes in BMD are expected to be small and possibility undetectable. Two different DXA scanners were used in the present study. Although consistency in the scanning device used is preferred, a multi-centre approach was required in order to recruit a large cohort of high-level athletes. Furthermore, it has been shown that there is a high-level of agreement between bone and body composition characteristics for the brands of DXA used in the present study [42] and therefore it is unlikely that the use of separate devices influenced the results. The current study did not account for factors including diet, training status, training environment, individual biomechanics, hormonal status and psychological factors which have also been associated with stress fracture injury [3]. However, the monitoring of all these variables in a multi-centre cohort is costly and practically challenging, but nevertheless something that future collaborative studies should strive to accomplish. Due to the number of statistical tests conducted,

multiple comparison testing was conducted. However, the majority of the findings retained significance pre and post multiple comparison testing. The conservative nature and problems with conducting multiple comparison testing [43] increase the chances of a type two error occurring. However, the debate surrounding the merits and drawbacks of multiple comparisons testing goes beyond the scope of the current study.

Conclusion

The findings of the present study provide the largest-scale assessment of the bone and body composition characteristics of high-level athletes with and without a history of stress fracture injury. Overall, no differences in DXA derived bone characteristics and body composition were shown among athletes with and without a history of stress fracture injury. Male endurance runners with a history of stress fracture had a greater T-, Z-score and body mass than those without a history of stress fracture, suggesting that there are sport-specific differences in risk factors. These normative data can be used by researchers and applied practitioners as a benchmark for their own cohorts and athletes.

Conflict of interests:

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors' contribution:

IAN VARLEY and ADAM HERBERT drafted the work. GEORGINA STEBBINGS, ALUN G. WILLIAMS, STEPHEN DAY, PHILIP HENNIS, REECE SCOTT and NEVAL GRAZETTE were involved in revising it critically for important intellectual content.

IAN VARLEY, ADAM HERBERT, GEORGINA STEBBINGS, ALUN G. WILLIAMS and STEPHEN DAY were involved in the conception and design of the work. IAN VARLEY, ADAM HERBERT, GEORGINA STEBBINGS, REECE SCOTT and NEVAL GRAZETTE were involved in the acquisition of data, IAN VARLEY, ADAM HERBERT, PHILIP HENNIS, GEORGINA STEBBINGS, ALUN G. WILLIAMS were involved in data analysis and interpretation of data.

All authors are in agreement to be accountable for ensuring that questions related to the accuracy or integrity of the work were appropriately investigated and resolved and approved the final version of the manuscript.

References

1. Bennell KL, Malcolm SA, Thomas SA, Reid SJ, Brukner PD, Ebeling PR, et al. Risk factors for stress fractures in track and field athletes. A twelve-month prospective study. *Am J Sports Med* 1996;24:810-8.
2. Fredericson M, Jennings F, Beaulieu C, Matheson GO. Stress fractures in athletes. *Top Magn Reson Imaging* 2006;17:309-25.
3. Bennell K, Matheson G, Meeuwisse W, Brukner P. Risk factors for stress fractures. *Sports Med* 1999;28:91-122.

4. Pegrum J, Crisp T, Padhiar N. Diagnosis and management of bone stress injuries of the lower limb in athletes. *BMJ* 2012;24:344
5. Pritchard NS, Smoliga JM, Nguyen AD, Branscomb MC, Sinacore DR, Taylor JB, et al. Reliability of analysis of the bone mineral density of the second and fifth metatarsals using dual-energy x-ray absorptiometry (DXA). *J Foot Ankle Res* 2017;28:10-52.
6. Alway P, Peirce N, King M, Jardine R, Brooke-Wavell, K. Lumbar bone mineral asymmetry in elite cricket fast bowlers. *Bone* 2019;127:537-43.
7. Popp KL, Hughes JM, Smock AJ, Novotny SA, Stovitz SD, Koehler SM et al. Bone Geometry, Strength, and Muscle Size in Runners With a History of Stress Fracture. *Med Sci Sports Exerc* 2009;41:2145-50.
8. Johnston TE, Dempsey C, Gilman F, Tomlinson R, Jacketti AK, Close J. Physiological Factors of Female Runners With and Without Stress Fracture Histories: A Pilot Study. *Sports Health* 2020;12:334-40.
9. Newsham-West RJ, Lyons B, Milburn PD. Regional bone geometry of the tibia in triathletes and stress reactions--an observational study. *J Sci Med Sport* 2014;17:150-4.
10. Schnackenburg KE, Macdonald HM, Ferber R, Wiley JP, Boyd SK. Bone quality and muscle strength in female athletes with lower limb stress fractures. *Med Sci Sports Exerc* 2011;43:2110-9.
11. Duckham RL, Brooke-Wavell K, Summers GD, Cameron N, Peirce N. Stress Fracture Injury in Female Endurance Athletes in the United Kingdom: A 12-month Prospective Study. *Scand J Med Sci Sports* 2015;25:854-9.
12. Kraus E, Tenforde AS, Nattiv A, Sainani KL, Kussman A, Deakins-Roche M, et al. Bone Stress Injuries in Male Distance Runners: Higher Modified Female Athlete Triad Cumulative Risk Assessment Scores Predict Increased Rates of Injury. *Br J Sports Med* 2019;53:237-242.
13. Wentz L, Liu PY, Ilich JZ, Haymes EM. Dietary and Training Predictors of Stress Fractures in Female Runners. *Int J Sport Nutr Exerc Metab* 2012;22:374-82.
14. McNaughton SA, Wattanapenpaiboon N, Wark JD, Nowson CA. An Energy-Dense, Nutrient-Poor Dietary Pattern Is Inversely Associated With Bone Health in Women. *J Nutr* 2011;141:1516-23.
15. Tagliaferri C, Wittrant Y, Davicco MJ, Walrand S, Coxam V. Muscle and bone, two interconnected tissues. *Ageing Res Rev* 2015;21:55-70.
16. Cao JJ. Effects of obesity on bone metabolism. *J Orthop Surg Res* 2011;6:30.
17. Tencerova M, Figeac F, Ditzel N, Taipaleenmäki H, Nielsen TK, Kassem M. High-Fat Diet-Induced Obesity Promotes Expansion of Bone Marrow Adipose Tissue and Impairs Skeletal Stem Cell Functions in Mice. *J Bone Miner Res* 2018;33:1154-65.
18. Bonewald L. Use it or lose it to age: A review of bone and muscle communication. *Bone* 2019;120:212-18.
19. Knapik JJ, Sharp MA, Montain SJ. Association between stress fracture incidence and predicted body fat in United States Army Basic Combat Training recruits. *BMC Musculoskelet Disord* 2018;19:161.
20. Cosman F, Ruffing J, Zion M, Uhorchak J, Ralston S, Tendy S, et al. Determinants of stress fracture risk in United States Military Academy cadets. *Bone* 2013;55:359-66.
21. Hoffman JR, Chapnik L, Shamis A, Givon U, Davidson B. The Effect of Leg Strength on the Incidence of Lower Extremity Overuse Injuries During Military Training. *Mil Med* 1999;164:153-6.
22. Yagi S, Muneta, Sekiya I. Incidence and Risk Factors for Medial Tibial Stress Syndrome and Tibial Stress Fracture in High School Runners. *Knee Surg Sports Traumatol Arthrosc* 2013; 21:556-63.

23. Pamukoff DN, Blackburn JT. Comparison of plantar flexor musculotendinous stiffness, geometry, and architecture in male runners with and without a history of tibial stress fracture. *J Appl Biomech* 2015;31:41-7.
24. Nose-Ogura S, Yoshino O, Dohi M, KigAlun G. Williamsa M, Harada M, et al. Low Bone Mineral Density in Elite Female Athletes With a History of Secondary Amenorrhea in Their Teens. *Clin J Sport Med* 2018;30:245-50
25. Xu W, Chafi H, Guo B, Heymsfield SB, Murray KB, Zheng, et al. Quantitative Comparison of 2 Dual-Energy X-ray Absorptiometry Systems in Assessing Body Composition and Bone Mineral Measurements. *J Clin Densitom* 2016;19:298-304.
26. Varley I, Hughes DC, Greeves JP, Stellingwerff T, Ranson C, Fraser WD, et al. RANK/RANKL/OPG pathway: genetic associations with stress fracture period prevalence in elite athletes. *Bone*. 2015;71:131-6.
27. Norcross J, Van Loan MD. Validation of Fan Beam Dual Energy X Ray Absorptiometry for Body Composition Assessment in Adults Aged 18-45 Years. *Br J Sports Med* 2004;38:472-6.
28. Ward LC, Dyer JM, Byrne NM, Sharpe KK, Hills AP. Validation of a three-frequency bioimpedance spectroscopic method for body composition analysis. *Nutrition* 2007;23:657-64.
29. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple hypothesis testing. *J R Stat Soc B* 1995;57:289–300.
30. Kemmler W, Engelke K, Baumann H, Beeskow C, von Stengel S, Weineck J, et al. Bone status in elite male runners. *Eur J Appl Physiol* 2006;96:78-85.
31. Elloumi M, Ben Ounis O, Courteix D, Makni E, Sellami S, Tabka Z, et al. Long-term rugby practice enhances bone mass and metabolism in relation with physical fitness and playing position. *J Bone Miner Metab* 2009;27:713-20.
32. Wittich A, Mautalen CA, Oliveri MB, Bagur A, Somoza F, Rotemberg E. Professional football (soccer) players have a markedly greater skeletal mineral content, density and size than age- and BMI-matched controls. *Calcif Tissue Int* 1998;63:112-7.
33. Baker BS, Chen Z, Larson RD, Bemben MG, Bemben DA. Sex differences in bone density, geometry, and bone strength of competitive soccer players. *J Musculoskelet Neuronal Interact* 2020;20:62-76.
34. Nieves JW, Melsop K, Curtis M, Kelsey JL, Bachrach LK, Greendale G. Nutritional factors that influence change in bone density and stress fracture risk among young female cross-country runners. *PM&R* 2010;2:740-750.
35. Cobb KL, Bachrach LK, Greendale G, Marcus R, Neer RM, Nieves J, et al. Disordered eating, menstrual irregularity, and bone mineral density in female runners. *Med Sci Sports Exerc* 2003;35:711-9.
36. Jackman SR, Scott S, Randers MB, Ørntoft C, Blackwell J, Zar A, et al. Musculoskeletal health profile for elite female footballers versus untrained young women before and after 16 weeks of football training. *J Sports Sci* 2013;31:1468-74.
37. Kohrt WM, Barry DW, Schwartz RS. Muscle forces or gravity: what predominates mechanical loading on bone? *Med Sci Sports Exerc* 2009;41:2050-5.
38. Goodman CA, Hornberger TA, Robling AG. Bone and Skeletal Muscle: Key Players in Mechanotransduction and Potential Overlapping Mechanisms. *Bone* 2015;80:24-36.
39. Herrmann M, Engelke K, Ebert R, Müller-Deubert S, Rudert M, Ziouti F, et al. Interactions between Muscle and Bone-Where Physics Meets Biology. *Biomolecules* 2020;10;10:432.
40. Schipilow JD, Macdonald HM, Liphardt AM, Kan M, Boyd SK. Bone Micro-Architecture, Estimated Bone Strength, and the Muscle-Bone Interaction in Elite Athletes: An HR-pQCT Study. *Bone* 2013;56:281-9.

41. Herbert AJ, Williams AG, Hennis PJ, Erskine RM, Sale C, Day SH, et al. The Interactions of Physical Activity, Exercise and Genetics and Their Associations With Bone Mineral Density: Implications for Injury Risk in Elite Athletes. *Eur J Appl Physiol* 2019;119:29-47.
42. Hull H, He Q, Thornton J, Javed F, Wang F, Pierson Jr RN, et al. iDXA, Prodigy, and DPXL dual-energy X-ray absorptiometry whole-body scans: a cross-calibration study. *J Clin Densitom* 2009;12:95–102.
43. Streiner DL, Norman GR. Correction for multiple testing: is there a resolution? *Chest* 2011;140:16-18.

Table 1: Personal best selection criteria for both men and women runners.

Distances	Men	Women
3000 m	< 8 min 45 s	< 10 min 15 s
5000 m/5 km road	< 15 min 45 s	< 18 min 45 s
10000 m/10 km road	< 32 min 45 s	< 38 min 45 s
Half marathon	< 74 min 00 s	< 88 min 00 s
Marathon	< 2 h 45 min 00 s	< 3 h 15 min 00 s

Table 2. The location of stress fracture injuries.

Location	Number of Stress Fractures
Metatarsal	28
Tibia	16
Lumbar spine	9
Sacrum	4
Navicular	4
Fibula	2
Cuboid	2
Talus	2
Pubic ramus	1
Ulna	1
Femur	1
Calcaneus	1
Unspecified location	1

Table 3a. The bone and body composition characteristics of male athletes and non-athletes.

		Athletes			Non-athletes		
		Men			Men		
		All (n = 210)	Stress fracture (n=34)	Non-stress fracture (n=176)	Stress fracture vs. non-stress fracture p value	(n = 44)	Athletes vs. non-athletes p value
Body composition	Age (years)	26.5(7.4)	26.7(7.8)	26.4(7.3)	0.81	36.5(15.5)	<0.01*
	Body mass (kg)	82.0(13.9)	83.6(14.2)	81.7(13.8)	0.47	78.3(11.2)	0.46
	Height (m)	1.82(0.08)	1.82(0.07)	1.82 (0.08)	0.64	1.79(0.07)	0.76
	BMI(kg/m ²)	24.7(3.2)	25.1(3.6)	23.7(3.1)	0.48	24.5(3.3)	0.19
	Lean mass (kg)	65.4(9.9)	66.1(9.5)	65.3(9.9)	0.66	57.1(6.4)	0.15
	% body fat	16.3(5.0)	16.8(0.5)	16.2(5.0)	0.56	22.6(5.9)	<0.01*
Bone: Whole body	T-score	2.1(1.2)	2.3(1.1)	2.0(1.3)	0.31	1.2(1.1)	<0.01*
	Z-score	1.7(1.0)	1.8(0.9)	1.7(1.0)	0.45	1.2(1.0)	0.03*

Values are mean (\pm 1SD). * significant difference between sex-specific athletes and non-athletes ($P < 0.05$).

Table 3b. The bone and body composition characteristics of female athletes and non-athletes.

		Athletes				Non-athletes	
		Women		Women		Women	
		All (n =56)	Stress fracture (n=16)	Non-stress fracture (n=40)	Stress fracture vs. non-stress fracture p value	(n = 59)	Athletes vs. non-athletes p value
Body composition	Age (years)	32.5(12.6)	31.7(11.0)	32.9(13.2)	0.76	37.8(15.8)	0.05
	Body mass (kg)	53.2(5.3)	51.7(4.2)	53.8(5.6)	0.20	64.8(11.4)	<0.01*
	Height (m)	1.64(0.05)	1.64(0.04)	1.64(0.06)	0.81	1.64(0.04)	0.66
	BMI(kg/m2)	19.8(1.9)	19.3(1.4)	20.0(2.1)	0.24	24.0(3.0)	<0.01*
	Lean mass (kg)	38.7(3.6)	37.7(3.1)	39.1(3.7)	0.19	39.2(5.9)	0.57
	% body fat	23.0(4.6)	23.2(4.2)	22.9(4.8)	0.87	34.5(7.0)	<0.01*
Bone: Whole body	T-score	1.0(1.0)	0.7(0.9)	1.2(1.0)	0.13	1.0(1.3)	0.85
	Z-score	1.0(0.9)	0.7(0.8)	1.1(0.9)	0.09	1.0(1.2)	0.88

Values are mean ($\pm 1SD$). * significant difference between sex-specific athletes and non-athletes ($P < 0.05$).

Table 4a. Bone and body composition characteristics of footballers and endurance runners with and without a history of stress fracture injury.

		Football			Endurance Runners					
					Men			Women		
		All (n =96)	Stress fracture (n =13)	Non-stress fracture (n =83)	All (n = 43)	Stress fracture (n = 8)	Non-stress fracture (n = 35)	All (n=49)	Stress fracture (n= 16)	Non-stress fracture (n =33)
	Age (years)	24.7(4.2)	23.7(3.9)	24.9(4.3)	35.9(9.3)	35.9(10.2)	35.9(9.1)	34.4(12.7)	31.7(11.0)	35.8(13.2)
	Body mass (kg)	82.0(9.3)	80.3(8.7)	82.3(9.4)	67.3(6.9)	71.7(5.2)*	66.3(6.8)	52.4(5.2)	51.7(4.2)	53.8(5.6)
	Height (m)	1.82(0.08)	1.80(0.7)	1.82(0.08)	1.78(0.06)	1.82(0.06)	1.77(0.06)	1.64(0.05)	1.64(0.04)	1.64(0.06)
	BMI (kg/m ²)	24.7(1.8)	24.5(1.4)	24.7(1.8)	21.2(1.8)	21.8(2.0)	21.0(1.7)	19.4(1.7)	19.3(1.4)	19.5(1.8)
Body composition	Lean mass (kg)	67.1(7.4)	66.3(7.6)	67.2(7.4)	52.8(4.7)	52.8(5.9)	52.8(4.4)	38.1(3.0)	37.7(3.1)	38.2(3.0)
	% body fat	14.6(3.6)	14.0(2.9)	14.7(3.7)	16.9(0.6)	17.9(3.5)	16.7(5.8)	23.0(4.6)	23.2(4.2)	22.9(4.8)
Bone: Whole body	BMD (g/cm ²)	1.44(0.10)	1.43(0.09)	1.44(0.10)	1.28(0.10)	1.34(0.11)	1.27(0.09)	1.19(0.09)	1.16(0.08)	1.20(0.09)
	BMC (g)	3872(465)	3770(391)	3888(476)	2910(294)	3084(493)	2870(356)	2244(285)	2166(209)	2283(123)
	T-score	2.4(0.1)	2.6(1.0)	2.4(1.0)	0.8(0.9)	1.4(0.9)*	0.7(0.8)	1.0(1.0)	0.7(0.9)	1.2(1.1)
	Z-score	2.0(0.7)	1.9(0.9)	2.0(0.7)	0.8(0.8)	1.4(0.8)*	0.7(0.8)	0.9(0.9)	0.7(0.8)	1.1(0.9)
Legs	BMD (g/cm ²)	1.65(0.12)	1.66(0.15)	1.66(0.12)	1.47(0.11)	1.50(0.10)	1.46(0.11)	1.27(0.01)	1.25(0.08)	1.28(0.10)
	BMC (g)	1584(215)	1521(178)	1594(220)	1180(174)	1239(206)	1166(163)	822(118)	788(98)	838(123)

Values are mean (±1SD). * significant difference between athletes with and without a history of stress fracture injury (P < 0.05)

Table 4b. Bone and body composition characteristics of rugby players and cricketers with and without a history of stress fracture injury.

		Rugby			Cricket		
		All (n=38)	Stress fracture (n=7)	Non-stress fracture (n=31)	All (n =20)	Stress fracture (n=5)	Non-stress fracture (n =15)
Body composition	Age (years)	22.5(3.1)	24.1(4.1)	22.1(2.7)	24.4(3.9)	24.8(4.6)	23.6(4.5)
	Body mass (kg)	99.2(11.8)	103.0(14.8)	98.3(11.2)	86.5(12.3)	87.7(4.8)	86.4(13.5)
	Height (m)	1.85(0.08)	1.84(0.06)	1.85(0.08)	1.84(0.10)	1.87(0.09)	1.84(0.12)
	BMI (kg/m ²)	29.0(3.0)	30.3(3.8)	28.7(2.8)	25.4(2.5)	25.1(1.2)	25.7(3.4)
	Lean mass (kg)	76.5(7.0)	77.2(6.9)	76.4(7.1)	65.2(6.1)	68.5(4.1)	63.8(6.7)
	% body fat	18.8(5.4)	21.0(6.3)	18.3(5.2)	20.4(5.3)	17.8(2.7)	21.7(4.9)
Bone: Whole body	BMD (g/cm ²)	1.51(0.09)	1.56(0.05)	1.50(0.10)	1.39(0.08)	1.41(0.04)	1.38(0.044)
	BMC (g)	4312(407)	4421(335)	4287(422)	3721(373)	3815(283)	3697(450)
	T-score	3.2(0.8)	3.5(0.6)	3.1(0.9)	1.9(0.8)	2.1(0.4)	1.9(0.5)
	Z-score	2.4(0.8)	2.7(0.5)	2.3(0.9)	1.6(0.7)	1.7(0.4)	1.6(0.4)
Legs	BMD (g/cm ²)	1.64(0.10)	1.69(0.07)	1.63(0.10)	1.59(0.13)	1.65(0.11)	1.57(0.07)
	BMC (g)	1611(166)	1615(106)	1610(178)	1528(238)	1622(260)	1523(231)

Values are mean ($\pm 1SD$). * significant difference between athletes with and without a history of stress fracture injury ($P < 0.05$)