Selección de Resúmenes de Menopausia

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Secondary Osteoporosis

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Osteoporosis is a global public health problem, with fractures contributing to significant morbidity and mortality. Although post-menopausal osteoporosis is most common, up to 30% of post-menopausal women, >50% of premenopausal women, and between 50-80% of men have secondary osteoporosis. Exclusion of secondary causes is important as treatment of such patients often commences by treating the underlying condition. These are varied but often neglected, ranging from endocrine to chronic inflammatory and genetic conditions. General screening is recommended for all patients with osteoporosis with advanced investigations reserved for premenopausal women and men aged <50 years, for older patients in whom classical risk factors for osteoporosis are absent, and for all patients with the lowest bone mass (Z-score ≤-2). The response of secondary osteoporosis to conventional anti-osteoporosis therapy may be inadequate if the underlying condition is unrecognized and untreated. Bone densitometry, using dual energy x-ray absorptiometry (DXA), may underestimate fracture risk in some chronic diseases including glucocorticoid-induced osteoporosis, type 2 diabetes and obesity, and may overestimate fracture risk in others (e.g. Turner syndrome). FRAX ® and TBS may provide additional information regarding fracture risk in secondary osteoporosis, but their use is limited to adults aged ≥40 years and ≥50 years, respectively. In additional FRAX ® requires adjustment in some chronic conditions e.g. glucocorticoid dose, type 2 diabetes and HIV. In most conditions, evidence for antiresorptive or anabolic therapy is limited to increases in bone mass. Current osteoporosis management guidelines also neglect secondary osteoporosis and these existing evidence gaps are discussed.

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Association of Antiosteoporotic Medication Bisphosphonates and Denosumab with Primary Breast Cancer: An Electronic Health Record Cohort Study

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Background: The risks of osteoporosis and breast cancer are increasing in elderly women. Bisphosphonates and denosumab are recommended for treatment of osteoporosis. They have different and overlapping pharmacodynamics and previous studies have shown conflicting results regarding their risk association with breast cancer. We intend to further look into this issue through a comparative study. Methods: Electronic health records of 91,626 women older than 50 years with no previous history of malignancy and no nonbreast cancer during follow-up were retrieved from southern California and retrospectively analyzed using univariate, bivariate, and log-rank tests. Medication use, breast cancer risk, and associated demographic and clinical history were assessed. Results: Over an average of 3.6 years follow-up, the breast cancer relative risks (RRs) counted after 365 days of latency are 1.12 (95% confidence interval [CI]: 0.64-1.97) for denosumab ever users and 0.37 (95% CI: 0.21-0.66) for bisphosphonates ever users, when covariates are comparable. The significant difference is supported by the Log-rank test (p = 0.0004). Excluding statins coprescribers, the breast cancer RR is 1.31 (0.71, 2.43) in denosumab group and 0.26 (0.11, 0.62) in bisphosphonates group. There is a reduced RR in statins ever users (0.47, 95% CI: 0.38-0.58), and the breast cancer risk difference is not significant between concomitant denosumab/statins and bisphosphonates/statins ever users with RR 0.65 (0.16, 2.58) versus 0.55 (0.26, 1.16), p = 0.692. Conclusions: Our data support an association of lower breast cancer risk with bisphosphonates use in elderly women. We did not observe a lower breast cancer risk in denosumab group; however, our data revealed a potential lower breast cancer risk in denosumab users with concurrent statins use and this requires further study.

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Human gut microbiome impacts skeletal muscle mass via gut microbial synthesis of the short-chain fatty acid butyrate among healthy menopausal women

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Background: Increasing evidence suggests that human gut microbiome plays an important role in variation of skeletal muscle mass (SMM). However, specific causal mechanistic relationship of human gut microbiome with SMM remains largely unresolved. Understanding the causal mechanistic relationship may provide a basis for novel interventions for loss of SMM. This study investigated whether human gut microbiome has a causal effect on SMM among Chinese community-dwelling healthy menopausal women. Methods: Estimated SMM was derived from whole-body dual-energy X-ray absorptiometry. We performed integrated analyses on whole-genome sequencing, shotgun metagenomic sequencing, and serum short-chain fatty acids (SCFAs), as well as available host SMM measurements among community-dwelling healthy menopausal women (N = 482). We combined the results with summary statistics from genome-wide association analyses for human gut microbiome (N = 952) and SMM traits (N = 28 330). As a prerequisite for causality, we used a computational protocol that was proposed to measure correlations among gut metagenome, metabolome, and the host trait to investigate the relationship between human gut microbiome and SMM. Causal inference methods were applied to assess the potential causal effects of gut microbial features on SMM, through one-sample and two-sample Mendelian randomization (MR) analyses, respectively. Results: In metagenomic association analyses, the increased capacity for gut microbial synthesis of the SCFA butyrate was significantly associated with serum butyrate levels [Spearman correlation coefficient (SCC) = 0.13, P = 0.02] and skeletal muscle index (SCC = 0.084, P = 0.002). Of interest was the finding that two main butyrate-producing bacterial species were both positively associated with the increased capacity for gut microbial synthesis of butyrate [Faecalibacterium prausnitzii (SCC = 0.25, P = 6.6 × 10-7) and Butyricimonas virosa (SCC = 0.15, P = 0.001)] and for skeletal muscle index [F. prausnitzii (SCC = 0.16, P = 6.2 × 10-4) and B. virosa (SCC = 0.17, P = 2.4 × 10-4)]. One-sample MR results showed a causal effect between gut microbial synthesis of the SCFA butyrate and appendicular lean mass (β = 0.04, 95% confidence interval 0.029 to 0.051, P = 0.003). Two-sample MR results further confirmed the causal effect between gut microbial synthesis of the SCFA butyrate and appendicular lean mass (β = 0.06, 95% confidence interval 0 to 0.13, P = 0.06). Conclusions: Our results may help the future development of novel intervention approaches for preventing or alleviating loss of SMM.

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Impact of sleep disturbances on employment and work productivity among midlife women in the US SWAN database: a brief report

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Objective: Menopause is associated with an increased prevalence of sleep difficulties. We evaluated the economic burden of sleep disturbances among working midlife women. Methods: This retrospective, longitudinal cohort study collected data from the US Study of Women's Health Across the Nation (SWAN) database of women age 42-52 years at enrollment. We assessed the association between sleep disturbances (trouble falling asleep, waking early, or nocturnal awakenings) and workplace productivity (employment [yes/no] and work hours/wk) for women who were employed at the baseline visit and had ≥1 follow-up visit. We estimated overall economic burden by multiplying changes in productivity by median age-specific hourly US wages. Each woman's data were compared from visit to visit and were excluded after the first observed unemployment. Regression analysis was used to estimate associations between changes in sleep and changes in workplace productivity while controlling for relevant characteristics that varied over time. Results: The analysis included 2,489 working women (19,707 visits); 31% became unemployed during follow-up. Risk of unemployment was 31% higher for women with versus without new-onset sleep disturbances (P = 0.0474). Onset of sleep disturbances was associated with a 0.44-0.57 hours/wk reduction in work time (not significant). Using the more conservative reduction (0.44 h), sleep problems were associated with an annual loss of $517 to $524 per woman and $2.2 billion/yr in lost productivity among women age 42-64 nationwide. Conclusions: New-onset sleep problems in midlife women are associated with significant increases in risk of unemployment and ~$2 billion/yr in lost productivity nationwide.

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Neurodegenerative Disease: Roles for Sex, Hormones, and Oxidative Stress

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Neurodegenerative diseases cause severe impairments in cognitive and motor function. With an increasing aging population and the onset of these diseases between 50-70 years, the consequences are bound to be devastating. While age and longevity are the main risk factors for neurodegenerative diseases, sex is also an important risk factor. Sex is

multifaceted, encompassing sex chromosome complement, sex hormones (estrogens and androgens), and sex hormone receptors. Sex hormone receptors can induce various signaling cascades, ranging from genomic transcription to intracellular signaling pathways that are dependent on the health of the cell. Oxidative stress, associated with aging, can impact the health of the cell. Sex hormones can be neuroprotective under low oxidative stress conditions but not in high oxidative stress conditions. An understudied sex hormone receptor that can induce activation of oxidative stress signaling is the membrane androgen receptor (mAR). mAR can mediate NADPH oxidase (NOX) generated oxidative stress that is associated with several neurodegenerative diseases, such as Alzheimer's disease. Further complicating this is that aging can alter sex hormone signaling. Prior to menopause, women experience more estrogens than androgens. During menopause, this sex hormone profile switches in women due to the dramatic ovarian loss of 17β-estradiol with maintained ovarian androgen (testosterone, androstenedione) production. Indeed, aging men have higher estrogens than aging women due to aromatization of androgens to estrogens. Therefore, higher activation of mAR-NOX signaling could occur in menopausal women compared to aged men, mediating the observed sex differences. Understanding these signaling cascades could provide therapeutic targets for neurodegenerative diseases.

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Increased Fracture Risk After Bariatric Surgery: a Case-Controlled Study with a Long-Term Follow-Up

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Purpose: Bariatric surgeries are common procedures due to the high prevalence of obesity. This study aimed to investigate whether bariatric surgery increases fracture risk. Material and methods: It was a case-controlled study. Patients who underwent bariatric surgery during 2011 and 2012 were matched for age (± 5 years) and gender to patients on medical weight management during the same period with a ratio of 1:2. The index date was defined as the date of bariatric surgery for both groups. The subject's electronic medical records were reviewed retrospectively to identify fractures documented by radiology during January 2020. Results: Randomly selected 403 cases were matched to 806 controls with a median age of 36.0 years (IQR 14.0) and 37.0 years (IQR 14.0), respectively. Seventy per cent of the cohort were females. Eighty per cent received sleeve gastrectomy, and the remaining (17%) underwent gastric bypass. The mean duration of follow-up was 8.6 years. The fracture rate was higher in the surgical group as compared to the controls (9.4% vs 3.5%) with a crude odds ratio of 2.71 (95% CI 1.69-4.36). The median duration for time to fracture was 4.17 years for the surgical group and 6.09 years for controls (p-value = 0.097). The most common site of fractures was feet, followed by hands. Apart from a few wrist fractures, there was no typical osteoporotic sites fracture. Conclusion: Subjects who underwent bariatric procedures had more non-typical osteoporotic site fractures affecting mainly feet and hands, and fractures tend to occur earlier as compared to controls.