



## Selección de Resúmenes de Menopausia

Semana del 6 al 12 de diciembre de 2017

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### **Menopause-Related Appendicular Bone Loss is Mainly Cortical and Results in Increased Cortical Porosity.**

Bjørnerem Å, Wang X, Bui M, Ghasem-Zadeh A, Hopper JL, Zebaze R, Seeman E.

After menopause, remodeling becomes unbalanced and rapid. Each of the many remodeling transactions deposits less bone than it resorbed, producing microstructural deterioration. Trabecular bone is said to be lost more rapidly than cortical bone. However, because 80% of the skeleton is cortical, we hypothesized that most menopause-related bone loss and changes in bone microstructure are cortical, not trabecular in origin, and are the result of intracortical remodeling. Distal tibial and distal radial microstructure were quantified during 3.1 years (range, 1.5 to 4.5 years) of follow-up using high-resolution peripheral quantitative computed tomography and StrAx software in 199 monozygotic and 125 dizygotic twin pairs aged 25 to 75 years in Melbourne, Australia. The annual increases in tibial cortical porosity accelerated, being 0.44%, 0.80%, and 1.40% in women remaining premenopausal, transitioning to perimenopause, and from perimenopausal to postmenopause, respectively. Porosity increased in the compact-appearing, outer, and inner transitional zones of the cortex (all  $p < 0.001$ ). The annual decrease in trabecular bone volume/tissue volume (BV/TV) also accelerated, being 0.17%, 0.26%, and 0.31%, respectively. Little bone loss was observed before menopause. The reduction in BV/TV was due to a decrease in trabecular number ( $p < 0.001$ ). The greatest bone loss, 7.7 mg hydroxyapatite (HA) annually, occurred in women transitioning from perimenopausal to postmenopause and of this, 6.1 mg HA (80%) was cortical. Results were similar for the distal radius. Despite microarchitectural changes, no significant bone loss was observed before menopause. Over 90% of appendicular bone loss occurs during and after menopause, over 80% is cortical, and this may explain why 80% of fractures are appendicular.

**Nutrients. 2017 Dec 7;9(12). pii: E1331. doi: 10.3390/nu9121331.**

### **Dietary Factors and Female Breast Cancer Risk: A Prospective Cohort Study.**

Kim JH, Lee J, Jung SY, Kim J.

Breast cancer is the leading cause of cancer in females and has become a major global health priority. This prospective cohort study investigated the association of dietary factors, including food items and dietary habits, with the risk of breast cancer in Korean women. Study participants were women aged 30 years or older, recruited from the National Cancer Center in South Korea between August 2002 and May 2007. They were followed until December 2014 using the Korea Central Cancer Registry to identify breast cancer cases. Among 5046 non-pre-diagnosed cancer participants, 72 breast cancer cases were prospectively identified. Participants with breast cancer had a significantly higher educational level (college or higher: 58.3% vs. 39.5%,  $p = 0.01$ ), were more likely to have ever smoked (22.2% vs. 7.8%,  $p < 0.001$ ), and were more likely to have a history of benign breast tumors (10% vs. 4%,  $p = 0.02$ ) than non-cases. Consumption of grilled meat conferred a significantly higher risk of breast cancer in all women (hazard ratio (HR) 1.77, 95% confidence interval (CI) 1.09-2.85) and in postmenopausal women (HR 3.06, 95% CI 1.31-7.15). High-cholesterol food intake was associated with a higher risk in all women (HR 1.69, 95% CI 1.01-2.82). Irregular meal intake was associated with an elevated risk in all women (HR 2.19, 95% CI 1.20-3.98,  $p$  for trend = 0.01) and in premenopausal women (HR 2.35, 95% CI 1.13-4.91,  $p$  for trend = 0.03). Our findings suggest that grilled meat and high-cholesterol food intake and irregular eating habits may be associated with a higher risk of breast cancer. Further studies with longer follow-up periods that include information on portion size, hormone receptor status, carcinogen levels in grilled meat, and a classification of foods by source are required.

**Nutr Health. 2017 Dec;23(4):271-279. doi: 10.1177/0260106017727359.**

### **Combined exercise training reduces climacteric symptoms without the additive effects of isoflavone supplementation: A clinical, controlled, randomised, double-blind study.**

Costa JG, Giolo JS, Mariano IM, Batista JP, Ribeiro ALA, Souza TCF, de Oliveira EP, Resende APM1 Puga GM.

**BACKGROUND:** Exercise and supplementation with isoflavones are therapies used to prevent and treat climacteric symptoms. **AIM:** To verify the effects of 10 weeks of combined aerobic and resistance training and isoflavone supplementation on climacteric symptoms in postmenopausal women. **METHODS:** A randomised, double-blind, controlled clinical trial was performed. A total of 32 postmenopausal women, aged  $54.4 \pm 5.4$  years, with a body mass index of  $26.6 \pm 3.0$  kg/m<sup>2</sup> and  $5.6 \pm 4.6$  years after menopause, were randomly assigned to groups: placebo and exercise (PLA + EXE, n = 15) or 100 mg of isoflavone and exercise (ISO + EXE, n = 17). At the beginning and after 10 weeks of aerobic + resistance (20 min each, moderate intensity) training, climacteric symptoms were evaluated using the Blatt-Kupperman Menopausal Index, Cervantes Scale and Menopause Rating Scale. ANCOVA was used for analysis between groups and at different times, with the covariate adjusted by the pre-value. The level of significance considered was  $p < 0.05$ . **RESULTS:** A reduction in climacteric symptoms was observed in both groups, without differences between the interventions. The reductions were 45% and 50% for the Blatt-Kupperman Menopausal Index, 41% and 52% for the MRS and 39% and 39% for the Cervantes Scale in the ISO + EXE and PLA + EXE groups, respectively. In the descriptive analysis of the Blatt-Kupperman Menopausal Index values, there was an increase in the absence of symptoms from 48-77% in the ISO + EXE group and 24-58% in the PLA + EXE group. **CONCLUSIONS:** A period of 10 weeks of combined training was effective in improving climacteric symptoms in post-menopausal women. However, isoflavone supplementation did not promote additional effects in improving symptoms.

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### **Increased body fat mass explains the positive association between circulating estradiol and insulin resistance in postmenopausal women.**

Marchand GB, Carreau AM, Weisnagel SJ, Bergeron J, Labrie F, Lemieux S, Tchernof A.

The relationship between circulating estrogen levels and cardiometabolic risk factors such as insulin resistance is unclear in postmenopausal women. High estradiol (E2) levels have been reported to predict increased risk of type 2 diabetes in this population. We aimed to examine associations among estrogen levels, adiposity measurements and cardiometabolic risk variables including insulin resistance in postmenopausal women. 101 healthy participants (mean±SD: age  $57 \pm 4$  years; BMI  $27.9 \pm 4.8$  kg/m<sup>2</sup>) were included in the analysis. Fifteen plasma steroids or metabolites were measured by liquid chromatography-tandem mass spectrometry. Insulin sensitivity was assessed with a hyperinsulinemic-euglycemic clamp. Body composition and fat distribution were determined with hydrostatic weighing and computed tomography respectively. Blood lipids and circulating cytokines were also measured. Circulating E2 was positively correlated with all adiposity indices ( $r=0.62$  to  $0.42$ ,  $p<0.0001$ ) except waist-to-hip ratio. E2 was positively correlated with VLDL-cholesterol, plasma-, VLDL- and HDL-triglyceride levels ( $r=0.31$  to  $0.24$ ,  $p<0.02$ ) as well as with hs-CRP and IL-6 ( $r=0.52$  and  $0.29$ ,  $p<0.005$ ) and negatively with HDL-cholesterol, adiponectin and insulin sensitivity ( $r=-0.36$  to  $-0.20$ ,  $p<0.02$ ). When adjusting for percent body fat, correlations between E2 and metabolic risk variables were no longer significant. Similar results were observed for circulating estrone (E1) and estrone-sulfate (E1-S) levels. In conclusion, circulating estrogen concentrations are proportional to adipose mass in postmenopausal women although they remain in the low range. Insulin resistance as well as altered blood lipids and cytokines are observed when circulating estrogen levels are high within that range, but these differences are explained by concomitant variation in total adiposity.

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### **Trauma exposure and endothelial function among midlife women.**

Thurston RC, Barinas-Mitchell E, von Känel R, Chang Y, Koenen KC, Matthews KA.

**OBJECTIVE:** Trauma is a potent exposure that can have implications for health. However, little research has considered whether trauma exposure is related to endothelial function, a key process in the pathophysiology of cardiovascular disease (CVD). We tested whether exposure to traumatic experiences was related to poorer endothelial function among midlife women, independent of CVD risk factors, demographic factors, psychosocial factors, or a history of childhood abuse. **METHODS:** In all, 272 nonsmoking perimenopausal and postmenopausal women aged 40 to 60 years without clinical CVD completed the Brief Trauma Questionnaire, the Child Trauma Questionnaire, physical measures, a blood draw, and a brachial ultrasound for assessment of brachial artery flow-mediated dilation (FMD). Relations between trauma and FMD were tested in linear regression models controlling for baseline vessel diameter, demographics, depression/anxiety, CVD risk factors, health behaviors, and, additionally, a history of childhood abuse.

**RESULTS:** Over 60% of the sample had at least one traumatic exposure, and 18% had three or more exposures. A greater number of traumatic exposures was associated with lower FMD, indicating poorer endothelial function in multivariable models (beta,  $\beta$  [standard error, SE] -1.05 [0.40],  $P=0.01$ ). Relations between trauma exposure and FMD were particularly pronounced for three or more trauma exposures (b [SE] -1.90 [0.71],  $P=0.008$ , relative to no exposures, multivariable). **CONCLUSIONS:** A greater number of traumatic exposures were associated with poorer endothelial function. Relations were not explained by demographics, CVD risk factors, mood/anxiety, or a by history of childhood abuse. Women with greater exposure to trauma over life maybe at elevated CVD risk.

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### **Vasomotor symptom characteristics: are they risk factors for incident diabetes?**

Gray KE, Katon JG, LeBlanc ES, Woods NF, Bastian LA, Reiber GE, Weitlauf JC, Nelson KM, LaCroix AZ.

**OBJECTIVE:** Vasomotor symptoms (VMS), encompassing hot flashes and night sweats, may be associated with diabetes, but evidence is limited. We sought to estimate these associations. **METHODS:** Among 150,007 postmenopausal Women's Health Initiative participants from 1993 to 2014, we prospectively examined associations of incident diabetes with VMS characteristics at enrollment: any VMS, severity (mild/ moderate/severe), type (hot flashes/night sweats), timing (early [premenopausal or perimenopausal]/late [postmenopausal]), and duration. Cox proportional-hazards models estimated hazard ratios (HRs) and 95% confidence intervals (CIs). **RESULTS:** Mean duration of follow-up was 13.1 years. VMS prevalence was 33%. Reporting any VMS was associated with 18% increased diabetes risk (95% CI 1.14, 1.22), which increased with severity (mild: HR 1.13, 95% CI 1.08, 1.17; moderate: HR 1.29, 95% CI 1.22, 1.36; severe: HR 1.48, 95% CI 1.34, 1.62) and duration (4% per 5 years, 95% CI 1.03, 1.05), independent of obesity. Diabetes risk was more pronounced for women reporting any night sweats (night sweats only: HR 1.20, 95% CI 1.13, 1.26; night sweats and hot flashes: HR 1.22, 95% CI 1.17, 1.27) than only hot flashes (HR 1.08, 95% CI 1.02, 1.15) and was restricted to late VMS (late: HR 1.12, 95% CI 1.07, 1.18; early and late: HR 1.16, 95% CI 1.11, 1.22; early: HR 0.99, 95% CI 0.95, 1.04). **CONCLUSIONS:** VMS are associated with elevated diabetes risk, particularly for women reporting night sweats and postmenopausal symptoms. The menopause transition may be an optimal window for clinicians to discuss long-term cardiovascular/metabolic risk with patients and leverage the bother of existing symptoms for behavior change to improve VMS and reduce diabetes risk.

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### **A Randomized, Multicenter, Double-Blind, Study to Evaluate the Safety and Efficacy of Estradiol Vaginal Cream 0.003% in Postmenopausal Women with Vaginal Dryness as the Most Bothersome Symptom.**

Archer DF, Kimble TD, Lin FDY, Battucci S, Sniukiene V, Liu JH.

**BACKGROUND:** Vulvovaginal atrophy (VVA) is characterized by vaginal/vulvar dryness, irritation, dyspareunia, or dysuria. The objective of this study was to examine the efficacy and safety of a very low-dose estradiol vaginal cream (0.003%) applied twice per week in postmenopausal women with VVA-related vaginal dryness. **MATERIALS AND METHODS:** In this phase 3, randomized, double-blind, placebo-controlled, multicenter study, postmenopausal women with moderate-severe vaginal dryness as the most bothersome VVA symptom were randomized (1:1) to estradiol cream 0.003% (15  $\mu\text{g}$  estradiol; 0.5 g cream) or placebo (0.5 g cream). Treatments were applied vaginally once daily for 2 weeks followed by two applications/week for 10 weeks. Coprimary outcomes were changes in severity of vaginal dryness, percentage of vaginal superficial and parabasal cells, and vaginal pH at final assessment. Additional outcomes comprised changes in severity of other VVA signs and symptoms. Adverse events (AEs) were assessed. **RESULTS:** Of the 576 randomized participants, most were white and had an average age of 59 years. At final assessment, estradiol reduced vaginal dryness severity, decreased vaginal pH, increased superficial cell percentage, and decreased parabasal cell percentage versus placebo ( $p \leq 0.05$ , all). Estradiol also reduced vaginal dryness severity at Weeks 4-12 and dyspareunia at Week 8 versus placebo ( $p \leq 0.05$ , all). Improvements in vaginal/vulvar irritation/itching severity and dysuria were similar between estradiol and placebo. Estradiol had comparable rates of treatment-emergent AEs to placebo. No deaths occurred. **CONCLUSIONS:** Very low-dose estradiol vaginal cream (0.003%) dosed twice weekly is an effective and well-tolerated treatment for VVA symptoms and dryness associated with menopause.