Heart failure and osteoporosis: an association that merits further study

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We were invited to comment on the systematic review and meta-analysis by Gu et al examining the risk of incident heart failure in persons with osteoporosis. Both heart failure and osteoporosis are prevalent disorders in the aging population and cause substantial morbidity, excess mortality, and considerable economic burden.²⁴ Heart failure and osteoporosis or osteoporotic fractures share some risk factors, including age,²⁴ behavioral factors such as smoking and alcohol use,²⁴ medication exposures such as systemic glucocorticoids,⁴⁵ decreased exercise tolerance,⁴⁴ hypovitaminosis D,⁴⁷ renal disease,²⁴ and diabetes.²⁴ Whether there are common operative mechanisms underlying the development of heart failure and osteoporosis remains an area of study.

Three cohort studies, 2 retrospective and 1 prospective, including 70,697 individuals, mainly of Taiwanese descent, were included in the systematic review and meta-analysis by Gu et al.¹ In these analyses, the authors report a modest increased risk of incident heart failure in persons with osteoporosis (HR, 1.17; 95% CI, 1.08–1.26), which remained significant in men (HR, 1.30; 95% CI, 1.05–1.62) but not in women (HR, 1.14; 95% CI, 0.94–1.37) in a gender-stratified analysis. There was a significant association of increased risk of incident heart failure among patients of Asian ethnicity with osteoporosis (HR, 1.18; 95% CI, 1.06–1.30), who comprised the majority of the population included in the meta-analysis. However, in the component prospective study by Fohtung et al,¹⁹ there was an inverse association among Black men; lower total hip bone mineral density (BMD) was independently associated with a lower risk of heart failure (HR, 0.74; 95% CI, 0.59–0.94, for every 0.1 g/cm² decrement in BMD).

The pathophysiology of heart failure and osteoporosis may share some common underpinnings. Gu et al proposed 2 possible mechanisms: renin-angiotensin-aldosterone system activation and dysregulation of osteoprotegerin. Consideration should also be given to increased oxidative stress as a common pathway to heart failure and osteoporosis. Population-based evidence shows increased oxidative stress is negatively associated with BMD¹⁰ and that antioxidants are decreased in women with postmenopausal osteoporosis.¹² Likewise, oxidative stress is postulated to contribute to atherosclerotic cardiovascular disease and cardiomyopathy risk,¹³ common causes of heart failure. Hyperparathyroidism, whether primary or secondary to another underlying cause such as vitamin D deficiency and/or renal disease,¹¹ another possible shared determinant.¹³ Vitamin D, known to be essential for calcium absorption and bone mineralization as well as cardiovascular integrity as an antifibrotic and antihypertrophic agent, is associated with both osteoporosis and heart failure incidence.¹³ However, the absence of a benefit of vitamin D supplementation for heart failure prevention in the general population (including vitamin D-replete individuals) in randomized trials raises doubt about this mechanistic pathway,¹⁴ and further study is needed. Finally, we would be remiss to neglect the fact that the association of osteoporosis and heart failure may be due entirely to shared risk factors.

We noted a few limitations with this study. First, the study population was largely of Taiwanese descent, thus limiting the generalizability of the findings to other races and ethnicities. The examined MESH terms did not include osteoporotic fractures; in clinical practice, presence of a fragility fracture secures the diagnosis of osteoporosis regardless of BMD. Thus, there may have been other published studies that were not included but might have shed more light on this important topic.

One of the 3 cohort studies included¹⁴ was limited to persons with end-stage renal disease (ESRD). This is problematic as the ESRD...
population differs from the general elderly population in its risks for heart failure and osteoporosis. Moreover, there are a number of complex changes in bone and mineral metabolism, that is, renal osteodystrophy, that occur in ESRD that may have simply been labeled as osteoporosis inaccurately. Furthermore, this study only partially controlled for confounding, neglecting important shared risk factors such as smoking, alcohol use, glucocorticoid exposure, decreased exercise tolerance, and elevated parathyroid hormone levels, despite a suspected high prevalence of hyperparathyroidism in its exclusively ESRD population. Careful adjustment for potential confounders is essential to understanding the true association between heart failure and osteoporosis given the myriad of shared risk factors, both known and theoretical. These confounders may be of particular importance in men, who may be less likely to be screened with dual-energy X-ray absorptiometry for osteoporosis in the absence of risk factors, generating selection bias.

Of interest, in contrast to osteoporosis, heart failure is a heterogenous disease comprising acute and chronic presentations, systolic and diastolic variants, and a multitude of divergent but sometimes overlapping causes including coronary artery disease, arrhythmia, valvular disease, and hypertension, among others. In a prior study of incident osteoporotic fractures in persons with prevalent heart failure, similar hazards of incident fracture were found between persons with systolic (EF ≤40%) and diastolic (EF >40%) heart failure. Further studies that evaluate for incidence of different etiologies and categories (systolic vs diastolic) of heart failure in persons with osteoporosis would help to clarify the association of heart failure and osteoporosis.

In conclusion, while further studies including investigation of the role of race and gender and more complete control of confounders are needed to better understand the association of heart failure with osteoporosis, Gu et al have furthered our knowledge in showing a modest association in men. In clinical practice, one could consider being particularly vigilant for heart failure signs and symptoms as prudent in the evaluation of osteoporotic patients, especially Asian men.

REFERENCES