



## Selección de Resúmenes de Menopausia

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Juan Enrique Blümel. Departamento Medicina Sur. Universidad de Chile

**Am J Physiol Heart Circ Physiol. 2015 Jan 30;ajpheart.00681.2014. [Epub ahead of print]**

### Association of testosterone with estrogen abolishes the beneficial effects of estrogen treatment by increasing ROS generation in aorta endothelial cells.

Costa TJ, Ceravolo GS, dosSantos RA, de Oliveira MA, Araújo PX, Giaquinto LR, Tostes RC, Akamine EH, et al. Testosterone has been added to hormone replacement therapy to treat sexual dysfunction in postmenopausal women. Whereas estrogen has been associated with vascular protection, the vascular effects of testosterone are contradictory and the effects of its association with estrogen are largely unknown. In this study we determined the effects of testosterone associated with conjugated equine estrogen (CEE) on vascular function using a model of hypertensive post-menopausal female: ovariectomized spontaneously hypertensive rats (SHR). Female SHR were divided into Sham-operated (Sham), ovariectomized (OVX) and OVX treated for 15 days with either CEE alone (OVX+CEE) or associated with testosterone (OVX+CEE+T). Angiotensin II (Ang-II) induced contraction was markedly increased aortic rings from OVX compared to Sham. CEE treatment restored Ang-II responses, a beneficial effect abrogated with CEE+T. CEE treatment also increased endothelium-dependent relaxation, which was impaired in OVX rats. This effect was lost by CEE+T. Treatment of aortas with losartan (Ang-II type-1 receptor (AT1R) antagonist) or apocynin (NADPH-oxidase inhibitor) restored the endothelium-dependent relaxation in OVX and CEE+T, establishing an interplay between Ang-II and endothelial dysfunction in OVX and CEE+T. The benefits by CEE were associated with down-regulation of NADPH-oxidase subunits mRNA expression and decreased ROS generation. The association of testosterone with CEE impairs the benefits of estrogen on OVX-associated endothelial dysfunction and ROS generation in rat aorta, by a mechanism that involves phosphorylation of the cytosolic NADPH oxidase subunit p47phox.

**Clin J Am Soc Nephrol. 2015 Jan 29. pii: CJN.06030614. [Epub ahead of print]**

### Vascular Calcification and Bone Mineral Density in Recurrent Kidney Stone Formers.

Shavit L, Girfoglio D, Vijay V, Goldsmith D, Ferraro PM, Moochhala SH, Unwin R.

**BACKGROUND AND OBJECTIVES:** Recent epidemiologic studies have provided evidence for an association between nephrolithiasis and cardiovascular disease, although the underlying mechanism is still unclear. Vascular calcification (VC) is a strong predictor of cardiovascular morbidity and the hypothesis explored in this study is that VC is more prevalent in calcium kidney stone formers (KSFs). The aims of this study were to determine (1) whether recurrent calcium KSFs have more VC and osteoporosis compared with controls and (2) whether hypercalciuria is related to VC in KSFs. **DESIGN, SETTING, PARTICIPANTS, & MEASUREMENTS:** This is a retrospective, matched case-control study that included KSFs attending an outpatient nephrology clinic of the Royal Free Hospital (London, UK) from 2011 to 2014. Age- and sex-matched non-stone formers were drawn from a list of potential living kidney donors from the same hospital. A total of 111 patients were investigated, of which 57 were KSFs and 54 were healthy controls. Abdominal aortic calcification (AAC) and vertebral bone mineral density (BMD) were assessed using available computed tomography (CT) imaging. The prevalence, severity, and associations of AAC and CT BMD between KSFs and non-stone formers were compared. **RESULTS:** Mean age was  $47 \pm 14$  years in KSFs and  $47 \pm 13$  in non-stone formers. Men represented 56% and 57% of KSFs and non-stone formers, respectively. The prevalence of AAC was similar in both groups (38% in KSFs versus 35% in controls,  $P=0.69$ ). However, the AAC severity score (median [25th percentile, 75th percentile]) was significantly higher in KSFs compared with the control group (0 [0, 43] versus 0 [0, 10],  $P<0.001$ ). In addition, the average CT BMD was significantly lower in KSFs ( $159 \pm 53$  versus  $194 \pm 48$  Hounsfield units,  $P<0.001$ ). A multivariate model adjusted for age, sex, high BP, diabetes, smoking status, and eGFR confirmed that KSFs have higher AAC scores and lower CT BMD compared with non-stone formers ( $P<0.001$  for both). Among stone formers, the association between AAC score and hypercalciuria was not statistically significant ( $P=0.86$ ). **CONCLUSIONS:** This study demonstrates that patients with calcium kidney stones suffer from significantly higher degrees of aortic calcification than age- and sex-matched non-stone formers,

suggesting that VC may be an underlying mechanism explaining reported associations between nephrolithiasis and cardiovascular disease. Moreover, bone demineralization is more prominent in KSFs. However, more data are needed to confirm the possibility of potentially common underlying mechanisms leading to extrasosseous calcium deposition and osteoporosis in KSFs.

**Maturitas. 2015 Jan 12. pii: S0378-5122(14)00405-8. doi: 10.1016/j.maturitas.2014.12.015. [Epub ahead of print]**

### **Waist-to-hip ratio is better at predicting subclinical atherosclerosis than body mass index and waist circumference in postmenopausal women.**

Lee HJ, Hwang SY, Hong HC, Ryu JY, Seo JA, Kim SG, Kim NH, Choi DS, Baik SH, Choi KM, Yoo HJ.

**OBJECTIVE:** Body fat distribution becomes more central after menopause. Although some studies have identified the superiority of various anthropometric indices to assess general health outcomes, very limited studies have compared the efficacy of body mass index (BMI), waist circumference (WC), and waist-to-hip ratio (WHR) to predict subclinical atherosclerosis according to menopausal status. **METHODS:** In total, 442 participants (209 premenopausal women and 233 postmenopausal women) were prospectively enrolled from the Health Promotion Center of Korea University Guro Hospital. We examined subclinical atherosclerosis using carotid intima-media thickness (CIMT) and brachial-ankle pulse wave velocity (baPWV). **RESULTS:** In premenopausal women, all anthropometric parameters such as BMI, WC and WHR were positively correlated with baPWV and CIMT values, whereas in postmenopausal women, only WHR was positively correlated with baPWV values (0.27,  $P < 0.01$ ), and WC and WHR were positively correlated with CIMT (0.15,  $P < 0.05$  and 0.21,  $P < 0.01$ , respectively). By receiver operating characteristic (ROC) curve analyses, WHR was superior to the other anthropometric indices to predict carotid atherosclerosis in postmenopausal women. Furthermore, the normal weight (BMI  $< 23 \text{ kg/m}^2$ ) with higher WHR group had a significantly thicker CIMT when compared to the normal weight with lower WHR group (0.76mm vs. 0.68mm,  $P < 0.01$ ) and even the overweight subjects with BMI  $\geq 23 \text{ kg/m}^2$  (0.76mm vs. 0.70mm,  $P < 0.01$ ) in postmenopausal women. **CONCLUSIONS:** The present study shows that WHR has the best potential for predicting subclinical atherosclerosis compared to BMI and WC in postmenopausal women.

**Osteoporos Int. 2015 Jan 29. [Epub ahead of print]**

### **Targeted assessment of fracture risk in women at midlife.**

Davis SR, Tan A, Bell RJ.

Women's Health Research Program, Monash University, Melbourne, VIC, 3004, Australia, susan.davis@monash.edu.

This study establishes a profile for women at midlife, referred for a dual energy X-ray absorptiometry (DXA), most likely to have osteoporosis, and from this, a pre-DXA screening tool has been developed. These findings inform much needed evidence-based guidelines for targeted and effective screening for osteoporosis and osteoporotic fracture prevention in women at midlife. **INTRODUCTION:** There is no consensus as to whether women at midlife should undergo screening dual energy X-ray absorptiometry (DXA) to identify osteoporosis (T-score  $< -2.5$ ). **METHODS:** We investigated the prevalence of osteoporosis in women, aged 40-65 years, referred to 42 community-based Australian radiology centres, and identified the characteristics that best predict osteoporosis in women having a screening DXA. **RESULTS:** One thousand four hundred and two women completed the study questionnaire and had DXA reports available. After excluding women with an established indication for a DXA (58 %), users of bone-specific medication (10.5 %) and cancer (7.6 %), 466 women were classified as having a screening DXA. Forty of these women had osteoporosis at the lumbar spine (n: 32, 6.9 %) or femoral neck (n: 17, 3.6 %). Three predictors of osteoporosis (postmenopausal, nonuse of hormonal therapy and body mass index) were identified and incorporated into the Monash Osteoporosis Risk Score for women at midlife (MORS). In the screened study population, the MORS had a sensitivity of 70 % and specificity of 66 %, with a positive predictive value of 16.2 % and negative predictive value of 95.9 % for osteoporosis. **CONCLUSIONS:** Very few women referred for a screening DXA scan will be found to have osteoporosis. The MORS, a simple decision tool, would have identified 70 % of the women in our screening DXA study population and would have eliminated over 60 % of the screening DXA studies. Hence, use of the MORS may reduce unnecessary DXA scans and facilitate identification of the majority of cases of osteoporosis in women aged 40 to 65 years.

**Sci Rep. 2015 Jan 28;5:8076. doi: 10.1038/srep08076.**

## **Effect of menopausal status on carotid intima-media thickness and presence of carotid plaque in chinese women generation population.**

Zhou Y, Wang D, Yang X, Wang A, Gao X, Guo Y, Wu S, Zhao X.

Menopause is an important physiological stage in women's life. The potential association of menopause with carotid intima-media thickness as well as with occurrence and stability of carotid plaque in Chinese female population is unclear. We conducted a population-based, cross-sectional study by recruiting 2,131 participants aged above 40 years from northeast of China. Carotid intima-media thickness (CIMT), presence of carotid plaque and its stability were evaluated by carotid duplex sonography. Among the participants, 1,133 (53.2%) were identified to be postmenopausal. After adjusting for potential confounding factors, presence of CIMT at 50(th)- 75(th) and  $\geq 75$ (th) percentiles, carotid plaque and its unstable status were found to be significantly associated with the postmenopausal status ( $P < 0.001$ ). When matched the participants by age, post-menopausal status was still associated with a higher risk of having unstable plaque. Moreover, our data show that postmenopausal status is a risk factor for intracranial arterial stenosis when compared with premenopausal status in the univariate analysis ( $OR = 1.314$ ,  $P = 0.043$ ), and such relationship is lost when the confounding factors are adjusted ( $OR = 0.828$ ,  $P = 0.225$ ). In conclusion, the vascular risk factors increase as the menopausal status changes. Compared with premenopausal status, postmenopausal status is associated with higher morbidity of CIMT, carotid plaque and its unstable status.

**J Affect Disord. 2015 Jan 14;175C:176-183. doi: 10.1016/j.jad.2014.12.061. [Epub ahead of print]**

## **Hormone-related factors and post-menopausal onset depression: Results from KNHANES (2010-2012).**

Jae Jung S, Shin A, Kang D.

**BACKGROUND:** Although hypotheses have been proposed regarding the biological mechanisms of hormonal fluctuations in mood disorders, few epidemiological studies have addressed this issue. The aim of this study was to examine the association between hormone-related life events and postmenopausal depression. **METHODS:** Of 13,918 women who participated in the Korean National Health and Nutrition Examination Survey (KNHANES) V, a total of 4869 post-menopausal women who had completed information on depression onset age and additional reproductive factors were included in the analysis. A multivariate logistic regression was applied to calculate the odds ratios between reproductive factors and post-menopausal onset depression. **RESULTS:** A total of 276 women (5.7%) were diagnosed with depression after menopause. Longer reproductive years were associated with a reduced risk of depression (for more than 35 reproductive years:  $OR=0.41$ , 95% CI: 0.27-0.62,  $P$ -trend $<0.001$ ). Similarly, a later age of menopause (52 years and older) corresponded to a decreased risk of depression ( $OR=0.35$ , 95% CI: 0.22-0.55) compared to the women with a menopausal age younger than 46 years. Greater numbers of pregnancies and exogenous hormone use were also associated with increased risk of depression. **LIMITATIONS:** All data were collected from interviews using questionnaires. There may be some inaccuracies in recall of lifetime reproductive events, but women generally recalled their hormonal events correctly. **CONCLUSION:** Early menopause and the use of exogenous hormones were associated with the risk of post-menopausal depression. Clinicians should closely monitor and consider further screening for depressed women who undergo early menopause or those with exogenous hormone use.

**J Womens Health (Larchmt). 2015 Jan 26. [Epub ahead of print]**

## **Symptoms of Depressed Mood, Disturbed Sleep, and Sexual Problems in Midlife Women: Cross-Sectional Data from the Study of Women's Health Across the Nation.**

Prairie BA, Wisniewski SR, Luther J, Hess R, Thurston RC, Wisner KL, Bromberger JT.

**Background:** Women report many nonvasomotor symptoms across the menopausal transition, including sleep disturbances, depressed mood, and sexual problems. The co-occurrence of these three symptoms may represent a specific menopausal symptom triad. We sought to evaluate the interrelatedness of disturbed sleep, depressed mood, and sexual problems in the Study of Women's Health Across the Nation (SWAN) and determine the characteristics of women exhibiting this symptom triad. **Methods:** SWAN is a multisite, multiethnic observational cohort study of the menopausal transition in the United States. Sleep disturbance, sexual problems, and depressed mood were

determined based on self-report. Women who reported all three symptoms simultaneously were compared to those who did not. Logistic regression models estimated the association of demographic, psychosocial, and clinical characteristics with the symptom triad. Results: Study participants (n=1716) were 49.8 years old on average and primarily in very good or excellent health. Sixteen and a half percent had depressed mood, 36.6% had a sleep problem, and 42.2% had any sexual problem. Five percent of women (n=90) experienced all three symptoms. Women with the symptom triad compared with those without had lower household incomes, less education, were surgically postmenopausal or late perimenopausal, rated their general health as fair or poor, and had more stressful life events and lower social support. Conclusions: The symptom triad of sleep disturbance, depressed mood, and sexual problems occurred in only 5% of women, and occurred most often among women with lower socioeconomic status, greater psychosocial distress, and who were surgically menopausal or in the late perimenopause.

**J Natl Cancer Inst. 2015 Jan 24;107(3). pii: dju428. doi: 10.1093/jnci/dju428. Print 2015 Mar.**

### **Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies.**

Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, Hu FB, Giovannucci EL.

**BACKGROUND:** Adiposity, measured by body mass index, is implicated in carcinogenesis. While adult weight gain has diverse advantages over body mass index in measuring adiposity, systematic reviews on adult weight gain in relation to adiposity-related cancers are lacking. **METHODS:** PubMed and Embase were searched through September 2014 for prospective observational studies investigating the relationship between adult weight gain and the risk of 10 adiposity-related cancers. Dose-response meta-analyses were performed using a random-effects model to estimate summary relative risk (RR) and 95% confidence interval (CI) for each cancer type. All statistical tests were two-sided. **RESULTS:** A total of 50 studies were included. For each 5kg increase in adult weight gain, the summary relative risk was 1.11 (95% CI = 1.08 to 1.13) for postmenopausal breast cancer among no- or low-hormone replacement therapy (HRT) users, 1.39 (95% CI = 1.29 to 1.49) and 1.09 (95% CI = 1.02 to 1.16) for postmenopausal endometrial cancer among HRT nonusers and users, respectively, 1.13 (95% CI = 1.03 to 1.23) for postmenopausal ovarian cancer among no or low HRT users, 1.09 (95% CI = 1.04 to 1.13) for colon cancer in men. The relative risk of kidney cancer comparing highest and lowest level of adult weight gain was 1.42 (95% CI = 1.11 to 1.81). Adult weight gain was unrelated to cancers of the breast (premenopausal women, postmenopausal HRT users), prostate, colon (women), pancreas, and thyroid. An increase in risk associated with adult weight gain for breast cancer was statistically significantly greater among postmenopausal women (P heterogeneity = .001) and HRT nonusers (P heterogeneity = .001); that for endometrial cancer was alike among HRT nonusers (P heterogeneity = .04). **CONCLUSIONS:** Avoiding adult weight gain itself may confer protection against certain types of cancers, particularly among HRT nonusers.