EDITORIAL COMMENT

Does Low Bone Mineral Density Cause a Broken Heart?*

Kenneth W. Lyles, MD,‡† Cathleen S. Colon-Emeric, MD, MHSc‡†

Osteoporosis, with its attendant fractures, is one of the most common and heartbreaking conditions in our aging society. In the United States, 2 million osteoporotic fractures occur each year, of which some 600,000 are in men (1). These skeletal events cause significant pain, disability, and functional impairment. For patients with a hip fracture, two-thirds must spend time in a rehabilitation or nursing facility. Once home, 50% of these women and men never return to their previous level of ambulation and function (2). Hip and other osteoporotic fractures are morbid events; 15% to 25% of patients with a hip fracture die within 12 months of the fracture (3). Although these devastating consequences of osteoporosis have long been appreciated, new research in this issue of JACC: Heart Failure (4) suggests that osteoporosis may also be literally causing broken hearts.

A higher-than-expected prevalence of osteoporosis among patients with atherosclerotic cardiovascular disease, and vice versa, has been recognized for years because they share many risk factors including age, sedentary lifestyles, and smoking. It has also been recognized that osteoporotic fractures are associated with an increased risk of cardiac events; retrospective studies from the Mayo Clinic and Taiwan have revealed that 10% of their patients with hip fracture have a myocardial infarction in the first week after their hip fracture (5,6). High levels of inflammatory cytokines circulating after a fracture have been postulated to lead to the infarction. Other epidemiologic evidence suggests that patients with prevalent heart failure have a higher risk of osteoporosis and subsequent fractures (7,8). The mechanism(s) for this association is almost certainly multifactorial. Patients with heart failure are frail and are receiving drugs that put them at risk for falls with subsequent fractures; loop diuretics cause renal calcium loss; and heart failure causes an increase in inflammatory markers that could suppress bone formation. Some experts call for routine measurement of bone mineral density (BMD) in patients with heart failure to identify those at risk for fracture, so that therapy can be initiated to reduce the subsequent fracture risk.

However, until now, there has not been evidence that the association cuts both ways. Pfister et al. (4) show for the first time in a healthy cohort that lower BMD as assessed by calcaneal broadband ultrasound attenuation (BUAA) by quantitative ultrasound predicts the development of heart failure after 9.3 years of follow-up. The use of calcaneal BUAA to assess skeletal BMD and subsequent fracture risk is an accepted way to screen large patient populations and assess their future fracture risk. After adjusting for a large number of covariates in the EPIC-Norfolk prospective study, these investigators showed that for every 1 SD increase in BMD, there was a 23% decrease in the risk of heart failure (hazard ratio [HR]: 0.77; 95% confidence interval [CI]: 0.66 to 0.89). The investigators demonstrated that this association was more robust with heart failure without (HR: 0.75; 95% CI: 0.63 to 0.89) than with antecedent myocardial infarction (HR: 0.82; 95% CI: 0.62 to 1.09). The association remained under different modeling assumptions, after sensitivity analyses to reduce the chance that subclinical heart failure was present at the time of BUAA, and after

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From ‡Duke University and VA Medical Centers, Durham, North Carolina; and †The Carolinas Center for Medical Excellence, Cary, North Carolina. Drs. Lyles and Colon-Emeric are founders and equity owners of BisCardia, Inc.
adjustment for common risk factors including age, smoking, alcohol, medications, and (to some extent) physical activity.

The association of lower BMD as a risk factor for the development of heart failure raises a myriad of new questions that may yield insights into the prevention of both conditions. If confirmed in other cohorts, understanding the common pathophysiologic mechanism(s) will be an interesting and potentially fruitful quest. Do patients with lower BMD have a diminished stem cell reserve, making them less capable of maintaining a normal bone mass, and also less capable of repairing their myocardium when it becomes damaged? When there is an increase in bone remodeling after the age of 30 years, in most patients, bone formation does not keep pace with bone resorption so that bone loss occurs. Does a comparable event occur in the myocardium resulting in abnormal remodeling when tissue damage occurs? Do patients with lower bone mass have a larger inflammatory response to stressors resulting in lower BMD and heart failure? Others will develop additional hypotheses to test and explain this association.

Because both heart failure and osteoporosis are two of the chronic illnesses at the top of the list of expensive health care conditions, we are intrigued by the potential for simple interventions that may significantly reduce the burden caused by these disorders. Will increasing BMD in childhood or even young adulthood reduce the subsequent risk of heart failure? Are women and men who have bone loss with the decline in gonadal estrogen/testosterone levels more at risk for development of heart failure? Does an increase in BMD that is possible with anti-resorptive therapies (bisphosphonates, raloxifene, or denosumab) or bone formation stimulation therapies (teriparatide) affect the risk of heart failure? In short, interventions targeting bone may have the potential to prevent many broken hearts.

The next step after such a provocative finding will be to replicate the association in another large database. Fortunately, with the wealth of existing well-defined cohorts, such studies should be relatively easy to accomplish. With confirmation of the observations made by Pfister et al. (4), a new area of cardiovascular/bone biology research will begin.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Kenneth W. Lyles, Duke University School of Medicine, Durham VA Medical Center, 508 Fulton Street, Durham, North Carolina 27705. E-mail: Kenneth.lyles@dm.duke.edu.

REFERENCES


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