

Editorial

Osteoporosis is recognized as a major public health problem and its incidence is very likely to be exacerbated in the coming years, owing to the lack of prophylactic agents. Therefore, there is an urgent need to provide validated new tools for healthcare professionals in order to delay metabolic and functional alterations of the skeleton.

The major contribution of calcium is now well established. Nevertheless, for a multimodal approach to health, nutritional prevention of osteoporosis, typically involving calcium and vitamin D therapy, must evolve to new concepts which, in addition to fulfilling the metabolic needs related to each physiological stage, include the potential exerted by certain nutrients and micronutrients to modulate the plasticity of tissues. Indeed, research into human nutrition has led to an awareness of the health benefits that a diet rich in fruit and vegetables may provide protection against chronic diseases, including osteoporosis. The associative evidence comes from epidemiological studies reporting that consumption of fruit and vegetables is an independent predictor of bone size in early pubertal children. In the same way, some observational trials reported significant associations between past reported fruit intake and BMD in premenopausal women, and possibly in postmenopausal women.

To provide an update on this topic, Hamidi et al. carried out a meta-analysis of the existing literature. They reviewed observational and interventional studies dealing with the effect of fruit and vegetable intake on bone turnover, bone mineral density and the risk of fracture. It turns out that the scientific case is, actually, not sufficiently documented to draw definitive conclusions in women older than 45 years.

Nevertheless, Hardcastle et al. published the first epidemiological study providing evidence of a clear association of bone turnover and even bone mineral density and dietary flavonoids (key nutrients found widely in tea, fruits and vegetables, which are secondary metabolites involved in the defensive strategy of plant against environmental stresses) in over 3,000 postmenopausal women.

Besides, Mackinnon & Rao, investigated the effect of lycopene on bone health, another hopeful player (carried by tomatoes and watermelon) in the prevention of degenerative diseases, because of its anti-oxidant properties. Both the cross-sectional study and the randomized controlled trial based on lycopene supplementation, they performed, demonstrate that lycopene can exhibit bone sparing effects.

In conclusion, fruit and vegetables do have a potential promise for the improvement of clinical practice to optimize bone health food strategies; nevertheless, we still need to gather more data targeting postmenopausal women.

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Are fruits and vegetables beneficial for bone health in postmenopausal women?

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Fruits and vegetables contain calcium, potassium, magnesium, B vitamins, vitamins C, E and K, various antioxidants and phytochemicals, all of which can be beneficial for bone health. Some studies have reported that diets high in fruits and vegetables are linked to better bone health in postmenopausal women^{1,2}; however, these positive findings are not consistent across the current scientific literature. Because studies can be of different scientific quality, our group performed a systematic review of the existing literature, assessed the quality of the different studies, summarized the findings, and identified potential research gaps³. We reviewed studies that have examined the associations between fruit and vegetable intake and the incidence of osteoporotic fractures, bone mineral density and bone turnover markers in women >45 years.

Assessing studies for risk of bias

We searched electronic databases and reference lists of selected articles for peer reviewed manuscripts that were published in English scientific literature. We included observational studies and clinical trials that specifically reported fruits and vegetables intake as a main dietary exposure among community dwelling women. Two reviewers independently selected and extracted data from the studies and evaluated the risk of bias. To assess the risk of bias in observational studies, we developed a tool that consists of seven domains³. The risk of bias in clinical trials was assessed using the Cochrane Collaboration's tool⁴ slightly modified to reflect dietary studies. This tool also consists of seven domains. The assignment of low, moderate or high risk depended on the number of domains considered not to be biased. Studies are considered of high quality when there is low risk of bias and of low quality when there is a high risk of bias.

Our findings

After a detailed review of all the studies, we included eight studies. One cohort study reported cross-sectional as well as longitudinal data in the same study population. There was significant heterogeneity in design, definition and amount of fruit and vegetable intake, outcomes, analyses and reporting of results among the different studies. Two studies had low, two had

moderate and four had high risk of bias. Overall, randomized controlled trials and prospective cohort studies found no beneficial effects of fruits and vegetable intake, while one case-control and all the cross-sectional studies found favorable relationships between fruit and vegetables intake and indicators of bone health.

In general, randomized controlled trials and prospective cohort studies have less potential for biases, and are often viewed as better study designs to answer the question of whether a certain intervention has its desired effects. In cross-sectional studies, fruit and vegetable intake may be linked to better bone health not because of the effect of fruit and vegetables, but because of the other healthy behaviours and lifestyles that are associated with a high fruit and vegetable intake such as physical activity, not smoking or taking calcium and vitamin D supplements.

Recommendations for future research in this area

The studies assessed in our review had different methods of assessing intake, different definitions or classification of fruits and vegetables, different intake levels, different types and usage among the various study populations. For example, some studies included potatoes, pulses and starchy vegetables in the vegetable group, or fruit juices and nuts in the fruit group. This may dilute a positive effect of fruits and vegetables on bone health and reduce the ability to detect an association.

There is a need for researchers to assess dietary intake using comparable and standardized methods across populations. A World Health Organization report provides useful guidelines for the assessment of fruit and vegetable intake⁵. Complying with these guidelines will result in more comparable literature, facilitate future systematic reviews and meta-analyses and ultimately lead to the development of evidence-based dietary recommendations.

In conclusion, our systematic review of the scientific literature did not find a clear beneficial effect of fruits and vegetables on bone health for women aged >45 years. However, our review was limited by the small number of well-conducted studies in this area, and the differences in the assessment of fruit and vegetable intake.

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Associations between dietary flavonoids intakes and bone health

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It is estimated that one in two women and one in five men over the age of fifty in the United Kingdom will have an osteoporotic fracture¹, and the prevalence of osteoporosis and its related fractures is increasing². Poor nutrition is likely to have a role in the pathogenesis of osteoporosis, and nutritional research on bone health has concentrated on the nutrients calcium and vitamin D; although more recently there has been interest in the role of protein, and the nutrients found in fruit and vegetables. One family of compounds commonly found in fruit and vegetables are the flavonoids.

Dietary Flavonoids

All foods of plant origin potentially contain flavonoids, and over 5,000 different flavonoids have been characterised. However, the majority of these are not commonly eaten in the Western diet, nor have they attracted attention in terms of their health benefits. The flavonols, flavones, catechins, procyanidins and flavanones are dietary flavonoids which are regularly eaten by humans. Fruit contains flavonols (in apples and stone fruit), flavanones (in citrus fruit) and catechins (in red berries). Flavonols are abundant in most vegetables (onions and the Brassica family are rich sources), flavones are found in celery, lettuce and capsicum peppers, and the catechin and procyanidin family have been detected in legumes such as green and broad beans. Flavonols are found in fruit juice and tea, though catechins are the most abundant dietary flavonoids found in beverages due to their high concentrations in tea.

Flavonoid intakes across the world vary and this is to be expected as different populations obtain their flavonoids from different food sources; apples are major contributors to Finnish intakes, and in Italy red wine is important. Principal sources of flavonoids within countries will change as dietary patterns vary, as may be seen in Japan where onions were the principal sources of flavonols and flavones; whereas previously green tea provided the majority of flavonoids to the diet.

Associations between Bone Health and Flavonoid Intakes

Animal models have shown positive associations between

flavonoid intakes and better bone health³. Human studies have mostly concentrated on tea, as tea has been reported to protect against hip fracture⁴, however the relationship between tea and bone mineral density (BMD) is unclear with studies reporting conflicting results. The first epidemiological study to examine the influence of dietary flavonoids on BMD and bone turnover was performed in Scotland, and it included over 3,000 postmenopausal women who were all members of a longitudinal study⁵. They had bone mineral density scans of their lumbar spine (LS) and hips and provided urine for measurement of bone resorption markers (deoxypyridinoline (DPD) and pyridinoline (PYD)). Diet was assessed using a validated food frequency questionnaire, and intakes of flavonols, flavones, catechins, procyanidins and flavanones were calculated.

Mean total flavonoid intake of the diet was 307 mg/day. Tea was the main contributor of flavonoids to the diet (57%), and fresh fruit and fruit juice also contributed significant amounts of flavonoids to the diet (18% and 12% respectively). A significant association was seen between total flavonoid intakes and BMD at the hip and lumbar spine. Dietary flavanones were shown to have a negative correlation with bone resorption markers; and catechins and procyanidins were associated with annual change in hip and LS BMD.

A sub-study which only included flavonoids from fruit and vegetable sources showed that these were associated more strongly with lumbar spine BMD than flavonoids from all sources. Bone resorption markers were negatively associated with intakes of total flavonoids, flavonols, and flavanones from fruit and vegetable sources, thus showing that dietary flavonoids from fruit and vegetable sources alone were still associated with decreased bone resorption.

Conclusions

This study of over 3,000 women showed associations between greater intakes of dietary flavonoids and improved bone health, however these associations were not strong. Dietary flavonoids may be a marker of a healthy diet and this must lead us to the conclusion that although fruit and vegetables may be good for bone health, and flavonoids are part of this jigsaw, the puzzle is still incomplete.



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The Antioxidant Lycopene and Its Role in the Prevention of Risk for Osteoporosis in Postmenopausal Women

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Lycopene is a potent antioxidant

Lycopene is a 40-carbon, acyclic isomer of β -carotene¹. Among the carotenoid family, it is credited with the highest singlet oxygen quenching capacity², which makes it a powerful antioxidant. Lycopene is the most predominant carotenoid found in human serum¹. Over 80% of lycopene consumed in the diet is obtained through consumption of tomatoes and tomato products³. However, it is also found in watermelon, pink grapefruit, rosehips and pink guava⁴.

Lycopene is well documented for its ability to decrease biomarkers of oxidative stress. Research shows that it is capable of decreasing lipid, protein and DNA markers. The antioxidant properties of lycopene have been credited with its ability to decrease the risk of age-related chronic diseases often attributed to oxidative stress. Research suggests that through its antioxidant capacity, lycopene may decrease the risk of infertility, diabetes, dementia, cardiovascular disease and several types of cancer⁵. Our research suggests that lycopene may also act in its antioxidant capacity to decrease the risk of osteoporosis in postmenopausal women.



Intake of dietary lycopene is important to improve antioxidant status

In a cross-sectional study we have shown that those with a high daily intake of lycopene consumed on average, more cooked and processed tomato products, which usually contain higher amounts of lycopene. In order to increase serum concentrations of the antioxidant-rich 5-cis lycopene, an increased consumption of foods rich in bioavailable lycopene, such as processed tomato products, should be considered⁶.

We have recently reported data showing that lycopene restriction, for a period of only one month, resulted in important changes in biomarkers of oxidative stress and bone resorption markers in postmenopausal women aged 50-60⁷. Refraining from consuming lycopene-containing foods resulted in significantly lower serum

lycopene, which coincided with increases in oxidative stress parameters and the bone resorption marker NTx. This significant increase in NTx may lead to a long-term decrease in BMD and increased risk for osteoporotic fracture⁸, suggesting that a longer restriction period may be detrimental to bone health⁷.

Lycopene supplementation may decrease the risk of osteoporosis in postmenopausal women

Further support to the importance of lycopene in the daily diet is given by our randomized controlled trial in which supplementation with lycopene resulted in significant increase in total antioxidant capacity which corresponded to significantly lower oxidative stress parameters and the bone resorption marker N-telopeptide of Type I collagen (NTx). These findings show capsule or juice forms of lycopene, supplying at least 30 mg of lycopene day, may decrease the risk of osteoporosis by decreasing oxidative stress parameters and the bone resorption marker NTx. Based on these findings, the consumption of lycopene by women to improve overall bone health should be considered as a natural complementary or alternative supplement for the prevention and treatment of osteoporosis in postmenopausal women⁹.

Lycopene is present in only select number of foods⁴; therefore targeted consumption of these products as a part of the regular daily diet to decrease negative health consequences in women, particularly with respect to osteoporosis risk, should be considered. Presently, lycopene is not considered to be an essential nutrient with no formal daily intake levels specified, however, based on human intervention studies an intake of 8-10 mg per day is recommended. Results from our research also provide further proof of the importance of consuming tomatoes and tomato products as a source of lycopene in the daily diet in maintaining overall health and decreasing the risk for age-related chronic diseases, particularly osteoporosis, which is associated with oxidative stress.



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