



## Selección de Resúmenes de Menopausia

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### **Bone mineral density in primary care patients related to serum calcium concentrations: a longitudinal cohort study from Sweden.**

Dalemo S, Eggertsen R, Hjerpe P, Almqvist EG, Boström KB.

**OBJECTIVE:** Elevated calcium concentration is a commonly used measure in screening analyses for primary hyperparathyroidism (pHPT) and cancer. Low bone mineral density (BMD) and osteoporosis are common features of pHPT and strengthen the indication for parathyroidectomy. It is not known whether an elevated calcium concentration could be a marker of low BMD in suspected pHPT patients with a normal parathyroid hormone concentration.

**PURPOSE:** To study if low BMD and osteoporosis are more common after ten years in patients with elevated compared with normal calcium concentrations at baseline. **DESIGN:** Prospective case control study. **SETTING:**

Primary care, southern Sweden. **SUBJECTS:** One hundred twenty-seven patients (28 men) with baseline elevated, and 254 patients (56 men) with baseline normal calcium concentrations, mean age 61 years, were recruited. After ten years, 77% of those still alive (74 with elevated and 154 with normal calcium concentrations at baseline) participated in a dual energy x-ray absorptiometry measurement for BMD assessment and analysis of calcium and parathyroid hormone concentrations. **MAIN OUTCOME MEASURES:** Association between elevated and normal calcium concentration at base-line and BMD at follow-up. Correlation between calcium and parathyroid hormone concentrations and BMD at follow-up. **RESULTS:** A larger proportion of the patients with elevated baseline calcium concentrations who participated in the follow-up had osteoporosis ( $p$  value=0.036), compared with the patients with normal concentrations. In contrast, no correlation was found between calcium or parathyroid hormone concentrations and BMD at follow-up. **CONCLUSIONS:** In this study, patients with elevated calcium concentrations at baseline had osteoporosis ten years later more often than controls (45% vs. 29%), which highlights the importance of examining these patients further using absorptiometry, even when their parathyroid hormone level is normal. **Key Points**

Osteoporosis is common, difficult to detect and usually untreated. It is not known whether elevated calcium concentrations, irrespective of the PTH level, could be a marker of low bone mineral density. No correlation was found between calcium or parathyroid hormone concentrations and bone mineral density at follow-up. In this study, patients with elevated calcium concentrations at baseline had osteoporosis ten years later more often than controls (45% vs. 29%).

**Osteoporos Int. 2018 Apr 5. doi: 10.1007/s00198-018-4482-0. [Epub ahead of print]**

### **Exercise effects on bone mineral density in older men: a systematic review with special emphasis on study interventions.**

Kemmler W, Shojaa M, Kohl M, von Stengel S.

This systematic review detected only limited positive effects of exercise on bone mineral density in older men. Further, based on the present literature, we were unable to suggest dedicated exercise prescriptions for this male cohort that might differ from recommendations based on studies with postmenopausal women. The primary aim of this systematic review was to determine the effect of exercise on bone mineral density (BMD) in healthy older men. A systematic review of the literature according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement included only randomized or non-randomized controlled trials of exercise training  $\geq 6$  months with study groups of  $\geq$  eight healthy men aged 50 years or older, not using bone-relevant pharmacological therapy, that determined BMD by dual-energy X-ray absorptiometry. We searched PubMed, Scopus, Web of Science, Cochrane, Science Direct, and Eric up to November 2016. Risk of bias was assessed using the PEDro scale. We identified eight trials with 789 participants (PEDro-score, mean value 6 of 10) which satisfied our eligibility criteria. Studies vary considerably with respect to type and composition of exercise. Study interventions of six trials were considered to be appropriate for successfully addressing BMD in this cohort. Between-group differences were not or not consistently reported by three studies. Three studies reported significant exercise effects on BMD for proximal femur; one of them determined significant differences between the exercise groups. None of the exercise trials determined significant BMD effects at the lumbar spine. Based on the present studies, there is only limited evidence for a favorable effect of exercise on BMD

in men. More well-designed and sophisticated studies on BMD in healthy older men have to address this topic. Further, there is a need to define intervention quality standards and implement a universal scoring system that allows this pivotal determinant to be addressed much more intensively.

**Ther Adv Musculoskelet Dis. 2018 Apr;10(4):71-90. doi: 10.1177/1759720X18759291. Epub 2018 Mar 22.**

### **Aromatase inhibitors are associated with a higher fracture risk than tamoxifen: a systematic review and meta-analysis.**

Tseng OL, Spinelli JJ, Gotay CC, Ho WY, McBride ML, Dawes MG.

**Background:** In this paper, our aim was to systematically evaluate published evidence of bone fracture risk associated with tamoxifen and aromatase inhibitors in women aged 65 and under, and diagnosed with nonmetastatic breast cancer. **Methods:** We comprehensively searched MEDLINE, EMBASE and CINAHL databases from January 1997 through May 2015, and reference lists of the selected articles to identify English-language randomized controlled trials and cohort studies of fracture risk. Two independent reviewers screened articles and assessed methodological quality using Risk of Bias assessment for randomized controlled trials and the Newcastle-Ottawa Scale for cohort studies. Fracture risk was estimated as pooled risk ratios using a random-effects model and inverse variance method. **Results:** Of 1926 identified articles, 21 independent studies fulfilled our selection criteria. Similar fracture risk was observed in women treated and not treated with tamoxifen [pooled risk ratio (RR) 0.95; 95% confidence interval (CI) 0.84-1.07]. A 35% (95% CI 1.21-1.51) higher fracture risk was observed in the aromatase inhibitor group compared with the tamoxifen group. A 17% (95% CI 1.07-1.28) higher fracture risk was observed in the aromatase inhibitor group than the no aromatase inhibitor group. Compared with the tamoxifen group, aromatase inhibitor-associated fracture risk increased by 33% (pooled RR 1.33; 95% CI 1.21-1.47) during the tamoxifen/aromatase inhibitor treatment period, but did not increase (pooled RR 0.99; 95% CI 0.72-1.37) during the post-tamoxifen/aromatase inhibitor treatment period. **Conclusions:** Fracture risk is significantly higher in women treated with aromatase inhibitors, especially during the treatment period. Tamoxifen is not associated with lower fracture risk while tamoxifen could potentially preserve bone mass. Better osteoporosis management programs, especially during the treatment period, are needed for this group of women.

**Sleep. 2018 Mar 30. doi: 10.1093/sleep/zsy049. [Epub ahead of print]**

### **Sleep characteristics and inflammatory biomarkers among midlife women.**

Nowakowski S, Matthews KA, von Känel R, Hall MH, Thurston RC.

**Study Objectives:** Research suggests that sleep disturbances are associated with elevated levels of inflammation. Some evidence indicates that women may be particularly vulnerable; increased levels of inflammatory biomarkers with sleep disturbances are primarily observed among women. Midlife, which encompasses the menopause transition, is typically reported as a time of poor sleep. We tested whether poorer objectively measured sleep characteristics were related to a poorer inflammatory profile in midlife women. **Methods:** Two hundred ninety-five peri- and postmenopausal women aged 40-60 completed 3 days of wrist actigraphy, physiologic hot flash monitoring, questionnaires (e.g. Berlin sleep apnea risk questionnaire), and a blood draw for the assessment of inflammatory markers, including C-reactive protein (CRP), interleukin-6 (IL-6), and von Willebrand factor (VWF) antigen. Associations of objective (actigraphy) sleep with inflammatory markers were tested in regression models. Sleep efficiency was inverse log transformed. Covariates included age, race/ethnicity, education, body mass index, sleep apnea risk, homeostatic model assessment (a measure of insulin resistance), systolic blood pressure, low-density lipoprotein cholesterol, and physical activity. **Results:** In separate models controlling for age, race/ethnicity, and education, lower sleep efficiency was associated with higher IL-6 [b(SE) = .02 (.10), p = .003] and VWF [b(SE) = .02 (.08), p = .002]. More minutes awake after sleep onset was associated with higher VWF [b(SE) = .12 (.06), p = .01]. Findings persisted in multivariable models. **Conclusions:** Lower sleep efficiency and more minutes awake after sleep onset were independently associated with higher circulating levels of VWF. Lower sleep efficiency was associated with higher circulating levels of IL-6. These findings suggest that sleep disturbances are associated with greater circulating inflammation in midlife women.

**Ann Oncol. 2018 Mar 29. doi: 10.1093/annonc/mdy097. [Epub ahead of print]**

### **Oral bisphosphonate use and lung cancer incidence among postmenopausal women.**

Tao MH, Chen S, Freudenheim JL, Cauley JA, Johnson KC, Mai X, Sarto GE, Wakelee H, Boffetta P, et al.  
 Background: Bisphosphonates are common medications for the treatment of osteoporosis in older populations. Several studies, including the Women's Health Initiative (WHI), have found inverse associations of bisphosphonate use with risk of breast and endometrial cancer, but little is known about its association with other common malignancies. The objective of this study was to evaluate the association of bisphosphonate use on the incidence of lung cancer in the WHI. Patients and methods: The association between oral bisphosphonate use and lung cancer risk was examined in 151,432 postmenopausal women enrolled into the WHI in 1993-1998. At baseline and during follow-up, participants completed an inventory of regularly used medications including bisphosphonates. Results: After a mean follow-up of 13.3 years, 2,511 women were diagnosed with incident lung cancer. There was no evidence of a difference in lung cancer incidence between oral bisphosphonate users and never users (adjusted hazard ratio (HR), 0.91; 95% confidence intervals (CI), 0.80-1.04; P = 0.16). However, an inverse association was observed among those who were never smokers (HR = 0.57, 95% CI, 0.39-0.84; P < 0.01). Conclusion: In this large prospective cohort of postmenopausal women, oral bisphosphonate use was associated with significantly lower lung cancer risk among never smokers, suggesting bisphosphonates may have a protective effect against lung cancer. Additional studies are needed to confirm our findings.

**J Am Coll Nutr. 2018 Apr 4:1-11. doi: 10.1080/07315724.2018.1431161. [Epub ahead of print]**

## **The Association of Dietary and Urinary Sodium With Bone Mineral Density and Risk of Osteoporosis: A Systematic Review and Meta-Analysis.**

Fatahi S, Namazi N, Larijani B, Azadbakht L.

**OBJECTIVE:** Although some earlier studies have indicated an association between dietary/urinary sodium and bone mass density (BMD), bone mass content (BMC), and the risk of osteoporosis (OS), findings are still conflicting. The aim of this study was to summarize the relation of dietary/urinary sodium with BMD, BMC, and the risk of OS. **METHODS:** We conducted a systematic search up to April 2017 in PubMed/MEDLINE, SCOPUS, and Web of Science to find relevant studies. Articles with cross-sectional and cohort designs in which odds ratios (ORs), correlations ( $r$ ), or beta coefficients were reported for the association between dietary/urinary sodium and OS, BMD, or BMC were included. **RESULTS:** Pooling 11 effect sizes with a total of 39,065 people showed that higher sodium consumption significantly increased the risk of OS (OR = 1.20; 95% confidence interval [CI], 1.02-1.41;  $p = 0.026$ ), with high heterogeneity among studies ( $I^2 = 68.0\%$ ;  $p = 0.001$ ). Subgroup analyses showed significantly higher risk of OS in premenopausal women (OR = 1.31; 95% CI, 1.01-1.69;  $p = 0.036$ ), in participants with a mean age older than 50 years (OR = 1.15; 95% CI, 1.04-1.28;  $p = 0.005$ ), in dietary sodium intake subgroup (OR = 1.45; 95% CI, 1.19-1.77;  $p < 0.001$ ), and in individuals with adjustment for energy (OR = 1.77; 95% CI, 1.38-2.27;  $p < 0.001$ ). The correlation coefficients showed no significant association between urinary sodium and BMD ( $r = -0.46$ ; 95% CI, -0.74 to -0.18;  $p = 0.02$ ). **CONCLUSIONS:** We found a positive association between sodium intake and the risk of OS, while no association was found with urinary sodium. Furthermore, there was no significant correlation between sodium intake and BMD. Due to high heterogeneity in this research, more studies are suggested.

**Menopause. 2018 Apr 2. doi: 10.1097/GME.0000000000001105. [Epub ahead of print]**

## **Hormone therapy in menopausal women with fibroids: is it safe?**

Srinivasan V1, Martens MG.

Menopause is an important transition in the life of women. It has been estimated that by the year 2030, worldwide 1.2 billion women will be menopausal. The most bothersome symptoms of menopause are believed to be due to declines in estrogen levels in postmenopausal women. Thus, hormone therapy is an effective treatment option for menopausal women, although prolonged use of hormone therapy is associated with a slightly increased risk of breast cancer, thromboembolism, and stroke. A literature search for studies evaluating the effects of hormone therapy in menopausal women with asymptomatic fibroids demonstrated variable effects of hormone therapy on the volume and size of the fibroids. Some studies have demonstrated an increase in size of pre-existing asymptomatic fibroids and formation of new fibroids with higher doses of progestogen in combination therapy. The finding of low resistance index in uterine arteries of women with asymptomatic fibroids is associated with an increased risk of fibroid growth, and thus making the measurement of pulsatility index of uterine arteries a possible screening tool before initiating hormone therapy in menopausal women with fibroids. Although the effect of hormone treatment is variable and statistically insignificant in many cases, the newer selective estrogen receptor modulators having tissue-specific estrogen agonistic and

antagonistic actions such as raloxifene have a favorable clinical profile and may be better alternatives in women with asymptomatic fibroids.

**Fertil Steril. 2018 Mar 28. pii: S0015-0282(17)32112-X. doi: 10.1016/j.fertnstert.2017.11.035. [Epub ahead of print]**

### **Estrogen deprivation and cardiovascular disease risk in primary ovarian insufficiency.**

Christ JP1, Gunning MN2, Palla G3, Eijkemans MJC4, Lambalk CB5, Laven JSE6, Fauser BCJM2.

**OBJECTIVE:** To evaluate the association between estrogen (E) exposure and deficiency and cardiovascular disease (CVD) risk among women with primary ovarian insufficiency (POI). **DESIGN:** Cross-sectional study conducted between 1996 and 2016. **SETTING:** Tertiary referral centers. **PATIENT(S):** A total of 385 women with POI, defined by amenorrhea and FSH levels  $\geq 40$  IU/L before 40 years of age, were recruited. **INTERVENTION(S):** None. **MAIN OUTCOME MEASURE(S):** Women underwent a standardized intake questionnaire including data on menstrual cyclicity. Lifetime E exposure and E-free period were assessed. Serum was analyzed for endocrine and CVD profiles. The Framingham 30-year risk of CVD was calculated. **RESULT(S):** Lifetime E exposure (mean  $\pm$  SD) was  $19.3 \pm 7.0$  years, E-free period was  $3.1 \pm 4.1$  years, and age at screening was  $34.8 \pm 7.4$  years. In multivariate models E-free interval associated positively with estimated risk of hard and general CVD events ( $\beta$  0.18 [95% confidence interval 0.08, 0.29]; 0.20 [0.05, 0.35], respectively), and lifetime E exposure associated negatively with estimated risk of hard and general CVD events ( $-0.15$  [ $-0.24, -0.05$ ];  $-0.16$  [ $-0.29, -0.03$ ], respectively), as well as low density lipoprotein cholesterol ( $-0.03$  [ $-0.06, 0.00$ ]) and non-high density lipoprotein cholesterol ( $-0.04$  [ $-0.07, 0.00$ ]). **CONCLUSION(S):** Prolonged E deprivation is associated with an increased estimated risk of CVD, whereas prolonged E exposure is associated with a reduced estimated risk. These results support the policy of early and continued use of E replacement therapy in women with POI.