Selección de Resúmenes de Menopausia

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Transcriptomic Profiling Reveals 17β-Estradiol Treatment Represses Ubiquitin-Proteasomal Mediators in Skeletal Muscle of Ovariectomized Mice

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Background: With a decline of 17β-estradiol (E2) at menopause, E2 has been implicated in the accompanied loss of skeletal muscle mass and strength. We aimed at characterizing transcriptomic responses of skeletal muscle to E2 in female mice, testing the hypothesis that genes and pathways related to contraction and maintenance of mass are differentially expressed in ovariectomized mice with and without E2 treatment. Methods: Soleus and tibialis anterior (TA) muscles from C57BL/6 ovariectomized mice treated with placebo (OVX) or E2 (OVX + E2) for 60 days, or from skeletal muscle-specific ERα knockout (skmERαKO) mice and wild-type littermates (skmERαWT), were used for genome-wide expression profiling, quantitative real-time PCR and immunoblotting. Computational detection of estrogen response elements (EREs) was performed with EREFINDER. Results: We found 155 significantly regulated probe sets in response to E2 ($p \leq 0.001$). Pathway analyses identified proteasome and ubiquitin-mediated proteolysis as two downregulated pathways in the E2 group. We confirmed downregulation ($p \leq 0.05$) in levels of Fbxw7, Psmb6, Ube2h and Ubxn1, as well as pro-apoptotic Bnip3 and inflammatory factor Nfkbia. Computational analysis identified ERE in the promoter regions of Psmb6, Ube2h, Bnip3 and Nfkbia. The overall content of ubiquitinated proteins was modestly but significantly lower in TA muscles from OVX + E2 vs. OVX mice ($p = 0.039$). There were no differences between skmERαKO and skmERαWT mice or between skmERαKO/OVX and skmERαKO/OVX + E2 mice for any genes assessed, indicating that ERα is required for E2 regulation of those genes. Conclusions: These results suggest that a mechanism whereby E2 protects against losses of skeletal muscle mass and strength is regulation of ubiquitin-proteasomal mediators.

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Menopause and obstructive sleep apnea: revealing an independent mediating role of visceral fat beyond body mass index

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Background: Menopause is a significant phase in women's health, in which the incidence of obstructive sleep apnea (OSA) is significantly increased. Body fat distribution changes with age and hormone levels in postmenopausal women, but the extent to which changes in body fat distribution affect the occurrence of OSA is unclear. Methods: This research performed a cross-sectional analysis utilizing data from the 2015-2016 National Health and Nutrition Examination Survey (NHANES). Body fat distribution was quantified using dual-energy X-ray absorptiometry in kilograms. Menopausal status and OSA symptoms were determined by questionnaire. Weighted multivariable regression analysis was utilized to investigate the correlation between menopausal status and OSA symptoms and body fat composition. We did a mediation analysis to assess how much of the effect of menopausal status on OSA symptoms was mediated through in body fat composition. Results: The analysis comprised 1459 individuals from NHANES, consisting of 1188 premenopausal and 271 postmenopausal women. In the weighted sample, 36.01% of premenopausal women and 53.39% of postmenopausal women had OSA symptoms. After adjusting for body mass index (BMI) and other potential confounders, menopausal status was correlated with a higher prevalence of OSA symptoms (OR = 1.57; 95% CI: 1.16,2.13), and increased visceral fat mass (β = 0.12; 95% CI: 0.07, 0.17). In addition, visceral fat mass exhibited a significant correlation with OSA symptoms (OR = 3.79; 95% CI: 1.61, 8.94). Mediation analysis showed that 29.76% of the effect of menopausal status on OSA symptoms was mediated through visceral fat. In age-matched analysis, postmenopausal women had higher visceral fat mass (0.63 kg vs. 0.52 kg, P = 0.02) and a higher prevalence of OSA symptoms (68.3% vs. 45.7%, P = 0.02) compared with premenopausal women; however, there was no significant difference in BMI (P > 0.05). Conclusion: Our results suggest that menopausal status is associated with increased visceral fat accumulation and OSA symptoms prevalence. Visceral fat accumulation appears to play an important role in the

development of OSA in postmenopausal women, independent of BMI; this highlights the importance of further studying this relationship.

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Effects of physical activity on depressive and anxiety symptoms of women in the menopausal transition and menopause: a comprehensive systematic review and meta-analysis of randomized controlled trials

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Background: Depression and anxiety may significantly affect women in the menopausal transition and menopause. In addition to traditional treatment strategies such as hormone therapy, antidepressants, and psychotherapy, physical activity (PA) have been increasingly studied, but there is no consensus about their role in menopausal women with depression and anxiety. Objective: The current study aimed to evaluate the effect of PA on the severity of depressive (DS) and anxiety (AS) symptoms in women during the menopausal transition and menopause.Methods: We searched for relevant published studies in PubMed, Embase, Web of Science, Cochrane Library, and CI NAHL prior to 8 April 2024, focusing on randomized controlled trials documenting the effect of physical activity on DS and AS, and assessed study quality using the Newcastle-Ottawa Scale. Results: The data used for meta-analysis were derived from 21 studies (DS, n = 9; AS, n = 1; DS and AS combined, n = 11) involving 2020 participants. The results showed that PA groups demonstrated a statistically significant effect of depressive symptoms versus controls (DS [SMD: -0.66, 95% CI: -0.99 to -0.33; P < 0.001]; AS [SMD: -0.55, 95% CI: -0.82 to -0.27; P < 0.001]). As subgroup analyses demonstrated, physical exercise also reduced depressive symptom of women in menopausal status (SMD =-0.56, 95% CI: -0.96 to - 0.17, p = 0.006, I2 = 69%), postmenopausal status (SMD =-0.94, 95% CI: -1.46 to - 0.42, p = 0.0004, I2 = 94%), and both in menopausal transition and postmenopausal status (SMD =-0.30, 95% CI: -0.49 to - 0.12, p = 0.001, I2 = 0%), while it only reduced anxiety symptom of postmenopausal women (SMD =-0.96, 95% CI: -1.49 to - 0.43, p = 0.0004, I2 = 89%). Low-intensity and moderate-intensity exercise both produced increasingly benefits over depressive and anxiety symptoms. However, there is no statistically significant effect of exercise intensity on both depressive symptom and anxiety symptom. Conclusion: Physical activities with low to moderate intensity can impart remarkable improvements for managing menopausal women with depression and anxiety.

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Safety of topical estrogen therapy during adjuvant endocrine treatment among patients with breast cancer: A meta-analysis based expert panel discussion

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Importance: Endocrine treatments, such as Tamoxifen (TAM) and/or Aromatase inhibitors (AI), are the adjuvant therapy of choice for hormone-receptor positive breast cancer. These agents are associated with menopausal symptoms, adversely affecting drug compliance. Topical estrogen (TE) has been proposed for symptom management, given its' local application and presumed reduced bioavailability, however its oncological safety remains uncertain. Objective: The present systematic review, meta-analysis and expert panel review aimed to evaluate the strength of the available evidence on the risk of recurrence and mortality when TE is utilised in congruence with TAM or AI treatment, among BC survivors. Data sources: Six databases and two prospective registers, were interrogated from inception to January 3rd, 2024. Search terms were Breast cancer AND Hormone replacement therapy AND topical/vaginal oestrogen AND recurrence/mortality. Study selection: All study designs reporting the use vs. non-use of TE in breast cancer survivors receiving adjuvant endocrine treatment were included. Six observational studies were deemed eligible for inclusion. Data extraction and synthesis: Sources of heterogeneity were explored using subgroup analysis by risk of bias, median follow-up period, node positivity and menopausal status. Trial sequential analysis was performed to quantify outcome reliability. A global expert panel was called to deliberate on the data, pinpoint areas of limited understanding, and determine the most important areas for future research. Main outcomes and measures: Risk ratio effect sizes (RR) and corresponding 95 % Confidence Intervals (CI) of breast cancer recurrence and mortality in survivors on endocrine treatment (TAM and/or AI) exposed to TE were reported. Expert panel appraisal of meta-analysis evidence with definition of current knowledge gaps and future research aims. Results: In 38 050 female patients receiving adjuvant endocrine treatment, of whom 1805 had been exposed to TE, TE exposure of those on AI, did not increase all-cause mortality (RR 0.99 [95 %CI 0.58, 1.69], I2 = 81 %, P = 0.96; moderate GRADE certainty). However, such exposure may convey an increased risk of recurrence (RR 2.51 [95 % CI 1.10, 5.72], I2 = 9 %, P = 0.03; low-GRADE certainty). Exposure to TE during TAM did not increase either recurrence risk or all-cause mortality. Clinical factors such as lymph node positivity at the time of

diagnosis and menopausal status and follow-up time appeared to be significant confounders. Conclusions and relevance: The use of TE does not appear to increase either recurrence or mortality risk among BC survivors treated with TAM. An increased recurrence risk, without an increase in mortality, cannot be ruled out when TE is used during AI.

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Prevalence and predictors of genitourinary syndrome of menopause: a population-based study in middle-aged Brazilian women

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Objective: This study aimed to determine the prevalence and predictors of genitourinary syndrome of menopause (GSM) in Brazilian women.Methods: A cross-sectional population-based household survey was conducted among 749 women aged 45 to 60 years. Th e dependent variable was the presence of GSM, which was assessed using a pretested structured questionnaire. The independent variables included sociodemographic data, health-related habits and morbidities, self-perception of health, and gynecological background. Results: The mean age of the participants was 52.5 ± 4.4 years, and the mean age of menopause was 46.4 ± 6.2 years. GSM was prevalent in 51.4% of the women. The most prevalent symptoms were dyspareunia (35%), daily vaginal dryness (25.1%), and intercourse vaginal dryness (24%). Poisson regression analysis demonstrated that global GSM was associated with having a partner, topical estrogen treatment (TET), depression/anxiety, and rheumatological diseases. The genital symptoms of GSM were related to peri/postmenopausal status, TET, multimorbidity, sexual activity, and the absence of vaginal birth. Factors associated with GSM urinary symptoms were negative self-perception of health, having at least one vaginal birth, depression/anxiety, and rheumatological diseases. Sexual symptoms were associated with having a partner, using TET, depression/anxiety, and rheumatic disease. GSM affected the lives of 42.8% of the women to some degree, and 43% discussed their symptoms with their gynecologists. Conclusions: GSM was prevalent in half of the women in this study, and several factors were associated with its presence. These results highlight the compelling need to understand these factors, improve diagnoses, and increase access to treatment.

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Profiles of testosterone and pre-androgens and sexual function in premenopausal women

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Background: There is inconsistent evidence as to the role of testosterone and pre-androgens in premenopausal female sexual function, and reported associations between blood concentrations of these hormones and female sexual function vary in strength. Aim: To examine the patterns of testosterone and pre-androgen concentrations and variations in sexual function in premenopausal eumenorrheic women.Methods: This was a secondary analysis of a sample of 588 premenopausal eumenorrheic women from the Grollo-Ruzzene Foundation Young Women's Health Study. Socio-demographics, health information, and questionnaire data were collected using online surveys. Eligible women were invited to provide a blood sample. We ran latent profile analysis (LPA) and subsequent analyses in R using RStudio. Outcomes: Indicator variables in the LPA included sexual arousal and desire domains of the Profile of Female Sexual Function and testosterone, dehydroepiandrosterone (DHEA), and androstenedione, measured by liquid chromatography-tandem mass spectrometry. Results: Analyses resulted in a pattern of 3 latent classes. Classes reporting relatively lower and higher sexual arousal (LPA-derived means and 95% CIs: -0.79 [-1.24; -0.34] and 0.62 [0.51; 0.72]) did not differ significantly in sex steroid concentrations (testosterone: -0.21 [-0.38; -0.03] and -0.33 [-0.47; -0.20]; DHEA: -0.47 [-0.57; -0.37] and -0.26 [-0.39; -0.13]; androstenedione: -0.36 [-0.50; -0.22] and -0.39 [-0.49; -0.29]), while the class reporting relatively medium arousal (-0.11 [-0.31; 0.08]) showed the highest testosterone, DHEA, and androstenedione concentrations (testosterone: 0.8 [0.60; 1.01]; DHEA: 0.99 [0.76; 1.23]; androstenedione: 1.08 [0.88; 1.29]). There were no significant differences in sexual desire between classes (-0.08 [-0.23; 0.06]; 0.00 [-0.13; 0.14]; 0.10 [-0.09; 0.30]) differing significantly in sex steroid concentrations (-0.69 [-0.80; -0.58], -0.04 [-0.15; 0.07], 0.94 [0.71; 1.16] for testosterone) nor associations between the sex steroid concentrations and degrees of sexual desire. Clinical implications: These findings cast further doubt on the utility of measuring sex steroids for diagnosing female sexual dysfunction in premenopausal eumenorrheic women, even when considered in combination. Strengths and limitations: We analyzed a large community sample and controlled for potentially biasing factors. We analyzed sex steroid concentrations determined with gold-standard methodology. Excluding women with early menopause and menstrual dysfunction might have resulted in finding 3, rather than more, latent classes. Conclusion: Testosterone and pre-androgen profiles do not clearly identify premenopausal eumenorrheic women with low sexual arousal and desire.