Selección de Resúmenes de Menopausia

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The significance of recent fracture location for imminent risk of hip and vertebral fractures-a nationwide cohort study on older adults in Sweden

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The role of recent fracture site in predicting the most detrimental subsequent fractures, hip and vertebral, is unclear. This study found that most recent fracture sites were associated with an increased risk of both hip and vertebral fracture, a finding that may impact the design of secondary prevention programs. Background: Hip and vertebral fractures are the most serious in terms of associated morbidity, mortality, and societal costs. There is limited evidence as to which fracture types are associated with the highest risk for subsequent hip and vertebral fractures. This study aims to explore the dependency of imminent hip and vertebral fracture risk on the site of the recent index fracture. Methods: Conducted as a nationwide retrospective cohort study, we utilized Swedish national registers to assess the risk of hip and vertebral fractures based on the site of the recent (≤ 2 years) index fracture and an old (> 2 years) prevalent fracture. This risk was compared to that observed in individuals without any prevalent fractures. This study encompassed all Swedes aged 50 years and older between 2007 and 2010. Patients with a recent fracture were categorized into specific groups based on the type of their previous fracture and were followed until December 2017, with censoring for death and migration. The study assessed the risk of hip and vertebral fractures during the follow-up period. Results: The study included a total of 3,423,320 individuals, comprising 145,780 with a recent fracture, 293,051 with an old fracture, and 2,984,489 without a previous fracture. The median follow-up times for the three groups were 7.6 years (IQR 4.0-9.1), 7.9 years (5.8-9.2), and 8.5 years (7.4-9.7), respectively. Patients with a recent fracture at almost all sites exhibited a significantly increased risk of hip fracture and an elevated risk of vertebral fracture compared to controls. Patients with recent fractures had an increased risk of subsequent hip and vertebral fractures, regardless of the index fracture site. These results strengthen the notion that all patients with a recent fracture, regardless of fracture site, should be included in secondary prevention programs, to improve the prevention of the clinically most serious fractures.

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Relationship of psychotropic medication use with physical function among postmenopausal women

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To examine cross-sectional and longitudinal relationships of psychotropic medications with physical function after menopause. Analyses involved 4557 Women's Health Initiative Long Life Study (WHI-LLS) participants (mean age at WHI enrollment (1993-1998): 62.8 years). Antidepressant, anxiolytic, and sedative/hypnotic medications were evaluated at WHI enrollment and 3-year follow-up visits. Performance-based physical function [Short Physical Performance Battery (SPPB)] was assessed at the 2012-2013 WHI-LLS visit. Self-reported physical function [RAND-36] was examined at WHI enrollment and the last available follow-up visit-an average of 22 [±2.8] (range: 12-27) years post-enrollment. Multivariable regression models controlled for socio-demographic, lifestyle, and health characteristics. Anxiolytics were not related to physical function. At WHI enrollment, antidepressant use was cross-sectionally related to worse self-reported physical function defined as a continuous (β = -6.27, 95% confidence interval [CI]: -8.48, -4.07) or as a categorical (< 78 vs. ≥ 78) (odds ratio [OR] = 2.10, 95% CI: 1.48, 2.98) outcome. Antidepressant use at WHI enrollment was also associated with worse performance-based physical function (SPPB) [< 10 vs. ≥ 10] (OR = 1.53, 95% CI: 1.05, 2.21) at the 2012-2013 WHI-LLS visit. Compared to non-users, those using sedative/hypnotics at WHI enrollment but not at the 3-year follow-up visit reported a faster decline in physical function between WHI enrollment and follow-up visits. Among postmenopausal women, antidepressant use was cross-sectionally related to worse self-reported physical function, and with worse performance-based physical function after > 20 years of follow-up. Complex relationships found for hypnotic/sedatives were unexpected and necessitate further investigation.

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Modulation of neural gene networks by estradiol in old rhesus macaque females

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The postmenopausal decrease in circulating estradiol (E2) levels has been shown to contribute to several adverse physiological and psychiatric effects. To elucidate the molecular effects of E2 on the brain, we examined differential gene expression and DNA methylation (DNAm) patterns in the nonhuman primate brain following ovariectomy (Ov) and subsequent subcutaneous bioidentical E2 chronic treatment. We identified several dysregulated molecular networks, including MAPK signaling and dopaminergic synapse response, that are associated with ovariectomy and shared across two different brain areas, the occipital cortex (OC) and prefrontal cortex (PFC). The finding that hypomethylation ($p = 1.6 \times 10\text{-}51$) and upregulation ($p = 3.8 \times 10\text{-}3$) of UBE2M across both brain regions provide strong evidence for molecular differences in the brain induced by E2 depletion. Additionally, differential expression ($p = 1.9 \times 10\text{-}4$; interaction $p = 3.5 \times 10\text{-}2$) of LTBR in the PFC provides further support for the role E2 plays in the brain, by demonstrating that the regulation of some genes that are altered by ovariectomy may also be modulated by Ov followed by hormone replacement therapy (HRT). These results present real opportunities to understand the specific biological mechanisms that are altered with depleted E2. Given E2's potential role in cognitive decline and neuroinflammation, our findings could lead to the discovery of novel therapeutics to slow cognitive decline. Together, this work represents a major step toward understanding molecular changes in the brain that are caused by ovariectomy and how E2 treatment may revert or protect against the negative neuro-related consequences caused by a depletion in estrogen as women approach menopause.

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A Survey on Relation of Menopause to Metabolic Syndrome - SAFOMS STUDY (South Asian Federation of Menopause Societies) - Interim Analysis

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Background: Metabolic syndrome (MS) is a spectrum of disorders that includes dysglycemia, dyslipidemia, central obesity, and hypertension. South Asian Indians are more prone to harbor MS at a younger age compared to Caucasians. However, there is a lack of large-scale data correlating menopause to MS in South Asian settings. Aims and objectives: The study aimed to determine the prevalence of MS and its components in pre- and postmenopausal women. It also assessed the relationship of age, menopausal status, personal and family history, anthropometric parameters, and biochemical markers to MS. Materials and methods: It was an interim analysis of a multicountry cross-sectional study in the South Asian Federation of Menopause Society (SAFOMS) countries: India, Pakistan, Bangladesh, Nepal, and Sri Lanka conducted through both online and physical methods. The survey questionnaire consisted of questions about details of personal history, demographics, and family history related to MS. Anthropometric measurements such as height, weight, basal metabolic index (BMI), waist circumference, and blood pressure readings were noted. Relevant history, history of polycystic ovarian syndrome, hypertensive disorders of pregnancy, and vasomotor symptoms were enquired. Biochemical evaluation of markers associated with MS was undertaken. Results: In this interim analysis, 638 women were recruited. Out of them, 406 (63.6%) women were premenopausal and 232 (36.4%) were postmenopausal. 392 (61.4%) women had MS, while 246 (38.6%) women did not have MS. Increasing age, BMI, and visceral adiposity (waist circumference) were significantly correlated with incidence of MS. Raised fasting blood sugar, hemoglobin A1C, total cholesterol, low-density lipoprotein, serum triglyceride, and reduced high-density lipoprotein levels were significantly associated with the incidence of MS in both pre- and postmenopausal women. Peri- and postmenopausal hot flashes, night sweats, and sleep disturbances were also significantly associated with MS. Personal history of hypertension, diabetes, and dyslipidemia were the strongest factors to be associated with MS with a significantly high odds ratio. Conclusion: The study has highlighted the role of BMI and waist circumference as the first warning signs, which will encourage to go for regular biochemical screening through lipid profile and fasting blood glucose measurements. Our study is a stepping stone for all future studies for relation of menopause to MS.

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Early-onset vasomotor symptoms and development of depressive symptoms among premenopausal women

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Background: We investigated the association between vasomotor symptoms (VMSs) and the onset of depressive symptoms among premenopausal women. Methods: This cross-sectional study included 4376 premenopausal women aged 42-52 years, and the cohort study included 2832 women without clinically relevant depressive symptoms at baseline. VMSs included the symptoms of hot flashes and night sweats. Depressive symptoms were evaluated using the Center for Epidemiological Studies Depression Scale; a score of ≥16 was considered to define clinically relevant depressive symptoms. Results: Premenopausal Women with VMSs at baseline exhibited a higher prevalence of depressive symptoms compared with women without VMSs at baseline (multivariable-adjusted prevalence ratio 1.76, 95 % confidence interval [CI] 1.47-2.11). Among the 2832 women followed up (median, 6.1 years), 406 developed clinically relevant depressive symptoms. Women with versus without VMSs had a significantly higher risk of developing clinically relevant depressive symptoms (multivariable-adjusted hazard ratio, 1.72; 95 % CI 1.39-2.14). VMS severity exhibited a dose-response relationship with depressive symptoms (P for trend <0.05). Limitations: Self-reported questionnaires were only used to obtain VMSs and depressive symptoms, which could have led to misclassification. We also could not directly measure sex hormone levels. Conclusions: Even in the premenopausal stage, women who experience hot flashes or night sweats have an increased risk of present and developed clinically relevant depressive symptoms. It is important to conduct mental health screenings and provide appropriate support to middle-aged women who experience early-onset VMSs.

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Systematic review and meta-analysis of the effects of menopause hormone therapy on cognition

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Introduction: Despite evidence from preclinical studies suggesting estrogen's neuroprotective effects, the use of menopausal hormone therapy (MHT) to support cognitive function remains controversial. Methods: We used random-effect meta-analysis and multi-level meta-regression to derive pooled standardized mean difference (SMD) and 95% confidence intervals (C.I.) from 34 randomized controlled trials, including 14,914 treated and 12,679 placebo participants. Results: Associations between MHT and cognitive function in some domains and tests of interest varied by formulation and treatment timing. While MHT had no overall effects on cognitive domain scores, treatment for surgical menopause, mostly estrogen-only therapy, improved global cognition (SMD=1.575, 95% CI 0.228, 2.921; P=0.043) compared to placebo. When initiated specifically in midlife or close to menopause onset, estrogen therapy was associated with improved verbal memory (SMD=0.394, 95% CI 0.014, 0.774; P=0.046), while late-life initiation had no effects. Overall, estrogen-progestogen therapy for spontaneous menopause was associated with a decline in Mini Mental State Exam (MMSE) scores as compared to placebo, with most studies administering treatment in a late-life population (SMD=-1.853, 95% CI -2.974, -0.733; P = 0.030). In analysis of timing of initiation, estrogen-progestogen therapy had no significant effects in midlife but was associated with improved verbal memory in late-life (P = 0.049). Duration of treatment >1 year was associated with worsening in visual memory as compared to shorter duration. Analysis of individual cognitive tests yielded more variable results of positive and negative effects associated with MHT.D iscussion: These findings suggest time-dependent effects of MHT on certain aspects of cognition, with variations based on formulation and timing of initiation, underscoring the need for further research with larger samples and more homogeneous study designs.

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Targeting Cell Senescence and Senolytics: Novel Interventions for Age-Related Endocrine Dysfunction

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Multiple changes occur in hormonal regulation with aging and across various endocrine organs. These changes are associated with multiple age-related disorders and diseases. A better understanding of responsible underling biological mechanisms could help in the management of multiple endocrine disorders over and above hormone replacement therapy (HRT). Cellular senescence is involved in multiple biological aging processes and pathologies common in elderly individuals. Cellular senescence, which occurs in many older individuals but also across the lifespan in association with tissue damage, acute and chronic diseases, certain drugs, and genetic syndromes, may contribute to such endocrine disorders as osteoporosis, metabolic syndrome, and type II diabetes mellitus (T2DM). Drugs that selectively induce senescent cell removal, "senolytics", and drugs that attenuate the tissue-destructive secretory state

of certain senescent cells, "senomorphics", appear to delay the onset or alleviate multiple diseases, including but not limited to endocrine disorders such as diabetes, complications of obesity, age-related osteoporosis, and cancers as well as atherosclerosis, chronic kidney disease, neurodegenerative disorders, and many others. Over thirty clinical trials of senolytic and senomorphic agents have already been completed, are underway, or are planned for a variety of indications. Targeting senescent cells is a novel strategy that is distinct from conventional therapies such as HRT, and thus might address unmet medical needs and can potentially amplify effects of established endocrine drug regimens, perhaps allowing for dose decreases and reducing side effects.