# Selección de Resúmenes de Menopausia

Semana del 24 al 31 de Julio de 2018

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## Persistence of excess mortality following individual non-hip fractures: A relative survival analysis.

Tran T, Bliuc D, Hansen L, Abrahamsen B, van den Bergh J, Eisman JA, van Geel T, Geusens P, et al.

Little is known about long-term excess mortality following fragility non-hip fractures. Objective: The study aimed to determine which fracture was associated with excess mortality, and for how long the post-fracture excess mortality persisted. Design, Setting, and Patients: This nationwide, registry-based follow-up study included all individuals in Denmark aged 50+ years who first experienced fragility fractures in 2001 and were followed up to 10 years for their mortality risk. Main outcome measure: The contribution of fracture to mortality at precise time intervals post-fracture was examined using relative survival analysis, accounting for time-related mortality changes in the background population. Results: There were 21123 women (aged 72± 13 years) and 9481 men (67±12) with an incident fragility fracture in 2001 followed by 10668 and 4745 deaths, respectively. Excess mortality was observed following all proximal and lower leg fractures. The majority of deaths occurred within the first year post-fracture and thereafter excess mortality gradually declined. Hip fractures were associated with the highest excess mortality (33% and 20% at one year post-fracture in men and women, respectively). One-year excess mortality was 20-25% after femur or pelvis, 10% following vertebral, 5-10% following humerus, rib or clavicle, and 3% following lower leg fractures. A significant- although smaller- excess mortality was still observed until 10 years for hip, and approximately 5 years after femur, other proximal and lower leg fractures. Conclusion: This study highlights the important contribution of a wide variety of fragility fractures to long-term excess mortality, and thus the potential for benefit from early intervention.

Adv Exp Med Biol. 2018;1065:433-454. doi: 10.1007/978-3-319-77932-4_27.

## Sex-Specific Physiology and Cardiovascular Disease.

Shufelt CL, Pacheco C, Tweet MS, Miller VM.

Sex differences in cardiovascular diseases can be classified as those which are specific to one sex and those that differ in incidence, prevalence, etiology, symptomatology, response to treatment, morbidity, and mortality in one sex compared to the other. All sex differences in cardiovascular conditions have their basis in the combined expression of genetic and hormonal differences between women and men. This chapter addresses how understanding basic mechanisms of hormone responses, imaging diagnostics, and integration of genomics and proteomics has advanced diagnosis and improved outcomes for cardiovascular conditions, apart from those related to pregnancy that are more prevalent in women. These conditions include obstructive coronary artery disease, coronary microvascular dysfunction, spontaneous coronary artery dissection, diseases of the cardiac muscle including heart failure and takotsubo cardiomyopathy, and conditions related to neurovascular dysregulation including hot flashes and night sweats associated with menopause and effects of exogenous hormones on vascular function. Improvement in technologies allowing for noninvasive assessment of neuronally mediated vascular reactivity will further improve our understanding of the basic etiology of the neurovascular disorders. Consideration of sex, hormonal status, and pregnancy history in diagnosis and treatment protocols will improve prevention and outcomes of cardiovascular disease in women as they age.

Maturitas. 2018 Sep;115:1-22. doi: 10.1016/j.maturitas.2018.05.010. Epub 2018 Jun 5.

## Vitamin D and cardiovascular disease.

Apostolakis M, Armeni E, Bakas P, Lambrinoudaki I.

Vitamin D, a soluble steroid hormone synthesized in the skin after sun exposure, plays a crucial role in calcium metabolism and is also involved in cardiovascular pathophysiology. The aim of this review is to summarize the available evidence (a) on the association between endogenous vitamin D status and cardiovascular disease, and (b) on the effect of vitamin D supplementation on cardiovascular outcomes. Most studies have shown an inverse

association between vitamin D levels and cardiovascular outcomes. Randomized controlled trials, however, do not consistently support a beneficial effect of vitamin D administration on cardiovascular health. Population characteristics, comorbid conditions such as diabetes, the overall population prevalence of cardiovascular disease, vitamin D status and the regimen of vitamin D supplementation may account for the conflicting results.

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## Weight loss and metabolic health effects from energy-restricted Mediterranean and Central-European diets in postmenopausal women: A randomized controlled trial.

Bajerska J, Chmurzynska A, Muzsik A, Krzyżanowska P, Mądry E, Malinowska AM, Walkowiak J.

We conducted a randomized controlled trial to examine the effect of two energy-restricted diets on body weight (BW), visceral fat (VF) loss, and the risk factors for metabolic syndrome. A total of 144 centrally obese postmenopausal women were assigned to the moderate in fat Mediterranean diet (MED) or to the Central European diet (CED), which is moderate in carbohydrates and high in dietary fiber (DF), for 16 weeks. BW, waist circumference and VF were significantly reduced by 8.8%, 7.0%, and 24.6%, respectively, over the trial ($P < 0.001$), with no difference between groups. A similar trend was seen for total cholesterol, triglycerides, glucose, and blood pressure. Within each diet group, the more adherent participants lost significantly more BW than did their less adherent counterparts. VF was significantly reduced only in women who were more adherent to the CED, and the reduction in VF correlated with an increase in the proportion of DF. Short-term dietary treatment with the CED or the MED was associated with similar improvements in some anthropometric, lipid, and nonlipid parameters; however, adequate adherence to the prescribed diet is important in weight loss success and in achieving improvements in metabolic health.

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## Does AMH relate to timing of menopause? Results of an Individual Patient Data meta- analysis.

Depmann M, Eijkemans MJC, Broer SL, Tehrani FR, Solaymani-Dodaran M, Azizi F, Lambalk CB, et al.

Context: Anti-Müllerian hormone based (AMH) age at menopause predictions remain cumbersome due to predictive inaccuracy. Objective: To perform an Individual Patient Data (IPD) meta-analysis, regarding AMH based menopause prediction. Data sources: A systematic literature search was performed using PubMed, Embase and Cochrane databases. Study selection: Prospective cohort studies regarding menopause prediction using serum AMH levels were selected by consensus discussion. Data selection: Individual cases were included if experiencing a regular cycle at baseline. Exclusion criteria were hormone use and gynecological surgery. Data synthesis: 2596 women were included, 1077 experienced menopause. A multivariable Cox regression analysis assessed time to menopause (TTM) using age and AMH. AMH predicted TTM, however, added value on top of age was poor (age alone C-statistic 84%; age + AMH HR 0.66 95% CI 0.61-0.71, C-statistic 86%). Moreover, the capacity of AMH to predict early (≤45 years) and late menopause (≥55 years) was assessed. An added effect of AMH was demonstrated for early menopause (age alone C-statistic 52%; age + AMH HR 0.33, 95% CI 0.24-0.45, C-statistic 80%). A Weibull regression model calculating individual age at menopause revealed that predictive inaccuracy remained present and increased with decreasing age at menopause. Lastly, a check of non-proportionality of the predictive effect of AMH demonstrated a reduced predictive effect with increasing age. Conclusion: AMH was a significant predictor of TTM and especially of time to early menopause. However, individual predictions of age at menopause demonstrated a limited precision, particularly when concerning early age at menopause, making clinical application troublesome.

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## A ten-year prospective study of bone mineral density and bone turnover in males and females with type 1 diabetes.

Hamilton EJ, Drinkwater JJ, Chubb SAP, Rakic V, Kamber N, Zhu K, Prince RL, Davis WA, Davis TME.

Context: In a previous community-based, cross-sectional study, males with type 1 diabetes had lower bone mineral density (BMD) than matched people without diabetes but females with type 1 diabetes had normal BMD. Objective:

To determine whether BMD in the males continued to decline, the neutral effect of type 1 diabetes on BMD in females persisted, and temporal BMD changes reflected changes in bone turnover markers. Design: Longitudinal observational study. Setting: Urban community. Patients: 48 of the original 102 original cross-sectional study participants (20 males, 28 females) of mean age 42.0 years and median diabetes duration 14.6 years at baseline who were restudied a mean of 10.3 years later. Main outcome measures: BMD at total hip, femoral neck, lumbar spine (L1-L4) and distal forearm. Biochemical bone turnover markers. Results: After adjustment for age, body mass index (BMI) and renal function, there was no temporal change in BMD at the hip or forearm in the males ($P \geq 0.12$), but lumbar spine BMD increased ($P = 0.009$). Females exhibited no statistically significant change in BMD in similar multivariable models that also included postmenopausal status, except a mild increase at the forearm ($P = 0.046$). Age- and sex-related changes in bone turnover markers paralleled those in general population studies. Conclusions: There is a reduction in BMD in males with type 1 diabetes that occurs early in the course of the disease but which then stabilizes. BMD in females with type 1 diabetes remains similar to that expected for age, BMI and postmenopausal status.

**BMC Endocr Disord. 2018 Jul 21;18(1):48. doi: 10.1186/s12902-018-0277-8.**

## The effects of single high-dose or daily low-dosage oral colecalciferol treatment on vitamin D levels and muscle strength in postmenopausal women.

Apaydin M, Can AG, Kizilgul M, Beysel S, Kan S, Caliskan M, Demirci T, Ozcelik O, Ozbek M, Cakal E.

INTRODUCTION: Vitamin D deficiency is a common health problem. Vitamin D supplements are used to improve vitamin D status; however, there are contradictory data related to what doses to give and how often they should be given. Many studies have investigated the effects of vitamin D supplementation on muscle strength, but the results remain controversial. We aimed to compare the effects and safety of single high-dose with daily low-dose oral colecalciferol on 25(OH)D levels and muscle strength in postmenopausal women with vitamin D deficiency or insufficiency. METHODS AND DESIGN: Sixty healthy postmenopausal women who had serum vitamin D levels < 20 ng/mL (50 nmol/L) were enrolled in the study. Group 1 (n = 32) was given daily oral dosages of 800 IU vitamin D3, and group 2 (n = 28) was given a single oral dose of 300,000 IU vitamin D3. Serum vitamin D levels and muscle strengths were measured at the beginning, 4th, and 12th week. Muscle strength tests were performed at 60° using a Biodex system 3 isokinetic dynamometer. RESULTS: Pretreatment vitamin D levels did not differ between the two groups (10.2 ± 4.4 ng/mL (25,4 ± 10,9 nmol/L); 9.7 ± 4.4 ng/mL (24,2 ± 10,9 nmol/L), p > 0.05). A significant increase in vitamin D levels was observed in both groups at 4 and 12 weeks after vitamin D3 treatment. The increase in the single-dose group was significantly higher than the daily low-dosage group at the 4th week (35.9 ± 9.6 ng/mL (89,6 ± 23,9 nmol/L), 16.9 ± 5.8 ng/mL (42,1 ± 14,4 nmol/L), p = 0.01). The increase in the single-dose group was significantly higher than in the daily low dosage group at the 12th week (23.4 ± 4.7 ng/mL (58,4 ± 11,7 nmol/L), 19.8 ± 7.2 ng/mL (49,4 ± 17,9 nmol/L), p = 0.049). The quadriceps muscle strength score increased significantly in the daily group at the 4th week (p = 0.038). The hamstring muscle strength score increased significantly in the daily group at the 12th week (p = 0.037). CONCLUSION: Although daily administration routes are more effective in improving muscle strength, a single administration is more effective in increasing vitamin D levels.