International Journal of Medical and Health Research
ISSN: 2454-9142
Impact Factor: RJIF 5.54
www.medicalsciencejournal.com
Volume 4; Issue 4; April 2018; Page No. 136-139

Vitamin D deficiency and stress fractures in soldiers and athletes: A review

Dr. Rami Shenouda[1], Dr. Mark Daniel Wilson[2]
[1] MBBS Dip Anat, University of Tasmania Burnie, Tasmania, Australia
BSc MBBS Dip Anat, University of Tasmania Burnie, Tasmania, Australia

Abstract
Objective: The purpose of this systematic review was to evaluate the role of and importance of Vitamin D deficiency as a risk factor for stress fractures in soldiers and athletes.
Methods: A search of the current literature was performed, leading to the inclusion of 14 suitable papers for analysis. A search on EMbase conducted using the search items “Vitamin D deficiency” and “stress fracture” was performed. The outcomes of these papers were used to outline a better understanding of the role of Vitamin D deficiency as a risk factor for stress fractures in these unique patient populations.
Results/Discussions: Often implicated in the pathophysiology of stress fractures, Vitamin D deficiency is described as a risk factor for the development of this condition in both athletes and military personnel, although the exact pathophysiology still requires further delineation.
Conclusion: While sufficient intake and metabolism of Vitamin D is important for proper bone health and to attenuate the risks of stress fractures, the true impact of Vitamin D insufficiency and deficiency varies across different populations, including athletes and soldiers. Overall, large, long-term and prospective studies must be completed to further our current understanding of this important area of musculoskeletal medicine.

Keywords: vitamin D deficiency, stress fracture, pathophysiology, athletes, military, sports medicine

Introduction

Stress fractures of the bone are a condition that result from micro-fractures from repeated physical loading and can cause a significant amount of pain and loss of function. Individuals who undertake repetitive, strenuous activity such as military personnel and athletes have been hypothesised to have an increased risk of these injuries due to several reasons. There are a number of studies that have attempted to identify a link between stress fractures and various anthropometric measurements and biochemical markers including Vitamin D. Vitamin D is a vital component of bone metabolism and turnover as well as numerous other metabolic processes, including but not limited to inflammatory and immune responses. A number of reviews and studies have given evidence to suggest that vitamin D deficiency (VDD) is associated with stress fractures and thus the purpose of this systematic review is to critique and critically analyse the literature surrounding stress fractures, Vitamin D and military personnel and athlete populations.

Methods

A search of the Web of Science databases was performed using the University of Queensland library. The terms “stress fracture” and “Vitamin D” were used with the results limited to the last ten years. This search returned 167 studies, all of which were reviewed by a single author (RS). Of these studies 14 were deemed suitable after review of the title, abstract and content and six further articles were sourced from the references of these articles where there content was believed to add to the review findings. These studies were subsequently reviewed and critically analysed by the two authors (RS and MW) to determine whether a quantifiable link exists between Vitamin D deficiency and stress fracture risk in military personnel and athletes.

Critical Analysis: Differences in Nationality

USA

Many of the most recent investigations regarding Vitamin D and stress fracture risk has arisen from the United States. Davey *et al*. (2015) investigated stress fractures and Vitamin D in 1082 Royal Marine trainees over 32 weeks. During this time, 78 recruits suffered a total of 92 stress fractures. Using a threshold of 50 nmol/L the study found recruits with a baseline vitamin D < 50 nmol/L had a higher incidence of stress fracture than recruits with vitamin D concentration above this (odds ratio 1.6 (95 % confidence interval (CI) 1.0–2.6). This study took blood tests, anthropometric and physical fitness measurements at week one and then repeated the blood tests at week 15 and 32. It also found that subjects that fractured from week 0-10 had a baseline vitamin D of 49.5±18.7 nmol/L (n=8) vs. 66.4±29.2 nmol/L (n=70) for those who fractured later (p=0.043). Serum vitamin D concentration was lower at week 32 in the fractured recruits than in the non-fractured recruits (44.5±22.9 nmol/L (n=17) vs. 56.8± 22.4 nmol/L (n=365); p<0.05. A study by Cosman *et al*. (2013) [5] found further risk factors identified in the male cohort were smaller tibial cortical area (RR 1.12; CI 1.03, 1.23) and smaller femoral neck diameter (RR1.35, CI 1.01, 1.81). For women, fewer years since menarche was associated with increased risk; mean 4.9 years in fracture cases vs. 5.8 years in non-fracture cases (RR 1.44 per year; CI 1.19, 1.73) and smaller femoral neck diameter (RR 1.16; CI 1.01, 1.33).

A further study reviewed the longitudinal effects of basic combat training (BCT) in 74 female soldiers in South Carolina over eight weeks. In the total study population, Vitamin D levels decreased from 72.9 ± 30.0 to 63.3 ± 19.8 nmol/L and PTH levels increased from 36.2 ± 15.8 to 47.5 ± 21.2 pg/mL ($P < 0.05$). The study also found differences in ethnicity with Hispanic and non-Hispanic Caucasians having the largest decrease in Vitamin D, but not in non-Hispanic blacks (Anderson *et al*., 2010) [6]; Lutz *et al*. (2012) [7] later added that white individuals experienced the largest decrease in Vitamin D and non-white individuals experienced an increase. Interestingly, thi study found that at all times those non-whites subjects had lower Vitamin D levels than their white counterparts. This was added to in 2013 during a comparatively large retrospective cohort study investigating the difference of UV index and ethnicities on stress fracture rate. The study found that black individuals were the least likely to experience stress fractures and that surprisingly those individuals in areas of lower UV Index had a decreased rate of stress fracture, thus highlighting the multi-factorial nature of stress fractures. Burgi *et al*.'s (2011) [9] study also found that white female recruits had a higher stress fracture risk than black female recruits. Having divided the groups into quartiles, the study found that in the white population specifically, the odds ratio decreased as the Vitamin D level increased. A further multi-variate analysis continued to demonstrate Vitamin D concentration having an inverse relationship to risk of stress fracture, supporting the geographic and racial component of its etiology.

Israel

Israeli military recruits have had several investigatory research articles published reviewing stress fractures in their population. A 2012 article by Moran *et al*. reviewed 74 elite Israeli recruits undergoing basic and advanced combat training (ACT). Various anthropometric measurements and blood tests assessing overall health and nutrition were taken at entry and at the 4-month and 6-month mark of training. It was found that upon induction many of the recruits had decreased calcium and Vitamin D levels and that these were reduced in the stress fracture group compared to the non-stress fracture group (Calcium 589 ± 92 vs. 964 ± 373 mg/d ($p<0.001$) and Vitamin D 117.9 ± 34.3 vs. 157.4 ± 93.3 IU/d, respectively, $p < 0.001$). While these results stayed stable in the stress fracture group, these levels decreased in the non-stress fracture group. The researches also found that despite their high-energy needs, the recruits consumed only 70% of their daily requirement. Additionally in the stress fracture group, soldiers developed iron deficiency and anemia symptoms that were associated with 39% low transferrin saturation (< 16%), 36.4% ferritin deficiency (<20 ng/ml), and 37.9% hemoglobin deficiency (< 14 g/dl). While not the main outcome, this could give grounds for further research in stress fracture causes and markers. These findings added to Moran *et al*.'s (2008) [11] study that investigated risk factors for stress fractures in female recruits; finding that height, psychological stressors as well as iron deficiency and ferritin all had associations with stress fracture risk. An earlier Israeli study of 2591 soldiers referred for suspected stress fractures (using X-ray and technetium scans) found 318 soldiers with high-grade stress fractures (Grade 3-4 uptake) and 237 symptomatic soldiers (no uptake to Grade 1-2 uptake) and 2036 asymptomatic controls. However, only 40 high-grade and 40 symptomatic/low-grade soldiers underwent biochemical tests due to limitations imposed by the ethics council and these tests were done whilst patients were symptomatic. The high-grade group revealed elevated ALP and osteocalcin compared to the symptomatic control group; the latter showed decreased Vitamin D and other biochemical markers (ALP 37.6 vs. 26.2 U/L, osteocalcin 10.8 vs. 8.8 ng/mL and Vitamin D 25.3 vs. 29.8 ng/mL respectively) all of which were statistically significant. Despite these blood tests, the researchers hypothesized that the cause of stress fractures were multi-factorial, as they also found surprising results such as smoking being minimally protective for stress fracture (Givon *et al*., 2000) [12], which intuitively seems biologically implausible.

Europe

Välimäki *et al*. (2005) [13] prospectively reviewed 179 Finnish male military recruits throughout BCT. Numerous physical and biochemical measurements were recorded, in addition to the subjects completing muscle strength and Cooper's tests. Throughout their military service, 15 of the men experienced stress fractures (10 in metatarsals, four in tibia, and one in calcaneus); three of these men had multiple metatarsal fractures. The study found that following analysis those with stress fractures were taller, with poorer muscle conditioning, and that following adjustment for several demographic and lifestyle factors, had lower femoral neck BMD. Finally, stress fractures were associated with higher iPTH levels, but not with lower Vitamin D levels. This study had a cumulative incidence of stress fracture of 8%, which was similar to previous Finnish studies, however this was overall significantly lower than other countries, including Israeli. Additionally, the stress fractures were diagnosed with x-ray rather than other modalities that are much more sensitive, namely bone scans and MRI (Välimäki *et al*. 2005) [13]. Chatzipapas *et al*. (2008) [16] also found no difference in Vitamin D levels between a stress fracture and non-stress fracture group, although this was a small study with only 64 subjects. The study also identified significant differences in albumin, Osteocalcin and T- and Z-score on calcaneal stiffness index on ultrasound, thus furthering the concept of a multi-factorial origin of stress fractures (Chatzipapas *et al*., 2008) [16].

A 2006 paper by Ruohola *et al*. again reviewed Finnish military recruits and their risk of stress fracture over 90 days. Out of 756 recruits, 22 developed 30 stress fractures (2.9%) with the incidence being 11.6% per 100 person-years. These were diagnosed on plain radiographs looking for hallmark signs of stress fracture, as well as MRI for those with ongoing pain and normal x-rays. Following multi-variate analysis a below median serum Vitamin D level (75.8 nmol/L) demonstrated an odds ratio of 3.6 for developing a stress fracture, however no significant associations were found for BMI, age, smoking and stress fractures. This study thus demonstrated that a lower level of serum Vitamin D might be a predisposing factor for stress fractures. Välimäki *et al*. 's (2004) [13] previous cross-sectional study may give insight into the causes as it identified positive correlations (when adjusted for lifestyle and anthropometric measurements) between Vitamin D and BMD at the lumbar spine, femoral neck and trochanter (correlation coefficient = 0.35, 0.061, 0.056, 0.068 respectively). Additionally, it found that of the included study participants, 38.9% had Vitamin D deficiency during winter, whilst in summer this figure was 0.9%, presumably due to regional sunlight exposure differences.

Athletes and Supplementation

There are several studies that review Vitamin D status and outcomes in athletes of various levels. Shimasaki *et al*. (2016) [17] reviewed high-level soccer players at university with metatarsal stress fractures against controls. While initial uni-variate analysis failed to identify a significant difference, the two groups underwent a subsequent multi-variate analyses that revealed an adjusted odds ratio of 23.3 for stress fracture when Vitamin D <30 ng/mL. The analysis also found a slight increase in odds ratio of 1.1 for bone-specific isoform of alkaline phosphatase (AP), a measure of bone turnover and general bone homeostasis. While this study provided a strong link in the athletic population, it was an extremely small study with some selection bias due to the recruiting method and thus it does lose some of its power as a result. A previous study by Nieves *et al*. (2010) [18] assessed intake of energy, protein, vitamins and elements and while it did not investigate stress fracture rates, it did find that adequate Vitamin D intake had a 0.67 hazard ratio for stress fractures, as well as improving hip and spine BMD.

A 2016 review of stress fractures and athletes provided commentary and guidelines on the risk factors and their development. The review stated biological factors such as significant nutritional deficiencies in calcium and Vitamin D increase the risk for stress fractures in addition to certain medication (anticonvulsants, steroids, antidepressants and antacids), as well as female sex and several biomechanical factors. The study drew reference from other studies that demonstrated female runners have a 6-fold decreased stress fracture risk in those with 1500 vs. 800 mg calcium supplementation. It also referenced Lappe *et al*. (2008) that examined calcium and Vitamin D supplementation in a comparatively large cohort (5210) of female navy recruits over eight weeks. Lappe found that the supplementation group (2000mg calcium and 800 IU Vitamin D) had an approximately 20% lower incidence of stress fractures compared to a control group (Lappe *et al*., 2008) [20].

Gaffney-Stomberg *et al*. (2014) [21] also reviewed the effects of Calcium and Vitamin D supplementation on bone density and parathyroid hormone in military recruits over nine weeks using a well-designed, randomized and double-blinded placebo trial. Researchers determined the physiological outcomes in 247 subjects (168 completed) undergoing basic combat training when given two snack bars (2000mg + 1000 IU/d Vitamin C and D, respectively) per day. Following consumption of the supplemental Vitamin C + D, volumetric BMD increased 14% on peripheral quantitative CT, whilst circulating ionized calcium increased (from 1.24 to 1.26 nmol/L, P = 0.022), maintained PTH, and increased the osteoprotegerin: RANKL ratio (12.7 to 18.8 pg/ml). Whilst stress fracture rates were not recorded, all of these factors are theoretically protective from stress fracture pathogenesis and the maintenance of bone health during periods of increased stress.

Discussion

The studies included in this review aim to provide an international view of stress fractures and Vitamin D levels amongst military staff and athletes. A benefit of this is that these articles are able to provide a cross-section of Vitamin D status amongst a number of countries. Each nation had significantly different exposure to sun with the USA and Israel being brighter, warmer climates compared to Finland, as well as diet, highlighted by the recruits in the Finland-based studies having a significant rate of pre-study Vitamin D deficiency. Additionally, several studies highlighted the difference in Vitamin D levels and stress fracture risk between different races that may affect the proportion of those diagnosed.

However, these studies are not without limitations. A vast majority of the studies are small in size due to the nature of basic training and thus it is quite difficult to obtain large cohorts for analysis. Additionally, across the studies, there did not appear to be a clear definition for Vitamin D deficiency, with many of them using their own values for deficiency throughout the military and athlete population. Diagnostic techniques were also not standardised across each study. The athlete-based studies suffered from a paucity of a large number of randomised studies. While there were several literature reviews and commentaries, these did not add to the strength of the already performed review by Shimasaki *et al*. in 2016 [17].

Conclusion

Stress fractures have been identified in military personnel and athletes for quite a significant period of time. This review aimed to critically analyses the studies that investigated the link between Vitamin D deficiency and stress fracture risk in order to determine whether such a link existed. While the review did give evidence to suggest that decreased Vitamin D levels may be linked to an increased stress fracture risk, it did not conclusively support this statement and also highlighted several other concerns. Throughout the various studies there were other indicators of stress fracture risk that warrant investigation, including but not limited to, ALP, Osteocalcin, BMD, as well as Vitamin D, calcium and energy intake and expenditure. Further large studies are warranted to produce high-powered results that allow for significant results and conclusions to be drawn for the clinical benefit of patients.

References

1. Brukner P, Khan K. *Clinical Sports Medicine* (Vol. 3rd). Sydney: McGraw-Hill, 2007.
2. Larson-Meyer DE, Willis KS. Vitamin D and Athletes. *Current Sports Medicine Reports*, 2010, 220-26.
3. Dao D, Sodhi S, Tabasinejad R, Peterson D, Ayeni O, Bhandari M, *et al*. Serum 25-Hydroxyvitamin D Levels and Stress Fractures in Military Personnel. The American Journal of Sports Medicine. 2015; 43(8):2064-72.

4. Davey T, Lanham-New S, Shaw A, Hale B, Cobley R, Berry J, *et al*. Low serum 25-hydroxyvitamin D is associated with increased risk of stress fracture during Royal Marine recruit training. Osteoporosis International, 2015, 171-179.
5. 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, 359-366.
6. Anderson NE, Karl PK, Cable SJ, Williams KW, Rood JC, Young AJ, *et al*. Vitamin D status in female military personnel during combat training. Journal of the International Society of Sports Nutrition. 2010; 7(38):1-5.
7. Lutz LJ, Karl JP, Rood JC, Cable SJ, Williams KW, Young AJ, *et al*. Vitamin D status, dietary intake, and bone turnover in female Soldiers during military training: a longitudinal study. Journal of the International Society of Sports Nutrition. 2012; 9(13):1-7.
8. Montain SJ, McGraw SM, Ely MR, Grier TL, Knapik JJ. A retrospective cohort study on the influence of UV index and race/ethnicity on risk of stress and lower limb fractures. *BMC Musculoskeletal Disorders.* 2013; 14(135):1-9.
9. Burgi AA, Gorham ED, Garland CF, Mohr SB, Garland FC, Zeng K, *et al*. High Serum 25-Hydroxyvitamin D Is Associated With a Low Incidence of Stress Fractures. Journal of Bone and Mineral Research. 2011; 26(10):2371-77.
10. Moran DS, Heled Y, Arbel Y, Israeli E, Finestone AS, Evans RK, *et al*. Dietary intake and stress fractures among elite male combat recruits. Journal of the International Society of Sports Nutrition. 2012; 9(6):1-7.
11. Moran D, Israeli E, Evans R, Yanovich R, Constantini N, Shabshin N, *et al*. Prediction Model for Stress Fracture in Young Female Recruits during Basic Training. Medicine & Science In Sports & Exercise. 2008; 40(11):S636-44.
12. Givon U, Friedman E, Reiner A, Vered I, Finestone A, Shemer J. Stress Fractures in the Israeli Defense Forces From 1995 to 1996. *Clinical Orthopaedics And Related Research*, 2000, 227-232.
13. Välimäki VV, Alfthan H, Lehmushkallio EL, Sahi T, Suominem H, Välimäki MJ. Risk factors for clinical stress fractures in male military recruits: A prospective cohort study. *Bone*, 2005, 267-273.
14. Ruohola JP, Laaksi T, Ylikomi T, Haataja R, Mattila VM, Sahi T, *et al*. Association Between Serum 25(OH)D Concentrations and Bone Stress Fractures in Finnish Young Men. Journal of Bone And Mineral Research, 2006, 1483-1488.
15. Välimaki VV, Alfthan H, Lehmuskallio E, Loyttyniemi E, Sahi T, Stenman UH, *et al*. Vitamin D Status as a Determinant of Peak Bone Mass in Young Finnish Men. The Journal of Clinical Endocrinology & Metabolism, 2004, 76-80.
16. Chatzipapas CN, Drosos G, Kazakos K, Tripsianis G, Iatrou C, Verettas D. Stress Fractures in Military Men and Bone Quality Related Factors. International Journal of Sports Medicine, 2008, 922-926.
17. Shimasaki Y, Nagao M, Miyamori T, Aoba Y, Fukushi N, Saita Y, *et al*. Evaluating the Risk of a Fifth Metatarsal Stress Fracture by Measuring the Serum 25-Hydroxyvitamin D Levels. Foot & Ankle International. 2016; 37(3):307-11.
18. Nieves J, Melsop K, Curtis M, Kelsey J, Bachrach L, Greendale G, *et al*. Nutritional Factors That Influence Change in Bone Density and Stress Fracture Risk Among Young Female Cross-Country Runners. American Academy of Physical Medicine and Rehabilitation. 2010; 2:740-50.
19. Tenforde A, Kraus E, Fredericson M. Bone Stress Injuries in Runners. Physical Medicine & Rehabilitation Clinics of North America. 2016; 27:139-49.
20. Lappe J, Cullen D, Haynatzki G, Recker R, Ahlf R, Thompson K. Calcium and Vitamin D Supplementation Decreases Incidence of Stress Fractures in Female Navy Recruits. Journal of Bone and Mineral Research. 2008; 23:741-49.
21. Gaffney-Stomberg E, Lutz LJ, Rood JC, Cable SJ, Pasiakos SM, Young AJ, *et al*. Calcium and vitamin supplementation maintains parathyroid hormone and improves bone density during initial military training: A randomized, double-blind, placebo controlled trial. *Bone*, 2014, 46-56.