

Selección de Resúmenes de Menopausia

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Estrogen and the Vascular Endothelium: The Unanswered Questions

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Pre-menopausal women have a lower incidence of cardiovascular disease (CVD) compared to their age-matched male counterparts however this discrepancy is abolished following the transition to menopause or during low estrogen states. This, combined with a large amount of basic and preclinical data indicating that estrogen is vasculoprotective, supports the concept that hormone therapy could improve cardiovascular health. However, clinical outcomes in individuals undergoing estrogen treatment have been highly variable, challenging the current paradigm regarding the role of estrogen in the fight against heart disease. Increased risk for CVD correlates with long-term oral contraceptive use, hormone replacement therapy in older, post-menopausal cis-females, and gender affirmation treatment for trans-females. Vascular endothelial dysfunction serves as a nidus for the development of many cardiovascular diseases and is highly predictive of future CVD risk. Despite preclinical studies indicating that estrogen promotes a quiescent, functional endothelium, it still remains unclear why these observations do not translate to improved CVD outcomes. The goal of this review is to explore our current understanding of the effect of estrogen on the vasculature, with a focus on endothelial health. Following a discussion regarding the influence of estrogen on large and small artery function, critical knowledge gaps are identified. Finally, novel mechanisms and hypotheses are presented that may explain the lack of cardiovascular benefit in unique patient populations.

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Effectiveness of workplace-based interventions to promote wellbeing among menopausal women: A systematic review

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Menopausal symptoms are known to affect quality of life and work productivity. This systematic review aimed to describe the range and effectiveness of workplace-based interventions for menopause. MEDLINE, PubMed, Embase, CINAHL, Cochrane Library, Web of Science, PsycINFO, EconLit, and SCOPUS were searched from the inception until April 2022. Quantitative interventional studies evaluating physical/virtual workplace-based interventions aiming to improve wellbeing, work, and other outcomes, that involved women in menopausal transition, or their line managers/supervisors were eligible for inclusion. Two randomized controlled trials and three uncontrolled trials, comprising 293 women aged 40-60 years and 61, line managers/supervisors, were included in the review. Results were narratively synthesized due to the heterogeneity of interventions and outcomes and we found that only a limited range of interventions have been evaluated for their ability to support women going through menopausal transition in the workplace. Self-help cognitive behavioural therapy (CBT); Raja yoga; and health promotion (involving menopause consultations, work-life coaching and physical training) improved menopausal symptoms significantly. Self-help CBT was associated with a significant improvement in mental resources for work, presenteeism, and work and social adjustment. Awareness programs significantly improved knowledge and attitudes of both employees and line managers/supervisors about menopause. The interventions have mostly been evaluated in small studies with selected populations but have improved menopausal symptoms and work outcomes. A customizable menopause wellbeing intervention package incorporating these evidence-supported interventions should be developed and implemented on a wider scale within organizations alongside robust evaluation of its effectiveness.

Prz Menopauzalny. 2023 Mar;22(1):21-23. doi: 10.5114/pm.2023.126363. Epub 2023 Apr 3.

The relationship between carotid intima-media thickness and cognitive function and depression in postmenopausal women

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Introduction: Atherosclerosis, cognitive impairment, and depression are common entities in postmenopausal patients. Our aim was to ascertain the relationship between the carotid intima-media thickness (IMT) and cognitive function and depression in postmenopausal women. Material and methods: This was an observational, cross-sectional, comparative study among postmenopausal women. A carotid artery ultrasound was performed, and the IMT was measured. Mental

function was assessed with the mini-mental state examination (MMSE), and the presence of depression with the Hamilton Depression Rating Scale (HDRS). For statistical analysis the Mann-Whitney U test and Spearman correlation were used. Sensitivity, specificity, positive predictive value, negative predictive value, and odds ratio (OR) were calculated. Results: Seventy-five patients were studied. The median of age was 52 years (31-76), and the IMT was 1.1 mm (0.6-0.20). The HDRS score was 8.9 (1-21), and that of the MMSE was 29 (18-30). After dividing the group according to the presence or absence of depression, it was found that age and IMT were greater in the group with depression, and the MMSE score was greater in the group without depression. After dividing according to the MMSE score, age and HDRS score were significantly greater in the group with cognitive impairment. The intima-media thickness had an OR of 12.2 (2.6-58.0) for cognitive impairment and an OR of 5.2 (1.9-14.1) for depression. Conclusions: The intima-media thickness is associated with greater risk of cognitive impairment and depression.

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Cell-Based Therapies for Degenerative Musculoskeletal Diseases

Pengbin Yin 1 2, Yuheng Jiang 1 2 3, Xuan Fang 4, Daofeng Wang 1 2, Yi Li 1 2, Ming Chen 1 2, Hao Deng 5, et al. Degenerative musculoskeletal diseases (DMDs), including osteoporosis, osteoarthritis, degenerative disc disease, and sarcopenia, present major challenges in the aging population. Patients with DMDs present with pain, functional decline, and reduced exercise tolerance, which result in long-term or permanent deficits in their ability to perform daily activities. Current strategies for dealing with this cluster of diseases focus on relieving pain, but they have a limited capacity to repair function or regenerate tissue. Cell-based therapies have attracted considerable attention in recent years owing to their unique mechanisms of action and remarkable effects on regeneration. In this review, current experimental attempts to use cell-based therapies for DMDs are highlighted, and the modes of action of different cell types and their derivatives, such as exosomes, are generalized. In addition, the latest findings from state-of-the-art clinical trials are reviewed, approaches to improve the efficiency of cell-based therapies are summarized, and unresolved questions and potential future research directions for the translation of cell-based therapies are identified.

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Hormone exposure and venous thromboembolism in commercially insured women aged 50 to 64 years

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Background: Menopausal hormone therapy (MHT) can elevate venous thromboembolism (VTE) risk, but less is known about formulations and routes of exposures. Objective: To estimate hormone-associated VTE risk by route and formulation in exposed and unexposed women aged 50 to 64 years in the US. Methods: In a nested case-control study of US commercially insured women aged 50 to 64 years (2007-2019), cases were defined as incident VTE diagnoses and matched to 10 controls by date of VTE and age, excluding prior VTE, inferior vena cava filter placement, or anticoagulants. Filled prescriptions in the prior year defined hormone exposures. International Classification of Diseases and Current Procedural Terminology codes identified risk factors and comorbidities. Results: Odds ratios (ORs) were estimated with conditional logistic regression controlling for differences between cases (n = 20,359) and controls (n = 203,590) in comorbidities and VTE risk factors. For exposures within 60 days, oral MHT risk was almost twice as high as transdermal MHT (OR = 1.92; 95% CI, 1.43-2.60); transdermal MHT did not elevate risk compared with no exposure (unopposed OR = 0.70; 95% CI, 0.59-0.83; combined OR = 0.73; 95% CI, 0.56-0.96). Risk was highest for MHT combinations with ethinyl estradiol, followed by conjugated equine estrogen (CEE) (ethinyl estradiol-CEE: OR = 1.55; 95% CI, 1.07-2.25), and lowest for estradiol (CEE-estradiol: OR = 1.33; 95% CI, 1.02-1.72). Combined hormonal contraceptives elevated risk 5 times higher than no exposure (OR = 5.22; 95% CI, 4.67-5.84) and 3 times higher than oral MHT (OR = 3.65; 95% CI, 3.09-4.31). Conclusion: The risk of VTE is much lower with MHT than combined hormone contraceptives and varies by hormone formulation and route of exposure. Transdermal MHT did not elevate risk. Oral MHT combinations with estradiol were lower risk than other forms of estrogen. Oral combined hormone contraceptives had much higher risk than oral combined hormonal MHT.

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Menopause hormone therapy and urinary symptoms: a systematic review

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Importance: Urogenital changes associated with menopause are now classified as genitourinary syndrome of menopause (GSM), which includes symptoms of urgency, frequency, dysuria, and recurrent urinary tract infections for which the

recommended treatment is estrogen. However, the association between menopause and urinary symptoms and the efficacy of hormone therapy for these symptoms is uncertain. Objective: Our objective was to define the relationship between menopause and urinary symptoms including dysuria, urgency, frequency, recurrent urinary tract infections (UTIs), and urge and stress incontinence by conducting a systematic review of the effects of hormone therapy (HT) for urinary symptoms in perimenopausal and postmenopausal women. Evidence review: Eligible studies included randomized control trials with perimenopausal and postmenopausal women with a primary or secondary outcome of the following urinary symptoms: dysuria, frequent UTI, urgency, frequency, and incontinence, included at least one treatment arm of estrogen therapy, and were in English. Animal trials, cancer studies and pharmacokinetic studies, secondary analyses, and conference abstracts were excluded. PubMed, Scopus, and the Cochrane Central Register of Controlled Trials were searched until April 2022. Two authors reviewed each article with discrepancies resolved through whole group consensus. Data extracted included the following: publication date, country, setting, subject number, follow-up, duration, age, race/ethnicity, study design, inclusion criteria, and main findings. Findings: There is insufficient evidence to confirm that menopause is associated with urinary symptoms. The effect of HT on urinary symptoms depends on type. Systemic HT may cause urinary incontinence or worsen existing urinary symptoms. Vaginal estrogen improves dysuria, frequency, urge and stress incontinence, and recurrent UTI in menopausal women.

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The association of hysterectomy with or without ovarian conservation with subclinical atherosclerosis progression in healthy postmenopausal women

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Objective: While the deleterious associations of surgical menopause after bilateral oophorectomy with cardiovascular disease are documented, less is specifically known concerning subclinical atherosclerosis progression. Methods: We used data from 590 healthy postmenopausal women randomized to hormone therapy or placebo in the Early versus Late Intervention Trial with Estradiol (ELITE), which was conducted from July 2005 to February 2013. Subclinical atherosclerosis progression was measured as annual rate of change in carotid artery intima-media thickness (CIMT) over a median 4.8 years. Mixed-effects linear models assessed the association of hysterectomy and bilateral oophorectomy compared with natural menopause with CIMT progression adjusted for age and treatment assignment. We also tested modifying associations by age at or years since oophorectomy or hysterectomy. Results: Among 590 postmenopausal women, 79 (13.4%) underwent hysterectomy with bilateral oophorectomy and 35 (5.9%) underwent hysterectomy with ovarian conservation, a median of 14.3 years before trial randomization. Compared with natural menopause, women who underwent hysterectomy with and without bilateral oophorectomy had higher fasting plasma triglycerides while women who underwent bilateral oophorectomy had lower plasma testosterone. The CIMT progression rate in bilaterally oophorectomized women was 2.2 $\mu\text{m}/\text{y}$ greater than natural menopause ($P = 0.08$); specifically, compared with natural menopause, the associations were significantly greater in postmenopausal women who were older than 50 years at the time of bilateral oophorectomy ($P = 0.014$) and in postmenopausal women who underwent bilateral oophorectomy more than 15 years before randomization ($P = 0.015$). Moreover, the CIMT progression rate in hysterectomized women with ovarian conservation was 4.6 $\mu\text{m}/\text{y}$ greater than natural menopause ($P = 0.015$); in particular, compared with natural menopause, the association was significantly greater in postmenopausal women who underwent hysterectomy with ovarian conservation more than 15 years before randomization ($P = 0.018$). Conclusions: Hysterectomy with bilateral oophorectomy and ovarian conservation were associated with greater subclinical atherosclerosis progression relative to natural menopause. The associations were stronger for later age and longer time since oophorectomy/hysterectomy. Further research should continue to examine long-term atherosclerosis outcomes related to oophorectomy/hysterectomy.

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Obesity and risk of fracture in postmenopausal women: a meta-analysis of cohort studies

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Background: Obesity is associated with an increased risk of fracture in adults, but is unclear in postmenopausal women. We aim to determine the association of obesity with the risk of fracture in postmenopausal women. Methods: PubMed, EMBASE, Cochrane Library and Web of Science were searched up to 11 April 2022 for cohort studies. And the included studies regarding the relationship between obesity with all cause of fracture in postmenopausal women were included in our meta-analysis. Data were screened and extracted independently by two reviewers. The relative risks (RR) were estimated using a random-effects model. Between-study heterogeneity was assessed using Cochran's Q and I² statistics. Results: Eight cohort studies comprising 671,532 postmenopausal women and 40,172 fractures were included. Overall,

the pooling analysis shows that obesity in postmenopausal women is associated with an increased risk of all-cause fracture (relative ratio (RR) = 1.18; 95% confidence interval (CI):1.09-1.28, I² = 86.3%, p = .000). Sub-analyses for each site of fracture indicate that obesity was associated with an increased risk of vertebral fracture in postmenopausal women (RR = 1.154, 95% CI: 1.020-1.305, I² = 94.5%, p = .023), but reduced the risk of pelvic fracture (RR = 0.575, 95% CI:0.470-0.702, I² = 0.0%, p = .000). There is no statistically significant difference in the risk of hip and humerus fractures associated with obesity in postmenopausal women. Conclusion: Obesity is associated with an increased risk of all-cause and vertebral fractures in postmenopausal women, but is a protective factor for pelvic fractures. Our findings suggest that postmenopausal women who regulate their weight might lower their risk of fractures.

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Oxidative Stress in Postmenopausal Women with or without Obesity

Giulia Leanza 1, Caterina Conte 2 3, Francesca Cannata 1, Camilla Isgro 1 4, Alessandra Piccoli 1, Rocky Strollo, et al. Oxidative stress, a key mediator of cardiovascular disease, metabolic alterations, and cancer, is independently associated with menopause and obesity. Yet, among postmenopausal women, the correlation between obesity and oxidative stress is poorly examined. Thus, in this study, we compared oxidative stress states in postmenopausal women with or without obesity. Body composition was assessed via DXA, while lipid peroxidation and total hydroperoxides were measured in patient's serum samples via thiobarbituric-acid-reactive substances (TBARS) and derivate-reactive oxygen metabolites (d-ROMs) assays, respectively. Accordingly, 31 postmenopausal women were enrolled: 12 with obesity and 19 of normal weight (mean (SD) age 71.0 (5.7) years). Doubled levels of serum markers of oxidative stress were observed in women with obesity in women with obesity compared to those of normal weight (H₂O₂: 32.35 (7.3) vs. 18.80 (3.4) mg H₂O₂/dL; malondialdehyde (MDA): 429.6 (138.1) vs. 155.9 (82.4) mM in women with or without obesity, respectively; p < 0.0001 for both). Correlation analysis showed that both markers of oxidative stress increased with an increasing body mass index (BMI), visceral fat mass, and trunk fat percentage, but not with fasting glucose levels. In conclusion, obesity and visceral fat are associated with a greater increase in oxidative stress in postmenopausal women, possibly increasing cardiometabolic and cancer risks.