

## Selección de Resúmenes de Menopausia

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María Soledad Vallejo. Clínica Quilín. Universidad de Chile

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### **Temporal increases in 25-hydroxyvitamin D in midlife women: Longitudinal results from the Study of Women's Health Across the Nation (SWAN).**

Mitchell DM, Ruppert K, Udupa N, Bassir F, Darakananda I, Solomon DH, Lian Y, Cauley JA, et al.

**OBJECTIVE:** 25-hydroxyvitamin D (25(OH)D) is critical for bone mineralization and may prevent fractures. Understanding vitamin D deficiency trends in midlife women is particularly important given their concurrent menopausal changes that increase risk for fracture. We aimed to evaluate changes in mean 25(OH)D over time and their determinants in a racially, ethnically, and socioeconomically diverse cohort of midlife women. **DESIGN:** A multi-center prospective cohort study. **PATIENTS:** 1585 women ages 42-52 years at baseline. **MEASUREMENTS:** We measured serum 25(OH)D at 2 timepoints (1998-2000 and 2009-2011). Between-visit change was assessed in the whole cohort and in socioeconomic and demographic subgroups. Among those with vitamin D deficiency (25(OH)D <30 nmol/L) at baseline, we evaluated determinants of persistent deficiency at follow-up. **RESULTS:** Mean 25(OH)D increased from 53.8 to 70.0 nmol/L ( $p<0.001$ ), and the prevalence of deficiency decreased from 20.4 to 9.7% ( $p<0.001$ ). While baseline 25(OH)D differed among subgroups, the changes in 25(OH)D were similar among groups. The proportion of women reporting dietary supplement use increased from 40.8 to 67.1% ( $p<0.001$ ), and the increase in 25(OH)D was significantly higher in supplement users. Among women with vitamin D deficiency at baseline, White women and supplement users were less likely to remain deficient at follow-up. **CONCLUSIONS:** Among midlife women, temporal increases in 25(OH)D concentrations are driven largely by increases in supplement use. The proportion of women with 25(OH)D<30 nmol/L and thus at high risk for skeletal consequences remains substantial. Targeted screening for vitamin D deficiency in populations at risk for fragility fracture may be advisable.

**Menopause. 2019 Apr 8. doi: 10.1097/GME.0000000000001340. [Epub ahead of print]**

### **Tamoxifen use as a malignancy risk factor in postmenopausal women with endometrial polyps.**

Yela DA, Ikejiri TA, Machado CR, Mutta D, Benetti-Pinto CL.

**OBJECTIVE:** We analyzed tamoxifen use as a malignancy risk factor in women with endometrial polyps. **METHODS:** This retrospective study included 675 women who underwent hysteroscopic polypectomy in 2010 to 2015 at the University of Campinas. Women were divided into tamoxifen use ( $n=169$ ) and no tamoxifen use ( $n=506$ ) groups. The primary outcome was endometrial cancer prevalence. Dependent variables included age, parity, years since menopause, presence of abnormal uterine bleeding, endometrial pattern on hysteroscopy, and endometrial thickness. **RESULTS:** There were seven cases of endometrial cancer in the tamoxifen use group (4.14%) and 41 in the no tamoxifen use group (8.1%;  $P=0.083$ ). On performing multivariate analysis, tamoxifen use was not a risk factor for endometrial cancer (prevalence ratio 0.51, 95% confidence interval [CI] 0.23-1.14,  $P=0.101$ ). The no tamoxifen use group had an increased prevalence of malignancy when women presented with abnormal uterine bleeding (prevalence ratio 3.9, 95% CI 2.08-7.29,  $P<0.001$ ), age >60 years (prevalence ratio 2.1, 95% CI 1.12-3.93,  $P=0.021$ ), or nulliparous status (prevalence ratio 3.13, 95% CI 1.55-6.35,  $P=0.002$ ). The tamoxifen use group had increased prevalence of malignancy when women were >60 years (prevalence ratio 7.85, 95% CI 1.05-58.87,  $P=0.006$ ) or nulliparous (prevalence ratio 8.36, 95% CI 2.32-30.11,  $P<0.001$ ). **CONCLUSION:** Tamoxifen use was not related with a higher prevalence of endometrial cancer in women with endometrial polyps. Abnormal uterine bleeding, age > 60 years, and nulliparous status were associated with malignancy.

**Endocrine. 2019 Apr 8. doi: 10.1007/s12020-019-01919-8. [Epub ahead of print]**

### **The next step after anti-osteoporotic drug discontinuation: an up-to-date review of sequential treatment.**

Guañabens N, Moro-Álvarez MJ, Casado E, Blanch-Rubió J, Gómez-Alonso C, Díaz-Guerra GM, et al.

Several antiresorptive drugs, like bisphosphonates and denosumab, are currently available for the treatment of osteoporosis due to their evidenced efficacy in reducing fracture risk at mid-term. Osteoanabolic therapies, like teriparatide, whose treatment duration is limited to 2 years, have also shown efficacy in the reduction of fracture risk. However, depending on the severity of osteoporosis and the presence of other associated risk factors for fracture, some patients may require long-term treatment to preserve optimal bone strength and minimize bone fracture risk. Given the limited duration of some treatments, the fact that most of the antiresorptive drugs have not been assessed beyond 10 years, and the known long-term safety issues of these drugs, including atypical femoral fractures or osteonecrosis of the jaw, the long-term management of these patients may require an approach based on drug discontinuation and/or switching. In this regard, interest in sequential osteoporosis therapy, wherein drugs are initiated and discontinued over time, has grown in recent years, although the establishment of an optimal and individualized order of therapies remains controversial. This review reports the currently available clinical evidence on the discontinuation effects of different anti-osteoporotic drugs, as well as the clinical outcomes of the different sequential treatment regimens. The objective of this article is to present up-to-date practical knowledge on this area in order to provide guidance to the clinicians involved in the management of patients with osteoporosis.

**Int J Environ Res Public Health. 2019 Apr 6;16(7). pii: E1228. doi: 10.3390/ijerph16071228.**

### **The Association between Osteoporosis and Grip Strength and Skeletal Muscle Mass in Community-Dwelling Older Women.**

Taniguchi Y, Makizako H, Kiyama R, Tomioka K, Nakai Y, Kubozono T, Takenaka T, Ohishi M.

This cross-sectional study investigated the association between osteoporosis, grip strength, and skeletal muscle mass in community-dwelling older women. Data obtained from 265 older women who participated in a community-based health check survey (Tarumizu Study) were analyzed. Face-to-face interviews with participants revealed their history of osteoporosis. Appendicular skeletal muscle mass was assessed through bioelectrical impedance analysis, and appendicular skeletal muscle index was calculated. Dominant grip strength was also assessed. Loss of skeletal muscle mass (appendicular skeletal muscle mass < 5.7 kg/m<sup>2</sup>) and muscle weakness (grip strength < 18 kg) were determined based on criteria for sarcopenia put forth by the Asian Working Group for Sarcopenia. The prevalence rates of osteoporosis, muscle weakness, and loss of skeletal muscle mass were 27.2%, 28.7%, and 50.2%, respectively. Loss of skeletal muscle mass was more prevalent in participants with osteoporosis than in those without (65.3% vs. 44.6%,  $p < 0.01$ ). The association between osteoporosis and muscle strength was not significant (30.6% vs. 28.0%,  $p = 0.68$ ). After covariate adjustment, loss of skeletal muscle mass was found to be independently associated with osteoporosis (odds ratio 2.56, 95% confidence interval 1.33–4.91). In sum, osteoporosis was found to be associated with loss of skeletal muscle mass, but not with muscle weakness in community-dwelling older women.

**Scand J Work Environ Health. 2019 Apr 8. pii: 3822. doi: 10.5271/sjweh.3822. [Epub ahead of print]**

### **Postmenopausal breast cancer and occupational exposure to chemicals.**

Videnros C1, Selander J, Wiebert P, Albin M, Plato N, Borgquist S, Manjer J, Gustavsson P.

**Objectives** The aim of this study was to investigate if exposure to chemicals in the workplace was associated with an increased risk of postmenopausal breast cancer. **Methods** The study comprised women born 1923-1950 living in Malmö city, Sweden, 1991-1996, and enrolled for a prospective population cohort study. Occupational exposure to various chemicals was assessed from job-exposure matrices. An extensive set of individual data on hormonal breast cancer risk factors were collected via a baseline questionnaire and used for confounding control. First time diagnoses of invasive breast cancer were identified through the Swedish Cancer Registry until end of follow-up on 31 December 2013. **Results** Of 16 084 women, 1011 were diagnosed with breast cancer. Women exposed to chemicals in their occupational environment had a statistically significant increased risk [adjusted hazard ratio (HR adj) 1.26, 95% confidence interval (CI) 1.02-1.54] of breast cancer, and the risk correlated with duration of exposure. Investigation of risk in association with specific chemicals showed a non-significantly elevated risk after exposure to organic solvents. More than ten years of exposure to diesel exhaust was associated with an increased risk (HR adj 1.69, 95% CI 1.01-2.82). Occupational chemical exposures account for 2% of the breast cancer cases in this population. **Conclusions** Occupational exposure to chemicals in general was associated with an elevated risk of breast cancer. A slight elevation of risk was seen after exposure to organic solvents. A statistically significant elevation of risk after >10 years of exposure to diesel exhaust was an unexpected finding.

**J Cell Biochem. 2019 Apr 8. doi: 10.1002/jcb.28674. [Epub ahead of print]**

## **Loss of p27kip1 suppresses the myocardial senescence caused by estrogen deficiency.**

Yan Y1, Miao D1, Yang Z1, Zhang D1.

Estrogen deficiency accelerates the aging process and increases the risk of developing cardiovascular disease (CVD). Apoptosis is one of the important mechanisms of aging. p27kip1 is a cyclin-dependent kinase inhibitor that can regulate cell cycle, apoptosis, and cell motility. p27kip1 overexpression can inhibit cell cycle and increase apoptosis so it has been considered as a marker of aging. In the present study, bilateral ovariectomy (OVX) was performed as a model for menopause in wild-type (WT) and p27kip1 knockout (KO) mice to assess the effects of p27kip1 loss in myocardial aging caused by estrogen deficiency. We found that myocardial fibrosis and heart weight/body weight ratio of mice in the OVX group and p27kip1 KO group were significantly increased. Echocardiography showed that the left ventricular diameter and volume of the WT OVX group increased significantly and the cardiac function decreased. However, there was no significant difference in the results of echocardiography between the two p27kip1 KO groups. The aging and apoptosis indexes in OVX group were increased significantly, However, the indexes in p27kip1 KO mice were decreased. The expression of antioxidant indexes in OVX group was decreased significantly and p27kip1 KO can improve the antioxidant ability. These results provided that estrogen deficiency increased oxidative stress and apoptosis, accelerated aging of heart. p27kip1 KO can partly delay the aging and apoptosis of heart through upregulated antioxidant enzymes.

**Biomol Concepts. 2019 Apr 3;10(1):44-50. doi: 10.1515/bmc-2019-0005.**

## **Comparison of the effect of vitamin D on osteoporosis and osteoporotic patients with healthy individuals referred to the Bone Density Measurement Center.**

Shahnazari B1, Moghimi J, Foroutan M2, Mirmohammadkhani M3, Ghorbani A4.

**Objective** Osteoporosis is the most common metabolic disease of the bones. Osteoporosis reduces bone density, predisposes a person to fractures, and imposes high costs on societies. Osteoporosis develops from a variety of causes, one of the most significant is vitamin D deficiency. This study investigates the impact of vitamin D on osteoporosis. **Materials and Methods** In this clinical trial, 400 patients referred to the Bone Density Clinic of Kowsar Hospital in Semnan were selected by convenience sampling method. Bone densitometry tests were carried out using DEXA (x-ray absorptiometry) and serum vitamin D levels were measured by the ELISA method. Subjects with vitamin D deficiency were treated for 8 weeks with (50,000 Vitamin D units per week. At the end of the treatment period, all subjects were evaluated for bone density and the results of both groups were compared. **Results** 13% of subjects had osteoporosis and 14.2% had osteopenia. 19% of subjects had vitamin D deficiency, 38.8% had insufficient levels of vitamin D, and 42.3% had sufficient vitamin D levels. The level of vitamin D in patients with osteoporosis ( $5.50 \pm 5.5$  ng/ml) was less than those with osteopenia ( $7.83 \pm 4.8$  ng/ml) and those with normal bone mineral density ( $23.88 \pm 18.42$  ng/ml) ( $P < 0.001$ ). The prevalence of osteoporosis in the intervention group after intervention with vitamin D was significantly lower than the control group (32.3 versus 67.7 and  $P < 0.001$ ). **Conclusion** The prevalence of serum vitamin D deficiency in osteopenic and osteoporotic individuals was higher than in normal subjects, with a significant relationship between age and sex. Thus, treatment with vitamin D improves bone density indices.