Selección de Resúmenes de Menopausia

Semana del 3 al 9 de diciembre, 2025

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Vaginal use of estradiol is associated with a reduced risk of rectal cancer in postmenopausal women: A Finnish nationwide case-control study

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Study design: We identified in this nationwide case-control study primary rectal cancer cases with five age-matched control cases in 1994-2019 from our dataset of 1.1 million Finnish postmenopausal women. We excluded users of systemic hormone therapy. Then we traced users of vaginal estradiol (10-25 μg twice a week) from the reimbursement register in 1994-2013, a period in which users could be accurately traced in the database (which was not the case for 2014-2019). Main outcome measures: Odds ratios with 95 % confidence intervals were calculated for rectal cancer risk with adjusted logistic regression models separately for vaginal estradiol users in 1994-2013 (1640 cases, 7889 controls) and for the whole study period of 1994-2019 (2853 cases, 13865 controls). Results: During follow-up, 494 rectal cancer patients (17 %) and 2826 controls (20 %) used vaginal estradiol ($p < 0.001$). Users were diagnosed with rectal cancer on average nine years later than non-users (73.9 vs 65.1 years, $p < 0.001$). Use for ≥3 years was associated with a reduced risk of rectal cancer (OR 0.79, 95 % CI 0.63-0.97) in the 1994-2013 cohort. In the extended 1994-2019 follow-up, risk reductions were similar (0.79, 0.68-0.92), appeared already with <3 years' use (0.85, 0.74-0.97), and persisted for up to 5 years after cessation of vaginal estradiol (0.80, 0.71-0.91). Conclusions: Vaginal estradiol use may be associated with a reduced risk of rectal cancer - perhaps due to estradiol infiltration into the rectal mucosa. This possible protecting effect could be an important additional health benefit of vaginal estradiol.

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No causal links between estradiol and female's brain and mental health using Mendelian randomization

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The role of estradiol in depression and Alzheimer's disease - brain disorders that disproportionately affect females - is debated. Results from observational studies are inconsistent and limited by confounding and reverse causation. To overcome these limitations, we perform two-sample Mendelian randomization. We run genome-wide association studies on sex-specific brain age gap, a proxy of brain health, and female-specific estradiol levels using data from the UK Biobank. We test for causal links between genetically-predicted factors related to estradiol exposure (estradiol levels in pre- and postmenopausal samples, reproductive span, age at menarche, age at menopause, number of childbirths) and brain age gap, Alzheimer's disease and depression as outcomes. We replicate our analyses on estradiol levels in males. Here, we find no significant associations between estradiol exposure and brain health across samples and robust methods, indicating an absence of constant causal effects and suggesting that hormonal fluctuations may drive links between estradiol and brain health.

Nota. *Mendelian randomization: Algunas variantes genéticas están asociadas con un factor de riesgo modificable (por ejemplo, colesterol LDL, IMC, presión arterial). Si esa variante genética también se asocia con una enfermedad, se puede inferir que el factor de riesgo probablemente causa la enfermedad. Es un método que usa variantes genéticas para determinar si una asociación observacional es probablemente causal.*

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Reproductive Lifespan and Reproductive Factors in Relation to Dementia Risk in Postmenopausal Women With Type 2 Diabetes.

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Objective: Endogenous estrogen exposure has been linked to a reduced risk of cognitive decline. Our study examined the influence of reproductive factors on the risk of dementia among women with diabetes. Research design and methods:

We identified 159,751 postmenopausal women with type 2 diabetes aged over 40 years who underwent health examinations in 2009 from the National Health Information Database. Data on reproductive factors were obtained using self-administered questionnaires. Incident dementia was determined by diagnosis codes and records of antidementia medication prescriptions. Cox proportional hazards regression analyses estimated the risk of all-cause dementia, Alzheimer disease, and vascular dementia according to reproductive factors such as reproductive lifespan, parity, and hormone replacement therapy (HRT) use. Results: The mean age was 64.5 ± 8.0 years, and the mean reproductive lifespan was 33.6 ± 4.5 years. Over a median follow-up of 8.3 years, 24,218 cases of all-cause dementia were identified (18,819 cases of Alzheimer disease, 2,743 cases of vascular dementia). Compared with a reproductive lifespan of <30 years, ≥40 years was associated with lower risk of all-cause dementia (hazard ratio 0.73; 95% CI 0.69-0.78). Women with parity 1 had a 27% lower risk of all-cause dementia compared with women with parity 0, and women who used HRT for more than 5 years had a 17% lower risk compared with those who did not use HRT. Comparable effects were found for both Alzheimer disease and vascular dementia. Conclusions: A longer reproductive lifespan was linked to a reduced risk of dementia in postmenopausal women with type 2 diabetes.

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Diagnostic value and concordance of endometrial thickness, smear, and biopsy results in women with abnormal uterine bleeding

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OBJECTIVE: This study was conducted to investigate whether an effective screening method for endometrial hyperplasia and endometrial cancer can be identified by comparing the results of transvaginal ultrasonography (TV-USG), liquid-based endometrial cytology, and endometrial biopsy. MATERIALS AND METHODS: The study included a total of 200 patients with a mean age of 50.04 ± 10.39 years (range: 33-85), who presented with abnormal uterine bleeding during the premenopausal and postmenopausal periods. Following a detailed clinical examination, endometrial thickness was measured using TV-USG in all cases. Subsequently, liquid-based endometrial cytology was obtained using an endometrial brush, followed by an endometrial biopsy using a Karman cannula. All patients were evaluated by the same clinician, and both the cytological and biopsy specimens were assessed by the same pathologist. RESULTS: No endometrial pathology was detected in cases with an endometrial thickness of ≤ 5 mm as measured by TV-USG. The mean endometrial thickness was found to be 12.66 mm for simple hyperplasia without atypia, 18 mm for complex atypical hyperplasia, and 17.00 mm for endometrial adenocarcinoma. A statistically significant difference was observed among these three groups with endometrial thicknesses ($p < 0.05$). The endometrial thickness in cases with complex atypical hyperplasia and endometrial cancer was significantly higher compared to the others ($p < 0.05$). While 58% of endometrial cytology samples and 34% of biopsy samples were found to be insufficient for evaluation, cytology still appeared to be a useful method for detecting malignant lesions. The high insufficiency rate observed in our series likely reflects the sampling technique employed, as an endocervical-type brush was used rather than a dedicated endometrial sampler, which may have reduced cellular yield and affected adequacy rates. For the diagnosis of malignant lesions, cytology demonstrated a sensitivity of 100%, a specificity of 96.9%, a positive predictive value of 71.43%, and a negative predictive value of 100%. CONCLUSIONS: Although TV-USG is not a method that provides a definitive diagnosis, it is highly effective in identifying cases that require further investigation. Moreover, due to its non-invasive nature, it should be considered the first-line diagnostic tool in patients suspected of having endometrial pathology. Despite the high diagnostic accuracy of endometrial cytology in detecting malignant lesions, the relatively high rate of insufficient sample both in premenopausal and postmenopausal patients compared to biopsy represents a notable disadvantage. Therefore, we do not consider endometrial cytology to be a standalone method suitable for screening endometrial cancer and its precursors. However, since malignant lesions were reliably detected when adequate cytology material was obtained, dedicated endometrial samplers and emerging molecular adjuncts should be evaluated in future prospective studies to determine whether cytology can contribute to a multimodal screening strategy.

Int J Womens Health. 2025 Nov 25:17:4879-4890. doi: 10.2147/IJWH.S542278. eCollection 2025.

Nonlinear Association Between Oxidative Balance Score and Premature Menopause: A Cross-Sectional Analysis of NHANES 2007-2018 Data

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Background: Oxidative stress is a critical mediator in ovarian aging, a key process leading to premature menopause (PM), which is defined as menopause before age 40. While the Oxidative Balance Score (OBS), a composite measure

of dietary and lifestyle pro- and anti-oxidant exposures, provides valuable insight, its association with PM remains unclear. This study aimed to investigate the association between OBS and PM in a nationally representative US population. Methods: This cross-sectional study utilized data from 4,128 participants in the National Health and Nutrition Examination Survey (NHANES) 2007-2018. The OBS was calculated from 16 dietary and 4 lifestyle components. Multivariable logistic regression models were used to estimate odds ratios (ORs) and 95% confidence intervals (CIs), with all analyses accounting for the complex survey design using appropriate NHANES sample weights. The potential nonlinear relationship was explored using restricted cubic splines (RCS). Results: A higher total OBS was significantly associated with a lower risk of PM (Adjusted OR for the highest compared to the lowest quartile, 0.51; 95% CI, 0.31 to 0.83). The dietary OBS component showed a consistent inverse association. Subgroup analysis suggested potential ethnic variations, although the interaction did not reach statistical significance (P for interaction = 0.054). RCS analysis confirmed a nonlinear inverse association. Further threshold effect analysis identified a turning point at an OBS of 28; the association was significant below this threshold (OR per unit increase, 0.95; 95% CI, 0.93 to 0.97), but this was not observed above it (OR, 1.09; 95% CI, 1.00 to 1.18). Conclusion: In this nationally representative sample of US women, a higher OBS was associated with a lower risk of PM, particularly below a score of 28. These findings suggest that dietary and lifestyle factors contributing to antioxidant balance may play a role in preserving ovarian function, although prospective studies are required to confirm causality.

Calcif Tissue Int. 2025 Dec 1;116(1):137. doi: 10.1007/s00223-025-01450-1.

Beyond Estrogen Deficiency: The Independent Role of FSH in Site-Specific Bone Loss in Midlife Women

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Follicle-stimulating hormone (FSH) was independently associated with lumbar spine (LS) bone mineral density (BMD), while estradiol (E2) predicted femoral neck BMD. A threshold effect for FSH (~ 15 mIU/mL) suggests site-specific and non-linear hormonal influences on bone during the menopausal transition. To investigate the association between serum FSH levels and BMD in midlife women, and to determine whether these associations persist after adjustment for E2 and age, with particular attention to site-specific effects. We conducted a cross-sectional study of 224 women aged 45-60 years, selected from an institutional database. Inclusion required simultaneous measurements of serum FSH, E2, and BMD at the LS, femoral neck (FN), and total hip (TH) by dual-energy X-ray absorptiometry. Women using anti-osteoporotic drugs, hormone therapy, or medications affecting bone, were excluded. Analyses included non-parametric tests, Spearman's correlations, multivariable linear regression with log-transformed hormones and stepwise BIC selection, and segmented regression. FSH rose progressively across menopausal stages, while E2 declined,, paralleling lower BMD values. Higher FSH correlated inversely with LS ($\rho = -0.26$, $p < 0.001$) and FN-BMD ($\rho = -0.29$, $p = 0.041$), while E2 correlated positively with LS-BMD ($\rho = 0.22$, $p = 0.018$). In multivariable models, log-FSH remained independently associated with LS-BMD ($\beta = -0.072$, $p = 0.009$), whereas log-E2 was the only predictor at FN-BMD ($\beta = 0.138$, $p = 0.020$). No predictors were retained for TH-BMD. Segmented regression identified a breakpoint at ~ 15 mIU/mL of FSH, below which LS-BMD declined steeply ($\beta = -0.007$ g/cm2 per mIU/mL), with a plateau thereafter. FSH and E2 exert distinct, site-specific influences on bone. FSH was independently associated with LS-BMD and showed a threshold effect, while E2 was more relevant to FN. These findings suggest that menopausal bone loss is not solely estrogen-driven but also involves gonadotropin-mediated mechanisms.

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Postmenopausal sarcopenia and Alzheimer's disease: The interplay of mitochondria, insulin resistance, and myokines

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As life expectancy increases, cognitive impairments such as Alzheimer's disease (AD) create serious problems for older adults. Women regardless of ethnicity and age group, are disproportionately affected, accounting for two-thirds of AD cases, with post-menopausal women representing over 60 % of those affected. Sarcopenia, defined by gradual reduction of skeletal muscle mass, strength, and activities, is increasingly correlated with an elevated risk of cognitive decline in post-menopausal women. Menopause-related hormonal decline (particularly estrogen loss) and aging contribute to sarcopenia, characterized by muscle mitochondrial dysfunction, oxidative stress, and insulin resistance. This sarcopenia-driven reduction in muscle mass and functional capacity further reduces the production of myokines (e.g., BDNF, irisin), impairing neuronal proliferation, adult neurogenesis, and spatial learning/memory. These pathophysiological changes

show a contributing link between sarcopenia and AD progression in post-menopausal women. This review is unique in that it discusses the triangular interplay between menopause, sarcopenia, and AD, offering an integrated mechanistic framework that links hormonal decline, muscle loss, and neurodegeneration. We aim to clarify the pathophysiological causes behind the muscle-brain axis and suggest viable treatment approaches to slow down sarcopenia and cognitive deterioration in postmenopausal women based on current evidence. The formulation of targeted strategies for enhancing the quality of life and lessening healthcare expenditures in this expanding population depends on the advancement of understanding this complex interconnection between menopause, sarcopenia and cognition.