Selección de Resúmenes de Menopausia

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Comparative Evaluation of Osteoporosis Clinical Risk Assessment Tools in Postmenopausal Women Aged 50-64

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Objectives: To assess the performance of five osteoporosis clinical risk assessment tools (SCORE, ORAI, ABONE, OST and OSIRIS), in a subgroup of young postmenopausal women aged 50-64, who underwent DXA screening. Methods: The above-mentioned osteoporosis risk assessment tools were calculated for 258 young postmenopausal women (aged 50-64) who had a DXA scan, in Crete/Greece. Results: Patients with a T-score ≤ -2.5 or a T-score ≤ -2.0 had a statistically significant higher value of SCORE, ORAI and ABONE and a lower value of OST, OSIRIS, and OSIRIS Adjusted Score, compared to the patients with T-score > -2.5 and T-score > -2.0, respectively. ORAI (T-score≤ -2.0) and OST (T-score≤ -2.5) demonstrated the highest sum of sensitivity and specificity. CHAID analysis further confirmed the relative significance of the OST tool in the osteoporosis group (T-score≤ -2.5 vs. T-score > -2.5), for a cut-off of 2.8. In the other group (T-score ≤ -2.0 vs T-score > -2.0) the ORAI score showed a significantly important relationship for a cut-off of 8. Conclusion: OST, despite its performance limitations, correlates best with the DXA measurements of young (50-64), postmenopausal osteoporotic women, a fact which may suggest its' potential role as a screening tool in this specific age group.

Eur J Obstet Gynecol Reprod Biol. 2024 Nov 26:304:134-140. doi: 10.1016/j.ejogrb.2024.11.040. Online ahead

Effect of pelvic floor muscle training on urinary incontinence symptoms in postmenopausal women: A systematic review and meta-analysis

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Objective: Urinary incontinence (UI) is common in women of all age groups, but postmenopausal women (MW) have a higher incidence of these symptoms. The International Continence Society suggests that women with UI should first try a conservative treatment, such as pelvic floor muscle training (PFMT), which aims to enhance the strength and rectify the activation patterns of the pelvic floor muscles. The aim of this study was to examine the effectiveness of PFMT, either on its own, or in conjunction with other physical therapy, in reducing the severity of UI symptoms in MW. Methods: A comprehensive literature search was performed to identify relevant publications from major medical databases. A meta-analysis was carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) model. In addition, the included studies were assessed for quality, heterogeneity and publication bias. Results: After screening, application of the inclusion/exclusion criteria, and bias assessment, five randomized controlled trials were evaluated. PFMT was found to have a significant and substantial impact on the level of UI in the total patient population (standardized mean difference between the intervention and control groups -1.30, 95%CI: -1.97, -0.62, pz ≤ 0.01, I2 = 88.5 %; probability of benefit = 0.92). A second analysis, after the removal of studies that combined PFMT with electrostimulation or biofeedback, returned similar results. Conclusions: PFMT is an effective intervention for the management of UI in MW. Our analysis shows a 92% chance of significant improvement for patients receiving PFMT in comparison with controls. Future studies should examine its efficacy in MW subgroups with symptoms of genitourinary syndrome of menopause (GSM).

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Searching for the 'X' factor: investigating the genetics of primary ovarian insufficiency

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Primary ovarian insufficiency (POI) is the cessation of ovarian function before the age of 40. The causes of POI are heterogeneous, but substantial evidence exists to support a genetic basis of POI, particularly in the critical involvement

of genes on the X chromosome. Recent studies have revealed novel candidate genes through the identification of copy number variations associated with POI. This review summarizes the genes located on the X chromosome with variants shown to be associated with POI in humans and/or in mice. Additionally, we present evidence to support the potential involvement of these candidate genes in the etiology of POI. We conducted a literature search in PubMed to identify case studies and screenings for the genetic causes of POI. We then performed systematic searches for the proposed candidate genes to investigate their potential reproductive roles. Of the X-linked candidate genes investigated, 10 were found to have variants associated with cases of POI in humans. An additional 10 genes were found to play a supportive role in POI. Other genes were not implicated in any cases of POI but were associated with various roles in reproduction. In the majority of cases where variants were identified through whole-exome sequencing, rather than targeted screening of candidate genes, more than one genetic variant was identified. Overall, this review supports past findings that the X chromosome plays a critical role in ovarian function, as demonstrated by a link between POI and various disruptions to genes on the X chromosome. Current genetic screening for POI, which includes only FMR1, is inadequate to capture the majority of cases with a genetic origin. An expanded genetic testing may improve health outcomes for individuals with POI as it could lead to better early interventions and education about these health risks.

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Normal weight obesity, circulating biomarkers and risk of breast cancer: a prospective cohort study and meta-analysis

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Background: Individuals with normal weight obesity (NWO) often escape the attention of healthcare providers who may assume that a normal body mass index (BMI) correlates with low health risks. However, it remains unknown whether NWO increases the risk of breast cancer.Methods: This study included 22,257 and 52,506 pre- and postmenopausal females with nor mal BMI in the UK Biobank. NWO was defined as participants with a normal BMI (18.5-24.9 kg/m2) and an excess percent body fat (PBF > 33.3%). Cox proportional hazard models were used to investigate the associations of NWO and NWO-related biomarkers with incident breast cancer. Results: NWO was not associated with premenopausal breast cancer, whereas it was associated with a higher risk of postmenopausal breast cancer (hazard ratio = 1.19, 95% CI: 1.08-1.31). In our meta-analysis, per 5-unit increment in percent body fat level was linked to a 15% (95% CI: 10-19%) elevated risk of postmenopausal breast cancer in females with normal BMI. Stratified analyses showed a stronger positive association in females with higher genetic risk. In our NWO-biomarkers analyses, NWO was linked to 34 identified biomarkers, of which three inflammation markers (monocyte count, neutrophil count, and C-reactive protein), and one ketone body metabolite (β-Hydroxybutyrate) also indicated a positive association with postmenopausal breast cancer. Conclusions: NWO is associated with an increased risk of postmenopausal breast cancer, indicating that relying solely on BMI neglects the higher risk faced by non-obese postmenopausal women.

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Chronic kidney disease and menopausal health: An EMAS clinical guide

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Kidney diseases are related to the aging process. Ovarian senescence and the loss of estrogen's renoprotective effects are directly associated with a decline in renal function and indirectly with an accumulation of cardiometabolic risk factors. The latter can predispose to the development of chronic kidney disease (CKD). Conversely, CKD diagnosed during reproductive life adversely affects ovarian function. Aim: To set out an individualized approach to menopause management in women with CKD. Materials and methods: Literature review and consensus of expert opinion. Summary recommendations: Menopause hormone therapy can be given to women with CKD. The regimen should be selected on the basis of patient preference and the individual's cardiovascular risk. The dose of hormonal and non-hormonal preparations should be adjusted in accordance with the patient's creatinine clearance. The management of a postmenopausal woman with CKD should focus on lifestyle advice as well as regular monitoring of the main cardiovascular risk factors and evaluation of bone mineral density. Tailored multidisciplinary advice should be given to women with comorbidities such as diabetes, dyslipidemia, and hypertension. Management of osteoporosis should be based on the severity of the CKD.

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Mitochondria: the epigenetic regulators of ovarian aging and longevity

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Ovarian aging is a major health concern for women. Ovarian aging is associated with reduced health span and longevity. Mitochondrial dysfunction is one of the hallmarks of ovarian aging. In addition to providing oocytes with optimal energy, the mitochondria provide a co-substrate that drives epigenetic processes. Studies show epigenetic alterations, both nuclear and mitochondrial contribute to ovarian aging. Both, nuclear and mitochondrial genomes cross-talk with each other, resulting in two ways orchestrated anterograde and retrograde response that involves epigenetic changes in nuclear and mitochondrial compartments. Epigenetic alterations causing changes in metabolism impact ovarian function. Key mitochondrial co-substrate includes acetyl CoA, NAD+, ATP, and α-KG. Thus, enhancing mitochondrial function in aging ovaries may preserve ovarian function and can lead to ovarian longevity and reproductive and better health outcomes in women. This article describes the role of mitochondria-led epigenetics involved in ovarian aging and discusses strategies to restore epigenetic reprogramming in oocytes by preserving, protecting, or promoting mitochondrial function.

bioRxiv [Preprint]. 2024 Nov 12:2024.11.11.622997. doi: 10.1101/2024.11.11.622997.

The Interaction of Diet-Induced Obesity and Chronic Stress in A Mouse Model of Menopause

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Menopause is characterized by the cessation of ovarian hormone production. During postmenopause, cisgender women face increased risks of obesity, cognitive decline, and mood disorder. Mood disorders are associated with exposure to chronic stress. We investigated the combined effects of a high-fat diet (HFD) and chronic stress exposure in a mouse model of menopause using 4-vinylcyclohexene diepoxide (VCD), a selective ovotoxicant that gradually depletes ovarian follicles and hormones. Starting at 6 months, 82 female WT C57BL/6J mice received saline or VCD (130 mg/kg i.p.) 5 days per week for 3 weeks. One month after injection, mice were fed either low-fat diet (LFD) or HFD for 8 weeks followed by 6 weeks of chronic variable mild stress (CVMS). Post-CVMS, mice were either processed for gene expression of the anterodorsal BNST or behavior tests to assess cognitive and anxiety-related behaviors. Plasma samples were collected to analyze metabolic hormones and corticosterone levels. VCD-treated HFD-fed mice had higher fat and body mass, and elevated fasting glucose levels compared to controls and more pronounced avoidance behaviors and cognitive impairments. LFD-fed, VCD-treated mice exhibited less exploration of novel objects and open spaces compared to OIL and HFD counterparts. VCD elevated corticosterone levels on LFD and increased BNST Pacap gene expression on HFD. These findings highlight cognitive repercussions of estrogen deficiency and suggest a potential protective effect of a HFD against some of the adverse outcomes associated with menopause. Our study emphasizes the importance of considering dietary and hormonal interactions in the development of therapeutic strategies.

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Contemporary menopausal hormone therapy and risk of cardiovascular disease: Swedish nationwide register based emulated target trial

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Objective: To assess the effect of contemporary menopausal hormone therapy on the risk of cardiovascular disease according to the route of administration and combination of hormones. Design: Nationwide register based emulated target trial. Setting: Swedish national registries. Participants: 919 614 women aged 50-58 between 2007 and 2020 without hormone therapy use in the previous two years, identified from the Swedish population.Interventions: 138 nested trials were designed, starting each month from July 2007 until December 2018. Using the presc ription registry data for that specific month, women who had not used hormone therapy in the previous two years were assigned to one of eight treatment groups: oral combined continuous, oral combined sequential, oral unopposed oestrogen, oral oestrogen with local progestin, tibolone, transdermal combined, transdermal unopposed oestrogen, or non-initiators of menopausal hormone therapy. Main outcome measures: Hazard ratios with 95% confidence intervals were estimated for venous thromboembolism, as well as for ischaemic heart disease, cerebral infarction, and myocardial infarction separately and as a composite cardiovascular disease outcome. Treatment effects were estimated by contrasting initiators and non-initiators in observational analogues to "intention-to-treat" analyses and continuous users versus never users in "per protocol" analyses. Results: A total of 77 512 women were initiators of any menopausal hormone therapy and 842 102 women were non-initiators. 24 089 women had an event recorded during the follow-up: 10 360 (43.0%) had an ischaemic heart disease event, 4098 (17.0%) had a cerebral infarction event, 4312 (17.9%) had a myocardial infarction event, and 9196 (38.2%) had a venous thromboembolic event. In intention-to-treat analyses, tibolone was associated with an

increased risk of cardiovascular disease (hazard ratio 1.52, 95% confidence interval 1.11 to 2.08) compared with non-initiators. Initiators of tibolone or oral oestrogen-progestin therapy had a higher risk of ischaemic heart disease (1.46 (1.00 to 2.14) and 1.21 (1.00 to 1.46), respectively). A higher risk of venous thromboembolism was observed for oral continuous oestrogen-progestin therapy (1.61, 1.35 to 1.92), sequential therapy (2.00, 1.61 to 2.49), and oestrogen-only therapy (1.57, 1.02 to 2.44). Additional results in per protocol analyses showed that use of tibolone was associated with a higher risk of cerebral infarction (1.97, 1.02 to 3.78) and myocardial infarction (1.94, 1.01 to 3.73).mConclusions: Use of oral oestrogen-progestin therapy was associated with an increased risk of heart disease and venous thromboembolism, whereas the use of tibolone was associated with an increased risk of ischaemic heart disease, cerebral infarction, and myocardial infarction but not venous thromboembolism. These findings highlight the diverse effects of different hormone combinations and administration methods on the risk of cardiovascular disease.

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Earlier Age at Menopause, Plasma Metabolome, and Risk of Premature Mortality

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Background/objectives: Menopause and related metabolites are associated with mortality. However, the relationship between earlier menopause, premature mortality, and the role of metabolomic signatures remains underexplored. This study investigated the association between earlier menopause and premature mortality, and the mediating effect of metabolomic signatures. Methods: This prospective cohort study used data from the UK Biobank, including 33,687 post-menopausal women aged 40-69 years. Age at menopause was obtained from a baseline self-reported questionnaire and analyzed both as a continuous variable and in categories (<40, 40-49, and ≥50 years). Premature mortality was defined as deaths before 75 years. Cox regression was used to estimate hazard ratios (HRs), and elastic net regression identified metabolomic signatures related to menopause age. Mediation analysis was conducted to assess the proportion of the association explained by the metabolomic signature. Results: During a median follow-up of 13.7 years, 1612 cases of premature mortality occurred. Compared to menopause at ≥50 years, earlier menopause (HR 1.17, 95% CI 1.04-1.30) and premature menopause (HR 1.60, 95% CI 1.28-2.00) were associated with higher risks of premature mortality. A metabolomic signature inversely associated with premature mortality (HR per SD increment, 0.79; 95% CI, 0.75-0.83) mediated 13.6% (95% CI, 1.9%-28.3%) of the association between earlier menopause and premature mortality. Conclusions: Earlier menopause is associated with an increased risk of premature mortality, partially mediated by a metabolomic signature related to age at menopause. These findings highlight the importance of metabolomic profiling in understanding menopause and mortality risks.