

Selección de Resúmenes de Menopausia

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A review of epigenetics and its association with ageing of muscle and bone

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Ageing is defined as the 'increasing frailty of an organism with time that reduces the ability of that organism to deal with stress'. It has been suggested that epigenetics may underlie the observation that some individuals appear to age faster than others. Epigenetics is the study of changes which occur in an organism due to changes in expression of the genetic code rather than changes to the genetic code itself; that is, epigenetic mechanisms impact upon the function of DNA without changing the DNA sequence. It is important to recognise that epigenetic changes, in contrast to genetic changes, can vary according to different cell types and therefore can demonstrate significant tissue-specificity. There are different types of epigenetic mechanisms: histone modification, non-coding RNAs and DNA methylation. Epigenetic clocks have been developed using statistical techniques to identify the optimal combination of CpG sites (from methylation arrays) to correlate with chronological age. This review considers how epigenetic factors may affect rates of ageing of muscle and bone and provides an overview of current understanding in this area. We discuss studies using first-generation epigenetic clocks, as well as the second-generation iterations, which appear to show stronger associations with the ageing muscle phenotype. We also review epigenome-wide association studies that have been performed in various tissues examining relationships with osteoporosis and fracture. It is hoped that an understanding of this area will lead to interventions that might prevent or reduce rates of musculoskeletal ageing in later life.

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Combined Oral Contraceptives and Vascular Thrombosis: A Single-Center Experience

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Background Combined oral contraceptives (COCs) are frequently prescribed for contraception, to regulate ovulation and treat endometriosis, and to control menopausal symptoms. A major risk of hormonal contraceptives is vascular thrombosis. **Methods** A retrospective chart review of female patients with deep vein thrombosis (DVT), pulmonary embolism (PE), or other sites of thrombosis or emboli seen in the thrombosis clinic of the department of internal medicine at a tertiary care hospital in Saudi Arabia between March 2010 and February 2015 was performed to identify and characterize which women were taking COCs. **Results** Of 1,008 patients treated for DVT, PE, or other sites of thrombosis or emboli, 100 (9.9%) were taking COCs. Venous (98%) and arterial (2%) thromboses were seen. Overall, 62% of the patients experienced a DVT and 26% pulmonary emboli, and 20% of the patients experienced unusual sites of thrombosis. Furthermore, 53% were obese or morbidly obese. The incidence of venous thrombosis was the highest during the first year of COC use (73%). Of the patients, 8% had thrombophilia. **Conclusion** This study characterizes Saudi women with thrombotic events taking COCs and identifies risk factors, including unusual sites of thrombosis. Most patients experienced the vascular event during the first year of taking COCs. Age of 40-50 years, obesity, and thrombophilia were the commonly observed risk factors.

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Menopausal hormone therapy reduces the risk of fracture regardless of falls risk or baseline FRAX probability-results from the Women's Health Initiative hormone therapy trials

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In a combined analysis of 25,389 postmenopausal women aged 50-79 years, enrolled in the two Women's Health Initiative hormone therapy trials, menopausal hormone therapy vs. placebo reduced the risk of fracture regardless of baseline FRAX fracture probability and falls history. **Introduction:** The aim of this study was to determine if the anti-fracture efficacy of menopausal hormone therapy (MHT) differed by baseline falls history or fracture risk probability as estimated by FRAX, in a combined analysis of the two Women's Health Initiative (WHI) hormone therapy trials.

Methods: A total of 25,389 postmenopausal women aged 50-79 years were randomized to receive MHT (n = 12,739) or matching placebo (n = 12,650). At baseline, questionnaires were used to collect information on falls history, within the last 12 months, and clinical risk factors. FRAX 10-year probability of major osteoporotic fracture (MOF) was calculated without BMD. Incident clinical fractures were verified using medical records. An extension of Poisson regression was used to investigate the relationship between treatment and fractures in (1) the whole cohort; (2) those with prior falls; and (3) those without prior falls. The effect of baseline FRAX probability on efficacy was investigated in the whole cohort. Results: Over 4.3 ± 2.1 years (mean \pm SD), MHT (vs. placebo) significantly reduced the risk of any clinical fracture (hazard ratio [HR] 0.72 [95% CI, 0.65-0.78]), MOF (HR 0.60 [95% CI, 0.53-0.69]), and hip fracture (0.66 [95% CI, 0.45-0.96]). Treatment was effective in reducing the risk of any clinical fracture, MOF, and hip fracture in women regardless of baseline FRAX MOF probability, with no evidence of an interaction between MHT and FRAX ($p > 0.30$). Similarly, there was no interaction ($p > 0.30$) between MHT and prior falls. Conclusion: In the combined WHI trials, compared to placebo, MHT reduces fracture risk regardless of FRAX probability and falls history in postmenopausal women.

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The effects of psychological interventions on menopausal hot flashes: A systematic review

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Background: Menopause is a normal physiological phenomenon, closely identified with a great deal of physical-psychological symptoms, including hot flashes (HFs) with a prevalence rate of 20-80%. Various pharmacological and non-pharmacological interventions have been thus far practiced to reduce this common symptom of the menopausal transition. Objective: This systematic review was conducted to evaluate the effects of psychological interventions on menopausal HFs. Materials and methods: In this review, the databases of Google Scholar, Scopus, PubMed, Web of Science, Science Direct, the Cochrane Library, and Scientific Information Database were searched applying the Boolean searching operators as well as the keywords of 'hot flashes', 'menopause', 'psychological intervention', and 'vasomotor symptoms'. Accordingly, a total number of 20,847 articles published from January 2000 to June 2019 were retrieved. After excluding the duplicate and irrelevant ones, the risk of bias of 19 clinical or quasi-experimental clinical trials was assessed using the Cochrane collaboration tool. Results: The interventions implemented in the studies on menopausal HFs included cognitive behavioral therapy, mindfulness-based stress reduction, hypnotherapy, and relaxation techniques. All of the articles reported improvements in HFs in postmenopausal women, except for 4 studies. Conclusion: Based on the findings of this systematic review, psychological interventions, especially cognitive behavioral therapy and relaxation techniques, are potentially effective for vasomotor symptoms and HFs in healthy postmenopausal women, although the quality of published research on this topic is sometimes questionable.

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Sex Differences in Molecular Mechanisms of Cardiovascular Aging

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Cardiovascular disease (CVD) is still the leading cause of illness and death in the Western world. Cardiovascular aging is a progressive modification occurring in cardiac and vascular morphology and physiology where increased endothelial dysfunction and arterial stiffness are observed, generally accompanied by increased systolic blood pressure and augmented pulse pressure. The effects of biological sex on cardiovascular pathophysiology have long been known. The incidence of hypertension is higher in men, and it increases in postmenopausal women. Premenopausal women are protected from CVD compared with age-matched men and this protective effect is lost with menopause, suggesting that sex-hormones influence blood pressure regulation. In parallel, the heart progressively remodels over the course of life and the pattern of cardiac remodeling also differs between the sexes. Lower autonomic tone, reduced baroreceptor response, and greater vascular function are observed in premenopausal women than men of similar age. However, postmenopausal women have stiffer arteries than their male counterparts. The biological mechanisms responsible for sex-related differences observed in cardiovascular aging are being unraveled over the last several decades. This review focuses on molecular mechanisms underlying the sex-differences of CVD in aging.

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Adverse Changes in Body Composition During the Menopausal Transition and Relation to Cardiovascular Risk: A Contemporary Review

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The menopausal transition period in aging women is strongly associated with weight gain. Evidence shows that weight changes during menopause increases the risk of developing cardiovascular disease (CVD) in postmenopausal women. However, the potential mechanisms that cause weight gain and adverse changes to body composition specifically during the menopausal transition period remain to be elucidated. In this contemporary review, we examined recent evidence for adverse changes in body composition at midlife during the menopausal transition and the link to increased CVD risk and described factors that may contribute to these changes, including normal chronological aging, hormonal factors (decreased estrogen, etc.), behavioral factors (changes in diet, physical activity), or other emerging factors (e.g., sleep). This review focused on identifying factors that make the menopausal transition period a critical window for prevention of CVD. Future study is needed to decipher the extent to which hormonal changes, age-related factors, and behavioral factors interact with and contribute to increased CVD risk in women undergoing menopause. Understanding the causes of weight gain during the menopausal transition may help to inform strategies to mitigate adverse CVD outcomes for women transitioning through menopause.

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Air pollution and green spaces in relation to breast cancer risk among pre and postmenopausal women: A mega cohort from Catalonia

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Background: The association between air pollution and green spaces with breast cancer risk stratified by menopausal status has not been frequently investigated despite its importance given the different impact of risk factors on breast cancer risk depending on menopausal status. **Objectives:** To study the association between air pollution, green spaces and pre and postmenopausal breast cancer risk. **Methods:** We conducted a population-based cohort study using electronic primary care records in Catalonia. We included women aged 17-85 years free of cancer at study entry between 2009 and 2017. Our exposures were particulate matter $<2.5 \mu\text{m}$ (PM_{2.5}) & $<10 \mu\text{m}$ (PM₁₀), nitrogen dioxide (NO₂), normalized difference vegetation index (NDVI), and percentage of green spaces estimated at the census tract level. Breast cancer was identified with ICD-10 code C50. We estimated cause-specific hazard ratios (HR) for the relationship between each individual exposure and pre and postmenopausal breast cancer risk, using linear and non-linear models. **Results:** Of the 1,054,180 pre and 744,658 postmenopausal women followed for a median of 10 years, 6,126 and 17,858 developed breast cancer, respectively. Among premenopausal women, only very high levels of PM₁₀ ($\geq 46 \mu\text{g}/\text{m}^3$) were associated with increased cancer risk (compared to lower levels) in non-linear models. Among postmenopausal women, an interquartile range increase in PM_{2.5} (HR:1.03; 95%CI:1.01-1.04), PM₁₀ (1.03; 1.01-1.05), and NO₂ (1.05; 1.02-1.08) were associated with higher cancer risk. NDVI was negatively associated with decreased cancer risk only among postmenopausal women who did not change residence during follow-up (0.84; 0.71-0.99) or who were followed for at least three years (0.82; 0.69-0.98). **Discussion:** Living in areas with high concentrations of PM_{2.5}, PM₁₀, and NO₂ increases breast cancer risk in postmenopausal women while long-term exposure to green spaces may decrease this risk. Only very high concentrations of PM₁₀ increase breast cancer risk in premenopausal women.