

Mayo Clinic Proceedings ' June 2022 Issue Summary

Greetings, I am Dr Karl Nath, the Editor-in-Chief of *Mayo Clinic Proceedings*, and I am pleased to welcome you to the multimedia summary for the journal's June 2022 issue. There are three articles that have been selected as our Editor's Choice or Highlights articles this month.

The Editor's Choice this month is a Thematic Review article entitled "Skeletal Aging." It is authored by Dr Jad Sfeir and colleagues from the Robert and Arlene Kogod Center on Aging, and the Division of Endocrinology and Metabolism at Mayo Clinic in Rochester, Minnesota.

Aging predisposes to chronic disease and multimorbidity, prominent among which are osteoporosis and its complications. In their review, Sfeir et al expertly discuss the epidemiology, risk factors, pathogenesis, and treatment of osteoporosis, within the overarching framework of age-dependent skeletal changes and processes. As noted by the authors, in Americans aged 50 years and older, osteoporosis is present in more than 10% of Americans, with one third of women and one fifth of men developing fractures at age 50 years and older. The authors discuss such salient areas that include the assessment of skeletal fragility; the assorted factors which, along with aging, promote bone loss and fractures; the assessment of falls, frailty, and sarcopenia; the critical relevance of hormonal status on bone health; and the natural history of changes in bone. With regard to the latter, in the first two decades of life, bone modeling occurs, with peak bone mineral density occurring in the third decade for either sex; from the third decade onward, bone remodeling occurs. Besides bone mass and mineral density, the microarchitecture and material properties of bone may determine the risk for fractures; these characteristics may be affected by aging, type 2 diabetes mellitus, and glucocorticoids.

Remodeling of bone consists of cycles of resorption by osteoclasts; reversal by bone marrow-derived osteoblast precursors; bone formation by osteoblasts; and bone mineralization by osteocytes. Osteocytes aid in the coordination of the actions of osteoclasts and osteoblasts, and these remodeling cycles are influenced by mechanical stress and bony microdamage. By the fifth decade or so in women (at the time of menopause), and later in men, the balance between bone resorption and bone formation is tilted towards net resorption.

As noted by the authors, it is estimated that women and men exhibit lifespan losses of 55% and 45% of trabecular bone, respectively, and losses of 25% and 18% of cortical bone, respectively. Such net loss of bone may reflect, at least in part, increased death of bone-forming cells, increased marrow adiposity, and the accumulation of senescent cells which produce an inflammatory senescent secretory phenotype. Sfeir et al conclude their review by discussing and emphasizing the prevention and treatment of osteoporosis by physical activity, calcium and vitamin D, and pharmacotherapy with estrogen, raloxifene, bisphosphonates, and other therapeutic compounds. Reducing the risk of or treating osteoporosis by such approaches, as indicated, in turn reduces the risk of fractures and their attendant morbidity and mortality.

The first Highlight this month is an Original Article entitled "Prevalence and Natural History of Mitral Annulus Calcification and Related Valve Dysfunction." It is authored by Dr Nahoko Kato and colleagues from the Departments of Cardiovascular Medicine and Health Sciences Research at Mayo Clinic in Rochester, Minnesota.

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Mitral annulus calcification is characterized by three essential processes involving the fibrous annulus of the mitral valve: chronicity, degenerative changes, and deposition of calcium. Kato et al undertook a large retrospective analysis of adults undergoing transthoracic echocardiography in 2015 at Mayo Clinic Rochester in whom mitral annulus calcification was identified. In this population of almost 25,000 patients, the prevalence of mitral annulus calcification was 23%, the latter increasing with age. The mean age of patients with mitral annulus calcification was higher than those without mitral annulus calcification - 75 years versus 60 years.

Mitral annulus calcification predisposes to mitral valve dysfunction. Specifically, in this patient population, mitral regurgitation, without mitral stenosis, occurred in 9.5% of patients with mitral annulus calcification compared with 6.1% of those without such calcification; the analogous figures for mitral stenosis, irrespective of mitral regurgitation, were 6.6% and 0.5%, in patients with and without mitral annulus calcification, respectively. The odds for the presence of mitral annulus calcification were significantly increased by aortic stenosis, prior aortic valve replacement, and left ventricular outflow tract obstruction. Risk factors for mitral stenosis in patients with mitral annulus calcification included aortic stenosis, prior aortic valve replacement, left ventricular outflow tract obstruction, female sex, kidney dysfunction, chest irradiation, and coronary artery disease, whereas risk factors for mitral regurgitation included reduced left ventricular ejection fraction, left ventricular outflow tract obstruction, left ventricular mass index, kidney dysfunction, female sex, and age.

After relevant adjustments, and during a median follow up of 3 years, patients with mitral annulus calcification exhibited increased mortality, which was further increased if complicated by mitral valve dysfunction.

This study by Kato et al—the first large cohort study to date of the prevalence, clinical characteristics, predisposing conditions, consequences, and complications of mitral annulus calcification—shows that this valvular condition is neither uncommon nor benign.

The second Highlight this month is an Original Article entitled “Socioeconomic Deprivation and Premature Cardiovascular Mortality in the United States.” It is authored by Dr Graham Bevan from the Harrington Heart and Vascular Institute of the University Hospitals Cleveland Medical Center in Cleveland, Ohio, and colleagues from Case Western Reserve University, in Cleveland, and Houston Methodist, in Houston, Texas.

Traditional cardiovascular risk factors do not adequately account for premature cardiovascular mortality in the United States, especially in light of discernible trends and geographic variation in such mortality. Bevan et al examined whether socioeconomic deprivation - increasingly recognized as a determinant of disease - may underlie such regional and temporal profiles in premature cardiovascular mortality during the period of 1999 to 2018.

The authors obtained such mortality data at a county-level from the US National Center for Health and Statistics. County level prevalence of traditional cardiovascular risk factors was obtained from the 2020 Population Level Analysis and Community Estimates project. Socioeconomic deprivation was evaluated by the Social Deprivation Index, which is an

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integrated score based on poverty/income; unemployment/employment; considerations pertaining to home, housing, and household; level of education; and access to transportation. The authors also employed another validated index, the Area Deprivation Index, which is an integrated score based on 17 criteria pertaining to aspects of income, employment, and education. The findings of Bevan et al demonstrate that a significantly increased, total non-Hispanic Black/African American and female premature cardiovascular mortality occurred in counties with a higher quartile Social Deprivation Index and Area Deprivation Index; both these indices correlated with mortality. Notably, 44% and 40% of the county variability in cardiovascular mortality could be ascribed to Area Deprivation Index and Social Deprivation Index, respectively.

During the years of this analysis, 1999 to 2018, premature cardiovascular mortality decreased, but the decline in mortality was less in counties with a higher socioeconomic deprivation; this, as noted by the authors, suggests widening disparities. The basis for the relationship between socioeconomic deprivation and premature cardiovascular mortality is multifactorial, including, for example, access to health care and psychosocial stress, among other factors, and is highlighted by Bevan et al in their Discussion. These findings underscore that so much of disease processes – in this case premature cardiovascular mortality – have their provenance in socioeconomic deprivation, findings of particular relevance and importance to health care policies seeking to reduce cardiovascular mortality.

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