

Selección de Resúmenes de Menopausia

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Urolithiasis Causes Osteoporosis in Asians: Genetic Evidence from Mendelian Randomization and Pathway Analysis

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Background: It is an indisputable fact that patients with urolithiasis are prone to osteoporosis (OP), but the specific mechanism of their association is unclear. Previous studies have focused on the mediation of environmental factors such as diet; however, the potential of urolithiasis itself to induce OP remains uncertain. **Methods:** In this study, we used data from the Japan BioBank (6,638 urolithiasis and 7,788 OP cases) to investigate the direct causal relationship and mechanism between urolithiasis and OP, applying Mendelian randomization (MR), genetic correlation analysis, colocalization, and pathway analysis. We selected ten genetic variants as instrumental variables (IVs) for urolithiasis. **Results:** The results showed a positive association between genetically predicted urolithiasis and OP, with significant direct effects persisting after adjusting for OP-associated factors in four models. Reverse analysis revealed no significant causal effect of genetically predicted OP on urolithiasis. While genetic correlation analysis and colocalization did not find conclusive evidence, mediation analysis identified eGFR as a significant contributor. Co-risk factor analysis unveiled cardiovascular elements as common risks for both conditions. Bioanalysis implicates cytokine, metabolic, and calcium signaling pathways may bridge urolithiasis and OP, with BCAS3, DGKH, TBX2, and TBX2-AS1 identified as potential causal genes. **Conclusions:** In conclusion, the study establishes a direct causal link between urolithiasis and OP, independent of environmental factors. Regardless of lifestyle, urolithiasis patients should remain vigilant about the risk of OP and consider regular OP screening. The biological mechanism of urolithiasis combined with OP and related drugs still needs to be further explored.

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Resistin and omentin in breast cancer: A systematic review and meta-analysis

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Breast cancer (BC) is the most frequently diagnosed cancer and a leading cause of cancer-related mortality among women globally. Resistin, omentin and ghrelin, adipokines involved in inflammation and metabolic regulation, have been implicated in cancer development, yet their associations with BC remain unclear. This systematic review and meta-analysis aimed to elucidate the relationships between resistin, omentin, and ghrelin concentrations and BC, while exploring potential moderators such as body mass index (BMI) and menopausal status. A comprehensive search of electronic databases up to 13 May 2024 identified studies comparing resistin and omentin, but not ghrelin, concentrations in BC patients and healthy controls. Standardized mean differences (SMDs) were calculated using random-effects models, and meta-regression and subgroup analyses were performed to investigate sources of heterogeneity. Analysis of 11 studies showed that BC patients exhibited significantly higher resistin concentrations compared to controls, with a pooled SMD of 2.05 (95 % CI 1.24 to 2.86, $p < 0.001$). Meta-regression indicated that BMI significantly moderated the resistin-BC association ($p = 0.003$). In contrast, omentin concentrations presented a complex picture, with a pooled SMD of -0.27 (95 % CI -1.39 to 0.84, $I^2 = 96.2\%$, $p < 0.001$), indicating substantial heterogeneity and inconclusive results, whereas only one study investigated ghrelin. Our findings support a significant association between elevated resistin concentrations and BC, suggesting a potential role of resistin in BC pathophysiology. The data on omentin and ghrelin remain inconclusive, warranting further investigation. Future research should focus on large, longitudinal studies with standardized methodologies to validate these findings and clarify the role of adipokines in BC.

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Associations between menopausal symptoms and cardiovascular disease in middle-aged Chinese women

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Objective: This study aimed to examine the association between severity of menopausal symptoms and cardiovascular disease (CVD) risk among middle-aged Chinese women. **Methods:** A cross-sectional study recruited 9679 women aged 40-70 years from three socioeconomic regions of China in 2018. Menopausal symptoms were assessed by the modified Kupperman Menopausal Index (KMI). The severity of individual symptoms was classified as none (0 points), mild (1 points) and moderate-to-severe symptoms (2-3 points), and overall menopausal symptoms were classified as none (<15 points), mild (15-24 points) or moderate-to-severe (≥ 25 points) according to the sum score of the KMI. Logistic regression models were used to examine associations of the severity of menopausal symptoms with CVD risk. **Results:** A total of 5.6% of participants reported being diagnosed with CVD. Overall menopausal symptoms were more common in women aged 60-70 years than in women aged 40-59 years. After multiple adjustment, mild (odds ratio [OR] = 2.07, 95% confidence interval [CI]: 1.64-2.61) and moderate-to-severe (OR = 2.64, 95% CI: 1.92-3.63) overall menopausal symptoms were associated with increased risk of CVD compared with no symptoms. Significant positive associations between the severity of individual menopausal symptoms and CVD risk were observed for all 13 items. **Conclusion:** The severity of menopausal symptoms was positively associated with CVD risk in middle-aged Chinese women.

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Late reproduction is associated with extended female survival but not with familial longevity

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Research question: Are age at last childbirth and number of children, as facets of female reproductive health, related to individual lifespan or familial longevity? **Design:** This observational study included 10,255 female participants from a multigenerational historical cohort, the LINKing System for historical family reconstruction (LINKS), and 1258 female participants from 651 long-lived families in the Leiden Longevity Study (LLS). Age at last childbirth and number of children, as outcomes of reproductive success, were compared with individual and familial longevity using the LINKS dataset. In addition, the genetic predisposition in the form of a polygenic risk score (PRS) for age at menopause was studied in relation to familial longevity using the LLS dataset. **Results:** For each year increase in the age of the birth of the last child, a woman's lifespan increased by 0.06 years (22 days; $P = 0.002$). The yearly risk for having a last child was 9% lower in women who survived to the oldest 10% of their birth cohort (hazard ratio 0.91, 95% CI 0.86-0.95). Women who came from long-living families did not have a higher mean age of last childbirth. There was no significant association between familial longevity and genetic predisposition to age at menopause. **Conclusions:** Female reproductive health associates with a longer lifespan. Familial longevity does not associate to extended reproductive health. Other factors in somatic maintenance that support a longer lifespan are likely to have an impact on reproductive health.

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Mapping global prevalence of menopausal symptoms among middle-aged women: a systematic review and meta-analysis

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Background: Women at middle age are puzzled by a series of menopausal disturbances, can be distressing and considerably affect the personal, social and work lives. We aim to estimate the global prevalence of nineteen menopausal symptoms among middle-aged women by performing a systematic review and meta-analysis. **Methods:** Comprehensive search was performed in multiple databases from January, 2000 to March, 2023 for relevant studies. Random-effect model with double-arcsine transformation was used for data analysis. **Results:** A total of 321 studies comprised of 482,067 middle-aged women were included for further analysis. We found varied prevalence of menopausal symptoms, with the highest prevalence of joint and muscular discomfort (65.43%, 95% CI 62.51-68.29) and lowest of formication (20.5%, 95% CI 13.44-28.60). Notably, South America shared dramatically high prevalence in a sort of menopausal symptoms including depression and urogenital symptoms. Besides, countries with high incomes (49.72%) had a significantly lower prevalence of hot flashes than those with low (65.93%), lower-middle (54.17%), and upper-middle (54.72%, $p < 0.01$), while personal factors, such as menopausal stage, had an influence on most menopausal symptoms, particularly in vaginal dryness. Prevalence of vagina dryness in postmenopausal women (44.81%) was 2-fold higher than in premenopausal women (21.16%, $p < 0.01$). Furthermore, a remarkable distinction was observed between body mass index (BMI) and prevalence of sleep problems, depression, anxiety and

urinary problems. Conclusion: The prevalence of menopausal symptoms affected by both social and personal factors which calls for attention from general public.

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Should I stay for local hormone therapy or should I go for radiofrequency to treat vulvovaginal atrophy? A patient preference trial

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Objective: To compare patient satisfaction rate in postmenopausal women who chose dynamic quadripolar radiofrequency or topical estrogens as their preferred treatment for genitourinary syndrome of menopause. Methods: Patients were divided into two groups according to their preference: one was treated with estrogen therapy (ET) and the other with dynamic quadripolar radiofrequency treatment (RF). All patients included fulfilled a series of validated questionnaires, at baseline and at the 6-mo follow-up, in order to evaluate the discomfort degree associated with the presence of vulvovaginal atrophy and the impact of the reported symptoms on QoL and sexuality. Results: After propensity score matching, the proportion of women considering themselves satisfied with their genital health conditions was extremely small at study entry (5.2% of the RF group and 6.9% of the ET group), while at a 6-mo follow-up, it increased to 46.7% and 46.6%, respectively. No statistically significant between-group differences were found regarding mean numerical rating scale scores for dryness and dyspareunia at follow-up (5.6 ± 2.6 vs 5.3 ± 2.3 , $P = 0.5$; and 2.9 ± 2.5 vs 3.0 ± 2.7 , $P = 0.46$). At 6-mo follow-up, we observed no statistically significant differences between the two groups regarding the other items evaluated. RF treatment was overall well tolerated. Conclusion: The use of quadripolar radiofrequency devices seems effective, but it is not associated with better clinical outcomes compared with topical hormone treatment, which is a substantially cheaper and more convenient treatment for genitourinary syndrome of menopause. Therefore, we suggest limiting the use of dynamic quadripolar radiofrequency selectively when topical estrogens are not effective, not tolerated, or contraindicated.

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Reproductive hormones in relation to white matter hyperintensity volumes among midlife women

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Introduction: Although reproductive hormones are implicated in cerebral small vessel disease in women, few studies consider measured hormones in relation to white matter hyperintensity volume (WMHV), a key indicator of cerebral small vessel disease. Even fewer studies consider estrone (E1), the primary postmenopausal estrogen, or follicle-stimulating hormone (FSH), an indicator of ovarian age. We tested associations of estradiol (E2), E1, and FSH to WMHV among women. Methods: Two hundred twenty-two women (mean age = 59) underwent hormone assays (E1, E2, FSH) and 3T brain magnetic resonance imaging. Associations of hormones to WMHV were tested with linear regression. Results: Higher E2 (B[standard error (SE)] = $-0.17[0.06]$, $P = 0.008$) and E1 (B[SE] = $-0.26[0.10]$, $P = 0.007$) were associated with lower whole-brain WMHV, and higher FSH (B[SE] = $0.26[0.07]$, $P = 0.0005$) with greater WMHV (covariates age, race, education). When additionally controlling for cardiovascular disease risk factors, associations of E1 and FSH to WMHV remained. Discussion: Reproductive hormones, particularly E1 and FSH, are important to women's cerebrovascular health. Highlights: Despite widespread belief that sex hormones are important to women's brain health, little work has considered how these hormones in women relate to white matter hyperintensities (WMH), a major indicator of cerebral small vessel disease. We considered relations of estradiol (E2), estrone (E1), and follicle-stimulating hormone (FSH) to WMH in midlife women. Higher E2 and E1 were associated with lower whole-brain WMH volume (WMHV), and higher FSH with higher whole-brain WMHV. Associations of E1 and FSH, but not E2, to WMHV persisted with adjustment for cardiovascular disease risk factors. Findings underscore the importance of E2 and FSH to women's cerebrovascular health.