Selección de Resúmenes de Menopausia

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Senescent cells: A therapeutic target for osteoporosis

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Background: Osteoporosis (OP) is a prevalent disorder characterized by the loss of bone mass and the deterioration of bone microarchitecture. OP is attributed to various factors, including menopause (primary), ageing (primary) and the adverse effects of medications (secondary). Recently, cellular senescence has been shown to have a crucial role in the maintenance of cellular homeostasis and organ function. The purpose of this review is to summarize recent findings regarding the roles of bone cellular senescence and senescence-associated secretory phenotype (SASP) in OP. Methods: A comprehensive search of the PubMed database from inception to July 2022 was performed regarding the molecular mechanism of bone cell senescence in OP progression. Results: We describe the pathophysiology of senescent bone cells and SASP, and how each contributes to OP. We also provide new options for treating OP by targeting cellular senescence pathways.Conclusion: Cellular senescence plays an important role in bone homeostasis, with variations based on the different types of OP. These variations are associated with pathogenic factors, bone turnover rate and systemic metabolism. Understanding the molecular relationship between bone cells and senescence provides for the possible targeting of senescence as a means by which to treat OP.

Extensive Expertise in Endocrinology: Osteoporosis Management

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Fractures occur in about half of older white women, and almost a third of older white men. However, 80% of the older individuals who have fractures do not meet the bone density definition of osteoporosis, suggesting that this definition is not an appropriate threshold for offering treatment. Fracture risk can be estimated based on clinical risk factors with or without bone density. A combination of calculated risk, fracture history, and bone density is used in treatment decisions. Medications available for reducing fracture risk act either to inhibit bone resorption or to promote bone formation. Romosozumab is unique in that it has both activities. Bisphosphonates are the most widely used interventions because of their efficacy, safety and low cost. Continuous use of oral bisphosphonates for >5 years increases the risk of atypical femoral fractures, so is usually punctuated with drug holidays of 6-24 months. Denosumab is a further potent antiresorptive agent given as six-monthly subcutaneous injections. It is comparable to the bisphosphonates in efficacy and safety but has a rapid offset of effect after discontinuation so must be followed by an alternative drug, usually a bisphosphonate. Teriparatide stimulates both bone formation and resorption, substantially increases spine density and reduces vertebral and non-vertebral fracture rates, though data for hip fractures are scant. Treatment is usually limited to 18-24 months, followed by transition to an anti-resorptive. Romosozumab is given as monthly subcutaneous injections for one year, followed by an anti-resorptive. This sequence prevents more fractures than anti-resorptive therapy alone. Because of cost, anabolic drugs are usually reserved for those at very high fracture risk. 25-hydroxyvitamin D levels should be maintained above 30 nmol/L, using supplements if sunlight exposure is limited. Calcium intake has little effect on bone density and fracture risk but should be maintained above 500 mg/day using dietary sources.

Menopausal Symptoms and Sleep Quality in Women Aged 40-65 Years

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The study examined the relationship between menopausal symptoms and sleep disturbances and the related influencing factors. Methods. We recruited women aged 40-65 years who attended the menopause clinic at Shanghai Jiao Tong University's Sixth People's Hospital from February 2011 to November 2019. The Menopause Rating Scale (MRS) was used to collect women's menopausal symptoms, and the Pittsburgh Sleep Quality Index (PSQI) was used to evaluate the subjects' sleep condition. We used logistic regression models to identify the relationship between menopausal symptoms and sleep quality. Results. A total of 1341 participants were recruited in this study. The most frequent three symptoms assessed by MRS were fatigue (72.9%), sleep disturbance (67%), and hot flashes with night sweats (65%). Participants'

age was significantly associated with the severity of menopausal syndrome (P < 0.01). According to the PSQI sleep evaluation, 66.9 percent of participants had sleep disturbances (PSQI > 5). Logistic regression analysis revealed that women with mild, moderate, or severe menopausal syndrome had a 3-, 7-, and 17-fold increased chance of having sleep disturbances compared to women without menopausal syndrome. Conclusion. Women aged 40-65 years were found to have a significantly higher risk of menopausal syndrome and sleep disturbances.

Hot flushes and sweating, sleep problems, joint and muscular discomfort, and physical and mental exhaustion in breast cancer survivors during the first 24 months of tamoxifen therapy: a prospective observational study

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Purpose: This study aimed to explore symptom trajectories over 24 months for hot flushes and sweating, sleep problems, joint and muscular discomfort, and physical and mental exhaustion experienced by premenopausal women diagnosed with tamoxifen-treated breast cancer. Methods: A total of 104 patients participated in the study. The menopausal symptoms were examined using the Menopausal Rating Scale at baseline, 3-6, 12, and 18-24 months after initiating tamoxifen. The changes over four time points were analyzed using repeated measures analysis of variance. The chi-square test was used to examine the differences between "no symptom-to-mild" and "moderate-to-extremely severe" 3-6 months after initiating tamoxifen according to the patients' chemotherapy treatment experiences. Results: All menopausal symptoms occurred in > 70% of patients with breast cancer and persisted until 24 months. More than 50% of patients experienced four menopausal symptoms, with at least two at a serious severity level after initiating tamoxifen. Hot flushes and sweating occurred in the highest number of patients, recording high scores. Sleep problems and physical and mental exhaustion exhibited relatively high scores, even before tamoxifen initiation. There were significant changes over four time points in all symptoms. Young patients aged < 40 years experienced more severe sleep problems, and patients who had previously received chemotherapy experienced more severe joint and muscular discomfort. Conclusions: This study's findings may assist in alerting healthcare providers to menopausal symptoms that develop during tamoxifen therapy and the need for early and active intervention to minimize symptom occurrence and distress.

Cardiovascular health in the menopause transition: a longitudinal study of up to 3892 women with up to four repeated measures of risk factors

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Background: Women experience adverse changes in cardiovascular health in mid-life; whether the menopausal transition influences these remains strongly debated. The aim of this study was to examine associations of reproductive age (time since final menstrual period (FMP)) with change in carotid intima media thickness (CIMT) and cardiovascular risk factors and determine the role of chronological and reproductive age. Methods: We used data from 1702 women from a pregnancy-based UK cohort who had up to four repeat cardiovascular health measures between mean age 51 (SD = 4.0) and 56 (SD = 3.6) years and experienced a natural menopause. Multilevel models were used to assess the relationship between cardiovascular measures and time since FMP (reproductive age), whilst adjusting for the underlying effects of chronological age and confounders (socioeconomic factors, body mass index, smoking, alcohol, parity, age at menarche). In addition, we looked at the relationship between cardiovascular measures by chronological age according to menopausal stages (pre-menopause, peri-menopause and post-menopause) using information from women who had and had not experienced menopause (N = 3892). Results: There was no strong evidence that reproductive age was associated with CIMT (difference in mean 0.8 μm/year, 95% CI - 0.4, 2.1), whereas there was a strong positive association of chronological age (7.6 μm/year, 95% CI 6.3, 8.9). Consistent with this, we found weaker linear associations of reproductive compared with chronological age for atherosclerotic risk factors, such as with systolic blood pressure (- 0.1 mmHg/year, 95% CI - 0.3, 0.1, and 0.4 mmHg/year, 95% CI 0.2, 0.5, respectively) and non-HDL-cholesterol (0.02 mmol/l/year, 95% CI 0.005, 0.03, and 0.06, 95% CI 0.04, 0.07, respectively). In contrast, associations with fat mass (0.06 kg/m2/year, 95% CI 0.03, 0.10, and 0 kg/m2/year, 95% CI - 0.04, 0.04, respectively) and C-reactive protein (0.01, 95% CI 0.001, 0.02, and 0.01, 95% CI - 0.001, 0.02 natural logged mg/l/year, respectively) were stronger for reproductive compared with chronological age. Both reproductive and chronological age were (weakly) positively associated with glucose (0.002, 95% CI 0.0001, 0.003, and 0.002, 95% CI 0.0001, 0.003 natural logged mmol/l/year, respectively). Conclusions: Our results suggest that going through the menopausal transition does not further increase

women's risk of atherosclerosis (measured by CIMT) beyond effects of ageing. Menopausal transition may, in additional to ageing, modestly increase adiposity and glucose levels and therefore a possible associated diabetes risk.

Early menopause and weight loss are significant factors associated with risk of future fracture in middle-aged women

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Methods: In total, 18,326 women from the Malmö Diet and Cancer study were included in this prospective population-based cohort study. Participants were included 1991-1996 and followed to 2016. Using data from the National Patient Registry, linked with every participants' unique personal identification number, any first fracture affecting spine, thoracic cage, upper and lower extremities was identified. The association of baseline factors with incident fracture risk was analyzed using Cox regression models. Results: For participating women, median age 56.0 years, the multivariable Cox regression analysis observed that early menopause (40-44 years) (hazard ratio (HR) 1.14, 95% confidence interval (CI) 1.03-1.27) but not premature menopause < 40 years (HR 1.06, 95% CI 0.91-1.24) was associated with future fracture risk. Self-reported weight loss since age 20 was also associated with future fracture risk (HR 1.39, 95% CI 1.17-1.65) whereas a daily alcohol consumption in the third quartile (5.36-11.42 g/day) compared to the lowest quartile (0-0.80 g/day) was associated with decreased future fracture risk (HR 0.88, 95% CI 0.81-0.96). The multivariable Cox regression analysis also observed that increasing age and weight at baseline, current smoking, a positive history of previous fracture and family history of fractures were associated with increased fracture risk whereas an increasing BMI was associated with a decreased fracture risk. No association to parity or period of lactation was observed nor ever-use of oral contraceptives and menopausal hormone therapy. Conclusion: This study shows that early menopause between 40 to 45 years and self-reported weight loss since age of 20 are relevant factors associated with increased fracture risk in middle-aged women. These factors were Independent of traditional predictors of fracture risk among women and may be considered in preventive initiatives.

Health screening of middle-aged women: what factors impact longevity?

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Objective: The aim of this study was to measure the impact of different risk factors in middle-aged women on longevity evaluated after three decades of an initial health screening. Methods: Women who received an annual check-up between 1990 and 1993 were recruited. Anamnesis and physical examination were recorded. Blood samples for the measurement of glycemia and lipids were taken. Data are reported as of December 2021.Results: A total of 1,158 women aged 40 to 60 were studied. At 30.9 years of follow-up, the Kaplan-Meier overall survival was 75.6% (95% confidence interval, 72.6-78.3). The main causes of the 260 deaths observed were the following: cancer (n = 88; 33.8%), cardiovascular disease (n = 55; 21.2%), and infectious disease (n = 41; 15.8%). The following hazard ratios were found with the flexible parametric survival model: personal history of fracture (hazard ratio, 2.55; 95% confidence interval, 1.29-5.02; P = 0.007), type 2 diabetes mellitus (2.14; 1.18-3.88; P = 0.012), personal history of heart disease (1.85; 1.09-3.13; P = 0.022), chronic arterial hypertension (1.65; 1.25-2.17; P < 0.001), postmenopausal status (1.60; 1.13-2.26; P = 0.008), unskilled jobs (1.56; 1.17-2.07; P = 0.002), cigarette smoking (1.51; 1.17-1.94; P = 0.002), age (1.06; 1.03-1.09; P < 0.001), body mass index (1.04; 1.01-1.07; P = 0.004), multiparous (0.72; 0.56-0.93; P = 0.012), and active sexual intercourse (0.68; 0.52-0.87; P = 0.003). Lipid disorders did not reach statistical significance as a risk factor. Conclusions: In this cohort, it was observed that most of the classic risk factors for mortality were present. However, a history of fracture appears in middle-aged women as a strong predictor of mortality, surpassing diabetes and arterial hypertension. Multiparity, on the other hand, was a protective factor.

Differing effects of oral conjugated equine estrogen and transdermal estradiol on vitamin D metabolism in postmenopausal women: a 4-year longitudinal study

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Objective: The aim of this study was to examine the effect of either conjugated equine estrogen or transdermal estradiol on vitamin D metabolism in postmenopausal women. Methods: Twenty-five women from the Kronos Early Estrogen

Prevention Study who were randomized to conjugated equine estrogen 0.45 mg/d and 20 women who were treated with transdermal estradiol 50 mg/d (patch replaced weekly) were analyzed in the present study. All participants received micronized progesterone for 12 days per month. Results: There was no significant treatment effect on serum total 25-hydroxyvitamin D over 48 months in either study group, and there were no significant differences between treatment arms. In contrast, at 12 months, directly measured free 25-hydroxyvitamin D was significantly higher in the transdermal estradiol group than in the conjugated equine estrogen group. Directly measured free 25-hydroxyvitamin D subsequently increased significantly from 12 to 48 months in both treatment arms. Calculated free 25-hydroxyvitamin D was also significantly higher in the transdermal estradiol group at 36 months. Vitamin D-binding protein decreased significantly in both treatment groups from 12 to 48 months, but at 48 months, least square mean values were no different based on treatment assignment. Conclusions: Directly measured free 25-hydroxyvitamin D levels, but not serum total 25-hydroxyvitamin D levels, are different within the first 12 months of estrogen replacement depending on the preparation. However, this difference is transient, in that there were no differences at 36 or 48 months. These findings suggest that there may be a short-term benefit to prescribing transdermal estradiol for women who are either vitamin D deficient or vitamin D insufficient.

Estrogen therapy and breast cancer in randomized clinical trials: a narrative review

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Importance and objective: In the Women's Health Initiative (WHI) randomized trial with 10,739 postmenopausal women with prior hysterectomy, conjugated equine estrogen (CEE) alone significantly reduced breast cancer incidence and breast cancer mortality. In contrast, epidemiological studies in a meta-analysis from the Collaborative Group on Hormonal Factors in Breast Cancer (Collaborative Group) with 108,647 breast cancers and the Million Women's Study cohort significantly associated estrogen-alone therapy with higher breast cancer incidence and breast cancer mortality. The Collaborative Group included a meta-analysis of five smaller randomized trials and the WHI randomized trial; however, findings were restricted to the Collaborative Group appendix. Our objective is to facilitate understanding of these discordant results. Methods: Data sources supporting our review findings include the randomized WHI CEE-alone trial and the meta-analysis of five smaller randomized trials evaluating estrogen alone. We summarize the smaller randomized trials' details of breast cancer relevance and place the findings in clinical context. We review findings of the WHI randomized trial evaluating CEE alone in the context of issues raised by Collaborative Group and the Million Women Study authors. We trace the evolution of the time-from-menopause, "window of opportunity" concept and augment the Collaborative Group meta-analysis by including the most recent WHI findings. Discussion and conclusions: Consideration of the smaller randomized trials evaluating estrogen alone with breast cancer signals that the WHI findings of lower breast cancer incidence and lower breast cancer mortality with CEE-alone use are not a "stand-alone" outcome or due to the play of chance. The serial reports of consistent favorable breast cancer findings through 20 years of cumulative follow-up suggest CEE-alone use initiates changes that persist. After full consideration of risks and benefits, randomized trial evidence provides reassurance for postmenopausal women with prior hysterectomy who are close to menopause considering estrogen alone for climacteric symptom management.

The role of probiotics in vaginal health

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Probiotics have been widely used in the treatment of intestinal diseases, but the effect of probiotics on female reproductive tract health is still controversial. Lactobacillus is the most abundant microorganism in the vagina, which is related to the vaginal mucosal barrier. Lactobacillus adheres to the vaginal epithelium and can competitively antagonize the colonization of pathogens. The factors produced by Lactobacillus, such as bacteriocin and hydrogen peroxide (H2O2), can inhibit the growth of pathogenic microorganisms and maintain the low pH environment of the vagina. Probiotics play an important role in maintaining the stability of vaginal microenvironment, improving immune defense and blocking the progression of cervical cancer. We review the research progress of probiotics represented by Lactobacillus in gynecological diseases such as human papilloma virus (HPV) infection, bacterial vaginosis (BV) and Genitourinary Syndrome of Menopause (GSM), so as to provide basis for further exerting the role of probiotics in women's health.