



Selección de Resúmenes de Menopausia

Semana del 3 al 9 de julio de 2019

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Curr Opin Obstet Gynecol. 2019 Aug;31(4):267-278. doi: 10.1097/GCO.0000000000000548.

Postmenopausal endometriosis, where are we now?

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PURPOSE OF REVIEW: Postmenopausal endometriosis is a gynecologic disease, affecting 2-5% of postmenopausal woman. Current literature assessing the prevalence, pathogenesis, and treatment of this uncommon condition is limited, stressing the necessity for future research. This review examines the current literature on postmenopausal endometriosis to help inform clinical decision-making and point to novel approaches for treatment and management. **RECENT FINDINGS:** Although one unifying theory to explain the pathogenesis of endometriotic lesions has not been elucidated, estrogen dependence is central to the pathophysiological process. The total quantity of estrogen production is mediated by multiple enzymes in complex pathways. Recent studies have confirmed the presence of these necessary enzymes in endometriotic lesions thereby suggesting a local source of estrogen and a likely pathogenic contributor. More research is needed to fully elucidate the mechanism of local estrogen biosynthesis; however, the current data provide possible explanations for the presence of postmenopausal endometriosis in an otherwise systemically hypoestrogenic environment. **SUMMARY:** All suspected endometriosis lesions should be surgically excised for optimization of treatment and prevention of malignant transformation. If hormone replacement therapy is initiated, combined estrogen and progestin is recommended, even in the setting of previous hysterectomy, given the risk of disease reactivation and malignant transformation of endometriotic lesions. Further research is needed to understand the true prevalence, cause, and progression in this patient demographic. Histologic studies evaluating tissue lesions and peritoneal fluid for estrogen receptors, estrogen metabolizing enzymes, immune cells, and nerve fibers will aid in clinical management and treatment planning.

Biomed Res Int. 2019 May 29;2019:8584130. doi: 10.1155/2019/8584130. eCollection 2019.

Age at Menopause and Risk of Developing Endometrial Cancer: A Meta-Analysis.

Wu Y1, Sun W1, Liu H1, Zhang D1.

Object: The association of age at menopause with endometrial cancer remains controversial. Therefore, we quantitatively summarized the evidence from observational studies with a meta-analysis. **Methods:** We searched PubMed, Web of Science, Embase, Medline, Chinese National Knowledge Infrastructure (CNKI), and Wan Fang Med online up to March 2019, and all eligible case-control and cohort studies were included in the study. Pooled relative risks (RRs) with 95% confidence intervals (CIs) were calculated using the random-effects model. The dose-response relationship was assessed by restricted cubic spline model. The heterogeneity among studies was evaluated by I². Metaregression was used to explore the potential sources of between-study heterogeneity. Egger's test was used to estimate publication bias. **Results:** Eighteen articles including 957242 subjects with 4781 cases were included in the meta-analysis. The pooled RR (95% CI) of endometrial cancer for the highest versus the lowest age at menopause was 1.89 (95% CI: 1.58-2.26). For dose-response analysis, a nonlinear relationship was found between age at menopause and endometrial cancer, and the positive association became statistically significant when age at menopause was greater than 46.5 years old. **Conclusions:** This meta-analysis suggested that age at menopause was positively associated with endometrial cancer. For women whose menopausal age over 46.5 years old, the risk of endometrial cancer increased with the age at menopause.

Climacteric. 2019 Jul 4:1-7. doi: 10.1080/13697137.2019.1628734. [Epub ahead of print]

Vasomotor symptoms in aging Chinese women: findings from a prospective cohort study.

Li J1, Luo M1, Tang R1, Sun X1, Wang Y1, Liu B1, Cui J1, Liu G2, Lin S1, Chen R1.

Purpose: This study aimed to prospectively determine the prevalence, duration, and severity of vasomotor symptoms (VMS) during menopause in a Chinese longitudinal cohort. **Methods:** This longitudinal cohort study recruited 187 participants from an urban Chinese community. The presence, frequency, degree, and duration of VMS were measured and analyzed. **Results:** A total of 83.4% of participating women experienced hot flashes and 82.9% reported night sweats, with nearly half reporting moderate to severe VMS (more than 3 times per day, or rated 4 or greater on a 1-8 severity scale). The median duration for both hot flashes and night sweats was 4.5 years. In a generalized linear mixed model, presence of VMS was significantly related to menopause stages, serum follicle stimulating hormone concentrations, general distress levels, and baseline body mass index. **Discussion and conclusions:** The prevalence of VMS in this longitudinal cohort was higher than that of previous Chinese cross-sectional studies and consistent with prior studies in western women. Meanwhile, the duration of symptomatic years in our study was shorter than that of western women. These results indicate that the difference in VMS between western and Chinese women appears to be in terms of the duration of symptoms, not prevalence.

Gynecol Endocrinol. 2019 Jul 2:1-5. doi: 10.1080/09513590.2019.1582625. [Epub ahead of print]

Vasomotor symptoms and neurovegetative comorbidities on the menopause: insights from an Italian quantitative research.

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Vasomotor symptoms (VMSs) are the most common symptoms affecting women during the menopause. Besides, affective symptoms may share with VMS a common biological pathophysiology. The current multicenter quantitative research was based on an online survey aimed to evaluate the impact of VMS in peri- and post-menopausal Italian women and to identify the main barriers to seeking help. The most frequent bothersome VMSs were hot flashes (41%), night sweats (31%), and over-heating (31%). Almost 87% of women experienced three or more simultaneous symptoms. Emotions verbalized by women indicate how intensely hot flushes and neuro-vegetative symptoms impact life: embarrassment, confusion, depression, impact on social/personal relationships, and guiltiness. Up to 43% of all women suffering from VMS were not treating the symptoms. Although 92% of women reported prior knowledge of the VMS condition, only 12% do something about it straight away after the appearance of VMS. This survey provided real-life observational data from a large population of peri-menopausal women and highlighted the important impact of VMS, its neurovegetative comorbidities and its significant burden effect on social life. Physicians must be more adaptive and inquisitive to evaluate and detect incipient VMS, as this will indicate the vulnerability to severe symptomatology and pathological brain aging.

J Clin Endocrinol Metab. 2019 Jul 2. pii: jc.2019-00924. doi: 10.1210/jc.2019-00924. [Epub ahead of print]

Comparison of Teriparatide and Denosumab in Patients Switching from Long-Term Bisphosphonate Use.

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CONTEXT: Teriparatide and denosumab are effective treatments for osteoporosis and typically reserved as second-line options after patients have used bisphosphonates. However, limited head-to-head comparative effectiveness data exist between teriparatide and denosumab. **OBJECTIVE:** We compared changes in bone mineral density (BMD) between groups treated with teriparatide or denosumab after using bisphosphonates, focusing on the change in BMD while on either drug over 2 years. **DESIGN:** Observational cohort study using electronic medical records from two academic medical centers in the US. **PARTICIPANTS:** The study population included osteoporotic patients > 45 years who received bisphosphonates over one year prior to switching to teriparatide or denosumab. **OUTCOME MEASURES:** Annualized BMD change from baseline at the lumbar spine, total hip and femoral neck. **RESULTS:** Patients treated with teriparatide (n=110) were compared to those treated with denosumab (n=105); the mean (SD) age was 70 (10) years and median duration (IQR) of bisphosphonate use was 7.0 (5.6-9.7) years. Compared to denosumab users, teriparatide users had higher annualized BMD change at the spine by 1.3% (95% CI 0.02, 2.7%), but lower at the total hip by -2.2% (95% CI -2.9 to -1.5%) and the femoral neck by -1.1% (95% CI -2.1 to -0.1%). Those who switched to teriparatide had a transient loss of hip BMD for the first year, with no overall increase in the total hip BMD over two years. **CONCLUSIONS:** Among patients who use long-term bisphosphonates, the decision of switching to teriparatide should be made with caution, especially for patients at high risk of hip fracture.

Biol Rev Camb Philos Soc. 2019 Jul 1. doi: 10.1111/brv.12541. [Epub ahead of print]

The vascular protective role of oestradiol: a focus on postmenopausal oestradiol deficiency and aneurysmal subarachnoid haemorrhage.

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The steroid hormone, oestradiol, has pleiotropic functions. The protective effects of oestradiol are attributed to its anti-inflammatory, antioxidant, anti-atherogenic, anti-apoptotic, vasodilatory activities and regulation of micro RNA. Oestradiol upregulates endothelial nitric oxide synthase gene expression and increases the production of nitric oxide, an important vasodilator. It suppresses the renin-angiotensin system and monitors haemodynamic stress. The hormone maintains the integrity of blood vessels by reducing oxidative stress while upregulating the expression of antioxidant enzymes and prevents vascular inflammation by regulating pro- and anti-inflammatory cytokines. Aneurysmal subarachnoid haemorrhage (aSAH) occurring as a consequence of the rupture of an intracranial aneurysm is a devastating cerebrovascular event, representing 5-7% of all strokes. Postmenopausal women are more susceptible to aSAH compared to men in the same age group. This gender disparity has been attributed to reduced levels of the vascular protective hormone oestradiol following menopause. This review is focused on the protective role of oestradiol on vasculature and how the drop in oestradiol levels after menopause dramatically increases the incidence of aSAH in women. During menopause, oestradiol deficiency may affect vascular integrity causing dysregulation of vascular homeostasis by affecting the renin-angiotensin-aldosterone system (RAAS) and inflammatory and apoptotic cascades, resulting in the weakening of the cerebral arterial wall and potentially to development of an aneurysm and its rupture. In view of the role of oestradiol in maintaining vascular integrity, treatments involving hormone replacement could be a promising approach in postmenopausal women who are at risk of developing or rupturing an intracranial aneurysm.

Z Gerontol Geriatr. 2019 Jul 1. doi: 10.1007/s00391-019-01573-9. [Epub ahead of print]

Should vitamin D administration for fracture prevention be continued? : A discussion of recent meta-analysis findings.

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In consideration and critical review of four recent meta-analyses on vitamin D and fracture prevention, vitamin D supplementation with or without calcium is supported among older adults age 65 years and older at risk of vitamin D deficiency and fractures if given in daily or equivalent weekly or monthly doses of 800 to 1000 IU and with good adherence. Vitamin D supplementation might not be effective in primary prevention among adults age 50 years and older without vitamin D deficiency and osteoporosis; however, clinical trials on primary prevention are limited. Notably, large annual bolus administration of vitamin D is detrimental with regard to falls and fractures among older adults at risk of fractures and should not be continued in clinical care. Larger monthly doses of 100,000 IU need further evaluation with respect to efficacy and safety.

J Gerontol A Biol Sci Med Sci. 2019 Jun 29. pii: glz162. doi: 10.1093/gerona/glz162. [Epub ahead of print]

Creatine supplementation (3 g/day) and bone health in older women: a 2-year, randomized, placebo-controlled trial.

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BACKGROUND: Creatine supplementation could be a non-expensive, safe and effective dietary intervention to counteract bone loss. The aim of this study was to investigate whether long-term creatine supplementation can improve bone health in older, postmenopausal women. **METHODS:** A double-blind, placebo-controlled, parallel-group, randomized trial was conducted between November 2011 and December 2017 in Sao Paulo, Brazil. Two hundred postmenopausal women with osteopenia were randomly allocated to receive either creatine monohydrate (3 g/day) or placebo over 2 years. At baseline and after 12 and 24 months, we assessed areal bone mineral density (aBMD; primary outcome), lean and fat mass (through dual X-ray absorptiometry), volumetric BMD and bone microarchitecture parameters, biochemical bone markers, physical function and strength, and the number of falls and fractures. Possible adverse effects were self-reported. **RESULTS:** Lumbar spine ($p < 0.001$), femoral neck ($p < 0.001$) and total femur aBMD ($p = 0.032$) decreased across time; however, no interaction effect was observed (all $p > 0.050$). Bone markers, microarchitecture parameters, and the number of falls/fractures were not changed with creatine (all $p > 0.050$). Lean mass and appendicular skeletal muscle mass increased throughout the intervention ($p < 0.001$), with no additive effect of creatine ($p = 0.731$ and $p = 0.397$, respectively). Creatine did not affect health-related laboratory parameters.

CONCLUSION: Creatine supplementation over 2 years did not improve bone health in older, postmenopausal women with osteopenia, nor did it affect lean mass or muscle function in this population. This refutes the long-lasting notion that this dietary supplement alone has osteogenic or anabolic properties in the long run.

Eur Heart J. 2019 Jun 30. pii: ehz391. doi: 10.1093/eurheartj/ehz391. [Epub ahead of print]

Association between regional body fat and cardiovascular disease risk among postmenopausal women with normal body mass index.

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AIMS: Central adiposity is associated with increased cardiovascular disease (CVD) risk, even among people with normal body mass index (BMI). We tested the hypothesis that regional body fat deposits (trunk or leg fat) are associated with altered risk of CVD among postmenopausal women with normal BMI. METHODS AND RESULTS: We included 2683 postmenopausal women with normal BMI (18.5 to <25 kg/m²) who participated in the Women's Health Initiative and had no known CVD at baseline. Body composition was determined by dual energy X-ray absorptiometry. Incident CVD events including coronary heart disease and stroke were ascertained through February 2017. During a median 17.9 years of follow-up, 291 incident CVD cases occurred. After adjustment for demographic, lifestyle, and clinical risk factors, neither whole-body fat mass nor fat percentage was associated with CVD risk. Higher percent trunk fat was associated with increased risk of CVD [highest vs. lowest quartile hazard ratio (HR) = 1.91, 95% confidence interval (CI) 1.33-2.74; P-trend <0.001], whereas higher percent leg fat was associated with decreased risk of CVD (highest vs. lowest quartile HR = 0.62, 95% CI 0.43-0.89; P-trend = 0.008). The association for trunk fat was attenuated yet remained significant after further adjustment for waist circumference or waist-to-hip ratio. Higher percent trunk fat combined with lower percent leg fat was associated with particularly high risk of CVD (HR comparing extreme groups = 3.33, 95% CI 1.46-7.62). CONCLUSION: Among postmenopausal women with normal BMI, both elevated trunk fat and reduced leg fat are associated with increased risk of CVD.