



## Selección de Resúmenes de Menopausia

Semana del 7 al 13 de junio de 2017

Juan Enrique Blümel. Departamento Medicina Sur. Universidad de Chile

**J Aging Phys Act. 2017 May 22:1-27. doi: 10.1123/japa.2016-0132. [Epub ahead of print]**

### **Differences in Function and Fracture Risk in Postmenopausal Women With and Without a Recent Distal Radius Fracture.**

Crockett KL, Kontulainen S, Farthing J, Chilibeck P, Bath B, Baxter-Jones A, Arnold C.

A distal radius fracture (DRF) is commonly the first fracture to occur in early postmenopausal women. The reasons for sustaining a DRF may be related to fall risk, bone fragility or both. The objective of this study was to compare functional and fracture risk status in postmenopausal women with and without a recent DRF and explore the relationships between function, grip strength and fracture risk status. **METHODS:** Seventy-seven women age 50-78 with (n=32) and without (n=45) a history of DRF in the past 2 years participated. Balance, timed up and go (TUG), gait velocity, balance confidence, sit to stand, grip strength and fracture risk were assessed. **RESULTS:** There was a significant group difference after controlling for physical activity level (Pillai's Trace,  $p < 0.05$ ) where women with DRF had poorer outcomes on sit to stand, gait velocity, TUG and fracture risk status. Grip strength was associated with functional tests, particularly in women with DRF. **CONCLUSIONS:** Women with a recent DRF demonstrated lower functional status and higher fracture risk compared to women without. Grip strength was associated with measures of function and fracture risk, and may complement screening tools for this population.

**Osteoporos Int. 2017 Jun 7. doi: 10.1007/s00198-017-4091-3. [Epub ahead of print]**

### **FRAX for fracture prediction shorter and longer than 10 years: the Manitoba BMD registry.**

Leslie WD, Majumdar SR, Morin SN, Lix LM, Johansson H, Oden A, McCloskey EV, Kanis JA.

**INTRODUCTION:** FRAX® estimates 10-year probability of major osteoporotic fracture (MOF) and hip fracture. We examined FRAX predictions over intervals shorter and longer than 10 years. **METHODS:** Using a population-based clinical registry for Manitoba, Canada, we identified 62,275 women and 6455 men 40 years and older with baseline dual-energy X-ray absorptiometry scans and FRAX scores. Incident MOF and hip fracture were assessed up to 15 years from population-based data. We assessed agreement between estimated fracture probability from 1 to 15 years using linearly rescaled FRAX scores and observed cumulative fracture probability. The gradient of risk for FRAX probability and incident fracture was examined overall and for 5-year intervals. **RESULTS:** FRAX predicted incident MOF and hip fracture for all time intervals. There was no attenuation in the gradient of risk for MOF even for years >10. Gradient of risk was slightly lower for hip fracture prediction in years >10 vs years <5, though HRs remained high. Linear agreement was seen in the relationships between observed vs predicted (rescaled) FRAX probabilities ( $R^2$  0.95-1.00). Among women, there was near-perfect linearity in MOF predictions. Deviations from linearity, with a slightly higher observed than predicted MOF probability, were most evident in the first years following a fracture event and after 10 years for hip fracture prediction in women using FRAX with BMD. Simulations showed that results were robust to large differences in fracture rates and moderate differences in mortality rates. **CONCLUSIONS:** FRAX predicts incident MOF and hip fracture up to 15 years and could be adapted to predict fracture over time periods shorter and longer term than 10 years in populations with fracture and mortality epidemiology similar to Canada.

**Menopause. 2017 Jun 5. doi: 10.1097/GME.0000000000000879. [Epub ahead of print]**

### **Associations between high-risk alcohol consumption and sarcopenia among postmenopausal women.**

Kwon YJ, Lim HJ, Lee YJ, Lee HS, Linton JA, Lee JW, Kang HT.

**OBJECTIVE:** Sarcopenia is an age-related process, leading to cardio-metabolic diseases and disabilities. High-risk drinking is also closely related to diabetes, hypertension, and dyslipidemia, which are modifiable risk factors for sarcopenia. In the present study, we aimed to investigate the association between alcohol-drinking patterns and sarcopenia in Korean postmenopausal women. **METHODS:** Data from 2,373 postmenopausal women were analyzed from the 2008 to 2011 Korean National Health and Nutrition Examination Survey. We defined sarcopenia as two standard deviations

below the sex-specific means of the appendicular skeletal muscle/weight (percentage) values of a young reference group. Participants were categorized into three groups according to alcohol-drinking patterns, as assessed by the Alcohol Use Disorders Identification Test questionnaire. The odds ratios and 95% confidence intervals for sarcopenia were calculated using multiple logistic regression analyses. **RESULTS:** In total, 8.2% of Korean postmenopausal women met criteria for sarcopenia. The prevalence of sarcopenia increased from low-risk to high-risk alcohol-drinking groups as follows: 7.6, 11.0, and 22.7%, respectively. Compared with the low-risk group, the odds ratio (95% confidence interval) for the high-risk group was 4.29 (1.87-9.82) after adjusting for age, body mass index, systolic blood pressure, total cholesterol, fasting blood glucose, household income, education level, daily calorie intake, current smoking and regular exercise, and household food security status **CONCLUSIONS:** High-risk alcohol drinking was associated with a higher risk of sarcopenia in postmenopausal Korean women.

**Osteoporos Int. 2017 Jun 6. doi: 10.1007/s00198-017-4106-0. [Epub ahead of print]**

## **Breastfeeding as the sole source of milk for 6 months and adolescent bone mineral density.**

Blanco E, Burrows R, Reyes M, Lozoff B3 Gahagan S, Albala C.

**INTRODUCTION:** The aim of the study is to assess the role of breastfeeding BF on adolescent bone mineral density (BMD) in a cohort prospectively followed since infancy. **METHODS:** We studied 679 participants from an infancy iron deficiency anemia preventive trial in Santiago, Chile, followed to adolescence. Breast and bottle feeding were ascertained weekly from 4 to 12 months. At 16 years, whole body BMD was assessed by DEXA. Using linear regression, we evaluated associations between BF duration and BF as the sole source of milk and adolescent BMD z-score, adjusting for possible infancy, adolescent, and background confounders. **RESULTS:** Mean birth weight and length were 3.5 (0.3) kg and 50.7 (1.6) cm. For at least 6 months, BF was the sole source of milk for 26.3% and with supplementation for 36.7%. For 37%, BF was provided for less than 6 months. Mean 16-year BMD z-score was 0.25 (1.0). Covariates included male sex, birth length, and gestational age. BF as the sole source of milk  $\geq 6$  months, compared to BF  $< 6$  months, was associated with higher adolescent BMD z-score adjusting for covariates ( $\beta = 0.29$ ,  $p < 0.05$ ). Mixed BF was not significantly related to adolescent BMD z-score ( $\beta = 0.06$ ,  $p = 0.47$ ). For every 30 days of BF as the sole source of milk, adolescent BMD z-score increased by 0.03 ( $p = 0.01$ ). **CONCLUSION:** BF without formula supplementation for at least 6 months was associated with higher adolescent BMD z-score and a suggestive trend in the same direction for BMD suggests that exclusivity and duration of BF may play a role in adolescent bone health.

**Nutr Res Pract. 2017 Jun;11(3):223-231. doi: 10.4162/nrp.2017.11.3.223. Epub 2017 Apr 20.**

## **Effect of soy isoflavones supplement on climacteric symptoms, bone biomarkers, and quality of life in Korean postmenopausal women: a randomized clinical trial.**

Lee H, Choue R, Lim H.

**BACKGROUND/OBJECTIVES:** Soy isoflavones are expected to improve menopausal symptoms and osteoporosis in women. However, their efficacy is still inconclusive, and there was limited data for postmenopausal women in South Korea. We examined the effects of soy isoflavones on climacteric symptoms, bone biomarkers, and quality of life in Korean postmenopausal women. **SUBJECTS/METHODS:** A randomized, double-blind study design was used. Eighty-seven participants who had undergone natural menopause were randomly administered either 70 mg/day isoflavones ( $n = 43$ ) or placebo ( $n = 41$ ) for 12 weeks. We assessed the Kupperman index for climacteric symptoms and the menopause-specific quality of life (MENQOL) questionnaire for quality of the life. Biomarkers of bone metabolism were also measured in serum bone-specific alkaline phosphatase (BALP), osteocalcin (OC), N- and C-terminal cross-linking telopeptides of type I collagen (NTx, CTx), and urine-deoxypyridinolin (u-DPD). **RESULTS:** Scores of the Kupperman index were decreased in both the isoflavones group ( $-7.0 \pm 15.8$ ,  $P = 0.0074$ ) and placebo group ( $-6.3 \pm 14.6$ ,  $P = 0.0064$ ) during the intervention, but no significant difference was noted between the groups. Regarding the bone formation markers, the level of serum BALP increased by  $6.3 \pm 4.1\%$  ( $P = 0.004$ ) and OC increased by  $9.3 \pm 6.2\%$  ( $P < 0.001$ ), meanwhile those of the placebo were not changed. For the bone resorption markers, NTx, CTx, and u-DPD were not significantly different in either group. MENQOL was significant decreased in the isoflavone group ( $-0.6 \pm 0.5$ ) and placebo group ( $-0.6 \pm 0.4$ ), with a significant difference between groups ( $P = 0.0228$ ). **CONCLUSIONS:** Our study suggests that 70 mg isoflavones supplement has beneficial effects on bone formation markers; however, it showed no benefit compared to the placebo on climacteric symptoms or quality of life.

**J Sex Med. 2017 Jun;14(6):834-842. doi: 10.1016/j.jsxm.2017.03.258.**

## **Flibanserin in Postmenopausal Women with Hypoactive Sexual Desire Disorder: Results of the PLUMERIA Study.**

Portman DJ, Brown L, Yuan J, Kissling R, Kingsberg SA.

**BACKGROUND:** Hypoactive sexual desire disorder (HSDD) is a common sexual disorder in younger and older women. Flibanserin is approved for the treatment of acquired generalized HSDD in premenopausal women only. The efficacy of flibanserin for postmenopausal women with HSDD was demonstrated in the first of two North American randomized, double-blinded, placebo-controlled trials (SNOWDROP). **AIM:** To evaluate the safety and efficacy of flibanserin in postmenopausal women with HSDD in a second randomized, double-blinded, placebo-controlled trial (PLUMERIA). **METHODS:** Naturally postmenopausal women were randomly assigned to receive flibanserin (100 mg/d) or placebo. Efficacy outcomes were assessed using the last-observation-carried-forward imputation method. **OUTCOMES:** Safety assessment included incidence of adverse events. Primary efficacy outcomes were the number of satisfying sexual events and the Female Sexual Function Index desire domain (FSFI-d) score. **RESULTS:** The study population (flibanserin, n = 376; placebo, n = 369) included primarily white women (84.7%), with a mean age of 56.1 years and a mean HSDD duration of 5.0 years. When the study was discontinued early by the sponsor, 45.3% of randomly assigned patients had completed week 16 (which served as the primary analysis time point). The most common adverse events in flibanserin-treated patients were insomnia (7.7%), somnolence (6.9%), and dizziness (6.4%). Improvement from baseline to week 16 (last-observation-carried-forward) in FSFI-d score was significantly greater for flibanserin compared with placebo (P = .011); however, the between-group comparison for satisfying sexual events did not reach statistical significance. **CLINICAL IMPLICATIONS:** Considered with the findings of the previous randomized controlled trial (SNOWDROP), the results of this study support the safety and efficacy of flibanserin in postmenopausal women. **STRENGTHS AND LIMITATIONS:** This was a well-designed randomized, placebo-controlled trial. A key limitation was early discontinuation by the study sponsor, which decreased the sample size. In addition, the validity of satisfying sexual events as a primary outcome measurement in HSDD studies has been called into question (but was required by the US Food and Drug Administration as a primary end point in studies of female sexual dysfunction at the time this study was conducted). **CONCLUSION:** Flibanserin was generally well tolerated in this population of naturally postmenopausal women. Despite the greatly decreased power to detect improvement compared with placebo on the efficacy measurements used, results suggest that flibanserin could be efficacious in postmenopausal women with HSDD.

**Bone Rep. 2016 Aug 27;5:243-251. doi: 10.1016/j.bonr.2016.08.003. eCollection 2016 Dec.**

## **Estrogen depletion and drug treatment alter the microstructure of type I collagen in bone.**

Cauble MA, Muckley MJ, Fang M, Fessler JA, Welch K, Rothman ED, Orr BG, Duong LT, Holl MMB.

The impact of estrogen depletion and drug treatment on type I collagen fibril nanomorphology and collagen fibril packing (microstructure) was evaluated by atomic force microscopy (AFM) using an ovariectomized (OVX) rabbit model of estrogen deficiency induced bone loss. Nine-month-old New Zealand white female rabbits were treated as follows: sham-operated (Sham; n = 11), OVX + vehicle (OVX + Veh; n = 12), OVX + alendronate (ALN, 600 µg/kg/wk., s.c.; n = 12), and OVX + cathepsin-K inhibitor L-235 (CatKI, 10 mg/kg, daily, p.o.; n = 13) in prevention mode for 27 weeks. Samples from the cortical femur and trabecular lumbar vertebrae were polished, demineralized, and imaged using AFM. Auto-correlation of image patches was used to generate a vector field for each image that mathematically approximated the collagen fibril alignment. This vector field was used to compute an information-theoretic entropy that was employed as a quantitative fibril alignment parameter (FAP) to allow image-to-image and sample-to-sample comparison. For all samples, no change was observed in the average FAP values; however significant differences in the distribution of FAP values were observed. In particular, OVX + Veh lumbar vertebrae samples contained a tail of lower FAP values representing regions of greater fibril alignment. OVX + ALN treatment resulted in a FAP distribution with a tail indicating greater alignment for cortical femur and less alignment for trabecular lumbar vertebrae. OVX + CatKI treatment gave a distribution of FAP values with a tail indicating less alignment for cortical femur and no change for trabecular lumbar vertebrae. Fibril alignment was also evaluated by considering when a fibril was part of discrete bundles or sheets (classified as parallel) or not (classified as oblique). For this analysis, the percentage of parallel fibrils in cortical femur for the OVX group was 17% lower than the Sham group. OVX + ALN treatment partially prevented the proportion of parallel fibrils from decreasing and OVX + CatKI treatment completely prevented a change. In trabecular lumbar vertebrae, there was no difference in the percentage of parallel fibrils between Sham and any of the other treatment groups.