

## Selección de Resúmenes de Menopausia

Semana del 10 a 16 de mayo, 2023

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**Am J Obstet Gynecol. 2023 May 11;S0002-9378(23)00309-5.doi: 10.1016/j.ajog.2023.05.002.**

### **Efficacy of Vaginal Estrogen for Recurrent Urinary Tract Infection Prevention in Hypoestrogenic Women**

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**Background:** Vaginal estrogen is considered the standard of care for recurrent urinary tract infection prevention in hypoestrogenic women. However, the literature supporting its use is limited to small clinical trials with narrow generalizability. **Objectives:** The primary objective of this study was to assess the association between vaginal estrogen prescription and the frequency of urinary tract infections over the following year in a diverse population of hypoestrogenic women. Secondary objectives included evaluation of medication adherence and predictors of post-prescription urinary tract infection. **Study design:** This multicenter retrospective review included women who were prescribed vaginal estrogen for the indication of recurrent urinary tract infection from January 2009 through December 2019. Recurrent urinary tract infection was defined as three or more positive urine cultures (separated by at least 14 days) in the 12 months preceding index vaginal estrogen prescription. Patients were confirmed to fill their prescriptions and continue care within Kaiser Permanente Southern California for at least one year. Exclusion criteria included anatomic abnormalities, malignancy, or mesh erosion of the genitourinary tract. Data on demographics, medical comorbidities, and surgical history were collected. Adherence was captured through refill data after the index prescription. Low adherence was defined as no refills; moderate adherence was defined as one refill; high adherence was defined as two or more refills. Data were abstracted from the electronic medical record using the pharmacy database and diagnosis codes. A paired t-test was used to compare pre- and post-prescription urinary tract infections over the year preceding and following vaginal estrogen prescription. Multivariate negative binomial regression was used to evaluate predictors of post-prescription urinary tract infection. **Results:** The cohort included 5,638 women with mean ( $\pm$ standard deviation) age of 70.4 ( $\pm$ 11.9) years, body mass index of 28.5 ( $\pm$ 6.3) kg/m<sup>2</sup>, and baseline urinary tract infection frequency of 3.9 ( $\pm$ 1.3). Most were white (59.9%) or Hispanic (29.7%) and postmenopausal (93.4%). Mean urinary tract infection frequency in the year following index prescription decreased to 1.8 ( $P$ <0.001) from 3.9 in the year pre-prescription, a 51.9% reduction. During the 12 months after index prescription, 55.3% of patients experienced one or fewer urinary tract infections, and 31.4% experienced no urinary tract infections. Significant predictors of post-prescription urinary tract infection included: age 75-84 (incident rate ratio 1.24; 95% CI 1.05-1.46) and 85 plus years (1.41; 1.17-1.68), increased baseline urinary tract infection frequency (1.22; 1.19-1.24), urinary incontinence (1.14; 1.07-1.21), urinary retention (1.21; 1.10-1.33), diabetes mellitus (1.14; 1.07-1.21), and moderate (1.32; 1.23-1.42) or high medication adherence (1.33; 1.24-1.42). Highly-adherent patients demonstrated more frequent post-prescription urinary tract infections than low-adherence patients (2.2 versus 1.6,  $P$ <0.0001). **Conclusions:** In this retrospective review of 5,600 hypoestrogenic women prescribed vaginal estrogen for the prevention of recurrent urinary tract infection, the frequency of urinary tract infection decreased by over 50% in the following year. Baseline urinary tract infection frequency, increasing age, urinary incontinence/retention, and diabetes were associated with an increased risk of post-prescription urinary tract infection. The paradoxical finding that women with moderate and high adherence experienced the lowest-magnitude reduction in urinary tract infection frequency may represent unobserved selection or unmeasured confounding.

**Radiol Bras. 2023 Mar-Apr;56(2):75-80.doi: 10.1590/0100-3984.2022.0085-en.**

### **Amorphous breast calcifications: is BI-RADS 4a appropriate?**

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**Objective:** To evaluate the positive predictive value (PPV) of amorphous calcifications and to analyze the imaging variables that could alter the risk of malignancy associated with this finding. **Materials and methods:** This was a retrospective study of 138 stereotactically guided percutaneous vacuum-assisted biopsies of amorphous calcifications, performed between January 2012 and December 2017. All of the patients included were referred for radiological follow-up for a minimum of one year (if the histopathology showed a benign lesion) or for surgical treatment (if the histopathology showed malignancy or a lesion of uncertain malignant potential). **Results:** We found that the PPV of amorphous calcifications was 9.42%. However, most of the malignant amorphous calcifications were in cases of invasive carcinoma or high-grade ductal carcinoma in situ, indicating clinically relevant disease. The relative risk of malignancy associated with amorphous calcifications was 6.15 times higher in patients with a family or personal history of breast or

ovarian cancer. Neither being postmenopausal nor having dense breasts was found to be predictive of malignancy in patients with amorphous calcifications. Conclusion: Amorphous calcifications in the breast had a PPV for malignancy of 9.42%, indicating the possibility of placing the finding in subcategory 4a, which requires histopathological analysis. Our finding that the risk of malignancy associated with this subtype of calcifications is up to 6.15 times higher in patients with a family or personal history of breast cancer warrants greater concern regarding the clinical, radiologic, and histopathologic correlations after biopsy.

**Biomed Pharmacother. 2023 May 8;163:114834. doi: 10.1016/j.biopha.2023.114834. Online ahead of print.**

## **Oxidative stress: A common pathological state in a high-risk population for osteoporosis**

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Osteoporosis is becoming a major concern in the field of public health. The process of bone loss is insidious and does not directly induce obvious symptoms. Complications indicate an irreversible decrease in bone mass. The high-risk populations of osteoporosis, including postmenopausal women, elderly men, diabetic patients and obese individuals need regular bone mineral density testing and appropriate preventive treatment. However, the primary changes in these populations are different, increasing the difficulty of effective treatment of osteoporosis. Determining the core pathogenesis of osteoporosis helps improve the efficiency and efficacy of treatment among these populations. Oxidative stress is a common pathological state secondary to estrogen deficiency, aging, hyperglycaemia and hyperlipemia. In this review, we divided oxidative stress into the direct effect of reactive oxygen species (ROS) and the reduction of antioxidant enzyme activity to discuss their roles in the development of osteoporosis. ROS initiated mitochondrial apoptotic signaling and suppressed osteogenic marker expression to weaken osteogenesis. MAPK and NF- $\kappa$ B signaling pathways mediated the positive effect of ROS on osteoclast differentiation. Antioxidant enzymes not only eliminate the negative effects of ROS, but also directly participate in the regulation of bone metabolism. Additionally, we also described the roles of proinflammatory factors and HIF-1 $\alpha$  under the pathophysiological changes of inflammation and hypoxia, which provided a supplement of oxidative stress-induced osteoporosis. In conclusion, our review showed that oxidative stress was a common pathological state in a high-risk population for osteoporosis. Targeted oxidative stress treatment would greatly optimize the therapeutic schedule of various osteoporosis treatments.

**Menopause. 2023 May 9. doi: 10.1097/GME.0000000000002194. Online ahead of print.**

## **Association of parity with body mass index and cardiometabolic risk in high-parous women**

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Objective: Postpregnancy weight retention contributes to obesity, but the long-term effect of parity on body mass index (BMI) and other cardiometabolic risk factors is unclear. We aimed to evaluate the relationship between parity and BMI among highly parous Amish women, both before and after menopause, and to evaluate the associations of parity with glucose, blood pressure, and lipids. Methods: We conducted a cross-sectional study among 3,141 Amish women 18 years or older from Lancaster County, PA, who participated in our community-based Amish Research Program between 2003 and 2020. We evaluated the association between parity and BMI across different age groups, both before and after the menopausal transition. We further assessed associations between parity and cardiometabolic risk factors among the 1,128 postmenopausal women. Finally, we evaluated the association of change in parity with change in BMI in 561 women followed longitudinally. Results: Approximately 62% of women in this sample (mean age, 45.2 y) reported having four or more children, and 36% reported having seven or more. A one-child increase in parity was associated with increased BMI in both premenopausal women (estimate [95% confidence interval], 0.4 kg/m<sup>2</sup> [0.2-0.5]) and to a lesser degree in postmenopausal women (0.2 kg/m<sup>2</sup> [0.02-0.3], *P*int = 0.02), suggesting that the impact of parity on BMI decreases over time. Parity was not associated with glucose, blood pressure, total cholesterol, low-density lipoprotein, or triglycerides (*P*adj > 0.05). Conclusions: Higher parity was associated with increased BMI in both premenopausal and postmenopausal women, but more so in younger/premenopausal women. Parity was not associated with other indices of cardiometabolic risk.

**Menopause. 2023 May 9. doi: 10.1097/GME.0000000000002185. Online ahead of print.**

## **Hormone therapy for sexual function in perimenopausal and postmenopausal women: a systematic review and meta-analysis update**

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Importance: Distressing sexual problems are a common complaint of menopausal women. In 2013, a Cochrane review assessed the effect of hormone therapy on sexual function in menopausal women; however, new evidence has since been published, which should be considered. Objective: This systematic review and meta-analysis aims to update the evidence synthesis on the effect of hormone therapy, compared with control, on sexual function in perimenopausal and postmenopausal women. Evidence review: Thirteen databases and clinical trial registries were searched from December 2012 to March 30, 2022. Backward reference searching on all retrieved full texts was also performed. Study quality was assessed using the Cochrane ROB.2 tool. Data were pooled in random-effect model meta-analyses, which included all studies identified in the present search and all studies previously included in the 2013 Cochrane review. Findings: Forty-seven randomized controlled trials (35,912 participants) were included in the systematic review, and 34 randomized controlled trials (15,079 participants) were included in the meta-analysis. The meta-analysis revealed that, in comparison to control, estrogen therapy (standardized mean difference [SMD], 0.16; 95% confidence interval [CI], 0.02 to 0.29; I<sup>2</sup> = 59%; 2,925 participants, 16 studies), estrogen plus progestogen therapy (SMD, 0.11; 95% CI, -0.07 to 0.29; I<sup>2</sup> = 65%; 2,432 participants, 7 studies), tibolone (SMD, 0.15; 95% CI, 0.02 to 0.28; I<sup>2</sup> = 0%; 916 participants, 2 studies), and selective estrogen receptor modulators (SMD, 0.18; 95% CI, 0.06 to 0.30; I<sup>2</sup> = 0%; 1,058 participants, 4 studies) may result in no effect to small benefit on sexual function composite score. Conclusion and relevance: Hormone therapy may slightly improve sexual functioning. This potential small benefit should be considered when discussing treatment options for other menopausal symptoms.

**J Womens Health (Larchmt). 2023 May 8.doi: 10.1089/jwh.2022.0207. Online ahead of print.**

## **Hysterectomy with and without Oophorectomy, Tubal Ligation, and Risk of Cardiovascular Disease in the Nurses' Health Study II**

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 Background: Hysterectomy, oophorectomy, and tubal ligation are common surgical procedures. The literature regarding cardiovascular disease (CVD) risk after these surgeries has focused on oophorectomy with limited research on hysterectomy or tubal ligation. Materials and Methods: Participants in the Nurses' Health Study II (n = 116,429) were followed from 1989 to 2017. Self-reported gynecologic surgery was categorized as follows: no surgery, hysterectomy alone, hysterectomy with unilateral oophorectomy, and hysterectomy with bilateral oophorectomy. We separately investigated tubal ligation alone. The primary outcome was CVD based on medical-record confirmed fatal and nonfatal myocardial infarction, fatal coronary heart disease, or fatal and nonfatal stroke. Our secondary outcome expanded CVD to include coronary revascularization (coronary artery bypass graft surgery, angioplasty, stent placement). Cox proportional hazard models were used to calculate hazard ratios (HR) and 95% confidence intervals (CIs) and were adjusted a priori for confounding factors. We investigated differences by age at surgery ( $\leq 50$ ,  $>50$ ) and menopausal hormone therapy usage. Results: At baseline, participants were on average, 34 years old. During 2,899,787 person-years, we observed 1,864 cases of CVD. Hysterectomy in combination with any oophorectomy was associated with a greater risk of CVD in multivariable-adjusted models (HR hysterectomy with unilateral oophorectomy: 1.40 [95% CI: 1.08-1.82]; HR hysterectomy with bilateral oophorectomy: 1.27 [1.07-1.51]). Hysterectomy alone, hysterectomy with oophorectomy, and tubal ligation were also associated with an increased risk of combined CVD and coronary revascularization (HR hysterectomy alone: 1.19 [95% CI: 1.02-1.39]; HR hysterectomy with unilateral oophorectomy: 1.29 [1.01-1.64]; HR hysterectomy with bilateral oophorectomy: 1.22 [1.04-1.43]; HR tubal ligation: 1.16 [1.06-1.28]). The association between hysterectomy/oophorectomy and CVD and coronary revascularization risk varied by age at gynecologic surgery, with the strongest association among women who had surgery before age 50 years. Discussion: Our findings suggest that hysterectomy, alone or in combination with oophorectomy, as well as tubal ligation, may be associated with an increased risk of CVD and coronary revascularization. These findings extend previous research finding that oophorectomy is associated with CVD.

**Ren Fail. 2023 Dec;45(1):2209200.doi: 10.1080/0886022X.2023.2209200.**

## **The association between dietary inflammation index and bone mineral density: results from the United States National Health and nutrition examination surveys**

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Objective: To investigate the associations of dietary inflammation index (DII) with bone density and osteoporosis in different femoral areas. Methods: The study population was selected from the National Health and Nutrition Examination Survey (NHANES) with the exclusion criteria of age 18, pregnancy, or missing information on DII, femoral bone marrow density (BMD), estimated glomerular filtration rate (eGFR), and urine albumin-to-creatinine ratio (UACR), or had diseases which may influence systemic inflammation. DII was calculated based on the questionnaire interview of dietary

recall within 24 h. Subjects' baseline characteristics were collected. The associations between DII and different femoral areas were analysed. Results: After applying exclusion criteria, 10,312 participants were included in the study. Significant differences among DII tertiles were found in BMD or T scores ( $p < .001$ ) of the femoral neck, the trochanter, the intertrochanter, and the total femur. High DII was associated with low BMDs and T scores in all the femoral areas (all  $p < .01$ ). Compared to low DII (tertile1, DII  $< 0.380$  as reference), in the femoral neck, the intertrochanter, and the total femur, increased DII is independently associated with increased the possibility of the presence of osteoporosis (OR, 95% CI: 1.88, 1.11-3.20; 2.10, 1.05-4.20; 1.94, 1.02-3.69, respectively). However, this positive association was only observed in the trochanteric area of the non-Hispanic White population after full adjustment (OR, 95% CI: 3.22 (1.18, 8.79)). No significant difference in the association of DII and the presence of osteoporosis were found in subjects with or without impaired kidney function (eGFR  $< 60$  ml/min/1.73 m<sup>2</sup>).