



## Selección de Resúmenes de Menopausia

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**Bone Res. 2017 Oct 4;5:17046. doi: 10.1038/boneres.2017.46. eCollection 2017.**

### **Intestinal microbiota: a potential target for the treatment of postmenopausal osteoporosis.**

Xu X, Jia X, Mo L, Liu C, Zheng L, Yuan Q, Zhou X.

Postmenopausal osteoporosis (PMO) is a prevalent metabolic bone disease characterized by bone loss and structural destruction, which increases the risk of fracture in postmenopausal women. Owing to the high morbidity and serious complications of PMO, many efforts have been devoted to its prophylaxis and treatment. The intestinal microbiota is the complex community of microorganisms colonizing the gastrointestinal tract. Probiotics, which are dietary or medical supplements consisting of beneficial intestinal bacteria, work in concert with endogenous intestinal microorganisms to maintain host health. Recent studies have revealed that bone loss in PMO is closely related to host immunity, which is influenced by the intestinal microbiota. The curative effects of probiotics on metabolic bone diseases have also been demonstrated. The effects of the intestinal microbiota on bone metabolism suggest a promising target for PMO management. This review seeks to summarize the critical effects of the intestinal microbiota and probiotics on PMO, with a focus on the molecular mechanisms underlying the pathogenic relationship between bacteria and host, and to define the possible treatment options.

**J Midlife Health. 2017 Jul-Sep;8(3):103-109. doi: 10.4103/jmh.JMH\_67\_15.**

### **Study of Comparison between Autonomic Dysfunction and Dyslipidemia in Healthy Postmenopausal Women.**

Yalamudi K.

**BACKGROUND:** Obesity, physical inactivity, and altered estrogen levels play an important role in contributing to disease risk profile and autonomic dysfunction in healthy postmenopausal women. This study was conducted to test the correlation between autonomic dysfunction and dyslipidemia in healthy postmenopausal women. **MATERIALS AND METHODS:** This study was carried out on sixty healthy postmenopausal women before the age of 65 years, without any gross systemic disease. The following five autonomic functional tests were performed on the study group: heart rate response to deep breathing, heart rate response to Valsalva maneuver, heart rate response to standing up from supine position, blood pressure response to sustained hand grip, and blood pressure response to standing up from supine position. Fasting lipid profile of the study group was tested. **RESULTS AND CONCLUSION:** In the present study, autonomic dysfunction was found in 67% of healthy postmenopausal women. Among the sixty female healthy postmenopausal women included in the study, 68% were found to have dyslipidemia. In our study, there is a statistically significant correlation between autonomic dysfunction and dyslipidemia in healthy postmenopausal women. In these healthy postmenopausal women with increased serum cholesterol, serum low-density lipoprotein, and serum triglycerides, there was autonomic dysfunction which is statistically significant. There is no statistical significance on comparing serum high-density lipoprotein cholesterol with autonomic dysfunction in healthy postmenopausal women.

**Acta Obstet Gynecol Scand. 2017 Oct 5. doi: 10.1111/aogs.13239. [Epub ahead of print]**

### **Differential effect of the ultra-low dose and standard estrogen plus dydrogesterone therapy on thrombin generation and fibrinolysis in postmenopausal women.**

Piróg M, Jach R, Kacalska-Janssen O.

**INTRODUCTION:** The objective was to estimate the effects of different doses of oral hormone therapy (HT) on thrombin generation and fibrinolytic activity in postmenopausal women after 12-months treatment. **MATERIAL AND METHODS:** Thrombin generation, fibrinolysis activators and inhibitors were determined before, and after 12-months treatment. Participants (180) were assigned (1:1:1) as follows: 1) standard HT group, 17 $\beta$ -estradiol (1 mg/d) with

dydrogesterone (5 mg/d); 2) ultra-low-dose HT group, 17 $\beta$ -estradiol (0.5 mg/d) with dydrogesterone (2.5 mg/d); 3) control group, no treatment.

**RESULTS:** The standard HT led to higher prothrombin 1+2 fragments concentration (by 5.8%) with lower antithrombin activity (by 6.1%). Compared with baseline, we observed reduction in mean antithrombin activity in the standard HT group and increases in mean prothrombin 1+2 fragments levels in two HT groups. We found decreases after treatment in both standard and ultra-low-dose HT groups in plasminogen activator inhibitor-1 (PAI-1) activity (-32.4% and -19.6%, respectively) and PAI-1 antigen (-9.9% and -7.8%, respectively). Intergroup analysis revealed reduction in both mean PAI-1 activities and PAI-1 antigen levels in two treatment groups when compared to the control. **CONCLUSION:** In contrary to the standard estrogen plus dydrogesterone treatment, ultra-low-dose HT revealed positive effects on hemostasis by intensifying fibrinolysis through decrease in both PAI-1 activity and antigen levels, and with no impact on thrombin generation.

**Jpn J Clin Oncol. 2017 Oct 1;47(10):935-941. doi: 10.1093/jjco/hyx111.**

### **Comparative risks for cancer associated with use of calcitonin, bisphosphonates or selective estrogen receptor modulators among osteoporosis patients: a population-based cohort study.**

Hsiao FY, Hsu WW.

**Background:** This population-based cohort study was to compare the risks of incident cancer in osteoporosis patients who used bisphosphonates, calcitonin or selective estrogen receptor modulators (SERMs). **Methods:** We identified 9995 patients who were diagnosed with osteoporosis and prescribed osteoporosis drugs (bisphosphonate (n = 4675), calcitonin (n = 3993) and SERMs (n = 1327)) between 1 January 2000 and 31 December 2006 in Taiwan's National Health Insurance Research Database. Date of first prescription of osteoporosis drugs was assigned as the index date. The outcome measurement was incident cancer, defined by a first-ever inpatient visit with a primary diagnosis of cancer. All patients were followed until the occurrence of cancer. For those who did not develop cancer, we censored them at 1 year after their last prescription of osteoporosis drugs. Cox proportional hazard models were used to examine the association between risk of cancer and use of calcitonin, bisphosphonates or SERMs. **Results:** The incidence rate of cancer was 68.8, 34.0 and 29.6 per 1000 person years in the calcitonin, SERMs and bisphosphonate cohorts, respectively. Compared with bisphosphonate users, calcitonin users were associated with an increased risk of cancer (adjusted hazard ratio (HR) 2.11, 95% confidence interval (CI) 2.01-2.21, P < 0.001). SERM users were associated with an increased risk of cancer (adjusted HR 1.20, 95% CI 1.13-1.28, P < 0.001). **Conclusion:** Our findings suggest that calcitonin is associated with an increased risk of cancer than bisphosphonate, supporting the recent warning issued by the European Medicines Agency and US Food and Drug Administration. SERMs is found to be associated with an increased risk of cancer than bisphosphonate.

**MMWR Morb Mortal Wkly Rep. 2017 Oct 3;66(39):1052-1058. doi: 10.15585/mmwr.mm6639e1.**

### **Vital Signs: Trends in Incidence of Cancers Associated with Overweight and Obesity - United States, 2005-2014.**

Steele CB, Thomas CC, Henley SJ, Massetti GM, Galuska DA, Agurs-Collins T, Puckett M, Richardson LC.

**BACKGROUND:** Overweight and obesity are associated with increased risk of at least 13 different types of cancer. **METHODS:** Data from the United States Cancer Statistics for 2014 were used to assess incidence rates, and data from 2005 to 2014 were used to assess trends for cancers associated with overweight and obesity (adenocarcinoma of the esophagus; cancers of the breast [in postmenopausal women], colon and rectum, endometrium, gallbladder, gastric cardia, kidney, liver, ovary, pancreas, and thyroid; meningioma; and multiple myeloma) by sex, age, race/ethnicity, state, geographic region, and cancer site. Because screening for colorectal cancer can reduce colorectal cancer incidence through detection of precancerous polyps before they become cancerous, trends with and without colorectal cancer were analyzed. **RESULTS:** In 2014, approximately 631,000 persons in the United States received a diagnosis of a cancer associated with overweight and obesity, representing 40% of all cancers diagnosed. Overweight- and obesity-related cancer incidence rates were higher among older persons (ages  $\geq 50$  years) than younger persons; higher among females than males; and higher among non-Hispanic black and non-Hispanic white adults compared with other groups. Incidence rates for overweight- and obesity-related cancers during 2005-2014 varied by age, cancer site, and state. Excluding colorectal cancer, incidence rates increased significantly among persons aged 20-74 years; decreased among those aged  $\geq 75$  years; increased in 32 states; and were stable in 16 states and the District of Columbia.

**CONCLUSIONS:** The burden of overweight- and obesity-related cancer is high in the United States. Incidence rates of overweight- and obesity-related cancers except colorectal cancer have increased in some age groups and states. **IMPLICATIONS FOR PUBLIC HEALTH PRACTICE:** The burden of overweight- and obesity-related cancers might be reduced through efforts to prevent and control overweight and obesity. Comprehensive cancer control strategies, including use of evidence-based interventions to promote healthy weight, could help decrease the incidence of these cancers in the United States.

**Climacteric. 2017 Oct 5:1-6. doi: 10.1080/13697137.2017.1377696. [Epub ahead of print]**

### **FSH to estradiol ratio can be used as screening method for mild cognitive impairment in postmenopausal women.**

Hestiantoro A, Wiwie M, Shadrina A, Ibrahim N, Purba JS.

**OBJECTIVE:** To determine the role of anthropometric measurement, menopausal symptoms and biochemical marker changes as screening methods for mild cognitive impairment (MCI) in postmenopausal women **Methods:** A cross-sectional study included 282 postmenopausal women in Jakarta, further classified into two groups, with and without MCI. Some related variables such as age, body mass index (BMI), duration of menopause, vasomotor symptoms, hormone levels such as follicle stimulating hormone (FSH), luteinizing hormone, leptin, estradiol, and cognitive status, were assessed and analyzed. **RESULTS:** The FSH levels significantly correlated with MCI incidence ( $p = 0.018$ ), along with the ratio of FSH/estradiol levels ( $p = 0.029$ ) and ratio of FSH/soluble leptin receptor ( $p = 0.011$ ), while other variables did not. By multivariate analysis, the ratio of FSH/estradiol was known as the most significant factor with a probability of having MCI in menopausal women of 1.15. Using the ROC curve, the threshold of the ratio FSH/estradiol to predict MCI was 1.94, with sensitivity 66.5% and specificity 46.8%. **CONCLUSIONS:** The ratio of FSH to estradiol ( $>1.94$ ) can be used as a screening method for the occurrence of MCI in postmenopausal women.

**Eur J Nutr. 2017 Oct 3. doi: 10.1007/s00394-017-1544-6. [Epub ahead of print]**

### **Calcium and vitamin D fortified milk reduces bone turnover and improves bone density in postmenopausal women over 1 year.**

Kruger MC, Chan YM, Lau LT, Lau CC, Chin YS, Kuhn-Sherlock B, Todd JM, Schollum LM.

**PURPOSE:** In Malaysia, hip fracture incidence is higher in Chinese women than other ethnic groups. This study compared the effects of a high-calcium vitamin D fortified milk with added FOS-inulin versus regular milk over 1 year on aspects of bone health in Chinese postmenopausal women in Malaysia. **METHODS:** One-hundred and twenty-one women (mean age  $59 (\pm 4)$  years) were randomized into two groups: control ( $n = 60$ ; regular milk, 428 mg calcium per day) or intervention ( $n = 61$ ; fortified milk at 1200 mg calcium, 96 mg magnesium, 2.4 mg zinc, 15  $\mu\text{g}$  vitamin D and 4 g FOS-inulin per day). At baseline, weeks 12, 24, 36 and 52, parathyroid hormone (PTH), C-Telopeptide of Type I Collagen (CTx-1), Procollagen I Intact N-Terminal propeptide (PINP) and vitamin D levels were assessed. Bone density (BMD) was measured at baseline and week 52 using a GE Lunar iDXA. **RESULTS:** Body mass index, lumbar spine and femoral neck BMD did not differ between groups at baseline. Over 52 weeks, mean plasma 25 (OH) D3 levels increased to 74.8 nmol/L (intervention group) or remained at 63.1 nmol/L (control group) ( $p < 0.001$  between groups). PTH levels increased in the control group ( $p = 0.001$ ). The intervention resulted in a significant suppression of CTx-1 and PINP at  $p = 0.018$  and  $p = 0.004$ . Femoral neck BMD remained stable in the intervention group but decreased significantly in the controls, with a borderline treatment effect ( $p = 0.07$ ). **CONCLUSION:** Compared with regular milk, the fortified milk suppressed bone turnover markers and tended to increase femoral neck BMD.

**Cancer Causes Control. 2017 Oct 3. doi: 10.1007/s10552-017-0968-x. [Epub ahead of print]**

### **Sedentary time and postmenopausal breast cancer incidence.**

Nomura SJO, Dash C, Sheppard VB, Bowen D, Allison M, Barrington W, Chlebowski R, Coday M, Hou L, et al.

**PURPOSE:** The objective of this study was to evaluate the prospective association between sedentary time and postmenopausal breast cancer incidence, and whether associations differ by race/ethnicity, physical activity levels, and body measurements. **METHODS:** The Women's Health Initiative Observational Study is a prospective cohort among women ages 50-79 years at baseline (1994-1998) (analytic cohort = 70,233). Baseline questionnaire data were used to estimate time spent sitting and total sedentary time. Associations between time spent sitting and invasive breast cancer incidence overall ( $n = 4,115$  cases through September 2015), and by hormone receptor subtypes, were investigated

using Cox proportional hazards regression. Analyses were replicated stratified by race/ethnicity, body measurements, and physical activity. RESULTS: Among women in this study, 34.5% reported  $\leq 5$  h/day sitting, 40.9% reported 6-9 h/day and 24.7% reported  $\geq 10$  h/day. Time spent sitting ( $\geq 10$  vs.  $\leq 5$  h/day adjusted HR = 1.00, 95% CI 0.92-1.09) was not associated with breast cancer incidence, regardless of hormone receptor subtype. Associations did not differ by race/ethnicity, physical activity, or body measurements. CONCLUSIONS: Results from this study do not support an association between sedentary time and breast cancer incidence.

**Osteoporos Int. 2017 Oct 3. doi: 10.1007/s00198-017-4242-6. [Epub ahead of print]**

### **Significant bone loss after stopping long-term denosumab treatment: a post FREEDOM study.**

Zanchetta MB, Boailchuk J, Massari F, Silveira F, Bogado C, Zanchetta JR.

We evaluate 38 elderly women who had received long-term denosumab treatment after stopping the drug. Taking into account the gain during treatment and the loss after stopping treatment, they lost 35.5% of the total gain in the spine, 44.6% of the total gain in the femoral neck, and 103.3% in the total hip. INTRODUCTION: Denosumab (DMAb) is a soluble inhibitor of the receptor activator of nuclear factor-kappaB ligand (RANKL) and, therefore, does not incorporate into the bone matrix. Consistently, DMAb discontinuation is associated with reversal of the effects attained with treatment. PURPOSE: The aim of this study is to assess changes in BMD after a year of discontinuation of DMAb in a group of postmenopausal women treated with DMAb for 7 or 10 years. Secondly, is to evaluate the occurrence of fragility fractures. METHODS: Women who had participated in the FREEDOM study and its extension were invited to participate in this follow-up study. BMD at LS and hip and spine X-rays were obtained. Results were compared to the last value obtained while in treatment to assess changes after discontinuation. RESULTS: Thirty-eight women, mean age:  $81 \pm 3.4$  years completed study procedures; none had received bisphosphonates after stopping DMAb. Mean gap time between DMAb last dose and the follow-up visit was 17 months (range 16-20 months). Bone mineral density (BMD) decreased significantly in all regions: - 8.1% in LS, - 6% in FN, and - 8.4% in TH. Five (5/38, 13.15%) patients had a fragility fracture, one suffered a wrist fracture, and four experienced vertebral fractures. Three patients suffered one vertebral fracture and one of them had two vertebral fractures. Laboratory results showed the following mean values: CTX =  $996 \pm 307$  pg/ml (normal values  $550 \pm 226$  pg/ml); osteocalcin =  $55.2 \pm 18.6$  ng/ml (normal value 42 ng/ml); and 25 OH vitamin D =  $23.7 \pm 6.9$  ng/ml. CONCLUSION: Our results describe the rapid bone loss occurring after cessation of denosumab treatment. Further studies are needed to assess if patients have a higher risk of fracture after stopping DMAb and if so, which patients have the highest risk, and assess the role of transitioning to bisphosphonates in the long term.