Selección de Resúmenes de Menopausia

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Postmenopausal women with normal BMD who have fracture have deteriorated bone microarchitecture: A prospective analysis from the OFELY study

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Most postmenopausal women who sustain fragility fracture (Fx) have their areal bone mineral density (aBMD) above the osteoporosis threshold. A sizeable proportion of them have normal aBMD. The aim of this study was to prospectively investigate the association of fragility Fx with bone microarchitecture (MA) assessed by high resolution peripheral computed tomography (HR-pQCT) in postmenopausal women without low BMD. At the 14th annual follow-up of the OFELY study, we have measured bone MA at the distal radius and tibia with HR-pQCT in addition to areal BMD with DXA, in 586 postmenopausal women. Among them, 166 (29 %) women, mean (SD) age 65 (8) yr, had normal BMD defined as a T score ≥ -1 at the lumbar spine, femoral neck and total hip. During a median [IQR] 15 [14-15] yr of follow-up, 46 of those women sustained incident fragility Fx, including 19 women with a major osteoporotic Fx (clinical spine, forearm, proximal humerus, hip). Women who sustained Fx did not differ for age, BMI, tobacco and alcohol use, diabetes, falls, FRAX®, aBMD and TBS compared with women without incident Fx. In contrast, they had significant impairment of volumetric densities, cortical area (Ct.Ar) and thickness (Ct.Th), stiffness (K) and estimated failure load (FL) at the radius compared with women without incident Fx. At the radius, each SD decrease of volumetric densities, Ct.Ar, Ct.Th, K and estimated FL was significantly associated with an increased risk of all fragility fractures with hazard ratios (HR) from 1.44 to 1.56 and of major osteoporotic fractures (HR from 1.66 to 2.57). Lesser impairment of bone MA was seen at the tibia. We conclude that even in women with normal areal BMD fragility fractures are associated with deterioration of bone microarchitecture.

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A Contemporary View of Menopausal Hormone Therapy

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Enthusiasm for the use of hormones to ameliorate symptoms of perimenopause and menopause has waxed and waned over the years. Both treatment for symptoms and training of women's health care practitioners in the management of menopause have sharply declined since publication of the Women's Health Initiative initial results in 2002. Findings from that trial, which treated a population of older, asymptomatic patients, have been extrapolated over the past 21 years to all estrogen products, all menopausal women, and all delivery mechanisms. Our patients deserve a more nuanced, individualized approach. Conjugated equine estrogens and medroxyprogesterone acetate are no longer the predominant medications or medications of choice available for management of menopausal symptoms. All hormones are not equivalent any more than all antiseizure medications or all antihypertensives are equivalent; they have different pharmacodynamics, duration of action, and affinity for receptors, among other things, all of which translate to different risks and benefits. Consideration of treatment with the right formulation, at the right dose and time, and for the right patient will allow us to recommend safe, effective, and appropriate treatment for people with menopausal symptoms.

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Bacterial Persistence in Urinary Tract Infection Among Postmenopausal Population

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Importance: Urinary tract infections (UTIs) are common in older-aged women. Our study examined bacterial persistence with commonly prescribed antibiotics. Bacterial growth was demonstrated despite antibiotic treatment. Objectives: The aims of this study were to quantify the bacterial persister phenotype in urine collected from postmenopausal women with acute and recurrent UTI and to determine the capabilities of first-line antibiotics to

effectively treat persister cells. Study design: This was an institutional review board-approved cross-sectional analysis within a large academic referral center. Uropathogens were cultured from postmenopausal women with acute or recurrent UTI and screened for persister cells using persistence assays. Demographic and clinical variables were collected and analyzed. The entire experimental process was repeated in triplicate. Data were analyzed for significance ($P < 0.05$) between the persister culture and antibiotic treatments using a 1-way analysis of variance with multiple comparisons in Prism 9.3.0. Results: Forty participants were included: 62.5% White, 22.5% Black, 3% Asian, and 2% Hispanic with a mean age of 72.3 ± 11.62 years. The persister phenotype was demonstrated in all of Escherichia coli isolates. Treatment with fosfomycin demonstrated reduced colony-forming units per milliliter compared with control ($P < 0.01$). Among recurrent isolates, there was a statistically significant decrease in colony-forming units per milliliter after antibiotic treatment with all 4 antibiotics ($P < 0.05$). Conclusions: This study demonstrated in vitro bacterial persistence in uropathogens from urogynecology patients despite treatment with commonly prescribed antibiotics. Fosfomycin generated the least amount of persister cells. Results suggest that persistence may be one bacterial defense mechanism involved in UTIs. Further research is needed to understand the clinical implications.

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Brown Adipose Tissue Metabolism in Women is Dependent on Ovarian Status

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In rodents, loss of estradiol (E2) reduces brown adipose tissue (BAT) metabolic activity. Whether E2 impacts BAT activity in women is not known. BAT oxidative metabolism was measured in premenopausal (N=27, 35±9 years, body mass index (BMI) = 26.0±5.3 kg/m2) and postmenopausal (N=25, 51±8 years, BMI = 28.0±5.0 kg/m2) women at room temperature (RT) and during acute cold exposure using [11C]-acetate with positron emission tomography coupled with computed tomography (PET/CT). BAT glucose uptake was also measured during acute cold exposure using 2-deoxy-2-[18F]fluoro-D-glucose ([18F]FDG). To isolate the effects of ovarian hormones from biological aging, measurements were repeated in a subset of premenopausal women (N=8, 40±4 years, BMI = 28.0±7.2 kg/m2) after 6 months of gonadotropin-releasing hormone agonist (GnRHAG) therapy to suppress ovarian hormones. At RT, there was no difference in BAT oxidative metabolism between premenopausal (0.56±0.31.min-1) and postmenopausal women (0.63±0.28.min-1). During cold exposure, BAT oxidative metabolism (1.28±0.85 vs. 0.91±0.63.min-1, P=0.03) and net BAT glucose uptake (84.4±82.5 vs. 29.7±31.4 nmol.g-1.min-1, P<0.01) were higher in premenopausal than postmenopausal women. In premenopausal women who underwent GnRHAG, cold-stimulated BAT oxidative metabolism was reduced to a similar level (from 1.36±0.66.min-1 to 0.91±0.41.min-1) to that observed in postmenopausal women (0.91±0.63.min-1). These results provide the first evidence in humans that reproductive hormones are associated with BAT oxidative metabolism and suggest that BAT may be a target to attenuate age-related reduction in energy expenditure and maintain metabolic health in postmenopausal women.

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Sedentary behavior does not predict low BMD nor fracture - population-based Canadian Multicentre Osteoporosis Study (CaMos)

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Sedentary behavior (SB) or sitting is associated with multiple unfavorable health outcomes. Bone tissue responds to imposed gravitational and muscular strain with there being some evidence suggesting a causal link between SB and poor bone health. However, there are no population-based data on the longitudinal relationship between SB, bone change and incidence of fragility fractures. This study aimed to examine the associations of sitting/sedentary behavior (defined as daily sitting time), areal bone mineral density (BMD by dual energy X-ray absorptiometry) and incident low trauma (fragility) osteoporotic fractures (excluding hands, feet, face and head). We measured baseline (1995-7) and 10-yr self-reported SB, femoral neck (FN), total hip (TH) and lumbar spine (L1-4) BMD in 5708 women and 2564 men aged 25-80+ years from the population-based, nation-wide, nine-center Canadian Multicentre Osteoporosis Study (CaMos). Incident 10-yr fragility fracture data were obtained from 4,624 participants; >80% of fractures were objectively confirmed by medical-records or radiology reports. Vertebral fractures were confirmed by qualitative morphological methods. All analyses were stratified by sex. Multivariable regression models assessed SB-BMD relationships; Cox proportional models were fit for fracture risk. Models were adjusted for age, height, BMI, physical activity and sex-specific covariates. Versus women with the least SB (1st quartile), women in 3rd/4th quartiles had lower adjusted FN BMD; women in the SB 3rd quartile had lower adjusted TH BMD. Men in the SB 3rd quartile had lower adjusted FN BMD than those in SB 1st quartile. Neither baseline nor stable 10-year SB were related to BMD

change nor to incident fragility fractures. Increased sitting (SB) in this large, population-based cohort was associated with lower baseline FN BMD. Stable SB was not associated with 10-year BMD loss nor increased fragility fracture. In conclusion, habitual adult sedentary behavior was not associated with subsequent loss of BMD nor increased risk of fracture.

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Systematic review of neurokinin-3 receptor antagonists for the management of vasomotor symptoms of menopause

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Importance: Vasomotor symptoms (VMS) affect many postmenopausal persons and impact sleep and quality of life. Objective: This systematic review examines the literature describing the safety and efficacy of neurokinin-3 receptor antagonists approved and in development for postmenopausal persons with VMS. Evidence review: A search of MEDLINE, EMBASE, and International Pharmaceutical Abstracts was conducted using the search terms and permutations of neurokinin-3 receptor antagonist, elinzanetant, fezolinetant, and osanetant. Inclusion criteria of reporting on efficacy or safety of fezolinetant, elinzanetant, or osanetant; studies in participants identifying as female; full record in English; and primary literature were applied. Abstract-only records were excluded. Extracted data were synthesized to allow comparison of reported study characteristics, efficacy outcomes, and safety events. Eligible records were evaluated for risk of bias via the Cochrane Risk of Bias 2 tool for randomized studies and the Grading of Recommendations Assessment, Development and Evaluation system was used. This study was neither funded nor registered. Findings: The search returned 191 records; 186 were screened after deduplication. Inclusion criteria were met by six randomized controlled trials (RCT), four reported on fezolinetant, and two reported on elinzanetant. One record was a post hoc analysis of a fezolinetant RCT. An additional study was identified outside the database search. Three fezolinetant RCT demonstrated a reduction in VMS frequency/severity, improvement in Menopause-Specific Quality of Life scores, and improvement in sleep quality at weeks 4 and 12 compared with placebo without serious adverse events. The two RCT on elinzanetant also showed improvements in VMS frequency and severity. All eight records evaluated safety through treatment-emergent adverse events; the most common adverse events were COVID-19, headache, somnolence, and gastrointestinal. Each record evaluated had a low risk of bias. There is a strong certainty of evidence as per the Grading of Recommendations Assessment, Development and Evaluation system. Conclusions and relevance: Because of the high-quality evidence supporting the efficacy of fezolinetant and elinzanetant, these agents may be an effective option with mild adverse events for women seeking nonhormone treatment of VMS.