

Selección de Resúmenes de Menopausia

Semana del 12 al 18 de octubre, 2022

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Osteoporos Int. 2022 Oct 14. doi: 10.1007/s00198-022-06569-7. Online ahead of print.

Tea consumption and the risks of osteoporosis and hip fracture: a population-based longitudinal follow-up study

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Introduction: To investigate the association of tea consumption with the risks of osteoporosis and hip fracture. **Methods:** This study used the Keelung Community-based Integrated Screening database and Taiwan's National Health Insurance Research Database. A total of 42,742 subjects aged 45 to 74 years were enrolled. Each was classified as no tea consumption, low tea consumption, and high tea consumption, according to the results of an eating habits questionnaire. The diagnosis of osteoporosis and hip fracture was based on BMD measured by dual-energy X-ray absorptiometry and the X-ray findings. The median follow-up time was 8.5 years. **Results:** As compared with the no tea consumption group, the osteoporosis HRs for the low tea consumption and high tea consumption groups were 0.88 (95% confidence interval (CI) 0.80-0.96) and 0.87 (95% CI 0.80-0.94), respectively. Among those participants aged 59 or below, the osteoporosis HRs for low tea consumption and high tea consumption (vs. no tea consumption) were 0.85 (95% CI 0.74-0.96) and 0.79 (95% CI 0.69-0.90). The HRs of hip fracture for the low tea consumption and high tea consumption groups (vs. no tea consumption) were 0.85 (95% CI 0.67-1.08) and 0.69 (95% CI 0.55-0.86), respectively. **Conclusion:** Tea consumption was linked to a lower risk of osteoporosis, particularly among women and middle-aged people. High tea consumption was also associated with a reduced risk of hip fracture.

Eur Heart J. 2022 Aug 4;ehac364. doi: 10.1093/eurheartj/ehac364. Online ahead of print.

Age at menopause and risk of heart failure and atrial fibrillation: a nationwide cohort study

Jean Shin 1, Kyungdo Han 2, Jin Hyung Jung 3, Hyo Jin Park 1, Wonsock Kim 1, Youn Huh , Yang Hyun Kim, et al. **Aims:** This study aimed to examine the association of premature menopause and age at menopause with the risk of heart failure (HF) and atrial fibrillation (AF). **Methods and results:** A total of 1 401 175 postmenopausal women, who had undergone health examination provided by the Korean National Health Insurance Service, were included, and their reproductive histories were collected. Multivariable Cox proportional hazard models were performed to determine the hazard ratios (HRs) and 95% confidence intervals (CIs) of incident HF and AF, according to the history of premature menopause and age at menopause. At a mean follow-up of 9.1 years, there were 42 699 (3.0%) and 44 834 (3.2%) new cases of HF and AF, respectively. Women with history of premature menopause had an increased risk of HF (HR: 1.33, 95% CI: 1.26-1.40) and AF (HR: 1.09, 95% CI: 1.02-1.16), compared to women without the history. Compared with women aged ≥ 50 years at menopause, those aged 45-49, 40-44, and < 40 years at menopause showed a significantly increased trend in HRs for the incident risk of both HF and AF (P for trend < 0.001). The robustness of the results of a series of sensitivity analyses further strengthens the main findings. **Conclusion:** Our findings suggest that postmenopausal women with a history of premature menopause or early menopausal age may have an increased risk of HF and AF. These reproductive factors need to be considered for preventing the future risk of HF and AF.

J Clin Med. 2022 Sep 20;11(19):5512. doi: 10.3390/jcm11195512.

Nephrolithiasis: A Red Flag for Cardiovascular Risk

Alessia Gambaro 1, Gianmarco Lombardi 2, Chiara Caletti 2, Flavio Luciano Ribichini, Pietro Manuel Ferraro, et al. **Epidemiological evidence** shows that nephrolithiasis is associated with cardiovascular (CV) morbidities. The association between nephrolithiasis and CV disease is not surprising because both diseases share conditions that facilitate their development. Metabolic conditions, encompassed in the definition of metabolic syndrome (MS), and habits that promote nephrolithiasis by altering urine composition also promote clinical manifestations of CV disease. By inducing oxidative stress, these conditions cause endothelial dysfunction and increased arterial stiffness, which are both well-known predictors of CV disease. Furthermore, the subtle systemic metabolic acidosis observed in stone formers with CV disease may have a pathogenic role by increasing bone turnover and leading to reduced mineral

content and osteoporosis/osteopenia. Heart valves and/or coronary artery and aortic calcifications are frequently associated with reduced mineral density. This is known as the 'calcification paradox' in osteoporosis and has also been observed in subjects with calcium nephrolithiasis. Evidence supports the hypothesis that osteoporosis/osteopenia is an independent risk factor for the development of CV calcifications. In the long term, episodes of renal stones may occur from the onset of metabolic derangements/MS to arterial stiffness/atherosclerosis and CV morbidities. These episodes should be considered a warning sign of an ongoing and silent atherosclerotic process. The evaluation of cardiometabolic risk factors and MS components should be routine in the assessment of renal stone formers. This would allow for treatment and prevention of the development of CV complications, which are much more severe for the patient and for public health.

Int J Environ Res Public Health. 2022 Sep 23;19(19):12074. doi: 10.3390/ijerph191912074.

Effect of Exercise on Vascular Function and Blood Lipids in Postmenopausal Women: A Systematic Review and Network Meta-Analysis

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This study aimed to compare and rank the effectiveness of aerobic exercise (AE), resistance training (RT), combined training (CT), and water exercise (WE) on vascular function and blood lipids in postmenopausal women using a network meta-analysis (NMA). Methods: We searched the PubMed, Cochrane, Embase, Web of Science, and EBSCO (SPORTDiscus) databases to identify randomized controlled trials investigating the effects of exercise on vascular function and blood lipids in postmenopausal women. The retrieval period was from inception to March 2022. Two reviewers independently screened the retrieved articles, extracted pertinent data, and assessed the risk of bias of the included studies. Results: A total of 38 studies involving 1407 patients were included in this study. The results of the NMA indicated that WE had the greatest effect on systolic blood pressure (SBP) (surface under the cumulative ranking [SUCRA] = 84.9) and total cholesterol (TC) (SUCRA = 93.1); CT had the greatest effect on triglycerides (TG) (SUCRA = 96.2), high-density lipoprotein cholesterol (HDL-C) (SUCRA = 94.8), and diastolic blood pressure (DBP) (SUCRA = 91.1); RT had the greatest effect on low-density lipoprotein cholesterol (LDL-C) (SUCRA = 79.4). Conclusion: The results suggest that exercise can effectively improve the PWV, SBP, and DBP and the levels of TC, TG, and LDL-C in postmenopausal women. WE had the best effect on improving TC and SBP. CT had the best effect on improving TG, HDL-C, and DBP. To improve LDL-C, RT can achieve a good effect. Considering the limitations of NMA, more RCTS need to be performed in the future to provide more direct evidence of the effectiveness of various exercise interventions on vascular health in postmenopausal women.

Int J Environ Res Public Health. 2022 Sep 20;19(19):11871. doi: 10.3390/ijerph191911871.

Possible Association of Hysterectomy Accompanied with Opportunistic Salpingectomy with Early Menopause: A Retrospective Cohort Study

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Opportunistic salpingectomies (OSs) are concurrently performed with hysterectomies to prevent epithelial ovarian cancer. This study aimed to investigate the correlation between OS and early menopause in females who have undergone hysterectomies. This was a retrospective cohort study involving 79 females who had undergone a hysterectomy, with or without an OS, between January 2007 and December 2015. Their ages at surgery, at menopause, and the lengths of time from surgery to menopause were compared. An OS had been performed in 54 and not performed in 25 of the enrolled patients, comprising the OS and non-OS groups. Body mass index was significantly higher in the OS group (OS: 25.27 ± 4.17 vs. non-OS: 22.97 ± 3.27 , $p = 0.01$). Additionally, menopausal sleep problems were more prevalent in the OS group than in the non-OS group (41% vs. 12%, $p = 0.01$). Notably, the time from surgery to menopause was significantly shorter in the OS group than in the non-OS group (OS: 1.84 ± 1.85 vs. non-OS: 2.93 ± 2.43 , $p = 0.031$). After adjusting the covariates, the OS group was associated with a significantly shorter period between surgery and menopause ($p = 0.029$). In conclusion, these results showed that a hysterectomy plus an OS might cause earlier menopause than a hysterectomy only. An OS should be preoperatively discussed with patients regarding the possibility of early menopause. The findings of this study require further large-scale investigations to reinforce the results.

Neurology. 2022 Oct 12;10.1212/WNL.000000000201401. doi: 10.1212/WNL.000000000201401.

Menopausal Vasomotor Symptoms and White Matter Hyperintensities in Midlife Women

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Background and objectives: The menopause transition is increasingly recognized as a time of importance for women's brain health. A growing body of work indicates that the classic menopausal symptom, vasomotor symptoms (VMS), may be associated with poorer cardiovascular health. Other work links VMS to poorer cognition. We investigate whether VMS, when rigorously assessed using physiologic measures, are associated with greater white matter hyperintensity volume (WMHV) among midlife women. We consider a range of potential explanatory factors in these associations and explore whether VMS are associated with the spatial distribution of WMHV. **Methods:** Women aged 45-67 and free of hormone therapy underwent 24 hours of physiologic VMS monitoring (sternal skin conductance), actigraphy assessment of sleep, physical measures, phlebotomy, and 3 Tesla neuroimaging. Associations between VMS (24-hour, wake, and sleep VMS, with wake and sleep intervals defined by actigraphy) and whole brain WMHV were considered in linear regression models adjusted for age, race, education, smoking, body mass index, blood pressure, insulin resistance, and lipids. Secondary models considered WMHV in specific brain regions (deep, periventricular, frontal, temporal, parietal, occipital) and additional covariates including sleep. **Results:** The study sample included 226 women. Physiologically-assessed VMS were associated with greater whole brain WMHV in multivariable models, with the strongest associations observed for sleep VMS [24-hour VMS, $B(SE)=.095 (.045)$, $p=.032$; Wake VMS, $B(SE)=.078 (.046)$, $p=.089$, Sleep VMS, $B(SE)=.173 (.060)$, $p=.004$]. Associations were not accounted for by additional covariates including actigraphy-assessed sleep (wake after sleep onset). When considering the spatial distribution of WMHV, sleep VMS were associated with both deep WMHV, periventricular WMHV, and frontal lobe WMHV. **Discussion:** VMS, particularly VMS occurring during sleep, were associated with greater WMHV. Identification of female-specific midlife markers of poor brain health later in life is critical to identify women who warrant early intervention and prevention. VMS have the potential to serve as female-specific midlife markers of brain health in women.

Menopause. 2022 Oct 11. doi: [10.1097/GME.0000000000002089](https://doi.org/10.1097/GME.0000000000002089). Online ahead of print.

The severity of individual menopausal symptoms, cardiovascular disease, and all-cause mortality in the Women's Health Initiative Observational Cohort

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Objective: The aim of this study was to examine the association between common menopausal symptoms (MS) and long-term cardiovascular disease (CVD) and all-cause mortality. **Methods:** In an observational cohort of 80,278 postmenopausal women with no known CVD at baseline from the Women's Health Initiative, we assessed individual MS severity (mild vs none; moderate/severe vs none) for night sweats, hot flashes, waking up several times at night, joint pain or stiffness, headaches or migraines, vaginal or genital dryness, heart racing or skipping beats, breast tenderness, dizziness, tremors (shakes), feeling tired, forgetfulness, mood swings, restless or fidgety, and difficulty concentrating. Outcomes included total CVD events (primary) and all-cause mortality (secondary). Associations between specific MS, their severity, and outcomes were assessed during a median of 8.2 years of follow-up. All results were multivariable adjusted, and individual associations were Bonferroni corrected to adjust for multiple comparisons. A machine learning approach (least absolute shrinkage and selection operator) was used to select the most parsimonious set of MS most predictive of CVD and all-cause mortality. **Results:** The severity of night sweats, waking up several times at night, joint pain or stiffness, heart racing or skipping beats, dizziness, feeling tired, forgetfulness, mood swings, restless or fidgety, and difficulty concentrating were each associated with total CVD. The largest hazard ratio (HR) for total CVD was found for moderate or severe heart racing or skipping beats (HR, 1.55; 95% confidence interval [CI], 1.29-1.86). The individual severities of heart racing or skipping beats, dizziness, tremors (shakes), feeling tired, forgetfulness, mood swings, restless or fidgety, and difficulty concentrating were associated with increased all-cause mortality. Moderate or severe dizziness had the largest HR (1.58; 95% CI, 1.24-2.01). Multiple symptom modeling via least absolute shrinkage and selection operator selected dizziness, heart racing, feeling tired, and joint pain as most predictive of CVD, whereas dizziness, tremors, and feeling tired were most predictive of all-cause mortality. **Conclusion:** Among postmenopausal women with no known CVD at baseline, the severity of specific individual MS was significantly associated with incident CVD and mortality. Consideration of severe MS may enhance sex-specific CVD risk prediction in future cohorts, but caution should be applied as severe MS could also indicate other health conditions.

Climacteric. 2022 Oct 11;1-7. doi: [10.1080/13697137.2022.2127352](https://doi.org/10.1080/13697137.2022.2127352). Online ahead of print.

Pulmonary embolism in menopausal hormone therapy: a population-based register study

Micaela Sundell 1 2, Anna-Clara Spetz Holm 2 3, Mats Fredrikson 2, Mats Hammar 2, Mikael Hoffmann 4, et al.

Objective: Oral but not transdermal menopausal hormone therapy (MHT) increases the risk of venous thromboembolism. There is no evidence regarding the risk of the serious complication pulmonary embolism (PE). The aim was to investigate the risk of PE in women using MHT depending on administration route, type of progestin and treatment duration. Method: The population-based case-control study covered 1,771,253 women aged 40-69 years, during 2006-2015. Diagnoses of PE (n = 13,974) and drug dispensations were received from national validated registers. Results: Current MHT users had a higher risk of PE than non-users (odds ratio [OR] 1.15, 95% confidence interval [CI] 1.05-1.26). First ever users had the highest risk (OR 2.07, 95% CI 1.23-3.50). Transdermal administration was not associated with increased risk of PE. The OR was slightly but non-significantly higher with estrogen combined with medroxyprogesterone acetate than with norethisterone acetate. Discussion: The risk of PE was significantly increased in users of oral but not transdermal MHT, with the highest risk in first ever users of oral estrogen combined with medroxyprogesterone acetate. The risk was considerably lower in women with recurrent treatment, probably because of the healthy user effect. Conclusion: PE was most common close to initiation of oral treatment. Transdermal MHT did not increase the risk of PE.

Alzheimers Dement. 2022 Sep 15. doi: 10.1002/alz.12759. Online ahead of print.

Menopause hormone therapy significantly alters pathophysiological biomarkers of Alzheimer's disease

Herman Depypere 1, Andrea Vergallo 2, Pablo Lemercier 2, Simone Lista 2, Andrea Benedet, Nicholas Ashton, et al.

Introduction: This increasing body of literature indicates that menopause hormonal replacement therapy (MHT) may substantially mitigate the risk of developing late-life cognitive decline due to progressive Alzheimer's disease (AD) pathophysiology. For the first time, we investigated the question whether MHT impacts AD biomarker-informed pathophysiological dynamics in de-novo diagnosed menopausal women. Methods: We analyzed baseline and longitudinal differences between MHT-taking and -not women in terms of concentrations of core pathophysiological AD plasma biomarkers, validated in symptomatic and cognitively healthy individuals, including biomarkers of (1) the amyloid- β (A β) pathway, (2) tau pathophysiology, (3) neuronal loss, and (4) axonal damage and neurodegeneration. Results: We report a prominent and significant treatment response at the A β pathway biomarker level. Women at genetic risk for AD (APOE e4 allele carriers) have particularly shown favorable results from treatment. Discussion: To our knowledge, we present first prospective clinical evidence on effects of MHT on AD pathophysiology during menopause.

BJGP Open. 2022 Oct 10;BJGPO.2022.0126. doi: 10.3399/BJGPO.2022.0126. Online ahead of print.

Hormonal replacement therapy prescribing in menopausal women in the UK: A descriptive study

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Background: Recent studies on the prescribing of hormonal replacement therapy (HRT) medicines to treat symptoms of menopause are lacking. Aim: To describe the prescribing of HRT in a cohort of UK menopausal women. Design & setting: Population-based drug utilization study using IQVIA Medical Research Database. Method: Primary care data of women with recorded menopause and/or 50 years and older between January 2010 and November 2021 were extracted from the database. The incidence rate (IR) of women who received their first prescription for HRT was calculated annually using person-years at risk (PYAR) as the denominator. IRs of HRT were estimated by type and route of administration. Relative changes in annual IR were expressed as percentages and the average percentage change was assessed using linear regression. Annual prescribing prevalence per 100 women was calculated using mid-year menopausal population estimates. Results: The IR of prescribing of HRT increased from 5.01 in 2010-18.16 per 1000 PYAR in 2021, a relative increase of 13.64% (95% CI 6.97-20.30) per year. IR of fixed combinations of HRT increased from 3.33 to 12.23 per 1000 PYAR in 2010 and 2021, respectively. Transdermal formulations of HRT increased from 1.48 to 14.55 per 1000 PYAR in 2010 and 2021, respectively. The overall proportion of women in receipt of a prescription for HRT changed from 7.89% in 2010 to 6.8% in 2020. Conclusion: Our study shows steady increase in the number of women receiving their first prescription for HRT during the study period which suggests regained acceptance of HRT medicines.