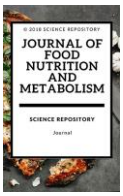

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Review Article

The Role of Diet in Osteoporotic Fracture Risk

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ABSTRACT

Introduction: Osteoporosis-related fractures constitute a considerable public health burden and nutrition is an important modifiable factor influencing bone health. Numerous micronutrients, macronutrients, and dietary components influence bone health, as well as dietary patterns. This short review describes the role of diet on osteoporosis fracture risk, investigating those dietary factors which improve bone health.

Materials and Methods: Searching Pubmed and Web of Science, we performed a review of current literature.

Results: This review reported the beneficial effects of micronutrients (e.g. calcium, vitamin D, potassium, magnesium, vitamin K, and vitamin B12), macronutrients (e.g. protein and carbohydrates), and foods (e.g. fish and seafood, fruits and vegetables) on osteoporotic fracture risk. A healthy diet, such as the Mediterranean diet, is important for decreasing osteoporotic fracture risk. A potential benefit on fracture risk is attributed to the "Healthy" and "Milk/dairy" dietary patterns which emphasise the intake of fruit, vegetables, whole grains, poultry and fish, nuts and legumes, and low-fat dairy products. By contrast, the unhealthy "Meat/Western" dietary pattern, characterised by high consumption of soft drinks, fried foods, meat and processed products, sweets and desserts, and refined grains, increased osteoporosis fracture risk.

Conclusions: Diet plays an important role in bone health. A healthy diet prevents osteoporosis and reduces osteoporotic fracture risk.

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Introduction

Osteoporosis is a systemic skeletal disorder, characterised by low bone mineral density (BMD) and compromised bone strength [1, 2]. Osteoporosis represents a significant risk factor for bone fractures [1]. Low BMD and osteoporosis-related fractures represent a growing socioeconomic and public health concern [3, 4]. Fragility fractures are associated to increased mortality and can affect considerably the quality of life [3, 5, 6]. The percentage of global burden of deaths attributable to low BMD increased in both sexes from 0.22% in 1990 and to 0.36% in 2010 and percentage of global burden of DALYs (Disability-Adjusted Life Years) almost doubled from 0.12% in 1990 to 0.21% in 2010 [3]. Factors, such as sex, age, physical inactivity, smoking, excessive alcohol consumption, loss of oestrogen, and nutritional factors mainly related to adequate intakes of calcium and vitamin D, contribute to BMD and osteoporosis [2]. Nutrition has relevant influence on bone health. The aim of this short report is to summarise the influence of diet (micronutrients, macronutrients, food, and dietary pattern) on risk of osteoporosis fracture and identifying pro- and anti-osteogenic nutritional factors.

Materials and Methods

A literature search was carried out on Pubmed and Web of Science. Supplementary sources were obtained from references of articles selected. A review of current literature was performed.

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Results

I Micronutrients

Phosphorus and calcium are major constituents of bone mineral content. Bone health and normal metabolism require many micronutrients, such as calcium, phosphorus, magnesium, zinc, copper, iron, fluoride, vitamins D, A, C, and K.

i Phosphorus

The recommended dietary daily allowance for phosphorus is 700 mg for men and women aged 51 years and older, but in many Western countries the daily dietary intake is higher than the recommended level [7]. Phosphorus is ubiquitous in foods, especially in high-protein foods in high-fat fast foods and processed snacks [8, 9]. High phosphorus dietary intake interferes with calcium homeostasis with potential adverse effects on bone metabolism and contributes to osteoporosis [8, 10]. High phosphorus dietary intake increases the risk of osteoporotic fractures in both sexes and serum phosphate is positively associated with fracture risk independently of BMD [11, 12].

ii Calcium

The recommended dietary daily calcium intake is 1,000 mg for men aged 51-70 years and 1,200 mg for women aged 51-70 years and older adults [13]. The meta-analysis by Bolland *et al.* showed no significant beneficial effect of dietary calcium on the risk of fractures [14]. The meta-analysis by Wang *et al.* performed on eight prospective cohort studies found no association of high calcium intake with the diet and/or supplementations and hip fracture risk; a continuously high calcium intake for more than eight years, however, significantly reduced relative risk of hip fracture [15]. A positive balance between intake and excretion of calcium plays a crucial role in preserving bone health [16]. The association of high intake of calcium with proteins reduced the risk of fractures [17].

iii Vitamin D

Vitamin D plays an important role for the intestinal absorption of calcium and serum concentrations of 25-hydroxyvitamin D tend to decline with age [18]. The recommended daily dietary intake of vitamin D should be around 400–800 IU [13]. Vitamin D deficiency can result in mineralisation defects, osteoporosis, and fractures [19]. Even though calcium and vitamin-D deficiency is a major risk factor for osteoporosis and the study by Fisher *et al.* describes that adequate calcium and vitamin D supply post-fracture is essential for callus-mineralization, the calcium and vitamin D supplementation showed no significant effect on fracture healing [20, 21].

iv Other Micronutrients

Dietary potassium and magnesium are associated with reduced risk of osteoporotic fracture [22]. Excessive dietary sodium intake represents a risk factor for osteoporosis [23]. High dietary intake of sodium leads to increased urinary calcium excretion, affecting bone remodelling and bone loss [24, 25]. Vitamin B12 deficiency has been associated with low bone mineral density and low serum concentration of vitamin B12 increased the risk of hip fracture [26, 27]. High dietary vitamin K intake resulted positively associated with better bone mineral density and reduced risk of fractures [28-30].

II Macronutrients

i Proteins

The role of dietary protein in bone metabolism has been controversial. Both low and high dietary intake can influence calcium absorption and affect bone health [31, 32]. Adequate protein intake, however, has been positively associated with bone mineral density and content and with reduced bone resorption markers [33, 34]. Indeed, dietary proteins contribute to collagen formation and stimulate the production of growth factors involved in bone formation [32]. High protein intake has shown a positive association with increased bone mass and bone health [35, 36]. Indeed, the Framingham Osteoporosis Study reported that higher intakes of proteins reduced the risk of hip fracture [37]. On the other hand, the meta-analysis by Shams-White *et al.* found no significant association between dietary protein intake and fracture risk [34]. Other nutrients in the diet could contribute to the complex role of protein in bone health [38].

ii Other Macronutrients

A diet rich in carbohydrates reduces the risk of osteoporotic fractures [39]. While a high-fat diet influences negatively bone remineralisation and the absorption of dietary calcium [40]. Accordingly, high intake of lipids increases fracture risk in postmenopausal women [39].

III Foods

i Fish and Seafood

Fish and seafood are rich in polyunsaturated fatty acids, especially n–3 (ω-3) fatty acids, which have an anti-inflammatory effect that benefits bone health [41]. Moreover, fish with dark flesh is rich in vitamin D and fish consumption has been associated with reduced risk of hip fracture [42].

ii Beverages

The consumption of cola has negative effect on bone mineral density and resulted associated with the risk of fracture in older women [43, 44]. Dietary compounds not usually categorised as nutrients, such as alcohol, can affect bone health. High alcohol consumption increases the risk of hip fractures and osteoporotic fractures [45, 46]. The meta-analysis by Sheng *et al.* found that coffee consumption had no significant effect on the risk of hip fracture, while a nonlinear association between tea consumption and the risk of hip fractures has been observed [47]. However, a previous meta-analysis by Liu *et al.* showed a positive association of coffee intake with fracture risk in women [48]. Caffeine at high doses can increase urinary calcium excretion and contribute to the risk of fractures [49].

iii Fruits and Vegetables

Fruits and vegetables contain important micronutrients, such as potassium and magnesium, which have been associated with increased bone mineral density [50].

IV Vegetarian and Vegan Diet

Vegetarian diet can place individuals at risk of inadequate intakes for several nutrients important to bone health [51]. The recent meta-analysis by Iguacel *et al*. reported that the risk of low bone mineral density and of fracture was higher in vegetarians and vegans than in omnivores [52]. Moreover, vegans showed a higher risk of low bone mineral density and of fracture than vegetarians [52].

V Dietary Patterns

Nutritional epidemiology has recently applied dietary patterns to investigate the relation between diet and chronic diseases rather than focusing on individual foods and nutrients [53,54]. Dietary patterns provide a closer representation of the actual conditions in which foods and nutrients are consumed and permit to estimate the effect of overall dietary habits. Dietary patterns are defined by *a priori* or by *a posteriori* methods. Dietary patterns defined by *a priori* approach consist in dietary indices and scores (i.e. glycaemic index, Mediterranean score) based on current nutritional knowledge of the healthy or unhealthy effects of various dietary constituents and identify a desirable pattern, the adherence to which could maximise health benefit. Dietary patterns defined by *a posteriori* approach identify dietary patterns (e.g. Western, healthy, and dairy patterns) on the basis of available dietary data directly obtained from the studied population [53].

i A priori

a Inflammatory Index

Higher dietary inflammatory index has been demonstrated to increase the risk of osteoporosis and incident fractures in women, while no significant effect resulted in men after adjusting for potential confounders [55, 56].

b Glycaemic Index

A recent trial conducted in 870 subjects aged 55-80 years at high cardiovascular disease risk has demonstrated that high dietary glycaemic index and the dietary glycaemic load increase the risk of osteoporotic fracture [57].

c Mediterranean Diet

The recent meta-analysis by Malmir *et al.* has reported that adherence to Mediterranean diet reduced the risk of osteoporosis fracture and was positively associated with a higher BMD [58]. Mediterranean diet is characterised by alkali-forming food groups (fruits and vegetables) and acid forming food groups (cereals, nuts and dairy product). Greater consumption of such dietary pattern can affect the inflammation process and might change the acid–base balance and influencing bone density [59-63].

ii A posteriori

a "Meat/Western" Dietary Pattern

The "Meat/Western" pattern is a dietary pattern characterised by a high loading of red meat, processed meat, animal fat, eggs, and sweets. The strong adherence to the "Western" diet involves a high dietary intake of lipids, protein, refined carbohydrates, sodium, and phosphorus. The "Meat/Western" pattern increased the risk of low bone mineral density of 22% and the risk of osteoporotic fractures of 11% [64].

b "Healthy" Dietary Pattern

The "Healthy" pattern is a dietary pattern characterised by a high loading of vegetables and fruits, poultry, fish, and whole grains. The high consumption of fruit and vegetables observed in this dietary pattern is related to high intake of important micronutrients, such as potassium, magnesium, vitamin C, vitamin K, folate, and carotenoids [65]. Adherence to "Healthy" pattern reduced the risk of low bone mineral density of 18% and the risk of osteoporotic fractures of 21% [64].

c "Milk/Dairy" Dietary Pattern

The "Milk/dairy" pattern is a dietary pattern characterised by a high loading of milk and dairy products, which are rich in calcium and magnesium and represent a relevant source of proteins, vitamin D, vitamin B-12, riboflavin, zinc, and potassium [66]. The strong adherence reduced the risk of low bone mineral density of 41%, while it showed no significant effect on fracture risk [64].

VI Malnutrition

A poor nutritional state has been associated with the increased risk of osteoporotic fractures and with mortality in older adults with hip fracture [67, 68].

Conclusions

This review reported the beneficial effects of micronutrients (e.g. calcium, vitamin D, potassium, magnesium, vitamin K, and vitamin B12), macronutrients (e.g. protein and carbohydrates), and foods (e.g. fish and seafood, fruits and vegetables) on osteoporotic fracture risk. A healthy diet, such as the Mediterranean diet, is important for decreasing osteoporotic fracture risk. A potential benefit on fracture risk is attributed to the "Healthy" and "Milk/dairy" dietary patterns which emphasise the intake of fruit, vegetables, whole grains, poultry and fish, nuts and legumes, and low-fat dairy products. By contrast, the unhealthy "Meat/Western" dietary pattern, characterised by high consumption of soft drinks, fried foods, meat and processed products, sweets and desserts, and refined grains, increased osteoporosis fracture risk. The high content of phosphorus in Western diet can affect bone health and contribute to osteoporosis. Nutrition is a relevant modifiable factor influencing bone health. Public health efforts are needed to provide

guidance for nutritional intervention and approaches directed to prevent osteoporosis and osteoporotic fractures.

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Conflicts of Interest

None.

REFERENCES

1. NIH Consensus Development Panel on Osteoporosis Prevention Diagnosis and Therapy (2001) Osteoporosis Prevention, Diagnosis, and Therapy. *JAMA* 285: 785-795. [Crossref]
2. Kanis JA on behalf of the World Health Organization Scientific Group (2007) Assessment of osteoporosis at the primary health-care level. *Technical Report*. World Health Organization Collaborating Centre for Metabolic Bone Diseases, University of Sheffield, UK.
3. Sànchez-Riera L, Carnahan E, Vos T, Veerman L, Norman R et al. (2014) The global burden attributable to low bone mineral density. *Ann Rheum Dis* 73: 1635-1645. [Crossref]
4. Cummings SR, Melton LJ (2002) Epidemiology and outcomes of osteoporotic fractures. *Lancet* 359: 1761-1767. [Crossref]
5. Center JR, Nguyen TV, Schneider D, Sambrook PN, Eisman JA (1999) Mortality after all major types of osteoporotic fracture in men and women: An observational study. *Lancet* 353: 878-882. [Crossref]
6. Cauley JA, Thompson DE, Ensrud KC, Scott JC, Black D (2000) Risk of mortality following clinical fractures. *Osteoporos Int* 11: 556-561. [Crossref]
7. Institute of Medicine (US) Standing Committee on the Scientific Evaluation of Dietary Reference Intakes (1997) Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. Washington (DC): National Academies Press (US). [Crossref]
8. Calvo MS, Park YK (1996) Changing Phosphorus Content of the U.S. Diet: Potential for Adverse Effects on Bone. *J Nutr* 126: 1168S-1180S. [Crossref]
9. Calvo MS (2000) Dietary considerations to prevent loss of bone and renal function. *Nutrition* 16: 564-566. [Crossref]
10. Vorland CJ, Stremke ER, Moorthi RN, Hill Gallant KM (2017) Effects of Excessive Dietary Phosphorus Intake on Bone Health. *Curr Osteoporos Rep* 15: 473-482. [Crossref]
11. Pinheiro MM, Schuch NJ, Genaro PS, Ciconelli RM, Ferraz MB et al. Nutrient intakes related to osteoporotic fractures in men and women - The Brazilian Osteoporosis Study (BRAZOS). *Nutr J* 8: 6. [Crossref]
12. Campos-Obando N, Koek WNH, Hooker ER, van der Eerden BC, Pols HA et al. (2017) Serum Phosphate Is Associated With Fracture Risk: The Rotterdam Study and MrOS. *J Bone Miner Res* 32: 1182-1193. [Crossref]
13. Ross AC, Taylor CL, Yaktine AL, Del Valle HB, Committee to Review Dietary Reference Intakes for Calcium and Vitamin D (2011) Dietary Reference Intakes for Calcium and Vitamin D. Washington, DC: National Academies Press (US); 2011. [Crossref]
14. Bolland MJ, Leung W, Tai V, Bastin S, Gamble GD et al. (2015) Calcium intake and risk of fracture: Systematic review. *BMJ* 351: h4580. [Crossref]
15. Dong Wang, Xiao-Hu Chen, Guo Fu, Li-Qiang Gu, Qing-Tang Zhu et al. (2015) Calcium intake and hip fracture risk: a meta-analysis of prospective cohort studies. *Int J Clin Exp Med* 8: 14424-14431. [Crossref]
16. Isaia G, D'Amelio P, Di Bella S, Tamone C (2007) Protein intake: the impact on calcium and bone homeostasis. *J Endocrinol Invest* 30: 48-53. [Crossref]
17. Sahni S, Cupples LA, McLean RR, Tucker KL, Broe KE et al. (2010) Protective effect of high protein and calcium intake on the risk of hip fracture in the Framingham offspring cohort. *J Bone Miner Res* 25: 2770-2776. [Crossref]
18. Delmas PD (2002) Treatment of postmenopausal osteoporosis. *Lancet* 359: 2018-2026. [Crossref]
19. Lips P, Van Schoor NM (2011) The effect of vitamin D on bone and osteoporosis. *Best Pract Res Clin Endocrinol Metab* 25: 585-591. [Crossref]
20. Fischer V, Haffner-Luntzer M, Prystaz K, Scheidt A Vom, Busse B et al. (2017) Calcium and vitamin-D deficiency marginally impairs fracture healing but aggravates posttraumatic bone loss in osteoporotic mice. *Sci Rep* 7: 7223. [Crossref]
21. Chiavarini M, Naldini G, Fabiani R (2020) The Role of Diet in Osteoporotic Fracture Healing: a Systematic Review. *Curr Osteoporos Rep*. [Crossref]
22. Hayhoe RP, Lentjes MA, Luben RN, Khaw KT, Welch AA (2015) Dietary magnesium and potassium intakes and circulating magnesium are associated with heel bone ultrasound attenuation and osteoporotic fracture risk in the EPIC-Norfolk cohort study. *Am J Clin Nutr* 102: 376-384. [Crossref]
23. Heaney RP (2006) Role of Dietary Sodium in Osteoporosis. *J Am Coll Nutr* 25: 271S-276S. [Crossref]
24. Kwon SJ, Ha YC, Park Y (2017) High dietary sodium intake is associated with low bone mass in postmenopausal women: Korea National Health and Nutrition Examination Survey, 2008-2011. *Osteoporos Int* 28: 1445-1452. [Crossref]
25. Park Y, Kwon SJ, Ha YC (2016) Association between Urinary Sodium Excretion and Bone Health in Male and Female Adults. *Ann Nutr Metab* 68: 189-196. [Crossref]
26. Tucker KL, Hannan MT, Qiao N, Jacques PF, Selhub J et al. (2005) Low plasma vitamin B12 is associated with lower BMD: The Framingham osteoporosis study. *J Bone Miner Res* 20: 152-158. [Crossref]
27. McLean RR, Jacques PF, Selhub J, Fredman L, Tucker KL et al. (2008) Plasma B vitamins, homocysteine, and their relation with bone loss and hip fracture in elderly men and women. *J Clin Endocrinol Metab* 93: 2206-2212. [Crossref]
28. Booth SL, Broe KE, Gagnon DR, Tucker KL, Hannan MT et al. (2003) Vitamin K intake and bone mineral density in women and men. *Am J Clin Nutr* 77: 512-516. [Crossref]
29. Booth SL, Tucker KL, Chen H, Hannan MT, Gagnon DR et al. (2000) Dietary vitamin K intakes are associated with hip fracture but not with bone mineral density in elderly men and women. *Am J Clin Nutr* 71: 1201-1208. [Crossref]

30. Feskanich D, Weber P, Willett WC, Rockett H, Booth SL et al. (1999) Vitamin K intake and hip fractures in women: A prospective study. *Am J Clin Nutr* 69: 74-79. [Crossref]
31. Kerstetter JE, O'Brien KO, Insogna KL (2003) Low Protein Intake: The Impact on Calcium and Bone Homeostasis in Humans. *J Nutr* 133: 855S-861S. [Crossref]
32. Cloutier GR, Barr SI (2003) Protein and bone health: Literature review and counselling implications. *Can J Diet Pract Res* 64: 5-11. [Crossref]
33. Darling AL, Millward DJ, Torgerson DJ, Hewitt CE, Lanham-New SA (2009) Dietary protein and bone health: a systematic review and meta-analysis. *Am J Clin Nutr* 90: 1674-1692. [Crossref]
34. Shams-White MM, Chung M, Du M, Fu Z, Insogna KL et al. (2017) Dietary protein and bone health: a systematic review and meta-analysis from the National Osteoporosis Foundation. *Am J Clin Nutr* 105: 1528-1543. [Crossref]
35. Heaney RP, Layman DK (2008) Amount and type of protein influences bone health. *Am J Clin Nutr* 87: 1567S-1570S. [Crossref]
36. Mangano KM, Sahni S, Kerstetter JE (2014) Dietary protein is beneficial to bone health under conditions of adequate calcium intake: an update on clinical research. *Curr Opin Clin Nutr Metab Care* 17: 69-74. [Crossref]
37. Misra D, Berry SD, Broe KE, McLean RR, Cupples LA et al. (2011) Does dietary protein reduce hip fracture risk in elders? the Framingham osteoporosis study. *Osteoporos Int* 22: 345-349. [Crossref]
38. Calvez J, Poupin N, Chesneau C, Lassale C, Tomé D (2012) Protein intake, calcium balance and health consequences. *Eur J Clin Nutr* 66: 281-295. [Crossref]
39. Kato I, Toniolo P, Zeleniuch-Jacquotte A, Shore RE, Koenig KL et al. (2000) Diet, smoking and anthropometric indices and postmenopausal bone fractures: a prospective study. *Int J Epidemiol* 29: 85-92. [Crossref]
40. Wohl GR, Loehrke L, Watkins BA, Zernicke RF (1998) Effects of high-fat diet on mature bone mineral content, structure, and mechanical properties. *Calcif Tissue Int* 63: 74-79. [Crossref]
41. Mangano KM, Sahni S, Kerstetter JE, Kenny AM, Hannan MT (2013) Polyunsaturated fatty acids and their relation with bone and muscle health in adults. *Curr Osteoporos Rep* 11: 203-212. [Crossref]
42. Feskanich D, Willett WC, Colditz GA (2003) Calcium, vitamin D, milk consumption, and hip fractures: a prospective study among postmenopausal women. *Am J Clin Nutr* 77: 504-511. [Crossref]
43. Tucker KL, Morita K, Qiao N, Hannan MT, Cupples LA et al. (2006) Colas, but not other carbonated beverages, are associated with low bone mineral density in older women: The Framingham osteoporosis study. *Am J Clin Nutr* 84: 936-942. [Crossref]
44. Kim SH, Morton DJ, Barrett-Connor EL (1997) Carbonated beverage consumption and bone mineral density among older women: The Rancho Bernardo study. *Am J Public Health* 87: 276-279. [Crossref]
45. Kanis JA, Johansson H, Johnell O, Oden A, De Laet C et al. (2005) Alcohol intake as a risk factor for fracture. *Osteoporos Int* 16: 737-742. [Crossref]
46. Benetou V, Orfanos P, Pettersson-Kymmer U, Bergström U, Svensson O et al. (2013) Mediterranean diet and incidence of hip fractures in a European cohort. *Osteoporos Int* 24: 1587-1598. [Crossref]
47. Sheng J, Qu X, Zhang X, Zhai Z, Li H et al. (2014) Coffee, tea, and the risk of hip fracture: A meta-analysis. *Osteoporos Int* 25: 141-150. [Crossref]
48. Liu H, Yao K, Zhang W, Zhou J, Wu T et al. (2012) Coffee consumption and risk of fractures: a meta-analysis. *Arch Med Sci* 8: 776-783. [Crossref]
49. Bhatti SK, O'Keefe JH, Lavie CJ (2013) Coffee and tea: Perks for health and longevity? *Curr Opin Clin Nutr Metab Care* 16: 688-697. [Crossref]
50. New SA, Robins SP, Campbell MK, Martin JC, Garton MJ et al. (2000) Dietary influences on bone mass and bone metabolism: Further evidence of a positive link between fruit and vegetable consumption and bone health? *Am J Clin Nutr* 71: 142-151. [Crossref]
51. Tucker KL (2014) Vegetarian diets and bone status. *Am J Clin Nutr* 100: 329S-335S. [Crossref]
52. Iguacel I, Miguel-Berges ML, Gómez-Bruton A, Moreno LA, Julián C (2019) Veganism, vegetarianism, bone mineral density, and fracture risk: A systematic review and meta-analysis. *Nutr Rev* 77: 1-18. [Crossref]
53. Hu FB (2002) Dietary pattern analysis: a new direction in nutritional epidemiology. *Curr Opin Lipidol* 13: 3-9. [Crossref]
54. Michels KB, Schulze MB (2005) Can dietary patterns help us detect diet–disease associations? *Nutr Res Rev* 18: 241-248. [Crossref]
55. Veronese N, Stubbs B, Koyanagi A, Hébert JR, Cooper C et al. (2018) Pro-inflammatory dietary pattern is associated with fractures in women: an eight-year longitudinal cohort study. *Osteoporos Int* 29: 143-151. [Crossref]
56. Kim HS, Sohn C, Kwon M, Na W, Shivappa N et al. (2018) Positive Association between Dietary Inflammatory Index and the Risk of Osteoporosis: Results from the KoGES_Health Examinee (HEXA) Cohort Study. *Nutrients* 10: E1999. [Crossref]
57. García-Gavilán JF, Bulló M, Camacho-Barcia L, Rosique-Esteban N, Hernández-Alonso P et al. (2018) Higher dietary glycemic index and glycemic load values increase the risk of osteoporotic fracture in the PREvención con DIeta MEDiterránea (PREDIMED)-Reus trial. *Am J Clin Nutr* 107: 1035-1042. [Crossref]
58. Malmir H, Saneei P, Larijani B, Esmaillzadeh A (2018) Adherence to Mediterranean diet in relation to bone mineral density and risk of fracture: a systematic review and meta-analysis of observational studies. *Eur J Nutr* 57: 2147-2160. [Crossref]
59. Dai J, Miller AH, Bremner JD, Goldberg J, Jones L et al. (2008) Adherence to the mediterranean diet is inversely associated with circulating interleukin-6 among middle-aged men: A twin study. *Circulation* 117: 169-175. [Crossref]
60. Esposito K, Marfella R, Ciotola M, Di Palo C, Giugliano F et al. (2004) Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: A randomized trial. *JAMA* 292: 1440-1446. [Crossref]
61. Mundy GR (2007) Osteoporosis and Inflammation. *Nutr Rev* 65: S147-S151. [Crossref]
62. Remer T, Manz F (1995) Potential Renal Acid Load of Foods and its Influence on Urine pH. *J Am Diet Assoc* 95: 791-797. [Crossref]
63. Bushinsky DA (2001) Acid-base imbalance and the skeleton. *Eur J Nutr* 40: 238-244. [Crossref]
64. Fabiani R, Naldini G, Chiavarini M (2019) Dietary Patterns in Relation to Low Bone Mineral Density and Fracture Risk: A Systematic Review and Meta-Analysis. *Adv Nutr* 10: 219-236. [Crossref]
65. New SA (2003) Intake of fruit and vegetables: implications for bone health. *Proc Nutr Soc* 62: 889-899. [Crossref]

66. Rizzoli R (2014) Dairy products, yogurts, and bone health. *Am J Clin Nutr* 99: 1256S-1262S. [Crossref]
67. Cederholm T, Hedström M (2005) Nutritional treatment of bone fracture. *Curr Opin Clin Nutr Metab Care* 8: 377-381. [Crossref]
68. Malafarina V, Reginster JY, Cabrerizo S, Bruyère O, Kanis JA et al. (2018) Nutritional Status and Nutritional Treatment Are Related to Outcomes and Mortality in Older Adults with Hip Fracture. *Nutrients* 10: E555. [Crossref]