# Selección de Resúmenes de Menopausia

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## Effects of Advanced Glycation End Products on Differentiation and Function of Osteoblasts and Osteoclasts

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Background: Risk of fragility fractures increases in patients with diabetes mellitus, independent of bone mineral density. In the present study, the effects of advanced glycation end products (AGEs) on differentiation and function of osteoblasts and osteoclasts were investigated. Methods: AGEs and 25 mM glucose were administered to marrow-derived macrophages and MCT3T3-E1 cells. The effects of AGEs on osteoclast differentiation was investigated using tartrate-resistant acid phosphatase (TRAP) assay. The effects of AGEs on osteoblast differentiation was investigated using alkaline phosphatase (ALP) activity and bone nodule formation assays. Expression of osteoclast-specific and osteoblast-specific genes and effects on cell signaling pathways associated with cell differentiation were analyzed using reverse transcription polymerase chain reaction and western blotting. Results: AGEs significantly decreased TRAP-positive multinucleated cell formation in receptor activator of nuclear factor-κB ligand-induced marrow-derived macrophages in a dose-dependent manner. AGEs suppressed the expression of osteoclast-specific genes, JNK, p38, AKT, intercellular adhesion molecule 1, and lymphocyte function-associated antigen 1 in marrow-derived macrophages. AGEs decreased ALP activity and showed a tendency to decrease bone nodule formation in MC3T3-E1 cells. AGEs suppressed the expression of osteoblast-specific genes, lysyl hydroxylase and lysyl oxidase in MC3T3-E1 cells. Conclusion: AGEs suppressed differentiation and function of osteoclasts and osteoblasts, and collagen cross-linking activity. It suggests that AGE may induce bone fragility through low bone turnover and deterioration of bone quality.

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## Menopausal hormone therapy and risk of incident hypertension: role of the route of estrogen administration and progestogens in the E3N cohort

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Objectives: Although menopausal hormone therapy (MHT) remains the most effective treatment for vasomotor symptoms of menopause, its association with the development of arterial hypertension remains unclear. We sought to explore associations between different formulations of MHT and incident hypertension among menopausal women in a prospective cohort study. Methods: We used the Etude Epidémiologique de femmes de la Mutuelle Générale de l'Education (E3N) cohort, a French prospective population-based study initiated in 1990 on 98,995 women. Out of these, 49,905 menopausal women with complete information on the use of MHT, and without prevalent hypertension at inclusion were included. Results: The mean age of the population at baseline was 54.2 ± 4.3 years, and 32,183 (64.5%) reported ever using MHT. Among these women, 10,173 cases of incident hypertension were identified over an average follow-up time of 10.6 years. Compared with women who never used MHT, those who ever used it had an increased risk of incident hypertension (adjusted HR 1.07, 95% CI 1.02-1.12) after adjustment for body mass index and other potential confounders. Oral but not transdermal estrogen use was associated with an increased risk of hypertension (adjusted HR = 1.09; 95% CI: 1.04-1.14 and HR = 1.03; 95% CI: 0.99-1.07, respectively). However, the HRs associated with oral and transdermal estrogens did not differ significantly (P-homogeneity = 0.09). Regarding the role of concomitant progestogens, pregnane and norpregnane derivatives were significantly associated with hypertension risk (HR = 1.12; 95% CI: 1.06-1.19 and HR = 1.06; 95% CI: 1.01-1.13, respectively). Conclusions: MHT was associated with a modest but significant increased risk of incident hypertension, especially when using oral estrogen in combination with a progestogen such as pregnane and norpregnane derivatives. Surveillance of blood pressure should be added to the medical surveillance of MHT users.

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## Cross-sectional study on the impact of age, menopause and quality of life on female sexual function

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We sought to determine the prevalence of female sexual dysfunction (FSD) and to examine the influence of age, menopausal state and quality of life (QoL) on the female sexual function (FSF) of healthy women and those with benign gynaecological disease. With this purpose, we conducted a cross-sectional study, based on self-report questionnaires (sociodemographic, WHOQOL-BREF and FSFI), enrolling 107 women. Some 51.6% (n = 55) were diagnosed with FSD. We found no statistical significant differences between grouped reason for consultation and FSFI total score (p = .72) and its domains (p > .05). The results showed a negative strong correlation between age and FSFI total score (S= -0.71) and a positive moderate correlation between WHOQOL-BREF and FSFI total scores (S = 0.39). We observed statistically significant differences between menopausal state and FSFI total score (p = .001). In conclusion, the prevalence of FSD in our population was 51.6%. Our study results reveal that a reduction in FSFI scores has a negative impact on QoL and vice versa, regardless of the reason for consultation. Elderly age and postmenopausal state have deleterious effects on FSF.Impact statementWhat is already known on this subject? Poor QoL can adversely affect FSF and vice versa. The study of FSF is relatively recent and there is controversy regarding the deleterious effects of elderly age and menopause on FSF. The prevalence of FSD is difficult to precisely determine, given the studies' use of different definitions for FSD and the highly heterogeneous study populations, as well as the types of tests and questionnaires employed. Sexual difficulties are problems seldom discussed between patients and their physicians. Lack of time, misconceptions, shame and frustration, considering sexuality as too intimate to discuss in the doctor's office, uncertainty regarding therapeutic options and insufficient training of health professionals are just some of the reasons mentioned for not addressing sexual dysfunction in a general consultation. What do the results of this study add? Our study is the first research in Spain on the impact of age, menopause and QoL on gynaecological patients´ FSF. Our results indicate that an impaired FSF could be related to poorer well-being and QoL; however, benign gynaecological disease does not appear to affect FSF. Elderly age and postmenopausal state can have deleterious effects on FSF.What are the implications of these findings for clinical practice and/or further research? Sexuality is an important aspect of QoL. Therefore, gynaecologists should discuss issues of sexuality with their patients in routine visits, especially in case of elderly and postmenopausal women. In addition, gynaecologists should train in the diagnosis and treatment of the female sexual dysfunction.

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## Treatment of osteoporosis after hip fracture is associated with lower all-cause mortality: A nationwide population study

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Purpose: Mortality after osteoporotic hip fractures is high. Postoperative care is as important as surgery itself to prevent a second fracture and improve outcomes, and the effect of anti-osteoporosis treatment after hip fractures on overall mortality is controversial. This nationwide population study aimed to determine whether anti-osteoporosis treatment might reduce overall mortality after hip fracture surgery. Methods: We conducted this cohort study using the National Health Insurance Research Database (NHIRD) of Taiwan to identify patients admitted for surgery due to hip fractures from 2008 to 2018. The subsequent use and duration of anti-osteoporotic medication and other parameters were analyzed, and national death registration records were retrieved to investigate mortality. Results: A total of 59,943 patients admitted for hip fracture surgery were identified. The 22,494 patients (37.5%) who received anti-osteoporotic medication showed a lower all-cause mortality rate compared with the 37,449 patients (62.5%) who did not receive further treatment (hazard ratio (HR): 0.69, 95% confidence interval (CI): 0.67-0.70, p < 0.0001). Patients who received anti-osteoporotic medication for more than 1, 2, and 3 years exhibited 0.57 (0.54-0.60), 0.42 (0.38-0.46), and 0.29 (0.26-0.33) fold reductions in all-cause mortality, respectively. Conclusion: Anti-osteoporosis treatment was associated with lower all-cause mortality after hip fracture surgery. A longer duration of treatment was also associated with lower mortality. Postoperative osteoporosis is crucial for patients with hip fracture.

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## The associations of statin intake and the trabecular bone score and bone mineral density status in elderly Iranian individuals: a cross-sectional analysis of the Bushehr Elderly Health (BEH) program

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Introduction: In recent years, a growing interest has been established to evaluate the impact of statin intake on bone health, although the reported results are controversial. This study aimed to evaluate the association of statin intake with bone health status according to BMD and TBS. Methods: This cross-sectional analysis used data from the elderly Iranian individuals who participated in the Bushehr Elderly Health (BEH) program. Dual x-ray absorptiometry (DXA) device was used to evaluate the BMD at lumbar spine (L1-L4), femoral neck, and total hip, as well as TBS at lumbar spine. Results: Among 2426 (1260 women and 1166 men) study participants, 778 were statin users. A positive significant association, irrespective of sex, was observed between statin intake and BMD at L1-L4, even after controlling for potential variables in total population ($\beta = 0.016$, $p = 0.013$). The mean TBS values at L1-L4 were negatively associated with statin intake in total population ($\beta = - 0.009$, $p = 0.001$), while in the full adjusted model, significant positive association between TBS and statin intake was detected only in men ($\beta = 0.013$, $p = 0.02$). Conclusion: The results of this study revealed that BMD at lumbar spine has a significant association with statin intake. However, such an association appears to be weaker regarding TBS values compared to BMD.

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## Ovarian Cancer Incidence and Death in Average-Risk Women Undergoing Bilateral Salpingo-Oophorectomy at Benign Hysterectomy

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Background: Opportunistic bilateral salpingo-oophorectomy (BSO) is often offered to patients undergoing benign hysterectomy to prevent ovarian cancer, but the magnitude of risk reduction obtained with BSO in this population remains unclear, and must be weighed against potential risks of ovarian hormone deficiency. Objective: To quantify the relative and absolute risk reduction in ovarian cancer incidence and death associated with BSO at the time of benign hysterectomy. Study design: We performed a population-based cohort study of all adult women (>20 years) undergoing benign hysterectomy from 1996 to 2010 in Ontario, Canada. Patients with ovarian pathology, prior breast/gynecologic cancer, or evidence of genetic susceptibility to malignancy were excluded. Inverse probability of treatment weighted Fine & Gray subdistribution hazard models were used to quantify the effect of BSO on ovarian cancer incidence and death, while accounting for competing risks and adjusting for demographic characteristics, gynecologic conditions, and comorbidities. Analyses were performed in all women, and specifically in women of postmenopausal age (>50 years) at the time of hysterectomy. Results: We identified 195,282 patients (BSO 24%; ovarian conservation 76%) with median age 45 years (interquartile range [IQR] 40-51). Over median follow-up of 16 years (IQR 12-20), 548 patients developed ovarian cancer (0.3%) and 16,170 died (8.3%) from any cause. BSO was associated with decreased ovarian cancer incidence (HR 0.23, 95% CI 0.14-0.38, $p<0.001$) and decreased ovarian cancer death (HR 0.30, 95% 0.16-0.57, $p<0.001$). At 20 years follow-up, the weighted cumulative incidence of ovarian cancer was 0.08% and 0.46% with BSO and ovarian conservation respectively, yielding an absolute risk reduction [ARR] of 0.38% (95% CI 0.32-0.45; number needed to treat [NNT] 260). After restricting to women aged >50 years at hysterectomy, the ARR was 0.62% (95% CI 0.47-0.77; NNT 161). Conclusion: BSO results in a significant absolute reduction in ovarian cancer among women undergoing benign hysterectomy. Population-average risk estimates derived in this study should be balanced against other potential implications of BSO in order to inform practice guidelines, patient decision-making, and surgical management.