Selección de Resúmenes de Menopausia

Semana del 10 al 16 de noviembre de 2021

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The effect of hormone replacement therapy on the survival of UK women: a retrospective cohort study 1984-2017

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Objective: To estimate the effect of oestrogen-only and combined hormone replacement therapy (HRT) on the hazards of overall and age-specific all-cause mortality in healthy women aged 46 to 65 at first prescription. Design: Matched cohort study. Setting: Electronic primary care records from The Health Improvement Network (THIN) database, UK (1984-2017).Population: 105,199 HRT users (cases) and 224,643 non-users (controls) matched on age and general practice. Methods: Weibull-Double-Cox regression models adjusted for age at first treatment, birth cohort, type 2 diabetes, hypertension and hypertension treatment, coronary heart disease, oophorectomy, hysterectomy, body mass index, smoking, and depri vation status. Main outcome measures: All-cause mortality. Results: A total of 21,751 women died over an average of 13.5 years follow-up per participant, of whom 6,329 were users and 15,422 non-users. The adjusted hazard ratio (HR) of overall all-cause mortality in combined HRT users was 0.91 (95%CI 0.88-0.94), and in oestrogen-only users was 0.99 (0.93-1.07), compared to non-users. Age-specific adjusted HRs for participants aged 46-50, 51-55, 56-60, and 61-65 years at first treatment were 0.98 (0.92-1.04), 0.87 (0.82-0.92), 0.88 (0.82-0.93), and 0.92 (0.85-0.98), for combined HRT users compared to non-users, and 1.01 (0.84-1.21), 1.03 (0.89-1.18), 0.98 (0.86-1.12), and 0.93 (0.81-1.07) for oestrogen-only users, respectively. Conclusions: Combined HRT was associated with a 9% lower risk of all-cause mortality and oestrogen-only formulation was not associated with any significant changes.

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Obesity and Risk of Diabetes Mellitus by Menopausal Status: A Nationwide Cohort Study

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Although both obesity and menopause are associated with increased risk of diabetes mellitus (DM), the association between obesity and DM according to menopausal status remains uncertain. Therefore, we conducted a study to examine the relationship between obesity and incidence of diabetes mellitus (DM) in premenopausal and postmenopausal women. Total of 926,196 premenopausal and 1,193,881 postmenopausal women who underwent health examinations from 2009 to 2014 were identified using the database of the Korean National Health Insurance Service. We compared the incidence and risk of DM according to body mass index (BMI) and waist circumference (WC) in the two groups of women. Cox proportional hazards analyses were performed to evaluate the association between the presence of obesity and risk of DM according to menopausal state. During the 7.8-year follow-up period, 37,736 (4.1%) premenopausal women and 121,102 (10.1%) postmenopausal women were diagnosed with DM. Compared to the reference group (BMI 18.5-23), a stronger association between obesity and risk of DM was observed in both pre- and postmenopausal women: multivariable-adjusted hazard ratios and 95% confidence intervals for BMI subgroups <18.5, 23-25, 25-30, and >30 were 0.62 (0.54, 0.70), 1.91 (1.85, 1.97), 3.38 (3.28, 3.47), and 6.25 (6.02, 6.48), respectively (p trend < 0.001) in premenopausal women and 0.87 (0.82, 0.92), 1.44 (1.41, 1.46), 2.00 (1.97, 2.03), and 2.96 (2.89, 3.02) in postmenopausal women (p trend < 0.001, p-interaction < 0.001). A similar trend was observed for WC. Subgroup analyses of women aged 45 to 55 also showed a stronger association with DM in premenopausal than in postmenopausal women. In conclusion, the association between obesity and DM was stronger in premenopausal women than in postmenopausal women. As estrogens are synthesized in adipose tissue by aromatization of androgens after menopause, increased estrogen levels in obese postmenopausal might have a protective effect against DM.

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Association between Bone Mineral Density and Metabolic Syndrome among Reproductive, Menopausal Transition, and Postmenopausal Women

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The menopausal transition stage brings physiological changes associated with the development of metabolic syndrome (MetS), which can affect bone mineral density (BMD), and may be more evident in the postmenopausal stage. The aim of this study was assessing the association between low BMD and MetS and its components among reproductive/menopausal transition and postmenopausal women in the northeast region of Mexico. A descriptive cross-sectional study was carried out (2015-2016) in 40-60-year-old women (n = 376) who were residents in the metropolitan area of Monterrey, in Nuevo Leon State, Mexico. Anthropometric measurements, blood pressure, a dual-energy X-ray absorptiometry (DXA) evaluation of BMD of two anatomical sites (lumbar spine and dual femur), and a biochemical analysis were obtained. The prevalence of MetS was 57.2%. In participants without MetS, the prevalence of osteopenia was 27.3% in the lumbar spine and 18.6% in the dual femur, while in participants with MetS, the prevalence of osteopenia was 35.8% in the lumbar spine and 14.4% in the dual femur. Osteoporosis in participants without MetS was present in 6.8% in the lumbar spine and in 1.8% in the dual femur, while in women with MetS, its prevalence was 4.7% in the lumbar spine and 0.5% in the dual femur. An association between low BMD at the lumbar spine and dual femur and components of MetS diseases was identified in Mexican women as follows: waist circumference ≥ 88 cm showed an increase risk for low BMD at femoral site in both reproductive/menopausal transition (OR 7.638; 95% CI: 1.607-36.298; p = 0.011) and postmenopausal women (OR 2.600; 95% CI: 1.023-6.609; p = 0.045); HDL < 50 mg/dL was associated with low BMD in both the femur (OR 3.639; 95% CI: 1.039-12.743; p = 0.043) and lumbar spine (OR 2.654; 95% CI: 1.092-6.447; p = 0.031); hypertension in postmenopausal women increased the risk for low BMD in the femur (OR 2.634; 95% CI: 1.150-6.035; p = 0.022). In conclusion, we found that components of the MetS were associated with low BMD, thus indicating that MetS increases the risk for developing osteopenia or osteoporosis. Furthermore, age was found to be an independent risk factor for low BMD.

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Denosumab in the Treatment of Osteoporosis: 10 Years Later: A Narrative Review

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The fully human monoclonal antibody denosumab was approved for treatment of osteoporosis in 2010 on the basis of its potent antiresorptive activity, which produces clinically meaningful increases in bone mineral density (BMD) and reduces fracture risk at key skeletal sites. At that time, questions remained regarding the long-term safety and efficacy of this receptor activator of nuclear factor kappa-B ligand (RANKL) inhibitor; and with clinical experience, new questions have arisen regarding its optimal use. Here, we examine these questions through the lens of data from the FREEDOM trial program and other studies to determine where denosumab fits in the osteoporosis treatment landscape. Clinical consensus and evidentiary support have grown for denosumab as a highly effective anti-osteoporosis therapy for patients at high risk of fracture. In the 10-year FREEDOM Extension study, denosumab treatment produced progressive incremental increases in BMD, sustained low rates of vertebral fracture, and further reduction in nonvertebral fracture risk without increased risk of infection, cancer, or immunogenicity. There was no evidence that suppression of bone turnover or mineralization was excessive, and rates of osteonecrosis of the jaw (ONJ) and atypical femoral fracture (AFF) were very low. It is now recognized, however, that transitioning to another anti-osteoporosis therapy after denosumab discontinuation is essential to mitigate a transient rebound of bone turnover causing rapid BMD loss and increased risk of multiple vertebral fractures (MVFs). Taken together, the available data show that denosumab has a favorable benefit/risk profile and is a versatile agent for preventing osteoporotic fractures in the short and long term.

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Association of Premenopausal Bilateral Oophorectomy With Cognitive Performance and Risk of Mild Cognitive Impairment

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Importance: The associations of bilateral oophorectomy among premenopausal women, age at oophorectomy, and use of estrogen therapy after oophorectomy with cognitive performance later in life remain controversial. Objective: To investigate whether women who underwent premenopausal bilateral oophorectomy were at increased risk of mild

cognitive impairment (MCI) and experienced decreased global or domain-specific cognitive performance. Design, setting, and participants: This case-control study and cross-sectional study were made possible by combining data from the Mayo Clinic Study of Aging (MCSA) and the Rochester Epidemiology Project (REP) medical record-linkage system. The studies were conducted among a population-based sample in Olmsted County, Minnesota, consisting of 2732 women aged 50 to 89 years who participated in the MCSA study from 2004 to 2019 and underwent a clinical evaluation and comprehensive cognitive testing. Data were analyzed from January to May 2021. Exposures: Medical record documentation of bilateral oophorectomy abstracted from a medical record-linkage system (ie, REP). Main outcomes and measures: Odds of MCI and global or domain-specific z scores on cognitive tests were measured at the first MCSA visit. The median (IQR) lag time between bilateral oophorectomy performed before menopause and before age 50 years and cognitive evaluation was 30 (22-38) years. Results: Among 2732 women aged 50 to 89 years (median [IQR] age at evaluation, 74 [66-81] years) who participated in the MCSA, the case-control study included 283 women with MCI (10.4%) and 2449 women without cognitive impairment (89.6%). Bilateral oophorectomy before menopause and before age 46 years was associated with clinically diagnosed MCI (adjusted odds ratio [aOR], 2.21; 95% CI, 1.41-3.45; P < .001) compared with no bilateral oophorectomy. The presence of an association with MCI varied by surgical indication, with an association among 259 women with bilateral oophorectomy before menopause and before age 50 years for the indication of benign ovarian condition (aOR, 2.43; 95% CI, 1.36-4.33; P = .003) but not for cancer or no ovarian condition. The presence of an association did not vary by estrogen therapy after bilateral oophorectomy, with associations among women aged less than 46 years with estrogen therapy (aOR, 2.56; 95% CI, 1.24-5.31; P = .01) and without estrogen therapy (aOR, 2.05; 95% CI, 1.18-3.52; P = .01). The cross-sectional study included 625 women with a history of bilateral oophorectomy (median [IQR] age, 75 [70-82] years) and 2107 women without a history of bilateral oophorectomy (median [IQR] age, 73 [65-80] years). Premenopausal bilateral oophorectomy was performed before age 46 years among 161 women and was associated with decreased global cognition z score (β, -0.17; 95% CI, -0.32 to -0.03; P = .02), attention and executive domain z score (β, -0.21; 95% CI, -0.36 to -0.05; P = .009), and Short Test of Mental Status score (β, -0.51; 95% CI, -0.95 to -0.08; P = .02) compared with no bilateral oophorectomy. Conclusions and relevance: This study found that women who underwent bilateral oophorectomy before menopause had increased odds of MCI and poorer performance on cognitive tests approximately 30 years later compared with women who did not undergo bilateral oophorectomy.

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Management of sleep disorders in the menopausal transition

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The menopausal transition is associated with increasing sleep disorders including sleep apnoea and restless leg syndrome. Insomnia is the most common and is recognised as a core symptom of the menopause. Guidelines to support decision making for women with sleep problems during the menopausal transition are lacking. Sleep problems are associated with negative impacts on healthcare utilisation, quality of life and work productivity. Sleep deprivation is a risk factor for cardiovascular disease, diabetes, obesity and neurobehavioral dysfunction. Declining oestrogen is implicated as a cause of menopausal sleep disruption. Vasomotor symptoms (VMS) and menopausal mood disturbance are also factors in the complex aetiology. VMS commonly precipitate insomnia and, due to their prolonged duration, they often perpetuate the condition. Insomnia in the general population is most effectively treated with cognitive behavioural therapy (CBT) (also effective in the menopausal transition.) The associations of menopausal sleep disturbance with VMS and depression mean that other treatment options must be considered. Existing guidelines outline effectiveness of hormone replacement therapy (HRT), CBT and antidepressants. HRT may indirectly help with sleep disturbance by treating VMS and also via beneficial effect on mood symptoms. The evidence base underpinning menopausal insomnia often references risks associated with HRT that are not in line with current international menopause guidelines. This may influence clinicians managing sleep disorders, leading to hesitation in offering HRT, despite evidence of effectiveness. Viewing sleep symptoms on an axis of menopausal symptoms - towards vasomotor symptoms or towards mood symptoms may help tailor treatment options towards the symptom profile.

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Low bone mineral density and coronary artery disease: A systematic review and meta-analysis

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Coronary artery disease (CAD) and osteoporosis both cause significant morbidity and mortality. Recent interest in inflammation and the bone-vascular axis suggests a mechanistic link between the two conditions. This review and meta-analysis was conducted to examine the potential association between low bone mineral density (BMD) and CAD in adults. Two authors searched for studies that examined the association between low BMD and CAD. Risk of bias assessment was conducted using the modified Newcastle Ottawa score. Ten studies were selected from the 2258 unique records identified. Pooled analysis showed a significant association between low BMD and CAD (OR 1.65, 95%CI 1.37-2.39, $p < 0.01$). Subgroup analysis investigating males and females separately was not significant. The subgroup analyses looking for any differences across geographic locations and differences between coronary imaging modalities were also negative. Studies with adjusted ORs ($n = 4$) were also pooled (OR 3.01, 95%CI 0.91-9.99, $p = 0.07$). Low BMD is associated with CAD; however, it is unclear whether this result is confounded by common risk factors given the heterogeneity between study populations and methodologies. Further large-scale epidemiological studies are required.