Selección de Resúmenes de Menopausia

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María Soledad Vallejo. Clínica Quilín. Universidad de Chile

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FRAX tool in type 2 diabetic subjects: the use of HbA1c in estimating fracture risk.

Valentini A, Cianfarani MA, De Meo L, Morabito P, Romanello D, Tarantino U, Federici M, Bertoli A.

AIMS: Patients with type 2 diabetes mellitus (T2DM) have an increased risk of fractures, despite having greater bone mineral density (BMD) than non-diabetic subjects. This has led to the hypothesis that the presence of impaired bone quality among diabetics reduces bone strength. The Fracture Risk Assessment Score (FRAX) algorithm, introduced to facilitate the evaluation of fracture risk, underestimates the risk of fracture in diabetic patients. The purpose of this study is to confirm the relationship between the degree of metabolic compensation and the 10-year probability of a major fracture or a hip osteoporotic fracture observed in our previous study and to ascertain whether glycosylated hemoglobin (HbA1c) can improve the predictive value of FRAX in patients with T2DM. METHODS: Our data derive from a retrospective clinical study conducted at the "Tor Vergata" Polyclinic in Rome on 6355 subjects over 50 years of age evaluated for osteoporosis. All available clinical records were examined. HbA1c was available for 242 of these subjects and all had had a Dual-energy X-ray Absorption (DXA) scan of the lumbar spine and femoral neck. The risk of fracture was estimated using the Italian version of the FRAX algorithm. RESULT: Patients with T2DM had BMD and T-scores higher than those of non-diabetic subjects, while FRAX average values were higher in the non-diabetic group. HbA1c and FRAX are inversely correlated with each other: for each incremental percentage point of HbA1c growth, the FRAX major osteoporotic fracture probability is reduced by 0.915 points and the FRAX hip osteoporotic fracture probability by 1.438 points. The introduction of a correction factor derived from HbA1c, resulted in mean FRAX values of diabetic patients equivalent to those of non-diabetic subjects. CONCLUSIONS: We propose a correction factor derived from HbA1c that could enhance the predictive ability of fracture risk estimated by the FRAX algorithm in subjects with T2DM.

Medicine (Baltimore). 2018 Jul;97(27):e11345. doi: 10.1097/MD.0000000000011345.

Association between serum leptin levels and breast cancer risk: An updated systematic review and meta-analysis.

Pan H, Deng LL, Cui JQ, Shi L, Yang YC, Luo JH, Qin D, Wang L.

BACKGROUND: Many studies have indicated that leptin is correlated with breast cancer occurrence and tumor behavior. However, this issue remains controversial. Therefore, we conducted an updated meta-analysis to investigate the role of leptin in breast cancer. METHODS: We performed a systematic literature search and identified relevant papers up to 1 September 2017. Standardized mean differences (SMDs) with 95% confidence intervals (CIs) were used to evaluate effect sizes. RESULTS: Thirty-five eligible studies were included in the current meta-analysis. Serum leptin levels were related to breast cancer risk as demonstrated by calculations of the overall SMD=0.46 (95% CI=0.31-0.60, I=93.5%). A subgroup analysis of BMI identified an association between breast cancer and serum leptin levels in patients who are overweight and obese (overweight: SMD=0.35, 95% CI=0.13-0.57, I=88.1%; obesity: SMD=1.38, 95% CI=0.64-2.12, I=89.6%). Additionally, menopausal status subgroup analysis revealed a significant association in postmenopausal women (SMD=0.26, 95% CI=0.12-0.40, I=77.9%). Furthermore, we identified a significant association between breast cancer and serum leptin levels in Chinese women (SMD=0.61, 95% CI=0.44-0.79, I=40.6%). CONCLUSION: The results of this meta-analysis suggested that leptin could be a potential biomarker for breast cancer risk in women, especially overweight/obese or postmenopausal women. Therefore, it may be useful for identifying subjects with a high risk for breast cancer who may benefit from preventive treatments.

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Difference in carotid intima-media thickness between pre and postmenopausal women.

Ieamtairat P, Soontrapa S, Kaewrudee S, Promsorn J, Takong W, Somboonporn W.

OBJECTIVES: To examine whether carotid intima-media thickness (CIMT), the prevalence of increased CIMT, and the presence of carotid plaque differ according to menopausal status. METHODS: In this analytical cross-sectional study, we enrolled 61 premenopausal women and 61 postmenopausal women. We matched the two groups for age. Participants were classified as either premenopausal or postmenopausal according to menstrual history and follicular-stimulating hormone level. Two skilled radiologists measured CIMT and carotid plaque in all participants by using B-mode ultrasound. RESULTS: The mean age was 49.25±2.0 years. The mean number of years since menopause in the postmenopausal group was 1.9±0.92 years. After adjusted analysis, the mean CIMT of the common carotid artery of postmenopausal women was significantly higher than that of premenopausal women, with a mean difference of 0.068 mm (95% confidence interval 0.023, 0.113). There was no significant association between number of years since menopause and mean CIMT. Although the prevalence of increased CIMT and the presence of carotid plaque were significantly higher in the postmenopausal group than in the premenopausal group according to crude analysis, this difference was not statistically significant after adjusted analysis. Multiple linear regression analysis for assessing potential risk factors for the alteration of mean CIMT showed that only menopausal status and body mass index were independently associated factors. CONCLUSIONS: Our findings indicate that postmenopausal status is a significant factor of high mean CIMT. These findings add to the growing evidence showing that menopause transition is a critical period for subclinical atherosclerosis development.

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Mechanisms in Endocrinology: Bone Marrow Adiposity And Bone, A Bad Romance?

Rharass T, Lucas S.

Bone marrow adipocytes (BMA) constitute an original and heterogeneous fat depot whose development appears interlinked with bone status throughout life. The gradual replacement of the hematopoietic tissue by BMA arises in a well-ordered way during childhood and adolescence concomitantly to bone growth and continues at a slower rate throughout the adult life. Importantly, BM adiposity quantity is found well associated with BMD (Bone Mineral Density) loss at different skeletal sites in primary osteoporosis such as in ageing or menopause but also in secondary osteoporosis consecutive to anorexia nervosa. Since BMA and osteoblasts originate from a common mesenchymal stem cell, adipogenesis is considered as a competitive process that disrupts osteoblastogenesis. Besides, most factors secreted by bone and bone marrow cells (ligands and antagonists of the Wnt/β-catenin pathway, BMP and others) reciprocally regulate the two processes. Hormones such as oestrogens, glucocorticoids, parathyroid and growth hormones that control bone remodelling also modulate the differentiation and the activity of BMA. Actually, BMA could also contribute to bone loss through the release of paracrine factors altering osteoblast and /or osteoclast formation and function. Based on clinical and fundamental studies, this review aims at presenting and discussing these current arguments that support but also challenge the involvement of BMA in the bone mass integrity.

Cell Rep. 2018 Jul 3;24(1):181-196. doi: 10.1016/j.celrep.2018.06.019.

Estrogens Promote Misfolded Proinsulin Degradation to Protect Insulin Production and Delay Diabetes.

Xu B, Allard C, Alvarez-Mercado AI, Fuselier T, Kim JH, Coons LA, Hewitt SC, Urano F, Korach KS, et al.

Conjugated estrogens (CE) delay the onset of type 2 diabetes (T2D) in postmenopausal women, but the mechanism is unclear. In T2D, the endoplasmic reticulum (ER) fails to promote proinsulin folding and, in failing to do so, promotes ER stress and β cell dysfunction. We show that CE prevent insulin-deficient diabetes in male and in female Akita mice using a model of misfolded proinsulin. CE stabilize the ER-associated protein degradation (ERAD) system and promote misfolded proinsulin proteasomal degradation. This involves activation of nuclear and membrane estrogen receptor-α (ERα), promoting transcriptional repression and proteasomal degradation of the ubiquitin-conjugating enzyme and ERAD degrader, UBC6e. The selective ERα modulator bazedoxifene mimics CE protection of β cells in females but not in males.

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The Use of Antidepressive Agents and Bone Mineral Density in Women: A Meta-Analysis.

Schweiger JU, Schweiger U, Hüppe M, Kahl KG, Greggersen W, Jauch-Chara K, Fassbinder E.

Antidepressive agents are one of the fastest-growing classes of prescribed drugs. However, the effects of antidepressive agents on bone density are controversial. The aim of this meta-analysis is to evaluate the state of research on the relationship between the use of tricyclic antidepressants (TCAs) or selective serotonin reuptake inhibitors (SSRIs) and bone mineral density (BMD) in women. The database searched was Pubmed. The meta-analysis included human studies in women fulfilling the following criteria: (i) an assessment of bone mineral density in the lumbar spine, the femoral neck or the total hip; (ii) a comparison of the BMD of depressed individuals using antidepressive agents (SSRIs or TCAs), and a control group that did not use antidepressive agents; (iii) measurement of BMD using dual-energy X-ray absorptiometry (DXA); and (iv) calculations of the mean BMD and standard deviation or standard error. Four studies were identified, which, in total, included 934 women using antidepressive agents and 5767 non-using individuals. The results showed that no significant negative composite weighted mean effect sizes were identified for the comparisons between SSRI users and non-users. Similarly, no significant negative composite weighted mean effect sizes were identified for the comparisons between TCA users and non-users, indicating similar BMD in SSRI or TCA users and non-users. The meta-analysis shows that the association between antidepressant medication and bone mineral density has not been extensively researched. Only four studies fulfilled the inclusion criteria. The global result of the literature review and meta-analysis was that the use of antidepressive agents was not associated with lower or higher BMD. This result applies to both SSRIs and TCAs and to all measurement locations (lumbar, femoral neck, total hip).

Clin Rev Bone Miner Metab. 2018 Mar;16(1):33-47. doi: 10.1007/s12018-018-9242-3. Epub 2018 Feb 5.

Glucocorticoid Excess in Bone and Muscle.

Sato AY, Peacock M, Bellido T.

Glucocorticoids (GC), produced and released by the adrenal glands, regulate numerous physiological processes in a wide range of tissues. Because of their profound immunosuppressive and anti-inflammatory actions, GC are extensively used for the treatment of immune and inflammatory conditions, the management of organ transplantation, and as a component of chemotherapy regimens for cancers. However, both pathologic endogenous elevation and long-term use of exogenous GC are associated with severe adverse effects. In particular, excess GC has devastating effects on the musculoskeletal system. GC increase bone resorption and decrease formation leading to bone loss, microarchitectural deterioration and fracture. GC also induce loss of muscle mass and strength leading to an increased incidence of falls. The combined effects on bone and muscle account for the increased fracture risk with GC. This review summarizes the advance in knowledge in the last two decades about the mechanisms of action of GC in bone and muscle and the attempts to interfere with the damaging actions of GC in these tissues with the goal of developing more effective therapeutic strategies.

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Progesterone for the prevention and treatment of osteoporosis in women.

Prior JC.

Estradiol (E2) is women's dominant 'bone hormone' since it is essential for development of adolescent peak bone mineral density (BMD) and physiological levels prevent the rapid (3-week) bone resorption that causes most adult BMD loss. However, deceasing E2 levels trigger bone resorption/loss. Progesterone (P4) is E2's physiological partner, collaborating with E2 in every cell/tissue; its bone 'job' is to increase P4-receptor-mediated, slow (3-4 months) osteoblastic new bone formation. When menstrual cycles are normal length and normally ovulatory, E2 and P4 are balanced and BMD is stable. However, clinically normal cycles commonly have ovulatory disturbances (anovulation, short luteal phases) and low P4 levels; these are more frequent in teen and perimenopausal women and increased by everyday stressors: energy insufficiency, emotional/social/economic threats and illness. Meta-analysis shows that almost 1%/year spinal BMD loss occurs in those with greater than median (~31%) of ovulatory disturbed cycles. Prevention of osteoporosis and fragility fractures requires the reversal of stressors, detection and treatment of teen-to-perimenopausal recurrent cycle/ovulatory disturbances with cyclic oral micronized progesterone. Low 'Peak Perimenopausal BMD' is likely the primary risk for fragility fractures in later life. Progesterone plus estradiol or other antiresorptive therapies adds 0.68%/year and may be a highly effective osteoporosis treatment. Randomized controlled trials are still needed to confirm progesterone's important role in women's bone formation.