Selección de Resúmenes de Menopausia

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Vasomotor symptoms and cardiovascular health: findings from the SWAN and the MsHeart/MsBrain studies

Vasomotor symptoms (VMS) are often considered the classic menopausal symptom and are experienced by most women during the menopause transition. VMS are well established to be associated with decrements in quality of life during the menopause. More recent research also links VMS to poorer cardiovascular health. This review summarizes key insights about links between VMS and cardiovascular disease (CVD) risk that come from the Study of Women's Health Across the Nation (SWAN), a longitudinal epidemiologic cohort study of the menopause transition, as well as from the MsHeart/MsBrain studies, clinical studies that leverage vascular imaging and brain imaging as well as wearable technologies that provide objective indicators of VMS. Using a range of methodologies and extensive consideration of confounders, these studies have shown that frequent and/or persistent VMS are associated with adverse CVD risk factor profiles, poorer underlying peripheral vascular and cerebrovascular health, and elevated risk for clinical CVD events. Collectively, the SWAN and MsHeart/MsBrain studies form complementary epidemiologic and clinical studies that point to the importance of VMS to women's cardiovascular health during the menopause transition and beyond.

Estradiol mitigates stress-induced cardiac injury and inflammation by downregulating ADAM17 via the GPER-1/PI3K signaling pathway

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Stress-induced cardiovascular diseases characterized by inflammation are among the leading causes of morbidity and mortality in postmenopausal women worldwide. Estradiol (E2) is known to be cardioprotective via the modulation of inflammatory mediators during stress. But the mechanism is unclear. TNFα, a key player in inflammation, is primarily converted to its active form by 'A Disintegrin and Metalloprotease 17' (ADAM17). We investigated if E2 can regulate ADAM17 during stress. Experiments were performed using female FVB wild-type (WT), C57BL/6 WT, and G protein-coupled estrogen receptor 1 knockout (GPER-1 KO) mice and H9c2 cells. The study revealed a significant increase in cardiac injury and inflammation during isoproterenol (ISO)-induced stress in ovariectomized (OVX) mice. Additionally, ADAM17's membrane content (mADAM17) was remarkably increased in OVX and GPER-1 KO mice during stress. However, in vivo supplementation of E2 significantly reduced cardiac injury, mADAM17, and inflammation. Also, administering G1 (GPER-1 agonist) in mice under stress reduced mADAM17. Further experiments demonstrated that E2, via GPER-1/PI3K pathway, localized ADAM17 at the perinuclear region by normalizing β1AR-Gαs, mediating the switch from β2AR-Gαi to Gαs, and reducing phosphorylated kinases, including p38 MAPKs and ERKs. Thus, using G15 and LY294002 to inhibit GPER-1 and its down signaling molecule, PI3K, respectively, in the presence of E2 during stress resulted in the disappearance of E2's modulatory effect on mADAM17. In vitro knockdown of ADAM17 during stress significantly reduced cardiac injury and inflammation, confirming its significant inflammatory role. These interesting findings provide novel evidence that E2 and G1 are potential therapeutic agents for ADAM17-induced inflammatory diseases associated with postmenopausal females.

Vitamin D Deficiency and Cardiovascular Mortality: Retrospective Analysis "Siena Osteoporosis" Cohort

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Vitamin D is a fat-soluble vitamin that plays a key role in bone metabolism, particularly concerning the regulation of calcium and phosphate homeostasis. Cardiovascular disease (CVD) is the main cause of morbidity and mortality in Western countries. Knowledge of the role of vitamin D in CVD arose from evidence of the vitamin D receptor (VDR) inside the cardiovascular system. In this retrospective analysis, we investigated the relationships between vitamin D

status and hospitalization for heart failure (HF), overall mortality and cardiovascular mortality. Between 2004 and 2009, age-stratified, random sampling of elderly men and postmenopausal women in the primary care registers of Siena residents was performed. In total, 174 males (mean ± SD, 65.9 ± 6 years) and 975 females (62.5 ± 6 years) were enrolled in the study. We investigated the association between 25OHD status and hospitalization for HF or causes of mortality. A total of 51 subjects (12 males and 39 females) had been hospitalized for acute HF. At the end of the survey, 931 individuals were alive, while 187 had died (43 males and 144 females). A greater proportion of deceased patients showed low 25OHD (particularly patients with levels below 20 ng/mL). A similar trend was observed concerning the prevalence of patients with 25OHD levels below 20 ng/mL who died from stroke (RR = 2.15; 95% CIs 0.98-4.69; p = 0.06). Low 25OHD levels may be predictive of cardiovascular mortality. Whether vitamin deficiency represents a primitive cause or is a simple bystander in increased cardiovascular mortality should be further investigated in prospective large cohort studies specifically designed to assess CVD risk, including a detailed assessment of cardiac dysfunction and the characterization of atherosclerotic lesions.

Previous fracture and subsequent fracture risk: a meta-analysis to update FRAX

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A large international meta-analysis using primary data from 64 cohorts has quantified the increased risk of fracture associated with a previous history of fracture for future use in FRAX. Introduction: The aim of this study was to quantify the fracture risk associated with a prior fracture on an international basis and to explore the relationship of this risk with age, sex, time since baseline and bone mineral density (BMD). Methods: We studied 665,971 men and 1,438,535 women from 64 cohorts in 32 countries followed for a total of 19.5 million person-years. The effect of a prior history of fracture on the risk of any clinical fracture, any osteoporotic fracture, major osteoporotic fracture, and hip fracture alone was examined using an extended Poisson model in each cohort. Covariates examined were age, sex, BMD, and duration of follow-up. The results of the different studies were merged by using the weighted β-coefficients. Results: A previous fracture history, compared with individuals without a prior fracture, was associated with a significantly increased risk of any clinical fracture (hazard ratio, HR = 1.88; 95% CI = 1.72-2.07). The risk ratio was similar for the outcome of osteoporotic fracture (HR = 1.87; 95% CI = 1.69-2.07), major osteoporotic fracture (HR = 1.83; 95% CI = 1.63-2.06), or for hip fracture (HR = 1.82; 95% CI = 1.62-2.06). There was no significant difference in risk ratio between men and women. Subsequent fracture risk was marginally downward adjusted when account was taken of BMD. Low BMD explained a minority of the risk for any clinical fracture (14%), osteoporotic fracture (17%), and for hip fracture (33%). The risk ratio for all fracture outcomes related to prior fracture decreased significantly with adjustment for age and time since baseline examination. Conclusion: A previous history of fracture confers an increased risk of fracture of substantial importance beyond that explained by BMD. The effect is similar in men and women. Its quantitation on an international basis permits the more accurate use of this risk factor in case finding strategies.

Association of type 2 diabetes mellitus with dementia-related and non-dementia-related mortality among postmenopausal women: A secondary competing risks analysis of the women's health initiative

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Introduction: Alzheimer's disease (AD) and AD-related dementias (ADRD) are leading causes of death among older adults in the United States. Efforts to understand risk factors for prevention are needed. Methods: Participants (n = 146,166) enrolled in the Women's Health Initiative without AD at baseline were included. Diabetes status was ascertained from self-reported questionnaires and deaths attributed to AD/ADRD from hospital, autopsy, and death records. Competing risk regression models were used to estimate the cause-specific hazard ratios (HRs) and 95% confidence intervals (CIs) for the prospective association of type 2 diabetes mellitus (T2DM) with AD/ADRD and non-AD/ADRD mortality. Results: There were 29,393 treated T2DM cases and 8628 AD/ADRD deaths during 21.6 (14.0-23.5) median (IQR) years of follow-up. Fully adjusted HRs (95% CIs) of the association with T2DM were 2.94 (2.76-3.12) for AD/ADRD and 2.65 (2.60-2.71) for the competing risk of non-AD/ADRD mortality. Discussion: T2DM is associated with AD/ADRD and non-AD/ADRD mortality. Highlights: Type 2 diabetes mellitus is more

strongly associated with Alzheimer's disease (AD)/AD and related dementias (ADRD) mortality compared to the competing risk of non-AD/ADRD mortality among postmenopausal women. This relationship was consistent for AD and ADRD, respectively. This association is strongest among participants without obesity or hypertension and with younger age at baseline, higher diet quality, higher physical activity, higher alcohol consumption, and older age at the time of diagnosis of type 2 diabetes mellitus.

Does the use of oral contraceptives or hormone replacement therapy offer protection against the formation or rupture of intracranial aneurysms in women?: a systematic review and meta-analysis

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Objective: The aim of this study was to carry out a systematic review of the literature with meta-analysis to evaluate the effect of using oral contraceptive and hormone replacement therapy as a protective factor in the formation of intracranial aneurysms and subarachnoid hemorrhage. Methods: This is a systematic review of the literature with meta-analysis, using PubMed and Embase as databases and the PRISMA method. Case-control and cohort studies published until December 2022 were included in this review. Results: Four studies were included in this review; three of which were eligible for meta-analysis. Regarding the use of oral contraceptive and the development of subarachnoid hemorrhage, there was a lower risk of aneurysm rupture with an odds ratio 0.65 (confidence interval 0.5-0.85). In the analysis of patients using hormone replacement therapy and developing subarachnoid hemorrhage, there was also a lower risk of aneurysm rupture with an OR 0.54 (CI 0.39-0.74). Only one article analyzed the formation of intracranial aneurysm and the use of hormone replacement therapy and oral contraceptive, and there was a protective effect with the use of these medications. oral contraceptive: OR 2.1 (CI 1.2-3.8) and hormone replacement therapy: OR 3.1 (CI 1.5-6.2). Conclusion: The use of hormone replacement therapy and oral contraceptive has a protective effect in intracranial aneurysm rupture and formation.