Behind the pathogenesis of osteoporosis and cardiovascular diseases

Commentary on
Osteoporosis, osteopenia and atherosclerosis vascular disease
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Over time the association between cardiovascular diseases (CVD) and osteoporosis has become more evident, especially as part of the aging process. At first the association of osteoporosis with CVD was considered as an artefact of aging, but it was revealed that after adjusting for age, the association still persists [1, 2].

Although several former and recent studies have indicated the strong association between CVD, atherosclerosis, antihypertensive drugs, statins and bone density [3-7], hypertension seems to be an independent predictor of low bone density [8]. In fact, the common pathophysiological pathway of both diseases remains unknown, although different mechanisms and pathways seem to have a critical role, including inflammation, oxidative stress, lipid metabolism, and the sympathetic nervous system [9]. However, the role of vitamin D is under debate [10].

Leukocyte (monocyte) and platelet activation induces inflammation by stimulating cytokine production, including growth factors, chemokines, and vasoactive molecules, as well as T cell migration [9]. According to this, interleukin-6 (IL-6), IL-1, tumour necrosis factor-α, macrophage colony stimulating factor, receptor activator of nuclear factor κB (RANKL) and its receptor, osteoprotegerin (OPG), osteopontin, C-reactive protein and interferons orchestrate the atherosclerotic process which is common in bone remodelling [9]. In addition, there are resorptive and remodelling sites in atherosclerotic plaques similar to bone which have abundant monocytes and preosteoclasts [9].

On the other hand, the critical role of platelets in wound healing, haemostasis, fracture repair and atherosclerosis should be deeply evaluated. According to our review, platelets and platelet-derived factors can be viewed as new therapeutic targets for both diseases [11].

Other than the mentioned inflammatory mediators and cytokines, several enzymes and metabolic pathways are linked to both senile

diseases, of which cyclooxygenase (COX), and homocysteine can be indicated. COX-derived prostaglandins contribute to various cellular biological functions and influence both diseases. However, the net effect and the role of each of COX-1 or COX-2 is not completely understood. In this regard, and according to the different controversial effects observed from nonsteroidal anti-inflammatory drugs, the issue needs more investigations [12]. In addition, the effect of n-3 fatty acids on bone density as well as atherosclerosis originates from its effect on COX enzyme is interesting. Our study on postmenopausal women showed a negative effect of n-3 fatty acids on a bone resorption marker (pyridinoline) [13, 14].

Furthermore, there is a strong link between hyperhomocysteinaemia, osteoporosis and CVD, which needs to be investigated in detail [15]. The link between cholesterol biosynthesis and bone metabolism was proposed and confirmed in several studies, and also it was revealed that statins affect bone density, although the therapeutic pathway which affects both is not obvious [7]. In addition to the above-mentioned pathways, the role of the sympathetic nervous system in bone metabolism should be considered [16].

Supporting above-mentioned findings, a positive correlation was found between bone mineral density and total body fat, and with abdominal fat [17]. Also it has been shown that children with juvenile rheumatoid arthritis have lower BMD and higher serum OPG and RANKL [18].

Taken together, we have a long way into surveying the strong link between osteoporosis and CVD, and it is far more than finding one or two biomarkers. In fact, both diseases should be viewed as one complex senile disease which several risk factors and pathogenesis affects it.

Furthermore, an interesting new issue in the treatment of osteoporosis is the adverse effect of calcium supplementation on the cardiovascular system, which is a new, challenging issue and will be discussed in detail in our next paper.

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