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Impact of physical activity on incidence of osteoporotic fractures - a review

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Abstract

Introduction and purpose: The purpose od this study is to describe influence of participating in sporting activities on health of the bones. Osteoporosis is a disease of elderly people in which bone mineral density lowers. Physical activity was reported to increase bone mineral density.

A brief description of the state of knowledge: Better physical performance is a positive factor that lowers the possibility of fracturing the bones of the elderly. Another factor that plays protective role is lean body mass and development of muscles. Training in young age can help to increase the bone mineral density, but the effect ceases with the passing of time, being much lower after decades. Multiple genes have impact on bone mineral density of the individual. Professional athletes have usually higher bone mineral density, but accumulation of microdamage in their bones can result in stress fractures. Training in elderly age is proven to increase bone mineral density of an individual, especially performing weight-bearing sports.

Conclusions: Physical activity has been proven to positively affect health in many ways. One of them is strengthening the bones by increasing bone mineral density. As it increases, the possibility to break the bone lowers, which makes it an effective way to support the fight

against the osteoporosis. It is especially important for women, who are more susceptible to osteoporotic fractures in post-menopausal age.

Key words: Osteoporosis; Fracture; physical activity; osteoporotic fracture

1. Introduction

Main characteristics of the osteoporosis is increased susceptibility to fractures, caused by lowering of bone mineral density (BMD) and bone quality. Bone Mineral Density usually gets lower with age. Dual-emission x-ray absorptiometry (DXA) is a routine method of measuring BMD. In adults, bone remodelling is the main mechanism of bone renewal and adaptation. The bone remodelling is significantly faster in postmenopausal women, making them more likely to get a fracture. What is more, fractures can happen on a background of microdamage, which accumulates with age [1,2].

Osteoporotic fractures happen in areas of lowered BMD, and with increased incidence in that location after age of 50 years. The risk of getting an osteoporotic fracture is 40-50% and 13-22% respectively for women and men. With such a high incidence comes and increase of mortality of the elderly and also huge socioeconomic costs of treatment and rehabilitation [3,4].

The most common cause of osteoporotic fracture is fall. There is literature evidence, that practising sports can result in higher bone mineral density and positively impact postural balance, resulting in lowering the impact of two factors important in developing a fracture [5,6]

2. Purpose of the study

To describe current state of knowledge available on PubMed database on impact of physical activity on a risk of developing an osteoporotic fracture.

3. State of knowledge

3.1. Physical performance as a measure of risk of osteoporotic fracture

In the elderly population, falls are the most common cause of the fractures. Accounting for 10% of hospitalisations of the elderly, they pose a threat to osteoporotic people, whose bones break more easily. Therefore, discovering risk factors of the falls in the population over 65 years has become an important task [7,8].
During The Osteoporotic Fractures in Men (MrOS) International Study researchers have proven, that lower physical condition of the elderly is a risk factor of a fall. Participants took part in 4 tests: grip strength test, standing up from a fully sitting position without using arms test, six-metre walk test and the twenty-centimetre narrow walk test. The correctness of performing the tasks and the needed time was proven to correlate with history of previous falls and fractures of the participant. The „non-falling'' group performed better that „falling with a fracture'' group in all tasks. The „falling without a fracture'' group performed better

than the „falling with a fracture'' group in grip strength test and six-metre walk test. What is worth to be noted, the „falling with a fracture'' group was the least physically active, while the group of elderly people who didn't have a history of falls were the most active. [7,9,10] In Study of Osteoporotic Fractures (SOF) performed on >65 old women of Caucasian and African-American Ethnicity the clinical characteristics that predict the hip fracture or „any non-vertebral fracture'' were examined. The most important risk factors are: low bone mineral density, previous fractures, poor cognitive function, walking speed and using arms to stand from sitting on a chair position. The last two are dependent on the physical condition of the individual. The Japanese Research on Osteoarthritis/osteoporosis Against Disability (ROAD) study confirms that low walking speed is an important risk factor for osteoporotic fractures [11,12,13].

3.2. Muscle mass and fractures

The correlation between muscle mass and incidence of fractures has already been proven. In a study from 2019 on group of men with average age of 84,2, muscle mass was measured using D3-creatine and bone density was measured with dual energy x-ray absorptiometry (DXA). Results show that in patients with the lowest muscle mass the probability of severe trauma, including fracture was 2,5 times higher compared with group of higher muscle mass [14]. Cohort study from southern Finland suggests, that lean body mass is correlated with risk of vertebral fracture. Participants were anthropometrically measured in age of 31 and 46, and what is more in age of 46 their body composition was measured and lumbar MRI was performed to calculate surface area of lumbar vertebrae. Results suggest that from anthropometric measures, height and lean body mass have the most notorious correlation with surface area of vertebrae [15].
In Beijing Jishuitan Hospital relationship between Bone Mineral Density of femur, lumbar vertebrae and iliac bone and density of surrounding muscles was verified using CT in group of women. The highest correlation was observed between the density of greater gluteal muscle and femoral trochanter density [16].

3.3. Training in youth and fractures in old age

Research from Norway has investigated the impact of recreational physical activity of adults and incidence of fractures of the vertebrae. Participants in age between 38 and 87 years filled out the questionnaires about their physical activity and DXA was performed on them. Results suggest that there is no impact of physical activity on incidence of vertebral fractures, irrespectively of type of activity [17].
Recreational physical activity of teenagers and young adults may give better results. Using ultrasounds, bone density of calcaneus was measured in adolescents, and in individuals of higher physical activity BMD was higher. The small size of study group has limited the possibility to verify if the relation is equally strong in men and women. Weight bearing sports had a higher impact on bone density [18].
Similar results were obtained in group of men from South Dakota in age ranging from 20 to 66 years. Their current physical activity and activity of school age and studies was compared with their BMD measured in DXA. In people that had at least 7 active sport seasons in their life BMD of hip bone was higher, and they were also taller and stronger than people with less physical activity. What should be noted, due to bone mass loss in young adulthood, the differences between groups were lesser in age of 50 [19].

Cohort study from Finland shows that physical activity of moderate intensity has a positive impact on vertebrae surface area and lowers the incidence of vertebral fractures in men and women. Activity was measured using water proof accelerometers worn by people of average age of 48,8 [20].
Research conducted in Silesia in 2016 on 362 women in post menopausal age (55-87) has proven similar results. Participants have filled the questionnaires about their physical activity in age 20-30 and 50-60 years. Their current physical capacity was measured, their bone density was measured with ultra sounds and DXA was performed on lumbar vertebrae. The results suggest that current physical capacity has significant influence on BMD, but physical activity in youth has no impact on it [21].

3.4. The relationship between genetics and sports impact on the incidence of bone fractures

Bone fractures occur when exposure to external factors results in a transfer of force to the bone that exceeds a person's tolerance threshold, what may be a result of high-impact force or repeated stresses with insufficient recovery (stress fractures) [22]. Exercise is an important factor in the prevention of osteoporotic fractures, but also exposure to stimuli that cause non-osteoporotic fractures [23,24]. Fracture risk is a complex trait that is also influenced by genetic variation [25]. It has been shown that fracture susceptibility is related to genetic factors in 20% depending on the fracture site and in 54% depending on age [26,27]. Genome wide association studies (GWAS) have identified single nucleotide polymorphisms (SNPs) which influence fracture risk in genes involved in skeletal structure and homeostasis via alterations in bone mineral density [22,25]. SNPs may change the composition or expression of the protein products, which directly affect the risk of fracture. There is evidence that SNPs in the collagen type 1 alpha 1 (COL1A1), vitamin D receptor (VDR) and LDL 5 receptor-associated protein (LRP5) genes have been correlated with a three- to eight-fold increase in fracture risk among physically active participants, however, some research show no association with the same SNPs [28-31]. In terms of the risk of non-osteoporotic fractures, the collagen 1 gene is the best studied, as it is the main bone building protein. Meta-analysis indicated a trivial reduction in fracture risk for the T allele of the COL1A1 rs1800012 SNP in physically active females, but not males [1]. Additionally, the T allele has been repeatedly associated with a reduced risk of ligament damage in active women and men [32-34]. T allele of collagen 1 may result in the production of a more durable protein that protects against ligament and bone injuries at an earlier age in physically active people. However, the results of studies aren't always conclusive. For example, analysis of theP allele of the collagen 1-COL1A2 gene presented conflicting results, one research reported that the 'PP' genotype reduced fracture risk in half while the other suggested that the P allele (or PP or the Pp genotype) increased the risk of fractures [29, 35].
Low bone mineral density (BMD) was identified as the main risk predictor of osteoporosis which may also have important implications for the health of athletes and the risk of injury in the sports environment. BMD is a highly multi-factorial phenotype influenced by diet, hormonal characteristics and physical activity [36-38]. There is also a large genetic component of BMD. It is estimated that BMD heritability is 50–85% depending on the anatomical location [39]. Over 66 genetic loci have been associated with dual-energy X-ray absorptiometry (DXA)-derived BMD or fracture via genome-wide association studies (GWAS) [40,41]. However, many of the identified genes are not related with biological functions or have not yet been replicated in subsequent studies. . In vitro studies have shown

alterations in gene expression following mechanical load [42,43]. Unfortunately, small number of studies have been conducted in athletes with different bone phenotypes [42,43]. A small number of studies have also been conducted in athletes with different bone phenotypes. For example, higher BMD in weight-bearing athletes than in control group was observed in the FF (7.7%) and Ff (6.9%) but not ff (1.8%) genotypes of the vitamin D receptor (VDR) FokI rs2228570 polymorphism, whilst lower total BMD was only observed in the FF (- 4.5%) genotype when comparing swimmers with a control group [44]. What's more, variants in the purinergic receptor P2X7 (P2RX7), human TNF receptor superfamily member 11a (TNFRSF11A) and sclerostin (SOST) genes have been associated with stress fracture in athletes [31,36,45]. More genetic research associated with BMD is needed to better understand its correlation with bone fractures, which could translate into benefits in public health and elite sport.

3.5. The relationship between professional sport and bone fractures

The cardiovascular benefits of physical activity are fairly well known and studied. However, there is also an orthopaedic advantage has been proposed as a potential mechanism for increased bone turnover [46, 47]. The osteogenic stimulus from exercise is the result of the action of the muscles, joints and ground reaction forces transmitted through the skeleton [48,49]. An important exponent of the orthopaedic benefits of sports and predictor of the bone fractures is bone mineral density (BDM). BMD is the ratio of mass to the area or volume of bone, which is known as areal (g/cm2) or volumetric (g/cm3) BMD, depending upon the measurement methodology used [36]. Bone mineral density accounts for 60–65% of the variance in bone strength so other factors such as bone geometry, collagen properties are also important determinants [50,51]. BMD is highly multi-factorial, being influenced by diet, hormonal characteristics and physical activity [36-38]. Preliminary studies estimate that physical activity accounts for up to 30% of bone mineral density [52]. Athletes tend to achieve a higher BMD because after physical activity, osteocytes detect muscles shape and volume changes, increasing or decreasing the liberation of specific bone mediators, which consequently influences bone formation and resorption [53].. Elite athletes can achieve from 3 to 22% higher BDM compared to non-athletic control group. The type of sport determines the bone location of the increased bone mineral density. For example, in the group of professional volleyball players high rates of BDM were recorded in lumbar spine and femoral neck [54-56]. Despite the benefits of weight-bearing activity for BMD, at the elite sporting level, too much activity to the point of overtraining can result in stress fractures. Stress fractures occur due to repetitive mechanical stress that stimulates an incomplete remodelling response [57]. The increased risk of stress fracture is influenced by biomechanical gait, bone size and mechanical properties, nutritional factors, training volume and rapid volume gain, small musculature and low BMD [36]. Therefore, higher incidence of lower limb stress fractures is observed in endurance runners in comparison with non-athletic controls. Significant amounts of site-specific loading, combined with other factors typical of this group, such as low energy availability, can result in a lower BMD and a higher risk of stress fractures which account for 50% of injuries suffered by runners [58,59]. Professional road cyclists have a lower bone mineral density in the hips compared to recreational cyclists [60].

3.6. Impact of training in elderly age on bones and health

The retrospective cohort study published in 2019 examined the effects of 24-week aerobic dance program on bone mineral density (BMD). The study involved 80 postmenopausal women with osteopenia. They were divided into two groups - 40 practiced dance (the intervention group) and the other 40 were the control group. Before the start of the training phase, BMD was examined in both groups. BMD was examined again after 24 weeks of the study. A significant increase in femoral neck BMD was observed in the group of exercising women (before 0,626±0,097 g/cm2 vs. after 0,643±0,09 g/cm2), while in the control group they have changed from 0,646±0,115 g/cm2, to 0,637±0,112 g/cm2 [61].

Another study involved 93 postmenopausal women (aged 50-75 years) diagnosed with osteoporosis. They were divided into three groups that have performed: aerobic exercises, anaerobic exercises and osteoanabolic exercises. After 12 weeks of training, a significant improvement was observed in the osteoanabolic group compared to the other groups. [62].

Researchers performed a meta-analysis that included 15 randomized controlled trials and analysed the effectiveness of Tai chi training as an adjuvant treatment for osteopenia and primary osteoporosis. The meta-analysis contained three subgroups: 1) Tai chi vs. no treatment, 2) Tai chi vs. conventional treatment, and 3) Tai chi and conventional treatment vs. conventional treatment. There were statistically significant differences in BMD between groups 1 and 2, with weighted mean difference (WMD) 0.05 g/cm2 and 0.16 g/cm2 respectively. In subgroup 3, the differences were not significant. Thus, Tai chi was proved to have a positive effect on BMD, and the therapeutic effect was better than in conventional treatment [63].

In study on 656 Australian men, aged 60-96, the influence of different types of physical activity was verified. Men were divided depending on their level of activity: sporting, household and leisure. 82 men suffered at least one fracture during the study The study has shown that performing even one sporting activity reduces risk of fractures in 6-year period after the study. [64].

In another study, on 1,283 men with mean age of 79,1 years, activity was measured in steps per day by SenseWear® Pro Armband. The study found that 1 standard deviation - 3,092 step increase in daily step count was associated with a 34% lower risk of hospitalization in the base model (adjusted for age and centre) and a 21% lower risk of hospitalization in the fully adjusted models (adjusted for age, centre, body mass index, marital status, depressive symptoms, multimorbidity, cognitive function and prior hospitalization) [65].

Research on elderly women with osteoporosis and vertebral fractures in medical history has investigated the effect of a 12-week exercise programme on gait walking speed over a distance of 10 meters. The secondary objectives were to investigate the effects on physical mobility, fear of falling, and quality of life. The randomized controlled trial included 149 women in age at least 65 years, complying with the study aims. The 12-week exercise programme included resistance training and balance training in intervention group. The women in the control group did not exercise with the programme. When the training period ended, walking speed was not significantly different between the intervention group and the control group (mean difference 0.04 m/s). Walking speed was measured again in both groups after 3 months and there was also no statistically significant difference (0.03 m/s) [66,67]. The research by Diem S. J. et al. concluded that women with slow walking speed were less likely to be independent than women with good walking speed [68]. Nevertheless, a significant improvement in balance and reduction in fear of falling was observed for the intervention group in both measurements [66,67]. Additionally, a study by Otero M. et al. also confirmed the positive effect of a physical exercise program based on balance and strength exercises on improving balance but also strength in women with osteoporosis [69].

4. Conclusions

Participating in sporting activities is an efficient way to increase BMD and help patients with osteoporosis and maintain in good health. Improving one's physical performance can lead to better body balance which lowers the risk of potentially dangerous fall. Weight-bearing exercises have more impact on BMD than non-weight-bearing exercises. Non-professional physical activity is available to wider circle of patients and allows them to strengthen their bones with lower risk of developing microdamage in their bones that professional sport. Training in both, young and elderly age is able to increase BMD, but effects fade away if physical activity of a person declines.

Bibliography

1. Armas LA, Recker RR. Pathophysiology of osteoporosis: new mechanistic insights. Endocrinol Metab Clin North Am. 2012 Sep;41(3):475-86. doi: 10.1016/j.ecl.2012.04.006. Epub 2012 Jun 9. PMID: 22877425.
2. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. JAMA. 2001 Feb 14;285(6):785-95. doi: 10.1001/jama.285.6.785. PMID: 11176917.
3. Johnell O, Kanis J. Epidemiology of osteoporotic fractures. Osteoporos Int. 2005 Mar;16 Suppl 2: S3-7. doi: 10.1007/s00198-004-1702-6. Epub 2004 Sep 8. PMID: 15365697.
4. Kanis JA, Oden A, Johnell O, Jonsson B, de Laet C, Dawson A. The burden of osteoporotic fractures: a method for setting intervention thresholds. Osteoporos Int. 2001;12(5):417-27. doi: 10.1007/s001980170112. PMID: 11444092.
5. Del Corso L, Giuliano G, Romanelli AM, Protti MA, Moruzzo D, Amato V, Agelli M, Pentimone F. Cadute e fratture nell'anziano. Cause e consequenze [Falls and fractures in the elderly. Causes and consequences]. Minerva Med. 1994 May;85(5):245-51. Italian. PMID: 8028754.
6. Oja P, Titze S, Kokko S, Kujala UM, Heinonen A, Kelly P, Koski P, Foster C. Health benefits of different sport disciplines for adults: systematic review of observational and intervention studies with meta-analysis. Br J Sports Med. 2015 Apr;49(7):434-40. doi: 10.1136/bjsports-2014-093885. Epub 2015 Jan 7. PMID: 25568330.
7. Rosengren BE, Ribom EL, Nilsson JÅ, Mallmin H, Ljunggren O, Ohlsson C, Mellström D, Lorentzon M, Stefanick M, Lapidus J, Leung PC, Kwok A, Barrett-Connor E, Orwoll E, Karlsson MK. Inferior physical performance test results of 10,998 men in the MrOS Study is associated with high fracture risk. Age Ageing. 2012 May;41(3):339-44. doi: 10.1093/ageing/afs010. Epub 2012 Feb 6. PMID: 22314696; PMCID: PMC3335372.
8. Tinetti ME. Clinical practice. Preventing falls in elderly persons. N Engl J Med. 2003 Jan 2;348(1):42-9. doi: 10.1056/NEJMcp020719. PMID: 12510042.

9. Harvey NC, Odén A, Orwoll E, Lapidus J, Kwok T, Karlsson MK, Rosengren BE, Ribom E, Cooper C, Cawthon PM, Kanis JA, Ohlsson C, Mellström D, Johansson H, McCloskey E. Measures of Physical Performance and Muscle Strength as Predictors of Fracture Risk Independent of FRAX, Falls, and aBMD: A Meta-Analysis of the Osteoporotic Fractures in Men (MrOS) Study. J Bone Miner Res. 2018 Dec;33(12):2150-2157. doi: 10.1002/jbmr.3556. Epub 2018 Aug 29. PMID: 30011086; PMCID: PMC6272117.
10. Cöster ME, Karlsson M, Ohlsson C, Mellström D, Lorentzon M, Ribom E, Rosengren B. Physical function tests predict incident falls: A prospective study of 2969 men in the Swedish Osteoporotic Fractures in Men study. Scand J Public Health. 2020 Jun;48(4):436-441. doi: 10.1177/1403494818801628. Epub 2018 Sep 29. PMID: 30269679.
11. Weycker D, Edelsberg J, Barron R, Atwood M, Oster G, Crittenden DB, Grauer A. Predictors of near-term fracture in osteoporotic women aged ≥65 years, based on data from the study of osteoporotic fractures. Osteoporos Int. 2017 Sep;28(9):2565-2571. doi: 10.1007/s00198-017-4103-3. Epub 2017 Jun 7. PMID: 28593447; PMCID: PMC5550536.
12. Muraki S, Akune T, Oka H, Ishimoto Y, Nagata K, Yoshida M, Tokimura F, Nakamura K, Kawaguchi H, Yoshimura N. Physical performance, bone and joint diseases, and incidence of falls in Japanese men and women: a longitudinal cohort study. Osteoporos Int. 2013 Feb;24(2):459-66. doi: 10.1007/s00198-012-1967-0. Epub 2012 Mar 21. PMID: 22434204.
13. Verghese J, Holtzer R, Lipton RB, Wang C. Quantitative gait markers and incident fall risk in older adults. J Gerontol A Biol Sci Med Sci. 2009 Aug;64(8):896-901. doi: 10.1093/gerona/glp033. Epub 2009 Apr 6. PMID: 19349593; PMCID: PMC2709543.
14. Cawthon PM, Orwoll ES, Peters KE, Ensrud KE, Cauley JA, Kado DM, Stefanick ML, Shikany JM, Strotmeyer ES, Glynn NW, Caserotti P, Shankaran M, Hellerstein M, Cummings SR, Evans WJ; Osteoporotic Fractures in Men (MrOS) Study Research Group. Strong Relation Between Muscle Mass Determined by D3-creatine Dilution, Physical Performance, and Incidence of Falls and Mobility Limitations in a Prospective Cohort of Older Men. J Gerontol A Biol Sci Med Sci. 2019 May 16;74(6):844-852. doi: 10.1093/gerona/gly129. PMID: 29897420; PMCID: PMC6521914.
15. Yin L, Xu Z, Wang L, Li W, Zhao Y, Su Y, Sun W, Liu Y, Yang M, Yu A, Blake GM, Wu X, Veldhuis-Vlug AG, Cheng X, Hind K, Engelke K. Associations of Muscle Size and Density With Proximal Femur Bone in a Community Dwelling Older Population. Front Endocrinol (Lausanne). 2020 Jul 28;11:503. doi: 10.3389/fendo.2020.00503. PMID: 32849289; PMCID: PMC7399084.
16. Oura P, Nurkkala M, Auvinen J, Niinimäki J, Karppinen J, Junno JA. The Association of Body Size, Shape and Composition with Vertebral Size in Midlife - The Northern Finland Birth Cohort 1966 Study. Sci Rep. 2019 Mar 8;9(1):3944. doi: 10.1038/s41598-019-40880-4. PMID: 30850701; PMCID: PMC6408584.
17. Mikkilä S, Calogiuri G, Emaus N, Morseth B. A cross-sectional and 6-year follow-up study of associations between leisure time physical activity and vertebral fracture in adults. BMC Musculoskelet Disord. 2019 Sep 17;20(1):435. doi: 10.1186/s12891-019-2821-8. PMID: 31526375; PMCID: PMC6747745.

18. Patel H, Sammut L, Denison H, Teesdale-Spittle P, Dennison E. The Relationship Between Non-elite Sporting Activity and Calcaneal Bone Density in Adolescents and Young Adults: A Narrative Systematic Review. Front Physiol. 2020 Mar 6;11:167. doi: 10.3389/fphys.2020.00167. PMID: 32210834; PMCID: PMC7069218.
19. Minett MM, Weidauer L, Wey HE, Binkley TL, Beare TM, Specker BL. Sports Participation in High School and College Leads to High Bone Density and Greater Rates of Bone Loss in Young Men: Results from a Population-Based Study. Calcif Tissue Int. 2018 Jul;103(1):5-15. doi: 10.1007/s00223-017-0383-z. Epub 2018 Jan 4. PMID: 29302709.
20. Modarress-Sadeghi M, Oura P, Junno JA, Niemelä M, Niinimäki J, Jämsä T, Korpelainen R, Karppinen J. Objectively Measured Physical Activity Is Associated with Vertebral Size in Midlife. Med Sci Sports Exerc. 2019 Aug;51(8):1606-1612. doi: 10.1249/MSS.0000000000001962. PMID: 30817715.
21. Tabor E, Zagórski P, Martela K, Glinkowski W, Kuźniewicz R, Pluskiewicz W. The role of physical activity in early adulthood and middle-age on bone health after menopause in epidemiological population from Silesia Osteo Active Study. Int J Clin Pract. 2016 Oct;70(10):835-842. doi: 10.1111/ijcp.12874. Epub 2016 Sep 22. PMID: 27655014.
22. Edward Ryan-Moore, Yiannis Mavrommatis, Mark Waldron, Systematic Review and Meta-Analysis of Candidate Gene Association Studies With Fracture Risk in Physically Active Participants, Front. Genet., 16 June 2020 | https://doi.org/10.3389/fgene.2020.00551
23. Kohrt, W. M., Bloomfield, S. A., Little, K. D., Nelson, M. E., and Yingling, V. R. (2004). Physical activity and bone health. Med. Sci. Sports Exercise 36, 1985–1996. doi: 10.1249/01.MSS.0000142662.21767.58
24. Santos, L., Elliott-Sale, K.J. & Sale, C. Exercise and bone health across the lifespan. Biogerontology 18, 931–946 (2017). https://doi.org/10.1007/s10522-017-9732-6
25. Trajanoska, K., Morris, J. A., Oei, L., Zheng, H.-F., Evans, D., Kiel, M., et al. (2018). Assessment of the genetic and clinical determinants of fracture risk: genome wide association and mendelian randomisation study. BMJ 362:k3225. doi: 10.1136/bmj.k3225
26. Andrew, T., Leto, A., Scurrah, K. J., MacGregor, A. J., and Spector, T. D. (2004). Risk of wrist fracture in women is heritable and is influenced by genes that are largely independent of those influencing BMD. J. Bone Mineral Res. 20, 67–74. doi: 10.1359/JBMR.041015
27. Michaëlsson, K., Melhus, H., Ferm, H., Ahlbom, A., and Pedersen, N. L. (2005). Genetic liability to fractures in the elderly. Arch. Inter. Med. 165:1825. doi: 10.1001/archinte.165.16.1825
28. Chatzipapas, C., Boikos, S., Drosos, G. I., Kazakos, K., Tripsianis, G., Serbis, A., et al. (2009). Polymorphisms of the vitamin D receptor gene and stress fractures. Hormone Metabol. Res. 41, 635–640. doi: 10.1055/s-0029-1216375
29. Blades, H. Z., Arundel, P., Carlino, W. A., Dalton, A., Crook, J. S., Freeman, J. V., et al. (2010). Collagen gene polymorphisms influence fracture risk and bone mass acquisition during childhood and adolescent growth. Bone 47, 989–994. doi: 10.1016/j.bone.2010.08.014

30. Korvala, J., Hartikka, H., Pihlajamäki, H., Solovieva, S., Ruohola, J.-P., Sahi, T., et al. (2010). Genetic predisposition for femoral neck stress fractures in military conscripts. BMC Gene. 11:95. doi: 10.1186/1471-2156-11-95
31. Varley, I., Hughes, D., Greeves, C., Stellingwerff, J. P. T., Ranson, C., Fraser, W., et al. (2018). The association of novel polymorphisms with stress fracture injury in elite athletes: further insights from the SFEA cohort. J. Sci. Sport 21, 564–568. doi: 10.1016/j.jsams.2017.10.038
32. Posthumus, M., September, A. V., Keegan, M., O'Cuinneagain, D., Van der Merwe, W., Schwellnus, M., et al. (2009). Genetic risk factors for anterior cruciate ligament ruptures: COL1A1 gene variant. Br. J. Sports Med. 43, 352–356. doi: 10.1136/bjsm.2008.056150
33. Stepien-Słodkowska, M., Ficek, K., Eider, J., Leonska-Duniec, A., Maciejewska-Karłowska, A., Sawczuk, M., et al. (2013). The +1245g/t polymorphisms in the collagen type i alpha 1 (col1a1) gene in polish skiers with anterior cruciate ligament injury. Biol. Sport 30, 57–60. doi: 10.5604/20831862.1029823
34. Ficek, K., Cieszczyk, P., Kaczmarczyk, M., Maciejewska-Karłowska, A., Sawczuk, M., Cholewinski, J., et al. (2013). Gene variants within the COL1A1 gene are associated with reduced anterior cruciate ligament injury in professional soccer players. J. Sci. Med. Sport 16, 396–400. doi: 10.1016/j.jsams.2012.10.004
35. Suuriniemi, M., Kovanen, V., Mahonen, A., Alén, M., Wang, Q., Lyytikäinen, A., et al. (2006). COL1A1 Sp1 polymorphism associates with bone density in early puberty. Bone 39, 591–597. doi: 10.1016/j.bone.2006.02.053
36. Herbert AJ, Williams AG, Hennis PJ, 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(1):29-47. doi:10.1007/s00421-018-4007-8
37. Darling AL, Millward DJ, Torgerson DJ, Hewitt CE, Lanham-New SA. Dietary protein and bone health: a systematic review and meta-analysis. Am J Clin Nutr. 2009;90(6):1674–1692.
38. Pluijm SMF, Visser M, Smit JH, Popp-Snijders C, Roos JC, Lips P. Determinants of bone mineral density in older men and women: body composition as mediator. J Bone Miner Res. 2001;16(11):2142–2151.
39. Ralston SH, Uitterlinden AG. Genetics of osteoporosis. Endocr Rev. 2010;31(5):629–662.
40. Hsu Y-H, Kiel DP. Genome-wide association studies of skeletal phenotypes: what we have learned and where we are headed. J Clin Endocrinol Metab. 2012;97(10):E1958–E1977
41. Estrada K, Styrkarsdottir U, Evangelou E, Hsu Y-H, Duncan EL, Ntzani EE, Oei L, Albagha OME, Amin N, Kemp JP. Genome-wide meta-analysis identifies 56 bone mineral density loci and reveals 14 loci associated with risk of fracture. Nat Genet. 2012;44(5):491.
42. Mantila Roosa SM, Liu Y, Turner CH. Gene expression patterns in bone following mechanical loading. J Bone Miner Res. 2011;26(1):100–112.
43. Mitchell JA, Chesi A, Elci O, McCormack SE, Roy SM, Kalkwarf HJ, Lappe JM, Gilsanz V, Oberfield SE, Shepherd JA. Physical activity benefits the skeleton of children genetically predisposed to lower bone density in adulthood. J Bone Miner Res. 2016;31(8):1504–1512.

44. Nakamura O, Ishii T, Mankyu H, Tsubakimoto S, Nomura T, Tokuyama K. Contribution of vitamin D receptor genotypes to bone mineral density in young male athletes with different impact loading. Eur J Sport Sci. 2002;2(2):1–8.
45. Varley I, Greeves JP, Sale C, Friedman E, Moran DS, Yanovich R, Wilson PJ, Gartland A, Hughes DC, Stellingwerff T. Functional polymorphisms in the P2X7 receptor gene are associated with stress fracture injury. Purinergic Signal. 2016;12(1):103–113.
46. Hind K, Gannon L, Whatley E, et al. Bone cross-sectional geometry in male runners, gymnasts, swimmers and non-athletic controls: a hipstructural analysis study. Eur J Appl Physiol. 2012;112:535–541.
47. Wilks DC, Winwood K, Gilliver SF, et al. Bone mass and geometry of the tibia and the radius of master sprinters, middle and long distance runners, race-walkers and sedentary control participants: a pQCT study. Bone. 2009;45:91–97.
48. Barry DW, Kohrt WM. Exercise and the preservation of bone health. J Cardiopulm Rehabil Prev. 2008;28:153–162.
49. Burr DB, Robling AG, Turner CH. Effects of biomechanical stress on bones in animals. Bone. 2002;30:781–786.
50. Fonseca H, Moreira-Gonçalves D, Coriolano H-JA, Duarte JA. Bone quality: the determinants of bone strength and fragility. Sports Med. 2014;44(1):37–53
51. Cheung AM, Frame H, Ho M, Mackinnon ES, Brown JP. Bone strength and management of postmenopausal fracture risk with antiresorptive therapies: considerations for women's health practice. Int J Women's Health. 2016;8:537.
52. Valdimarsson Ö, Kristinsson J, Stefansson S, Valdimarsson S, Sigurdsson G. Lean mass and physical activity as predictors of bone mineral density in 16–20-year old women. J Intern Med. 1999;245(5):489–496.
53. Nakashima T, Hayashi M, Fukunaga T, Kurata K, Oh-Hora M, Feng JQ, Bonewald LF, Kodama T, Wutz A, Wagner EF. Evidence for osteocyte regulation of bone homeostasis through RANKL expression. Nat Med. 2011;17(10):1231
54. Torstveit MK, Sundgot-Borgen J. Low bone mineral density is two to three times more prevalent in non-athletic premenopausal women than in elite athletes: a comprehensive controlled study. Br J Sports Med. 2005;39(5):282–287.
55. Chang RPY, Briffa KN, Edmondston SJ. Bone mineral density and body composition in elite female golf and netball players. Eur J Sport Sci. 2013;13(2):183–190.
56. Calbet JAL, Herrera PD, Rodriguez LP. High bone mineral density in male elite professional volleyball players. Osteoporos Int. 1999;10(6):468–474.
57. Jones BH, Thacker SB, Gilchrist J, Kimsey CD, Jr, Sosin DM. Prevention of lower extremity stress fractures in athletes and soldiers: a systematic review. Epidemiol Rev. 2002;24(2):228–247.
58. Loucks AB. Low energy availability in the marathon and other endurance sports. Sports Med. 2007;37(4–5):348–352.
59. Milner CE, Ferber R, Pollard CD, Hamill J, Davis IS. Biomechanical factors associated with tibial stress fracture in female runners. Med Sci Sports Exerc. 2006;38(2):323–328.
60. Mojock, Christopher D. PhD; Ormsbee, Michael J. PhD; Kim, Jeong-Su PhD; Arjmandi, Bahram H. PhD, RD; Louw, Gideon A. MS; Contreras, Robert J. PhD; Panton, Lynn B. PhD Comparisons of Bone Mineral Density Between Recreational

and Trained Male Road Cyclists, Clinical Journal of Sport Medicine: March 2016 - Volume 26 - Issue 2 - p 152-156 doi: 10.1097/JSM.0000000000000186

61. Yu PA, Hsu WH, Hsu WB, et al. The effects of high impact exercise intervention on bone mineral density, physical fitness, and quality of life in postmenopausal women with osteopenia: A retrospective cohort study. Medicine (Baltimore). 2019; 98(11): e14898. doi:10.1097/MD.0000000000014898
62. Khan AA, Farhad A, Siddiqui PQR, Ansari B. Effects of osteoanabolic exercises on bone mineral density of osteoporotic females: A randomized controlled trial. Int J Health Sci (Qassim). 2019; 13(1): 9-13.
63. Zhang Y, Chai Y, Pan X, et al. Tai chi for treating osteopenia and primary osteoporosis: a meta-analysis and trial sequential analysis. Clin Interv Aging. 2019;14:91-104. doi:10.2147/CIA.S187588
64. Holloway-Kew KL, Moloney DJ, Bucki-Smith G, et al. Sports participation and fracture in older Australian men. Arch Osteoporos. 2018;13(1):43. doi:10.1007/s11657-018-0459-z
65. Langsetmo L, Kats AM, Cawthon PM, et al. The Association Between Objectively Measured Physical Activity and Subsequent Health Care Utilization in Older Men. J Gerontol A Biol Sci Med Sci. 2019; 74(6): 820-826. doi:10.1093/gerona/glx191
66. Stanghelle B, Bentzen H, Giangregorio L, et al. Effects of a resistance and balance exercise programme on physical fitness, health-related quality of life and fear of falling in older women with osteoporosis and vertebral fracture: a randomized controlled trial. Osteoporos Int. 2020; 31(6): 1069-1078. doi:10.1007/s00198-019-05256-4
67. Stanghelle B, Bentzen H, Giangregorio L, et al. Physical fitness in older women with osteoporosis and vertebral fracture after a resistance and balance exercise programme: 3-month post-intervention follow-up of a randomised controlled trial. BMC Musculoskelet Disord. 2020; 21(1): 471. doi:10.1186/s12891-020-03495-9
68. Diem SJ, Lui LY, Langsetmo L, et al. Effects of Mobility and Cognition on Maintenance of Independence and Survival Among Women in Late Life. J Gerontol A Biol Sci Med Sci. 2018; 73(9): 1251-1257. doi:10.1093/gerona/glx209
69. Otero M, Esain I, González-Suarez ÁM, Gil SM. The effectiveness of a basic exercise intervention to improve strength and balance in women with osteoporosis. Clin Interv Aging. 2017;12:505-513. doi:10.2147/CIA.S127233