Osteoporosis and cardiovascular disease: is nonskeletal risk important in patients requiring an anti-osteoporotic treatment?

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Osteoporosis and osteoporosis-related fractures are major, and increasing, public health issues leading to increased mortality, morbidity and disability in Western countries. To determine whether nonskeletal risks should be considered in patients initiating anti-osteoporotic therapy, we reviewed epidemiological reports assessing the relationship between bone and cardiovascular diseases. Most studies reported an association between low bone mineral density and atherosclerosis. Individuals with decreased bone mass have an increased risk of dying from stroke, coronary heart disease and atherosclerosis. These data suggest that cardiovascular diseases should also be considered in patients with osteoporosis.

Some degenerative conditions occur with aging. Osteoporosis, characterized by abnormalities in the amount and microarchitectural arrangement of bone tissue, leads to decreased bone strength predisposing an individual to an increased risk of fracture. This generalized skeletal condition is common in elderly subjects. Nonskeletal risks, such as cardiovascular diseases (e.g., coronary heart diseases, cerebrovascular disorders and peripheral vascular events), are also critical chronic health problems. They play an important role in the decline in quality of life of the elderly population. Both osteoporosis and cardiovascular events, occurring in elderly men and women, are widely viewed as a major cause of mortality, morbidity and disability in most developed countries [1]. The number of elderly people is now rising and is expected to grow in the coming years due to the increase in life expectancy. This demographic shift will cause a dramatic increase in the prevalence of all chronic age-related diseases, including osteoporosis and cardiovascular conditions [2]. Therefore, they are major public health issues.

Osteoporosis and cardiovascular diseases have been traditionally considered as independent processes increasing with aging. In the last decade, mounting evidence suggested a link between the vessels and the skeleton. If this association is true, patients with osteoporosis should be treated with therapy that also prevents cardiovascular risk.

The present review describes the relationship between osteoporosis and cardiovascular events in epidemiological trials. Emphasis will be put on cardiovascular mortality, morbidity (atherosclerosis, stroke and myocardial infarction) and risk factors (hypertension, diabetes mellitus and dyslipidemia).

Osteoporosis

According to the current WHO operational definition, diagnosis of osteoporosis is based on a T-score of bone mineral density (BMD), at hip or spine, below -2.5 [3]. Low BMD (LBMD) is the best single predictor of future fracture risk. Therefore, epidemiological studies investigated alterations in bone mass, bone loss or the occurrence of fracture.

Vascular calcification due to atherosclerosis

Similarly to osteoporosis, atherosclerosis is a silent illness that may affect different parts of the vessels. This insidious process starts at adolescence, progresses into calcified plaques in early adulthood and results in thrombotic obstructions and sudden coronary heart disease during middle age and later [4]. Previously described as a purely degenerative process due to aging, vascular calcification is now increasingly viewed as an actively regulated process. Calcium deposition in the vasculature is well known to generate hypertension, congestive heart failure, myocardial ischemia and coronary insufficiency [5–6]. Vascular calcification is widely seen as valid surrogate marker for cardiovascular diseases.

Several trials conducted in humans during the last decade [7–29] predominantly explored the association between bone-mass loss and aortic calcification, carotid atherosclerosis, coronary artery diseases [16,20,22] or arterial disease of the lower limbs [10,14,30]. These studies used various methodologies and are summarized in **Tables 1–4**. Most [9–14,16–18,20–30], but not all studies [7–8,15,19], suggest a relationship between osteoporosis and atherosclerosis. However, the nature of the link remains uncertain and controversial. Several hypotheses have been raised to explain

future medicine

Table 1. Cross-sectional and longitudinal studies investigating the association between osteoporosis and atherosclerosis during the last decade.

Author	Method	Sample	Osteoporosis site(s)	Method	CVD site(s)	Method	Association	Ref.
Reid (1991)	Longitudinal, baseline	130 normal PMW; 45–71 years	Lumbar spine; left proximal femur	BMD; Lunar DEXA	AC	Lateral lumbar spine radiograph	No (even after adjusted for age)	[7]
Frye (1992)	Longitudinal, baseline	200 woman; ≥ 30 years	Mid and distal radius, lumbar spine, proximal femur (neck, intertrochanteric and shaft)	BMC; SPA/BMD; DPA	AC	Roentgenograms of the thoracic and lumbar spine	Negative association between calcified aortic plaques and BMD lumbar spine	[8]
Banks (1994)	Cross-sectional	115 healthy PMW; 49–64 years	Lumbar spine, proximal femur (neck and Ward's triangle)	BMD; DPA, QCT	CA	Lateral lumbar spine radiograph	Presence of AC associated with BMD	[9]
Laroche (1994)	Cross-sectional	18 men with symptomatic arterial disease of the lower limbs; 33–86 years	Both legs	BMC; Lunar DEXA	Both legs	Distal systolic indexes by Doppler ultrasonography	Reduced BMC in the leg that is more affected by arterial disease	[10]
Jie (1996)	Cross-sectional	113 PMW	Both hands	Metacarpal radiogrammetry	AC	Lateral lumbar spine radiograph	Presence of atherosclerotic calcification associated with bone mass	[11]
Hoshino (1996)	Cross-sectional	Autopsy cases: nine women, 11 men; 51–95 years	Lumbar spine phantom BMD	BMD; Lunar DPX DEXA	AC	Soft x-ray photographs	2.5% BMD increase in severe AC	[12]
Uyama (1997)	Cross-sectional	30 PMW; 67–85 years	Lumbar spine, total BMD	BMD; DEXA	CA	High resolution B-mode ultrasonography	A significant linear association between plaque score and low total BMD	[13]

AC: Aortic calcification; BMC: Bone mineral content; BMD: Bone mineral density; CA: Carotid atherosclerosis; CVD: Cardiovascular diseases; DEXA: Dual-energy x-ray absorptiometer; DPA: Dual-photon absorptiometry; PMW: Postmenopausal women; QCT: Quantitative computer tomography; SPA: Single photon absorptiometry.

Table 2. Cross-sectional and longitudinal studies investigating the association between osteoporosis and atherosclerosis during the last decade.

Author	Method	Sample	Osteoporosis site(s)	Method	CVD site(s)	Method	Association	Ref.
Vogt (1997a)	Longitudinal	1292 PMW; ≥ 65 years	Distal and proximal radius; calcaneus; proximal femur; spine	BMD; osteoanalyser, SEXA, Hologic QDR	LEAD; right and left tibial artery; right brachial artery	Blood flow; Doppler flowmeter; blood pressure; mercury manometer	Blood flow to the lower extremities associated with hip and appendicular skeleton bone mass	[14]
Vogt (1997b)	Cross-sectional	2051 PMW; ≥ 65 years	Hip; spine; calcaneus; proximal and distal radius	BMD; osteoanalyser; Hologic QDR	AC	Lateral lumbar spine radiograph	No	[15]
Barengolts (1998)	Cross-sectional	45 asymptomatic PMW;	Lumbar spine, proximal femur	BMD; DEXA	Coronary atherosclerosis	EBCT; heart	Total coronary calcium score with the severity of osteoporosis	[16]
Hak (2000)	Longitudinal Cross-sectional	236 premenopausal women; 45–57 years 720 PMW; 62.9 ± 5.6 years	Both hands	Metacarpal radiogrammetry	AC	High resolution B-mode ultrasonography; EBCT	AC associated with bone loss during menopause negative association between AC and metacarpal bone mass/density	[17]
Kiel (2001)	Longitudinal	364 women, 190 men	Second metacarpal on the right hand	Metacarpal radiogrammetry	AC	Lateral lumbar spine radiograph	No association in men; positive association between bone loss and severity of abdominal AC in women	[18]

AC: Aortic calcification; BMD: Bone mineral density; CVD: Cardiovascular diseases; DEXA: Dual-energy x-ray absorptiometer; EBCT: Electron beam computed tomography;
LEAD: Lower extremity arterial disease; PMW: Postmenopausal women; SEXA: Single-energy x-ray absorptiometry.

Table 3. Cross-sectional and longitudinal studies investigating the association between osteoporosis and atherosclerosis during the last decade.

Author	Method	Sample	Osteoporosis site(s)	Method	CVD site(s)	Method	Association	Ref.
Aoyagi (2001)	Cross-sectional	524 Japanese–American women; 43–80 years	Distal and proximal radius; calcaneus	SPA	AC	Lateral lumbar spine radiograph	No	[19]
Ramsey-Goldman (2001)	Cross-sectional	65 women with SLE; 44.6 years in average	Lumbar spine; hip	BMD; DEXA	Coronary calcification	EBCT	Association between BMD and carotid plaque index and presence of coronary artery calcification	[20]
Hirose (2003)	Cross-sectional	7865 Japanses: 4183 men, 3682 women; 50 ± 12 years	Calcaneus	OSI, QUS	Early stages of atherosclerosis	baPWV	Negative correlation between OSI and baPWV and is more important in women than in men	[21]
Tanko (2003)	Cross-sectional	963 PMW; 60–85 years	Distal radius; lumbar spine; proximal femur	BMD; DEXA	AC	Lateral lumbar spine radiograph	Negative association between BMD at the proximal femur and the severity of AC	[22]
Nakashima (2003)	Cross-sectional	39 women, 44 men; 23–83 years	Radius	BMD; DEXA	CA	High resolution B-mode ultrasonography	Negative correlation between Z-score and LDL-C and the carotid intima-media thickness	[23]
Schulz (2004)	Cross-sectional; Longitudinal	2348 healthy PMW; ≥50 years 228 women	Thoracic; lumbar spine	Fracture; radiograph	AC	EBCT/spine	Negative correlation between AC and BMD; Positive correlation between AC and fractures	[24]

AC: Aortic calcification; baPWV: Brachial-ankle pulse wave velocity; BMD: Bone mineral density; CA: Carotid atherosclerosis; CVD: Cardiovascular diseases; DEXA: Dual-energy x-ray absorptiometer; EBCT: Electron beam computed tomography; LDL-C: Low-density lipoprotein cholesterol; OSI: Osteo-sono assessment index; PMW: Postmenopausal women; QUS: Quantitative ultrasonography; SLE: Systemic lupus erythematosus; SPA: Single photon absorptiometry.

Table 4. Cross-sectional and longitudinal studies investigating the association between osteoporosis and atherosclerosis during the last decade.

Author	Method	Sample	Osteoporosis site(s)	Method	CVD site(s)	Method	Association	Ref.
Montalcini (2004)	Cross-sectional	157 healthy PMW; 45–75 years	Calcaneus; both heels	BMD; QUS	Extracranial CA	High resolution B-mode ultrasonography	PMW with LBMD and high OC levels have high prevalence of CA	[25]
Pennisi (2004)	Cross-sectional	Cases: 20 men, 16 women; 48–72 years Controls: 15 men, 15 women; 50–74 years	Total body; lumbar spine, hip left calcaneus	BMD; DEXA; QUS	CA and femoral atherosclerosis	High resolution B-mode ultrasonography	Presence of CA or femoral atherosclerotic plaques is associated with LBMD	[26]
Jørgensen (2004)	Cross-sectional	2726 PMW, 2543 men; 55–74 years	Distal; ultradistal forearm	BMD; SEXA	CA (six sites of the right carotid artery)	High resolution B-mode and pulse wave Doppler ultrasonography	Negative association between BMD and echogenic plaques	[27]
Bakhireva (2005)	Cross-sectional	180 men; 47–86 years 186 women; 58–81 years	Spine; hip	BMD; DEXA	Coronary artery calcification	EBCT/chest	Negative association between CACS only in women as current HT users	[28]
Tanko (2005)	Longitudinal	2576 PMW; 66.5 years on average	Lumbar spine; femoral neck	BMD; DEXA	CVD, including CHD and cerebrovascular event	Self-reported events	PMW with OP are at risk for CV events	[29]
Mangiafico (2006)	Cross-sectional	Cases: 345 PMW; 46–78 years Controls: 360 PMW	Lumbar spine; proximal femur	BMD; DEXA	Both arms Both legs	Sphygmomanometer Doppler	OP PMW with PAD had femoral neck BMD than those without PAD	[30]

BMD: Bone mineral density; CA: Carotid atherosclerosis; CACS: Coronary artery calcium score; CHD: Coronary heart disease; CV: Cardiovascular; CVD: Cardiovascular diseases; DEXA: Dual-energy x-ray absorptiometer; EBCT: Electron beam computed tomography; HT: Hormone therapy; LBMD: Low bone mineral density; OC: Osteocalcin; OP: Osteoporosis; PAD: Peripheral arterial disease; PMW: Postmenopausal women; QUS: Quantitative ultrasonnography; SEXA: Single-energy X-ray absorptiometry.

this association. Some claim that any association would be random, since prevalence of both disorders increases with aging. Others suggest a causal link between the two entities. Vascular calcification would result from osteoporosis, due to a shift in calcium from the skeleton to the vasculature. Conversely, osteoporosis would have a vascular etiology. These speculations are probably the consequence of recent findings. Actually, bone markers have been identified in calcified plaques, suggesting that both processes share similar mechanisms.

Populations recruited for these studies, most of them cross-sectional, usually include aged Caucasian postmenopausal women (PMW) [7–13,15–17,19–28,30]. Nevertheless, the association has also been assessed in other groups differing by age [17,20], gender [10,12,18,21,23,26–28] or ethnicity [19–20]. Some surveys recruited younger women. One of them, conducted in women (44.6 ± 11.4 years) presenting with systemic lupus erythematosus, pointed out an inverse relation between BMD and carotid plaque index [20]. At the menopause, atherosclerotic calcifications progress with increasing bone loss [17]. These data were consistent with outcomes from PMW. Few studies were performed in men [10,12,18,21,23,26–28]. One longitudinal study did not find any significant association [18]. A cross-sectional survey suggested a stronger relation in women compared with men [21], or a correlation only present in women currently using hormone replacement therapy [28]. After adjustment for age, two transversal studies performed in Japanese women reported no association between BMD and the presence of aortic calcification or a negative correlation between Osteo-sono Assessment Index (OSI) [19,21]. OSI was determined by calcaneal quantitative ultrasound measurements and brachial-ankle Pulse Wave Velocity (baPWV), a marker of early atherosclerosis [21]. Similar findings were extensively demonstrated with aortic calcifications, which only occur at later stages of atherosclerosis (Table 1). Prospective trials, conducted in women, observed the progression of the aortic plaques in parallel with bone loss. Women with the greatest rate of bone loss have the most severe progression of abdominal aortic calcification [18]. A total of 47% of the variance of the annual rate of bone loss (2.6%) is attributable to the progression in aortic calcification (13.8%) [24]. Higher odds ratios for vertebral and hip fractures are observed in women with calcifications compared with those without calcification. Aortic calcification is

viewed as a strong predictor for fragility fractures. Results from the placebo group of an osteoporosis treatment trial indicate that women with at least one vertebral fracture at baseline have a threefold increase in risk of cardiovascular events compared with women without vertebral fracture [29].

One study focussed on the analysis of morphological characteristics of carotid artery plaques [27]. Echogenic plaques (with calcium deposits and dense fibrous tissue) are related to low bone mass, whereas no association is found between BMD and echolucent plaques (lipid-rich plaques).

In summary, although these diseases have long been considered unrelated, the current epidemiological findings suggest that the illnesses may be more closely connected than previously suspected.

The following mediators are considered to potentially play a role in the link between cardiovascular diseases and bone loss: estrogen, vitamin K, vitamin D, matrix Gla protein, osteopontin, Type I collagen, osteoprotegerin, homocysteine, parathormone and several dietary factors (salt or potassium intake). However, these interesting findings do not identify a common pathway for these disorders; therefore, further investigations are still needed.

Stroke

Stroke that accounts for cerebrovascular diseases is a major cause of severe disability and death in both women and men. Osteoporosis is a significant complication in patients who survive an acute stroke, because of the reduced mechanical load resulting from hemiplegia or hemiparesis. Bone loss and increased propensity to falls are greater in the paretic side. They lead to an increased incidence of fracture (i.e., hip fracture), on the affected side. This happens mainly during the first year after stroke. These important aspects have been widely recognized in studies assessing the osteoporotic status after stroke [31–34]. It would be also of great interest to determine whether LBMD in patients is associated with an increased risk of incident stroke. This hypothesis was the main topic of a few longitudinal studies [35–39].

An association between LBMD and death from stroke was reported in a large cohort of PMW participating in the prospective Study of Osteoporotic Fractures (SOF) [35]. Each decrease in one standard deviation (1-SD) of BMD, measured at the calcaneus (0.09 g/cm^2), was associated with a 1.31-fold increase in the risk of stroke, after adjustment for age, follow-up

duration (2 years) and several confounding factors [36]. These results support the idea that women with LBMD are at increased risk for stroke. Common causes include dietary factors and estrogen deficiency, and are suspected to result in both bone loss and stroke.

A case-control study [37] and a large cross-sectional trial [38] using data from the Third National Health and Nutrition Examination Survey (NHANES III) evaluated the relationship between BMD and stroke in both women and men. Although different study designs (e.g., number of strokes, various inclusion and exclusion criteria, diagnosis of stroke and site of BMD measurement) were involved, surveys reported similar findings. A possible association between LBMD and risk of stroke was identified in women, but not in men.

A recent 20-year follow-up study of aged subjects from the NHANES I indicated no association between phalangeal BMD and the subsequent development of stroke [39].

These conflicting results may be partially explained by discrepancies in the methodologies used to investigate the association between both illnesses. More standardized studies are required to explore and further understand the possible common etiology of the two processes.

Myocardial infarction

Coronary heart diseases, representing one-third to one-half of cardiovascular diseases, include myocardial infarction among others. Only one study investigated BMD in survivors of heart attack [40]. This cross-sectional trial was conducted in a multi-ethnic population of 5050 women and men (USA) aged 50–79 years. The relationship between self-reporting a previous myocardial infarction and LBMD measured at the total femur was statistically significant in men (odds ratio [OR]: 1.39, confidence interval [CI]: 95%, 1.03 to 1.87]), but not in women. These results suggest that BMD should be measured in male survivors of myocardial infarction.

Cardiovascular mortality

Cardiovascular events are the leading cause of mortality in Western countries. Cardiovascular death constitutes a relevant indicator of the association between osteoporosis and cardiovascular disorders. The hypothesis that LBMD might predict cardiovascular mortality has been extensively tested, mainly in large prospective cohorts of elderly women (≥65 years). Cause-specific mortality was extracted from death certificates and hospital records. Bone mass was measured by conventional x-ray absorptiometry, ultrasonography and markers of bone resorption.

In late PMW, low bone mass or prevalent vertebral fracture were linked to an increase in the risk of cardiovascular death [41]. This confirms previous findings that LBMD at the proximal radius is strongly associated with nontrauma mortality, especially due to stroke (risk ratio [RR]: 1.74) [35]. Later, Kado and colleagues demonstrated that each 1-SD increase in the rate of BMD loss is associated with a 1.3-fold increase in mortality from CHD and with a 1.2-fold increased risk of death from atherosclerosis [42]. Another study reported a 19% increase in cardiovascular death for each 1-SD decrease in Broadband Ultrasonic Attenuation (BUA) [43]. Higher levels of serum osteoprotegerin, a cytokine that negatively affects osteoclastogenesis, are associated with elevated cardiovascular mortality (OR: 1.4) [44]. In early PMW, each 1-SD decrease in bone mass increases the risk of death from cardiovascular disease twofold (RR: 2.1) [41]. We only identified one study in elderly men. Each 1-SD increase of hip-BMD is associated with a 25% decrease in the risk of cardiovascular death [45]. Outcomes observed in men or in early menopausal women are consistent with those observed in PMW. Decrease of BMD, a well-established indicator of fracture risk, is strongly associated with cardiovascular death after adjustment for several confounding factors. LBMD also appears to be a significant predictor of cardiovascular mortality, and is even stronger than other risk factors, such as blood pressure and cholesterol [41,46]. These observations suggest that cardiovascular risk should be assessed in patients with osteoporosis.

Cardiovascular risk factors

Nonskeletal disorders, such as hypertension, diabetes mellitus and dyslipidemia, are well-established predictors for atherosclerotic cardiovascular disorders. Elevated bone mass loss is described in elderly women with high blood pressure [47]. Hypertensive women face higher urinary calcium excretion than normotensive subjects [48]. Recently, osteocalcin, a biochemical marker of bone formation, has been negatively related with increased blood pressure [49]. Longitudinal and cross-sectional studies suggest a significant association between high blood pressure and alterations in calcium metabolism. The relation between osteoporosis and diabetes mellitus is less obvious. Type 1 diabetes is generally

associated with moderate decreases in BMD [50]. Reduced bone mass found at the onset of Type 1 diabetes mellitus suggest that osteoporosis is not a late consequence of Type 1 diabetes mellitus [51]. Studies conducted in Type 2 diabetes mellitus patients report mainly increased [52], but also unchanged [53] or even decreased [54] BMD when compared with healthy controls. The conflicting results may be due to the different pathogenesis of Type 1 and 2 diabetes. In a recent longitudinal study, elderly white women with diabetes had higher bone mineral density at baseline, and had a greater bone loss at the femoral neck than those with normal glucose metabolism [52]. The increased bone loss exposes diabetic patients to elevated fracture risk [55]. The paradox of higher BMD with increased risk of fracture in patients with diabetes may be due to a high propensity to fall and to an altered bone strength and structure, which is not captured by BMD measurement. Diabetes may affect bone through various mechanisms, including obesity, hyperinsulinemia, higher concentrations of advanced glycation end-products in collagen, lower levels of insulin-like growth factor (IGF)-1, hypercalciuria, microangiopathy and inflammation.

Diabetes, a powerful contributor to atherosclerotic cardiovascular events, also affects the skeletal system. The lipid profile is a strong predictor of risk for cardiovascular disorders. Increased levels of low-density lipoprotein-cholesterol (LDL-C) and low concentrations of high-density lipoprotein-cholesterol (HDL-C) are associated with greater risk of cardiovascular diseases [56]. PMW with elevated plasma LDL-C levels have lower BMD at lumbar spine and femoral neck compared with normal control [57]. The risk of osteoporosis is more than twofold higher compared to women with normal levels [58]. Reduced HDL-C level protects against atherosclerosis and is associated with LBMD in PMW [59]. Lipid oxidation products promote osteoblastic differentiation of vascular cells and inhibit differentiation in bone cells [60]. Plasma lipid profile could be the common regulator underlying both osteoporosis and atherosclerosis. Further research is needed to investigate this potential explanation.

Conclusion & future perspectives

Although the aforementioned epidemiological studies were limited by study design and yielded discrepant findings, they suggest an age-independent association between cardiovascular disorders and osteoporosis. Moreover, preliminary results of preclinical studies are supportive of a common pathomechanism between these two degenerative diseases.

Further prospective and multicenter studies performed in large cohorts of men and women are needed to assess this association more accurately. They should use current, standardized and more sensitive technologies, such as dual energy x-ray absorptiometry or electron-beam computer tomography to obtain accurate estimates of the measured sites. Future biological studies should aim at discovering the mechanisms involved in the regulation of vascular and bone systems, thereby leading to a better understanding of each marker. This research will play an important role in the development of novel therapies.

Executive summary

Introduction

- Both osteoporosis and cardiovascular events, occurring in the elderly, are a major cause of mortality, morbidity and disability in most developed countries.
- Is there an association between these degenerative conditions?

Osteoporosis

- Osteoporosis is diagnosed when bone mineral density (BMD) T-score, at hip or spine, is below -2.5.
- BMD is the best single predictor of future fracture risk.

Vascular calcification due to atherosclerosis

- Atherosclerosis is a silent disease that may affect different parts of the vessels.
- Vascular calcification is widely considered as a valid surrogate for cardiovascular diseases.
- Most, but not all, epidemiological studies, which used variable study designs, suggest an association between osteoporosis (low [L]BMD or prevalent fracture) and atherosclerosis (aortic calcification, carotid atherosclerosis, coronary artery disease or peripheral arterial disease).
- Bone markers have been identified in calcified plaques, suggesting that both processes share similar mechanisms.
- Estrogen, vitamin K, vitamin D, osteocalcin, osteopontin, Type I collagen, osteoprotegerin, homocysteine, parathormone and several dietary factors (salt or potassium intake) are likely to play a role between cardiovascular diseases and bone loss.

Executive summary

Stroke

- Osteoporosis is a significant complication in patients who survive an acute stroke.
- Previous surveys investigating the link between LBMD and risk of incident stroke suggest an association in women, but not in men.
- A recent 20-year follow-up study (First National Health and Nutrition Examination Survey [NHANES I]) indicated no association.

Myocardial infarction

- One single study reports a statistically significant relationship between previous myocardial infarction and low hip-BMD in men.

Cardiovascular mortality

- Epidemiological studies suggest that LBMD is predictive of cardiovascular mortality in early- and late-postmenopausal women and in men.
- LBMD appears to be a significant predictor of cardiovascular mortality (stronger predictor than blood pressure or cholesterol levels).

Cardiovascular risk factors

- Longitudinal and cross-sectional studies suggest a significant association between high blood pressure and alterations in calcium metabolism.
- Diabetes, a powerful contributor to atherosclerotic cardiovascular events, also affects the skeleton.
- Increased levels of low-density lipoprotein cholesterol and low concentrations of high-density lipoprotein cholesterol, are associated with LBMD in postmenopausal women.

Conclusion

- Previous epidemiological studies support an association between cardiovascular disorders and osteoporosis independently of age. Cardiovascular risk should be considered in patients requiring anti-osteoporotic treatment.
- Further prospective studies using more sensitive technologies (dual-energy x-ray absorptiometry and electron-beam computer tomography) are needed to assess this association.
- Future biological studies should aim to discover the mechanisms involved in the regulation of vascular and bone systems.

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