

Selección de Resúmenes de Menopausia

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Type 2 diabetes and bone fragility- An under-recognized association

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Background and aims: Diabetes and osteoporosis are common chronic disorders with growing prevalence in the aging population. Skeletal fragility secondary to diabetes increases the risk of fractures and is underestimated by currently available diagnostic tools like fracture risk assessment (FRAX) and dual-energy X-ray absorptiometry (DXA). In this narrative review we describe the relationship and pathophysiology of skeletal fragility and fractures in Type 2 diabetes (T2DM), effect of glucose lowering medications on bone metabolism and the approach to diagnosing and managing osteoporosis and bone fragility in people with diabetes (PWD). **Methods:** A literature search was conducted on PubMed for articles in English that focused on T2DM and osteoporosis or bone/skeletal fragility. Articles considered to be of direct clinical relevance to physicians practicing diabetes were included. **Results:** T2DM is associated with skeletal fragility secondary to compromised bone remodeling and bone turnover. Long duration, poor glycemic control, presence of chronic complications, impaired muscle function, and anti-diabetic medications like thiazolidinediones (TZD) are risk factors for fractures among PWD. Conventional diagnostic tools like DXA and FRAX tool underestimate fracture risk in diabetes. Presence of diabetes does not alter response to anti-osteoporotic treatment in post-menopausal women. **Conclusion:** Estimation of fragility fracture risk should be included in standard of care for T2DM along with screening for traditional complications. Physicians should proactively screen for and manage osteoporosis in people with diabetes. It is important to consider effects on bone health when selecting glucose lowering agents in people at risk for fragility fractures.

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Comparison of methods to improve fracture risk assessment in chinese diabetic postmenopausal women: a case-control study

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Purpose: This study evaluated the predictive power of adjusted FRAX and standard FRAX models based on the actual prevalence of osteoporosis in type 2 diabetic (T2DM) postmenopausal women, and to explore the optimal strategy to better predicted fracture risk in postmenopausal women with diabetes in China. **Methods:** We recruited 434 patients from community-medical centers, 217 with T2DM and 217 without T2DM (non-T2DM). All participants completed self-reported questionnaires detailing their characteristics and risk factors. Bone mineral density (BMD) and spinal radiographs were evaluated. The China FRAX model calculated all scores. The area under the receiver operator characteristic curve (ROC-AUC) evaluated the sensitivity, specificity, and accuracy for predicting 10-year risk for major (MOF) and hip (OHF) osteoporotic fractures in T2DM patients. **Results:** T2DM patients had higher BMD but lower average FRAX values than non-T2DM patients. The unadjusted FRAX ROC-AUC was 0.774, significantly smaller than that for 0.5-unit femoral neck T-score-adjusted FRAX (0.800; $p = 0.004$). Rheumatoid arthritis (RA; AUC = 0.810, $p = 0.033$) and T-score (AUC = 0.816, $p = 0.002$) adjustments significantly improved fracture prediction in T2DM patients. **Conclusions:** Femoral neck T-score adjustment might be the preferred method for predicting MOF and OHF in Chinese diabetic postmenopausal women, while RA adjustment only effectively predicted HF risk.

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Use of Oral Contraceptives as a Potential Risk Factor for Breast Cancer: A Systematic Review and Meta-Analysis of Case-Control Studies Up to 2010

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Despite numerous studies evaluating the risk of breast cancer among oral contraception users, the effect of oral contraceptive on developing breast cancer remains inconclusive. Therefore, we conducted a systematic review of literature with meta-analysis in order to quantitative estimate this association. The bibliographic database MEDLINE and EMBASE, and reference lists of identified articles were searched, with no language restrictions, from the start of publication to August 2010. We performed a reanalysis and overall estimate of 79 case-control studies conducted

between 1960-2010, including a total of 72,030 incidents, histologically confirmed cases of breast cancer and 123,650 population/hospital controls. A decrease was observed in cancer risk in OC users before age 25 years (0.91, 0.83-1.00). However, the use of OCs before the first full-term pregnancy had a significant increased risk of breast cancer (OR, 1.14, 1.01-1.28, $p = 0.04$), as did OC use longer than 5 years (1.09, 1.01-1.18, $p = 0.02$). Pooled crude odds ratios of breast cancer in ever-users of oral contraceptives was 1.01 [95% confidence interval (CI), 0.95-1.07], compared with never-users. There was no significant increase in risk among premenopausal women (1.06, 0.92-1.22), postmenopausal women (0.99, 0.89-1.10), or nulliparous women (1.02, 0.82-1.26). Oral contraceptives do not appear to increase the risk of breast cancer among users. However, OC use before a first full-term pregnancy or using them longer than 5 years can modify the development of the breast cancer.

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The Dietary Inflammatory Index Is Associated with Low Muscle Mass and Low Muscle Function in Older Australians

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Age-associated chronic, low grade systemic inflammation has been recognised as an important contributing factor in the development of sarcopenia; importantly, diet may regulate this process. This cross-sectional study examined the association of diet-related inflammation with components of sarcopenia. Participants ($n = 809$) aged 60-95 years from the Geelong Osteoporosis Study were studied. Body composition was measured by dual energy X-ray absorptiometry. In this study, low appendicular lean mass (ALM/height², kg/m²) was defined as T-score < -1 and low muscle function as Timed-Up-and-Go >10 s over 3 m (TUG > 10). Dietary inflammatory index (DII®) scores, based on specific foods and nutrients, were computed using dietary data collected from a food frequency questionnaire. Associations between DII scores and low muscle mass and low muscle function, alone and combined, were determined using linear and logistic regression. After adjusting for covariates, higher DII score was associated with lower ALM/height² (β -0.05, standard error (SE) 0.02, $p = 0.028$), and higher natural log-transformed (ln) (TUG) (β 0.02, standard error 0.01, $p = 0.035$) and higher likelihood for these components combined (odds ratio 1.33, 95% confidence interval 1.05 to 1.69, $p = 0.015$). A pro-inflammatory diet, as indicated by higher DII score, is associated with lower muscle mass, poorer muscle function and increased likelihood for the combination of low muscle mass and low muscle function. Further studies investigating whether anti-inflammatory dietary interventions could reduce the risk of sarcopenia are needed.

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Protective effect of metformin against ovariectomy induced depressive- and anxiety-like behaviours in rats: role of oxidative stress

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Several studies have shown that low estrogen levels can lead to an increase in the incidence of depression and anxiety during menopause. The hippocampus and prefrontal cortex are parts of the brain involved in depressive- and anxiety-like behaviors. Recent studies have revealed that metformin has neuroprotective effects mainly due to its antioxidant properties. The aim of the present study was to examine the therapeutic potential of metformin in depressive- and anxiety-like behavior as well as oxidative stress in the prefrontal cortex and hippocampus of ovariectomized rats. Young female Wistar Albino rats were distributed into four groups ($n:8$): control, metformin-administered control, ovariectomized and metformin administered ovariectomized groups. Metformin (25 mg/kg) was administered daily by oral gavage for 2 weeks. Forced swimming test and open field test were performed to evaluate depression- and anxiety-like behaviors, respectively. Following the treatment with metformin, the tissues of the hippocampus and prefrontal cortex were isolated for the measurement of malondialdehyde, reduced glutathione and ascorbic acid contents. Ovariectomy resulted in depressive- and anxiety-like behaviors, and besides, increased content of malondialdehyde in both prefrontal cortex and hippocampus. The levels of ascorbic acid and glutathione were found to be reduced in ovariectomized rats. Metformin treatment significantly decreased depressive behaviour and malondialdehyde content in the prefrontal cortex. Reducing oxidative stress of the prefrontal cortex was suggested as a possible mechanism implicated in the beneficial effects of metformin on ovariectomy-induced depressive-like behaviour. We believe that the therapeutic efficiency of metformin needs to be tested for potential clinical use in surgical menopause or gonadal hormone deficiency women with depression.

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A core outcome set for vasomotor symptoms associated with menopause: the COMMA (Core Outcomes in Menopause) global initiative

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Objective: Vasomotor symptoms (VMS) (hot flashes and night sweats) affect most women over the menopause transition. Comparing the safety and effectiveness of treatments for vasomotor symptoms is limited by the use of inconsistent outcome measures, and uncertainty as to which outcomes are most important to symptomatic women. To address this, we have developed a Core Outcome Set (COS) for use in clinical trials of treatments for VMS. **Methods:** We systematically reviewed the primary outcomes measured in randomized controlled trials of treatments for VMS. These were refined and entered into a two-round modified Delphi survey completed by clinicians, researchers, and postmenopausal women between November 2019 and March 2020. Outcomes were scored on a nine-point scale from "not important" to "critically important." Two international consensus meetings were held to finalize the COS. **Results:** Based on the systematic review, 13 separate outcomes were included in the Delphi process. This was completed by 227 participants of whom 58% were postmenopausal women, 34% clinicians, and 8% researchers. Predefined thresholds were applied to categorize importance scores obtained during Round 2 of the Delphi survey. These informed discussions at the consensus meetings which were attended by 56 participants from 28 countries. The final COS includes six outcomes: 1) frequency of VMS, 2) severity of VMS, 3) distress, bother or interference caused by VMS, 4) impact on sleep, 5) satisfaction with treatment, and 6) side-effects of treatment. **Conclusion:** Implementation of this COS will: better enable research studies to accurately reflect the joint priorities of postmenopausal women, clinicians and researchers, standardize outcome reporting, and facilitate combining and comparing results from different studies, and ultimately improve outcomes for women with bothersome VMS.

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Topical estrogens and non-hormonal preparations for postmenopausal vulvovaginal atrophy: An EMAS clinical guide

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Introduction: Vulvovaginal atrophy (VVA) is a chronic condition caused by estrogen deficiency. It affects around 50% of postmenopausal women, reducing their general and sexual quality of life as well as the quality of their personal relationships. **Aim:** The aim of this clinical guide is to set out an individualized approach to the management of VVA with topical estrogens and non-hormonal preparations. **Materials and methods:** Literature review and consensus of expert opinion. **Summary recommendations:** An individualized approach is required for the management of VVA. Topical low-dose estrogens are effective and also alleviate urinary incontinence and prevent recurrent urinary tract infections. Women should not be denied long-term use of topical estrogens as long as they feel that this treatment is of benefit to them, because the safety data are reassuring. Non-hormonal preparations (lubricants and moisturizers) should be the first-line treatment for VVA in women taking adjuvant endocrine therapies for cancers considered to be hormone-dependent. They can be used over the long term.