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IN THE LIMELIGHT

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In the Limelight: June 2022

This month's feature highlights three articles that appear in the current issue of *Mayo Clinic Proceedings*. These articles are also featured on the *Mayo Clinic Proceedings*' YouTube Channel (https://youtu.be/W7NFAl_bNcQ).

THE AGING OF BONE AND ITS COMPLICATIONS

Aging predisposes to chronic disease and multimorbidity, prominent among which are osteoporosis and its complications. In the present issue of *Mayo Clinic Proceedings*, Sfeir et al expertly review 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 factures. The authors discuss assessment of skeletal fragility; 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. 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. In addition to 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, formation by osteoblasts, and mineralization by osteocytes; osteocytes aid in the coordination of 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 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.

See also pages 1094, 1108, 1194

Scan code to view video

Sfeir JG, Drake MT, Khosla S, Farr JN. Skeletal aging. *Mayo Clin Proc.* 2022;97(6):1194-1208.

MITRAL ANNULUS CALCIFICATION: NEITHER BENIGN NOR UNCOMMON

Mitral annulus calcification (MAC) is characterized by three essential processes involving the fibrous annulus of the mitral valve: chronicity, degeneration, 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 MAC was identified. In this population of 24,414 patients, the prevalence of MAC was 23%, the latter increasing with age; the mean age of patients with MAC was higher than those without MAC (75 years versus 60 years). Overall mitral valve dysfunction was more frequent in patients with MAC than those without MAC (16% versus 6.6%); the relevant figures for mitral regurgitation were (without mitral stenosis) 9.5% versus 6.1%, and for mitral stenosis (irrespective of mitral regurgitation) 6.6% versus 0.5%, in patients with and without MAC, respectively. Aortic stenosis, prior aortic valve replacement, and left ventricular outflow tract obstruction were associated with a 4-fold, 3-fold, and 2-fold increase in the odds for the presence of MAC, respectively. Aortic stenosis, prior aortic valve replacement, left ventricular outflow tract obstruction, female sex, eGFR, chest irradiation, and coronary artery disease were associated with an increase of mitral stenosis in patients with MAC, whereas reduced left ventricular ejection fraction, left ventricular outflow tract obstruction, left ventricular mass index, eGFR, female sex, and age were associated with mitral regurgitation in patients with MAC. After relevant adjustments, and during a median follow up of 3 years, patients with MAC exhibited an increased mortality, which was further increased if attended by mitral valve dysfunction. This study by Kato et al - the first large cohort study to date of the prevalence, clinical characteristics, consequences, and complications of MAC - shows that this condition is neither uncommon nor benign.

Kato N, Guerrero M, Padang R, et al. Prevalence and natural history of mitral annulus calcification and related valve dysfunction. *Mayo Clin Proc.* 2022;97(6):1094-1107.

SOCIOECONOMIC DEPRIVATION AS A DETERMINANT OF PREMATURE CARDIOVASCULAR MORTALITY

Traditional cardiovascular (CV) risk factors do not adequately account for premature CV mortality in the United States especially in light of discernible trends and geographic variation in such mortality. Bevan et al examined whether socioeconomic deprivation, increasingy recognized as a determinant of disease, would underlie such regional and temporal profiles in premature CV 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 CV risk factors was obtained from the 2020 Population Level Analysis and Community Estimates project. Socioeconomic deprivation was evaluated by the social deprivation index (SDI), which is an integrated score based on poverty/income; employment/non-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 (ADI), 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 greater total non-Hispanic Black/African American and female CV mortality was observed in counties with a higher quartile SDI and ADI, with both SDI and ADI correlating with mortality. Notably, 44% and 40% of the county variability in CV mortality could be ascribed to ADI and SDI,

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respectively. During the years of this analysis (1999 to 2018), premature CV 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 CV mortality is multifactorial, including, for example, access to health care and psychosocial stress, among other factors, and is highlighted by Bevan et al. These findings underscore that so much of disease processes — in this case premature CV mortality — have their provenance in socioeconomic deprivation, findings of particular relevance to health care policies seeking to reduce CV mortality.

Bevan GH, Nasir K, Rajagopalan S, Al-Kindi S. Socioeconomic deprivation and premature cardiovascular mortality in the United States. *Mayo Clin Proc.* 2022;97(6):1108-1113.

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