



## Selección de Resúmenes de Menopausia

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**Psychoneuroendocrinology. 2016 Aug 3;73:224-243. doi: 10.1016/j.psyneuen.2016.08.003. [Epub ahead of print]**

### **Age at menopause and duration of reproductive period in association with dementia and cognitive function: A systematic review and meta-analysis.**

Georgakis MK, Kalogirou EI, Diamantaras AA, Daskalopoulou SS, Munro CA, Lyketsos CG, Skalkidou A, Petridou  
INTRODUCTION: The preponderance of dementia among postmenopausal women compared with same-age men and the female sex hormones neuroprotective properties support a tentative role of their deficiency in the dementia pathogenesis. METHODS: Pairs of independent reviewers screened 12,323 publications derived from a search strategy for MEDLINE to identify articles investigating the association of age at menopause/reproductive period with (i) dementia and (ii) cognitive function; a snowball of eligible articles and reviews was conducted and authors were contacted for additional information. Random-effect models were used for the meta-analysis. RESULTS: Age at menopause (13 studies; 19,449 participants) and reproductive period (4 studies; 9916 participants) in the highest categories were not associated with odds of dementia (effect size [ES]: 0.97 [0.78-1.21]) and Alzheimer's disease (ES: 1.06 [0.71-1.58]). Significant heterogeneity was however noted in both analyses (I<sup>2</sup>: 63.3%,  $p=0.003$  and I<sup>2</sup>: 72.6%,  $p=0.01$ , respectively). Subgroup analyses by outcome assessment, study design, level of adjustment and study quality did not materially change the findings. In 9/13 studies assessing cognitive function, advanced age at menopause/longer reproductive period was significantly associated with better cognitive performance/lower decline. Due to statistical differences, no meta-analysis was possible for cognitive function. CONCLUSIONS: Existing evidence does not support an association between indices of prolonged exposure to female hormones and lower dementia risk. There are indications, however, for better cognitive performance and delayed cognitive decline, supporting a link between female hormone deficiency and cognitive aging. Current literature limitations, indicated by the heterogeneous study-set, point towards research priorities in this clinically relevant area.

**Osteoporos Int. 2016 Aug 20. [Epub ahead of print]**

### **Acute effects of calcium supplements on blood pressure: randomised, crossover trial in postmenopausal women.**

Billington EO, Bristow SM, Gamble GD, de Kwant JA, Stewart A, Mihov BV, Horne AM, Reid IR.

INTRODUCTION: Calcium supplements appear to be associated with increased cardiovascular risk; however, the mechanism of this is uncertain. We previously reported that blood pressure declined over a day in older women, and that this reduction was smaller following a calcium supplement. To confirm this finding, we investigated the acute effects of calcium supplements on blood pressure. METHODS: This was a randomised controlled crossover trial in 40 healthy postmenopausal women (mean age 71 years and BMI 27.2 kg/m<sup>2</sup>). Women attended on two occasions, with visits separated by  $\geq 7$  days. At each visit, they received either 1 g of calcium as citrate, or placebo. Blood pressure and serum calcium concentrations were measured immediately before, and 2, 4 and 6 h after each intervention. RESULTS: Ionised and total calcium concentrations increased after calcium ( $p < 0.0001$  versus placebo). Systolic blood pressure decreased after both calcium and placebo, but significantly less so after calcium ( $p = 0.02$ ). The reduction in systolic blood pressure from baseline was smaller after calcium compared with placebo by 6 mmHg at 4 h ( $p = 0.036$ ) and by 9 mmHg at 6 h ( $p = 0.002$ ). The reduction in diastolic blood pressure was similar after calcium and placebo. CONCLUSIONS: These findings are consistent with those of our previous trial and indicate that the use of calcium supplements in postmenopausal women attenuates the post-breakfast reduction in systolic blood pressure by around 6-9 mmHg. Whether these changes in blood pressure influence cardiovascular risk requires further study.

**Climacteric. 2016 Aug 18:1-6. [Epub ahead of print]**

### **The effect of surgical menopause on the intima-media thickness of the carotid and coronary arteries.**

Ozdemirci S, Kasapoglu T, Dilbaz B, Salgur F, Duran B, Koc O, Unverdi H, Hucumenoglu S.

**OBJECTIVE:** To evaluate the effect of prior bilateral oophorectomy on the intima-media thickness (IMT) of coronary and carotid arteries. **METHODS:** A total of 25 Wistar albino rats, aged 8-10 weeks, were assigned to three groups: ovariectomized (n = 10), control (n = 10) and sham (n = 5). The rats in the sham group only underwent midline laparotomy, while the other rats' ovaries were removed by the same type of laparotomy. All rats were sacrificed to evaluate microscopically the impact of a prolonged 26-week surgical menopause (menopausal period) on the IMT of the carotid and coronary arterial structure. **RESULTS:** The mean IMTs of both the carotid and coronary arteries in the ovariectomized group were significantly thicker than those of the control and sham groups (carotid arteries:  $268.69 \pm 53.67$ ,  $195.61 \pm 47.60$  and  $193.86 \pm 75.01$   $\mu\text{m}$ ,  $p = 0.014$ ; coronary arteries:  $182.40 \pm 30.22$ ,  $136.00 \pm 35.82$  and  $165.24 \pm 40.68$   $\mu\text{m}$ ,  $p = 0.022$ , respectively). **CONCLUSION:** According to the results of this study, surgical menopause results in a noteworthy increase in the IMT of the carotid and coronary arteries when compared with the controls. This interventional effect may have a significant role in accelerating the process of atherosclerosis.

**Bone. 2016 Aug 12. pii: S8756-3282(16)30229-0. doi: 10.1016/j.bone.2016.08.010. [Epub ahead of print]**

### **The effect of bisphosphonate treatment on osteoclast precursor cells in postmenopausal osteoporosis: The TRIO study.**

Gossiel F, Hoyle C, McCloskey EV, Naylor KE, Walsh J, Peel N, Eastell R.

Bisphosphonates are used to treat bone disease characterised by increased bone resorption by inhibiting the activity of mature osteoclasts, resulting in decreased bone turnover. Bisphosphonates may also reduce the population of osteoclast precursor cells. Our aims were to investigate the effect of bisphosphonates on i) osteoclast precursor cells and ii) circulating cytokine and cytokine receptor in postmenopausal women with osteoporosis compared with healthy premenopausal women. Participants were 62 postmenopausal women (mean age 66) from a 48-week parallel group trial of bisphosphonates. They received ibandronate 150mg/month (n=22), alendronate 70mg/week (n=19) or risedronate 35mg/week (n=21). Fasting blood was collected at baseline, weeks 1 and 48. At baseline, blood was also collected from 25 healthy premenopausal women (mean age 37) to constitute a control group. Peripheral blood mononuclear cells were extracted and stained for CD14, M-CSFR, CD11b and TNFR2 receptors. Flow cytometry was used to identify cells expressing CD14+ and M-CSF+ or CD11b+ or TNFR2+. RANKL and OPG were measured to evaluate potential mediation of the bisphosphonate effect. After 48 weeks of treatment, there was a decrease in the percentage of cells expressing M-CSFR and CD11b receptors by 53% and 49% respectively ( $p < 0.01$ ). Cells expressing M-CSFR and CD11b were decreased with ibandronate and risedronate after 48 weeks to the lower part of the premenopausal reference interval. These effects were not significantly different between each of the treatment groups. There was no significant effect on RANKL and OPG throughout the study period. Bisphosphonates inhibit bone resorption in the short-term by direct action on mature osteoclasts. There is also a later effect mediated in part by a reduction in the population of circulating osteoclast precursors.

**Semin Arthritis Rheum. 2016 Jul 26. pii: S0049-0172(16)30141-X. doi: 10.1016/j.semarthrit.2016.07.011. [Epub ahead of print]**

### **Calcium supplementation and inflammation increase mortality in rheumatoid arthritis: A 15-year cohort study in 609 patients from the Oslo Rheumatoid Arthritis Register.**

Provan SA, Olsen IC, Austad C, Haugeberg G, Kvien TK, Uhlig T.

**OBJECTIVE:** To investigate whether osteoporosis or use of calcium supplementations predict all-cause mortality, or death from CVD, in a longitudinal cohort of patients with rheumatoid arthritis (RA). **METHODS:** Patients in the Oslo RA register (ORAR) were examined, and bone mineral density was measured in 1996. The cohort was linked to the Norwegian Cause of Death registry on December 31, 2010. Death from CVD was defined in 3 following different outcomes: (1) primary atherosclerotic death, (2) atherosclerotic death as one of the 5 listed causes of death, and (3) CVD according to World Health Organization (WHO) definition as primary cause of death. Baseline predictors of all-cause mortality and death from CVD were identified in separate Cox regression models, using backwards selection. Sensitivity analyses were performed including analyses of interactions and competing risk. **RESULTS:** A total of 609 patients were examined in 1996/1997. By December 31, 2010, 162 patients (27%) had died, resulting in 7439 observed patient-years. Of the deceased, 40 (24.7%) had primary atherosclerotic death. In the

final model of all-cause mortality increased baseline ESR [hazard ratio (HR) 1.02 per mm/h, 95% CI: 1.01-1.03], calcium supplementation (1.74, 1.07-2.84), and osteoporosis, defined as a T score  $\leq$ 2.5 SD at any location, (1.58, 1.07-2.32) predicted higher mortality rates, in models adjusted for age, gender, and a propensity score. In the final model of primary atherosclerotic death, increased ESR (1.03 per mm/h, 1.01-1.05) and calcium supplementation (3.39, 1.41-8.08), predicted higher mortality.

CONCLUSIONS: Increased baseline ESR and use of calcium supplementation were predictors of increased all-cause mortality and risk of death from CVD in this longitudinal study of patients with RA.

**Endocrine. 2016 Aug 11. [Epub ahead of print]**

### **Efficacy of menopausal hormone therapy on sleep quality: systematic review and meta-analysis.**

Cintron D, Lipford M, Larrea-Mantilla L, Spencer-Bonilla G1, Lloyd R, Gionfriddo MR, Gunjal S, Farrell AM, Miller

Sleep complaints are reported by 40-60 % of menopausal women. Poor sleep is a risk factor for cardiovascular disease, diabetes, and obesity. The effect of menopausal hormone therapy on sleep quality is unclear. A systematic review and meta-analysis were conducted to summarize the efficacy of menopausal hormone therapy on self-reported sleep quality. Electronic databases (PubMed, Scopus, Ovid MEDLINE, EMBASE, EBM Reviews CENTRAL, and PsycInfo) were searched from 2002 to October 2015. Randomized trials assessing the effect of menopausal hormone therapy with a minimum follow up of 8 weeks were included. Titles, abstracts, and full texts were screened independently and in duplicate. Primary outcome included sleep items within a questionnaire, scale or diary. Standardized mean differences across trials were pooled using random-effects models. The search identified 424 articles, from which 42 trials were included. Seven trials at a moderate to high risk of bias enrolling 15,468 women were pooled in meta-analysis. Menopausal hormone therapy improved sleep quality in women who had vasomotor symptoms at baseline [standardized mean difference -0.54 (-0.91 to -0.18), moderate quality evidence]. No difference was noted when women without such symptoms were analyzed separately or combined. Across 31 sleep quality questionnaires, daytime dysfunction was the most evaluated sleep domain. Menopausal hormone therapy improves sleep in women with concomitant vasomotor symptoms. Heterogeneity of trials regarding study population, formulations, and sleep scales; limit overall certainty in the evidence. Future menopausal hormone therapy trials should include assessment of self-reported sleep quality using standardized scales and adhere to reporting guidelines.