Selección de Resúmenes de Menopausia

Semana del 26 de octubre a 1 de noviembre, 2022

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Eur Rev Med Pharmacol Sci. 2022 Oct;26(20):7616-7622. doi: 10.26355/eurrev_202210_30037.

Associations of coronary plaque characteristics and coronary calcification with bone mineral density in postmenopausal women

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Objective: We aimed at investigating the association of postmenopausal osteoporosis in different measurement locations, with the coronary plaque burden and morphology detected by coronary computed tomography angiography (CCTA). Patients and methods: We analyzed a total of 223 postmenopausal women who had undergone both dual-energy X-ray absorptiometry (DXA) and CCTA. Coronary plaque characteristics were analyzed using CCTA. Results: The number of burdens was higher in the osteoporosis/osteopenia group of patients than in the normal group. Agatston score and BMI were not significantly different between the two groups. T-score femur and bone mineral density (BMD) femur were higher in patients with severe coronary artery disease (CAD as compared to those with mild CAD (p=0.036 and p=0.049, respectively), whereas T-score lumbar and BMD lumbar were not significantly different. Non-calcified/mixed plaque burden was an independent predictor of osteopenia/osteoporosis (OR: 1.396, 95% CI 1.007-1.934; p=0.045) together with age (OR: 1.053, 95% CI 1.015-1.093; p=0.006). Conclusions: Non-calcified/mixed plaque burden was significantly and independently associated with osteoporosis/osteopenia at femoral neck but not at lumbar spine. Osteopenia/osteoporosis was not significantly associated with CAC

Front Aging Neurosci. 2022 Oct 14;14:993955. doi: 10.3389/fnagi.2022.993955. eCollection 2022.

Glutamatergic and GABAergic neurons in the preoptic area of the hypothalamus play key roles in menopausal hot flashes

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During menopause, when estrogen levels are low, abnormalities in the hypothalamic preoptic area (POA) of the thermoregulatory center can cause hot flashes. However, the involved neural population has not been identified. Proteomics showed that under low estrogen, differentially expressed proteins in the hypothalamus were associated with glutamatergic and GABAergic synapses. RNAscope, Western blotting and qRT-PCR indicated that the number of glutamatergic neurons in the POA was decreased, while the number of GABAergic neurons was increased. Chemogenetics showed that the rat body temperature decreased slowly after glutamatergic neurons were activated and increased quickly after glutamatergic neurons were inhibited, while it increased quickly after GABAergic neurons were activated and decreased slowly after GABAergic neurons were inhibited. RNAscope, immunofluorescence, Western blotting and qRT-PCR further showed that glutamate decarboxylase (GAD) 1 expression in the POA was increased, while GAD2 expression in the POA was decreased; that thermosensitive transient receptor potential protein (ThermoTRP) M (TRPM) 2 expression in glutamatergic neurons was decreased, while TRPM8 expression in GABAergic neurons was increased; and that estrogen receptor (ER) α and β expression in the POA was decreased, and ERα and ERβ expressed in both glutamatergic and GABAergic neurons. Estrogen therapy corrected these abnormalities. In addition, CUT&Tag and Western blot after injection of agonists and inhibitors of ERs showed that ERα and ERβ were both transcription factors in glutamatergic and GABAergic synapses. Mechanistically, during menopause, estrogen may regulate the transcription and expression of GADs and ThermoTRPs through ERs, impacting the number and function of glutamatergic and GABAergic neurons, resulting in unbalanced heat dissipation and production in the POA and ultimately triggering hot flashes.

Endocrine. 2022 Oct 28. doi: 10.1007/s12020-022-03231-4. Online ahead of print.

Serum 25 hydroxyvitamin D concentrations in individuals over 80 years old and their correlations with musculoskeletal and health parameters

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Purpose: The present study aims to evaluate the serum concentrations of 25 hydroxyvitamin D[25(OH)D] in individuals aged ≥80 years, independent, free-living in Sao Paulo, Brazil (Lat 23.5 oS), and to investigate their associations with musculoskeletal system, physical performance and health markers. Method: This cross-sectional study included 212 community dwellers aged ≥80 years and evaluated serum 25(OH)D, PTH, calcium, albumin,

phosphorus, creatinine, bone markers, and bone mineral density. Physical performance was evaluated with stationary march, Flamingo, and functional reach tests, questionnaires to assess falls and fractures in the previous year, energy expenditure (MET), and Charlson index. Physical activity was evaluated with the International Physical Activity Questionnaire. Results: Vitamin D deficiency (<20 ng/mL) was observed in 56% and severe vitamin D deficiency (<10 ng/mL) in 13% of those individuals. Serum concentrations of 25(OH)D were significantly and positively associated with BMD total hip (p = 0.001), femoral neck (p = 0.011) and 33% radius (p = 0.046) BMDs, MET (p = 0.03) and functional reach test (p = 0.037) and negatively with age (p = 0.021), PTH (p = 0.004) and osteoporosis diagnosis (p = 0.012). Long-lived individuals with 25(OH)D ≥ 20 ng/mL had higher total hip and femoral neck BMDs (p = 0.012 and p = 0.014, respectively) and lower PTH (p = 0.030). In multiple linear regression analysis, age and osteoporosis diagnosis remained negatively associated with 25(OH)D levels (p = 0.021 and p = 0.001, respectively), while corrected calcium and cholecalciferol use remained positively associated (p = 0.001 and p = 0.024, respectively). Conclusion: We observed high vitamin D inadequacy prevalence in those Brazilian community dwellers' oldest old. Serum concentrations of 25(OH)D were positively associated with bone mass and dynamic balance, and negatively with PTH and osteoporosis diagnosis. Additionally, 25(OH)D ≥ 20 ng/mL was associated with better bone mass and lower PTH levels.

Post Reprod Health. 2022 Oct 26;20533691221135906. doi: 10.1177/20533691221135906. Online ahead of print.

Intravaginal dehydroepiandrosterone for genitourinary symptoms of the menopause: Is the evidence sufficient?

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Intravaginal dehydroepiandrosterone (DHEA) is a locally metabolised oestrogen and androgen precursor, licensed in 2018 in the EU for moderate to severe vulvovaginal atrophy in postmenopausal women. A literature search revealed four original trials suitable for appraisal, three evaluating change in dyspareunia or dryness as a primary outcome, one evaluated safety as a primary outcome. In two trials of 255 and 558 women without cancer, the benefit of placebo (nightly vaginal suppositories with a lipophilic base) was a 0.9 and 1 point reduction in dyspareunia as measured on a 3 point scale, an unvalidated outcome measure. With nightly DHEA, dyspareunia was reduced by an additional 0.4 points compared to placebo. When 464 women with gynaecological cancer were randomised, those using nightly plain moisturiser gel reported a reduction of 'most bothersome symptom' (either dyspareunia or dryness) of 1.5 points on a 3 point scale. Those using nightly DHEA reported an additional symptom reduction of 0.3 points. This is also an unvalidated outcome measure. Data evaluating the efficacy of DHEA over placebo is unconvincing and based on unvalidated primary outcome measures that also do not reflect the complex psycho-sexual and socio-cultural components of genitourinary menopausal symptoms. The efficacy and safety data excluded women taking systemic HRT, applies to postmenopausal, not perimenopausal, women and had relatively short follow up. It is important further independent trials use sophisticated and validated assessment tools to better establish the efficacy, safety and cost effectiveness of intravaginal DHEA in clinically representative groups of women before being routinely prescribed.

Front Physiol. 2022 Oct 10;13:980843. doi: 10.3389/fphys.2022.980843. eCollection 2022.

The protective effect of 17 β-estradiol on human uterosacral ligament fibroblasts from postmenopausal women with pelvic organ prolapse

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This study aims to explore the protective effects of 17 β-estradiol on the human uterosacral ligament fibroblasts (hUSLFs) under static or stretched conditions. The experiments were performed on hUSLFs derived from pelvic organ prolapse (POP) and non-POP patients. Fibroblasts were cultured after collagenase digestion and identified by morphological observation and immunocytochemical methods. 17 β-estradiol (10-10 M and 10-9 M) and mechanical stress induced by the FX-5000 T-cell stress loading system under a loading strain of 1/2 sin waveform uniaxial cyclic stress with a tensile strain of 20% and a frequency of 0.5 Hz were either or both applied on hUSLFs. Cell proliferation was measured by CCK8, and cell apoptosis and death were detected using Annexin V/7-AAD staining and flow cytometric analysis. We found that the fibroblasts growth rate of POP patients was significantly lower than controls. The cell apoptosis and death rate increased as the mechanical load intensifying. After 20% mechanical stretching for 24 h, the dead cell rate was higher in POP than control. Notably, 17 β-estradiol treatment reversed mechanical stress induced hUSLFs apoptosis and death in both POP and Control cells. The protein and mRNA levels of anti-apoptotic PARP1 (poly-ADP-ribose polymerase) and Bcl-2 were increased by estrogen treatment. Meanwhile, expression of estrogen receptor α, a target of Poly-ADP-Ribosylation of PARP1, was also enhanced by 17 β-estradiol under the mechanical load. In conclusion, estrogen application ameliorates the mechanical strain induced cell apoptosis and death

in hUSLFs from POP patients. PARP1 might be involved in this protective process, providing novel insights into the mechanical biology of and possible therapies for POP.

Int J Environ Res Public Health. 2022 Oct 19;19(20):13501. doi: 10.3390/ijerph192013501.

Increased Risk of Fractures and Use of Proton Pump Inhibitors in Menopausal Women: A Systematic Review and Meta-Analysis

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Proton pump inhibitors (PPIs) can directly interfere with osteoclastic function, induce hypergastrinemia, and inhibit calcium absorption, leading to reduced bone mineral density (BMD), a measure of bone metabolism that may be associated with the risk of fractures. The current study involves a systematic review and meta-analysis aimed at assessing the relationship between prolonged use of PPI drugs and fractures in menopausal women. A systematic search and meta-analysis were performed on PubMed, Scopus, and Science Direct databases according to PRISMA guidelines. Two independent reviewers analyzed the articles. The five articles found in the databases, which met the eligibility criteria, covered participants who were menopausal women aged between 56 and 78.5 years, using or not using a PPI for a minimum of 12 months. All studies showed an increase in the rate of fractures related to using PPIs, as an outcome. Prolonged use of PPIs in menopausal women can affect bone metabolism and cause fractures. However, other factors, such as the use of other classes of drugs, obesity, low weight, poor diet, replacement hormones, and comorbidities, should also be considered for assessing the risk of fractures.

Fertil Steril. 2022 Oct 22;S0015-0282(22)01444-3. doi: 10.1016/j.fertnstert.2022.09.027. Online ahead of print.

Primary ovarian insufficiency has strong familiality: results of a multigenerational genealogical study

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Objective: To determine the familiality of primary ovarian insufficiency (POI) at population level through examination of multigenerational genealogical information linked to electronic medical records. Design: Case-control study. Setting: Not applicable. Patient(s): Women with POI were identified using International Classification of Disease 9 and 10 codes in electronic medical records (1995-2021) from 2 major health care systems in Utah and reviewed for accuracy. Cases were linked to genealogy information in the Utah Population Database (UPDB). All included POI cases (n = 396) were required to have genealogy information available for at least 3 generations of ancestors. The risk of POI in relatives was compared with population rates for POI matched by age, sex, and birthplace. Intervention(s): Not applicable. Main outcome measure(s): Relative risk of POI in first-, second-, and third-degree relatives. Result(s): We identified 396 validated cases of POI with an associated 2,132 first-degree relatives, 5,245 second-degree relatives, and 10,853 third-degree relatives. We found an increased risk of POI among the extended relatives of cases. Specifically, first-degree relatives demonstrated an 18-fold increased risk of POI compared with controls relative risk ([RR],18.52 95% confidence interval [CI], 10.12-31.07), second-degree relatives demonstrated a 4-fold increase (RR, 4.21; CI, 1.15-10.79), and third-degree relatives demonstrated a 2.7-fold increase (RR, 2.65; CI, 1.14-5.21]). Conclusion(s): This is the first population-based study to assess the familial clustering of POI. The data demonstrate excess familiality, familial clustering of POI in excess compared with matched population rates of disease, among first-, second-, and third-degree relatives. These findings support a genetic contribution to POI.

Osteoporos Int. 2022 Oct 25. doi: 10.1007/s00198-022-06567-9. Online ahead of print.

The need to distinguish intervention thresholds and diagnostic thresholds in the management of osteoporosis

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This position paper of the International Osteoporosis Foundation (IOF) and the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) addresses the rationale for separate diagnostic and intervention thresholds in osteoporosis. We conclude that the current BMD-based diagnostic criteria for osteoporosis be retained whilst clarity is brought to bear on the distinction between diagnostic and intervention thresholds.