



## Selección de Resúmenes de Menopausia

Semana del 12 al 18 de abril de 2017

Juan Enrique Blümel. Departamento Medicina Sur. Universidad de Chile

**Diabetol Metab Syndr. 2017 Apr 7;9:22. doi: 10.1186/s13098-017-0221-5. eCollection 2017.**

### **Impact of menopause and diabetes on atherogenic lipid profile: is it worth to analyse lipoprotein subfractions to assess cardiovascular risk in women?**

Fonseca MI, da Silva IT, Ferreira SR.

Cardiovascular disease is the leading cause of death in women at advanced age, who are affected a decade later compared to men. Cardiovascular risk factors in women are not properly investigated nor treated and events are frequently lethal. Both menopause and type 2 diabetes substantially increase cardiovascular risk in the female sex, promoting modifications on lipid metabolism and circulating lipoproteins. Lipoprotein subfractions suffer a shift after menopause towards a more atherogenic lipid profile, consisted of hypertriglyceridemia, lower levels of both total high density lipoprotein (HDL) and its subfraction HDL2, but also higher levels of HDL3 and small low-density lipoprotein particles. This review discusses the impact of diabetes and menopause to the lipid profile, challenges in lipoprotein subfractions determination and their potential contribution to the cardiovascular risk assessment in women. It is still unclear whether lipoprotein subfraction changes are a major driver of cardiometabolic risk and which modifications are predominant. Prospective trials with larger samples, methodological standardizations and pharmacological approaches are needed to clarify the role of lipoprotein subfractions determination on cardiovascular risk prediction and intervention planning in postmenopausal women, with or without DM.

**Am J Clin Nutr. 2017 Apr 12. pii: ajcn145110. doi: 10.3945/ajcn.116.145110. [Epub ahead of print]**

### **Dietary protein and bone health: a systematic review and meta-analysis from the National Osteoporosis Foundation.**

Shams-White MM, Chung M, Du M, Fu Z, Insogna KL, Karlsen MC, LeBoff MS, Shapses SA, Sackey J, et al.

Background: Considerable attention has recently focused on dietary protein's role in the mature skeleton, prompted partly by an interest in nonpharmacologic approaches to maintain skeletal health in adult life. Objective: The aim was to conduct a systematic review and meta-analysis evaluating the effects of dietary protein intake alone and with calcium with or without vitamin D (Ca±D) on bone health measures in adults. Design: Searches across 5 databases were conducted through October 2016 including randomized controlled trials (RCTs) and prospective cohort studies examining 1) the effects of "high versus low" protein intake or 2) dietary protein's synergistic effect with Ca±D intake on bone health outcomes. Two investigators independently conducted abstract and full-text screenings, data extractions, and risk of bias (ROB) assessments. Strength of evidence was rated by group consensus. Random-effects meta-analyses for outcomes with ≥4 RCTs were performed. Results: Sixteen RCTs and 20 prospective cohort studies were included in the systematic review. Overall ROB was medium. Moderate evidence suggested that higher protein intake may have a protective effect on lumbar spine (LS) bone mineral density (BMD) compared with lower protein intake (net percentage change: 0.87%; 95% CI: 0.18%, 1.56%; I<sup>2</sup>: 0%; n = 4) but no effect on total hip (TH), femoral neck (FN), or total body BMD or bone biomarkers. Limited evidence did not support an effect of protein with Ca±D on LS BMD, TH BMD, or forearm fractures; there was insufficient evidence for FN BMD and overall fractures. Conclusions: Current evidence shows no adverse effects of higher protein intakes. Although there were positive trends on BMD at most bone sites, only the LS showed moderate evidence to support benefits of higher protein intake. Studies were heterogeneous, and confounding could not be excluded. High-quality, long-term studies are needed to clarify dietary protein's role in bone health.

**Metabolism. 2017 May;70:116-124. doi: 10.1016/j.metabol.2017.02.010. Epub 2017 Feb 16.**

### **A prospective study of low fasting glucose with cardiovascular disease events and all-cause mortality: The Women's Health Initiative.**

Mongraw-Chaffin M, LaCroix AZ, Sears DD, Garcia L, Phillips LS, Salmoirago-Blotcher E, Zaslavsky O, et al.

BACKGROUND: While there is increasing recognition of the risks associated with hypoglycemia in patients with diabetes, few studies have investigated incident cause-specific cardiovascular outcomes with regard to low fasting

glucose in the general population. **OBJECTIVE:** We hypothesized that low fasting glucose would be associated with cardiovascular disease risk and all-cause mortality in postmenopausal women. **METHODS:** To test our hypothesis, we used both continuous incidence rates and Cox proportional hazards models in 17,287 participants from the Women's Health Initiative with fasting glucose measured at baseline. Participants were separated into groups based on fasting glucose level: low (<80mg/dL), normal/reference (80-99mg/dL), impaired (100-125mg/dL), and diabetic ( $\geq$ 126mg/dL). **RESULTS:** Participants were free of cardiovascular disease at enrollment, had mean age of 62years, and were 52% Caucasian, 24% African American, 8% Asian, and 12% Hispanic. Median follow-up was 15years. Graphs of continuous incidence rates compared to fasting glucose distribution exhibited evidence of a weak J-shaped association with heart failure and mortality that was predominantly due to participants with treated diabetes. Impaired and diabetic fasting glucose were positively associated with all outcomes. Associations for low fasting glucose differed, with coronary heart disease (HR=0.64 (0.42, 0.98)) significantly inverse; stroke (0.73 (0.48, 1.13)), combined cardiovascular disease (0.91 (0.73, 1.14)), and all-cause mortality (0.97 (0.79, 1.20)) null or inverse and not significant; and heart failure (1.27 (0.80, 2.02)) positive and not significant. **CONCLUSIONS:** Fasting glucose at the upper range, but not the lower range, was significantly associated with incident cardiovascular disease and all-cause mortality.

**Arch Ital Urol Androl. 2017 Mar 31;89(1):7-11. doi: 10.4081/aiua.2017.1.7.**

### **Tadalafil once daily: Narrative review of a treatment option for female sexual dysfunctions (FSD) in midlife and older women.**

Borghi CI, Dell'Atti L.

Female Sexual Disorders (FSD) include a complex, multidimensional, individual experience that can change as an individual age, suggesting that these problems are caused by multiple factors including psychosocial factors, personal relationships, pathologic changes caused by diseases, and pharmacologic influences. Menopause is an important time for middle aged women and postmenopausal physiological changes could have a significant role in the development of FSD. Few is still known about their correct definition and treatment. Their incidence, prevalence and risk factors are difficult to define because of a high level of overlap in the experience of problems with desire, arousal, and orgasm. Little evidences are known about the best therapeutic approach, and both non-pharmacological and pharmacological treatment options have been described. Among these, phosphodiesterase type 5 inhibitors could be an effective option for many subtypes of female sexual disorders, with an improvement in different aspects of sexual function, such as desire, arousal, orgasm and sexual satisfaction. In this paper authors reviewed what is already known about the use of these vasoactive agents, particularly tadalafil, as a treatment option for female sexual disturbances.

**Eur J Clin Nutr. 2017 Apr 12. doi: 10.1038/ejcn.2017.36. [Epub ahead of print]**

### **Chocolate intake and diabetes risk in postmenopausal American women.**

Greenberg JA, Manson JE, Tinker L, Neuhaus ML, Garcia L, Vitolins MZ, Phillips LS.

**BACKGROUND/OBJECTIVES:** Recent long-term prospective cohort studies found inverse associations between chocolate consumption and the risk of type 2 diabetes, but provided conflicting evidence on the nature of the association among women. To assess this association in a large cohort of American women. **SUBJECTS/METHODS:** Multivariable Cox regression was used with the data from 92 678 postmenopausal women in the prospective Women's Health Initiative study. Chocolate intake was assessed by food frequency questionnaire. Incidence of type 2 diabetes was determined by self-report of the first treatment with oral medication or insulin. **RESULTS:** Among women free of diabetes at baseline, there were 10 804 cases, representing an incidence rate of 11.7% during 13.1 years and 1 164 498 person-years of follow-up. There was no significant linear association between long-term chocolate intake and type 2 diabetes risk, but there was significantly reduced risk at moderate levels of intake. Compared to women who ate 1 oz. of chocolate <1 time per month, those who ate this amount 1- <1.5 times per month, 1.5-<3.5 times per month, 3.5 times per month to <3 times per week and  $\geq$ 3 times per week had hazard ratios of 0.97 (95% confidence interval: 0.92, 1.04), 0.92 (0.87, 0.98), 0.93 (0.88, 0.98) and 0.98 (0.92, 1.04) (P for linear trend=0.79). There was only evidence of such inverse associations for women with below-median physical activity (P for interaction <0.0001) and those with age<65 years (P=0.01). **CONCLUSIONS:** We only found an inverse association between chocolate consumption and type 2 diabetes at moderate levels of consumption in two subgroups of postmenopausal women in the Women's Health initiative cohort.

**Biomed Res Int. 2017;2017:7456853. doi: 10.1155/2017/7456853. Epub 2017 Mar 16.**

## **Estrogen Replacement Regulates Vaginal Innervations in Ovariectomized Adult Virgin Rats: A Histological Study.**

Li T, Ma Y, Zhang H, Yan P, Huo L, Hu Y, Chen X, Li T, Zhang M, Liu Z.

**Background.** Our previous Gräfenberg spot findings confirmed that the distal-third areas of the anterior vaginal wall bore a significantly greater number of nerves and sexual hormone may have certain degree of influence on these significant differences. However, the role of estrogen in vaginal innervations remains controversial. **Methods.** To investigate whether hormonal-neural interactions occur in the vagina, sixty rats were randomly divided into six groups: Sham-operated, ovariectomy, and 4 treatment groups. After 2 weeks of treatment, vaginal biopsies were prepared with hematoxylin and eosin and PGP9.5 using immunohistochemistry. **Results.** The density of small nerve fibers was significantly higher in the distal-half areas of intact vaginal walls than the proximal-half areas ( $P = 0.001$ ). In contrast, the overall PGP 9.5-ir fiber innervation density was significantly decreased in the OVX rats subjected to surgical menopause. Sustained estrogen administration for 2 weeks resulted in nerve fiber proliferation, with values reaching normal levels in the low-dose estradiol valerate group. **Conclusion.** Our findings indicate that systemic hormonal therapy with low-dose estradiol valerate is effective and safe for treating deficient vaginal innervation caused by low level of estrogen activity in menopausal women and may aid studies to identify an optimal estradiol dose to provide relief from vaginal discomfort.

**Menopause. 2017 Apr 10. doi: 10.1097/GME.0000000000000857. [Epub ahead of print]**

## **Physiologically assessed hot flashes and endothelial function among midlife women.**

Thurston RC, Chang Y, Barinas-Mitchell E, Jennings JR, von Känel R, Landsittel DP, Matthews KA.

**OBJECTIVE:** Hot flashes are experienced by most midlife women. Emerging data indicate that they may be associated with endothelial dysfunction. No studies have tested whether hot flashes are associated with endothelial function using physiologic measures of hot flashes. We tested whether physiologically assessed hot flashes were associated with poorer endothelial function. We also considered whether age modified associations. **METHODS:** Two hundred seventy-two nonsmoking women reporting either daily hot flashes or no hot flashes, aged 40 to 60 years, and free of clinical cardiovascular disease, underwent ambulatory physiologic hot flash and diary hot flash monitoring; a blood draw; and ultrasound measurement of brachial artery flow-mediated dilation to assess endothelial function. Associations between hot flashes and flow-mediated dilation were tested in linear regression models controlling for lumen diameter, demographics, cardiovascular disease risk factors, and estradiol. **RESULTS:** In multivariable models incorporating cardiovascular disease risk factors, significant interactions by age ( $P < 0.05$ ) indicated that among the younger tertile of women in the sample (age 40-53 years), the presence of hot flashes (beta [standard error] = -2.07 [0.79],  $P = 0.01$ ), and more frequent physiologic hot flashes (for each hot flash: beta [standard error] = -0.10 [0.05],  $P = 0.03$ , multivariable) were associated with lower flow-mediated dilation. Associations were not accounted for by estradiol. Associations were not observed among the older women (age 54-60 years) or for self-reported hot flash frequency, severity, or bother. Among the younger women, hot flashes explained more variance in flow-mediated dilation than standard cardiovascular disease risk factors or estradiol. **CONCLUSIONS:** Among younger midlife women, frequent hot flashes were associated with poorer endothelial function and may provide information about women's vascular status beyond cardiovascular disease risk factors and estradiol.

**Open Access J Sports Med. 2017 Mar 27;8:39-60. doi: 10.2147/OAJSM.S129182. eCollection 2017.**

## **Effects of water-based exercise on bone health of middle-aged and older adults: a systematic review and meta-analysis.**

Simas V, Hing W, Pope R, Climstein M.

**BACKGROUND:** Age-related bone loss is a major health concern. Only exercises associated with high-impact and mechanical loading have been linked to a positive effect on bone turnover; however, these types of exercises may not always be appropriate for middle-aged and older adults due to physical decline or chronic disorders such as osteoarthritis. Water-based exercise (WBE) has been shown to affect different components of physical fitness, has lower risks of traumatic fracture, and applies less stress to joints. However, the effects of WBE on bone health are unclear. **OBJECTIVE:** This study aimed to explore whether WBE is effective in preventing age-related bone

deterioration in middle-aged and older adults. **METHODS:** A search of relevant databases and the references of identified studies was performed. Critical narrative synthesis and meta-analyses were conducted. **RESULTS:** Eleven studies, involving 629 participants, met all inclusion criteria. All participants were postmenopausal women. Eight studies compared WBE to a sedentary control group, and four studies had land-based exercise (LBE) participants as a comparison group. Meta-analyses revealed significant differences between WBE and control group in favor of WBE for changes in bone mineral density (BMD) at the lumbar spine (mean difference [MD] 0.03 g/cm<sup>2</sup>; 95% confidence interval [CI]: 0.01 to 0.05) and femoral neck (MD 0.04 g/cm<sup>2</sup>; 95% CI: 0.02 to 0.07). Significant differences were also revealed between WBE and LBE in favor of LBE for changes in lumbar spine BMD (MD -0.04 g/cm<sup>2</sup>; 95% CI: -0.06 to -0.02). However, there was no significant difference between WBE and LBE for changes in femoral neck BMD (MD -0.03 g/cm<sup>2</sup>; 95% CI: -0.08 to 0.01). **CONCLUSION:** WBE may have benefits with respect to maintaining or improving bone health in postmenopausal women but less benefit when compared to LBE.

**Geburtshilfe Frauenheilkd. 2017 Mar;77(3):257-267. doi: 10.1055/s-0043-102694.**

### **Mammographic Density and Vitamin D Levels - A Cross-sectional Study.**

Straub L, Riedel J, Luppä PB, Wissing J, Artmann A, Kiechle M, Seifert-Klauss VR.

**Background** Some studies have already proposed an inverse association between vitamin D levels and breast density. As breast density is already considered an established risk factor for breast cancer, such a connection could offer a new starting point for the prevention of breast cancer. **Material and Methods** To investigate this suggested connection, a total of 412 pre- and 572 post-menopausal women for whom mammography was indicated were recruited into this cross-sectional study. In addition to a questionnaire-based interview on the patient's general and gynecological medical history, her eating habits and lifestyle, serum levels of 25-hydroxyvitamin D [25(OH)D], calcium, phosphate and creatinine were determined. Breast density was determined by mammography and categorized as 1 to 4 according to the ACR classification. In addition to performing descriptive analysis to get a better overview of the data, a number of multivariate regression models were developed to determine the impact of confounders and the connection between vitamin D and mammographic density. **Results** More than half of all participants had low levels of 25(OH)D (<20 ng/ml) and only a small minority of women (5.7%) had what are currently considered to be optimal serum levels of 25(OH)D of at least 30 ng/ml. The significant majority of the cohort had a medium mammographic density (n = 463 had ACR 2; n = 343 had ACR 3). Logistic regression analysis showed that lower 25(OH)D serum levels were associated significantly more often with high rather than medium breast density. This association remained, even after adjusting for other factors which influence breast density such as age, BMI and menopausal status (p = 0.032 for ACR 4 vs. ACR 2; p = 0.028 for ACR 4 vs. ACR 3). When the same analysis was done separately for pre-menopausal and post-menopausal women, BMI in both groups was found to be inversely correlated with breast density and this inverse correlation was highly significant. In post-menopausal women, age was found to be similarly correlated while 25(OH)D did not appear to be associated with ACR. In pre-menopausal women the opposite was the case: although there was no correlation between age and breast density, higher vitamin D levels tended to be associated with lower breast density (p = 0.06 for ACR 2 vs. ACR 4) in this smaller sample (n = 412). When vitamin D-rich food and food supplements were also taken into account, regular intake of vitamin D preparations was associated with lower breast density; this association achieved borderline statistical significance (p = 0.05 for ACR 3 vs. ACR 4). When the analysis also took menopausal status into account, the breast density of pre-menopausal women was lower following regular vitamin D intake and this lower breast density of pre-menopausal women was statistically highly significant (p < 0.001 for ACR 1 and ACR 2 vs. ACR 4, respectively). This effect was not found in post-menopausal women. Frequent intake of vitamin D-containing nutrition had no significant impact on ACR in either of the groups. **Conclusion** These results reinforce the assumption previously proposed by several authors that higher levels of 25(OH)D pre-menopause and vitamin D substitution are associated with lower breast density and could reduce the risk of breast cancer. The findings did not confirm any post-menopausal association between vitamin D and mammographic breast density.