Selección de Resúmenes de Menopausia

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María Soledad Vallejo. Clínica Quilín. Universidad de Chile

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Pathogenic mechanisms of glucocorticoid-induced osteoporosis

Meng Chen 1, Wenyu Fu 2, Huiyun Xu 3, Chuan-Ju Liu 4

Glucocorticoid (GC) is one of the most prescribed medicines to treat various inflammatory and autoimmune diseases. However, high doses and long-term use of GCs lead to multiple adverse effects, particularly glucocorticoid-induced osteoporosis (GIO). Excessive GCs exert detrimental effects on bone cells, including osteoblasts, osteoclasts, and osteocytes, leading to impaired bone formation and resorption. The actions of exogenous GCs are considered to be strongly cell-type and dose dependent. GC excess inhibits the proliferation and differentiation of osteoblasts and enhances the apoptosis of osteoblasts and osteocytes, eventually contributing to reduced bone formation. Effects of GC excess on osteoclasts mainly include enhanced osteoclastogenesis, increased lifespan and number of mature osteoclasts, and diminished osteoclast apoptosis, which result in increased bone resorption. Furthermore, GCs have an impact on the secretion of bone cells, subsequently disturbing the process of osteoblastogenesis and osteoclastogenesis. This review provides timely update and summary of recent discoveries in the field of GIO, with a particular focus on the effects of exogenous GCs on bone cells and the crosstalk among them under GC excess.

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Height loss as an indicator of ageing through its association with frailty and sarcopenia: An observational cohort study

Sunghwan Ji 1, Eunju Lee 2, Beom-Jun Kim 3, Ji Yeon Baek 4, Youngseok Yi 4, Il-Young Jang 4, Hee-Won Jung 4

Background: Height loss is associated with various health-related variables such as cardiovascular disease, osteoporosis, cognitive function, and mortality. We hypothesized that height loss can be used as an indicator of aging, and we assessed whether the degree of height loss for 2 years was associated with frailty and sarcopenia. Methods: This study was based on a longitudinal cohort, the Pyeongchang Rural Area cohort. The cohort included people aged 65 years or older, ambulatory, and living at home. We divided individuals according to the ratio of height change (height change for 2 years divided by height at 2 years from baseline): HL2 (<-2%), HL1 (-2%--1%), and REF (-1%≤). We compared the frailty index, diagnosis of sarcopenia after 2 years from baseline, and the incidence of a composite outcome (mortality and institutionalization). Results: In total, 59 (6.9%), 116 (13.5%), and 686 (79.7%) were included in the HL2, HL1, and REF groups, respectively. Compared with the REF group, groups HL2 and HL1 had a higher frailty index, and higher risks of sarcopenia and composite outcome. When groups HL2 and HL1 were merged, the merged group had higher frailty index (standardized B, 0.06; p = 0.049), a higher risk of sarcopenia (OR, 2.30; p = 0.006), and a higher risk of composite outcome (HR, 1.78; p = 0.017) after adjusting for age and sex. Conclusions: Individuals with greater height loss were frailer, more likely to be diagnosed with sarcopenia and had worse outcomes regardless of age and sex.

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Selected Genetic Factors Associated with Primary Ovarian Insufficiency

Mengchi Chen 1, Haotian Jiang 2, Chunping Zhang 2

Primary ovarian insufficiency (POI) is a heterogeneous disease resulting from non-functional ovaries in women before the age of 40. It is characterized by primary amenorrhea or secondary amenorrhea. As regards its etiology, although many POI cases are idiopathic, menopausal age is a heritable trait and genetic factors play an important role in all POI cases with known causes, accounting for approximately 20% to 25% of cases. This paper reviews the selected genetic causes implicated in POI and examines their pathogenic mechanisms to show the crucial role of genetic effects on POI. The genetic factors that can be found in POI cases include chromosomal abnormalities (e.g., X chromosomal aneuploidies, structural X chromosomal abnormalities, X-autosome translocations, and autosomal variations), single gene mutations (e.g., newborn ovary homeobox gene (NOBOX), folliculogenesis specific bHLH transcription factor (FIGLA), follicle-stimulating hormone receptor (FSHR), forkhead box L2 (FOXL2), bone morphogenetic protein 15

(BMP15), etc., as well as defects in mitochondrial functions and non-coding RNAs (small ncRNAs and long ncRNAs). These findings are beneficial for doctors to diagnose idiopathic POI cases and predict the risk of POI in women.

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Breast Cancer Risk and Breast-Cancer-Specific Mortality following Risk-Reducing Salpingo-Oophorectomy in BRCA Carriers: A Systematic Review and Meta-Analysis

Faiza Gaba 1 2, Oleg Blyuss 3 4, Alex Tan 3, Daniel Munblit 4 5 6, Samuel Oxley 2 3, Khalid Khan 7, et al.

Background: Risk-reducing salpingo-oophorectomy (RRSO) is the gold standard method of ovarian cancer risk reduction, but the data are conflicting regarding the impact on breast cancer (BC) outcomes. This study aimed to quantify BC risk/mortality in BRCA1/BRCA2 carriers after RRSO. Methods: We conducted a systematic review (CRD42018077613) of BRCA1/BRCA2 carriers undergoing RRSO, with the outcomes including primary BC (PBC), contralateral BC (CBC) and BC-specific mortality (BCSM) using a fixed-effects meta-analysis, with subgroup analyses stratified by mutation and menopause status. Results: RRSO was not associated with a significant reduction in the PBC risk (RR = 0.84, 95%CI: 0.59-1.21) or CBC risk (RR = 0.95, 95%CI: 0.65-1.39) in BRCA1 and BRCA2 carriers combined but was associated with reduced BC-specific mortality in BC-affected BRCA1 and BRCA2 carriers combined (RR = 0.26, 95%CI: 0.18-0.39). Subgroup analyses showed that RRSO was not associated with a reduction in the PBC risk (RR = 0.89, 95%CI: 0.68-1.17) or CBC risk (RR = 0.85, 95%CI: 0.59-1.24) in BRCA1 carriers nor a reduction in the CBC risk in BRCA2 carriers (RR = 0.35, 95%CI: 0.07-1.74) but was associated with a reduction in the PBC risk in BRCA2 carriers (RR = 0.63, 95%CI: 0.41-0.97) and BCSM in BC-affected BRCA1 carriers (RR = 0.46, 95%CI: 0.30-0.70). The mean NNT = 20.6 RRSOs to prevent one PBC death in BRCA2 carriers, while 5.6 and 14.2 RRSOs may prevent one BC death in BC-affected BRCA1 and BRCA2 carriers combined and BRCA1 carriers, respectively. Conclusions: RRSO was not associated with PBC or CBC risk reduction in BRCA1 and BRCA2 carriers combined but was associated with improved BC survival in BC-affected BRCA1 and BRCA2 carriers combined and BRCA1 carriers and a reduced PBC risk in BRCA2 carriers.

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Safety of Fezolinetant [(1)] for Vasomotor Symptoms Associated With Menopause: A Randomized Controlled Trial [(1)]antagonista de los receptores de neurokinina-3

Genevieve Neal-Perry, Antonio Cano, Samuel Lederman, Rossella E Nappi, Nanette Santoro, Wendy Wolfman, et al

Objective: To evaluate the safety, tolerability, and effect of fezolinetant on endometrial health over 52 weeks. Methods: We conducted a phase 3, randomized, double-blind, 52-week safety study (SKYLIGHT 4 [Study to Find Out How Safe Long-term Treatment With Fezolinetant is in Women With Hot Flashes Going Through Menopause]) of placebo, fezolinetant 30 mg, and fezolinetant 45 mg once daily (1:1:1). Participants were postmenopausal and seeking treatment for vasomotor symptoms associated with menopause. Primary endpoints were treatment-emergent adverse events, percentage of participants with endometrial hyperplasia, and percentage with endometrial malignancy. Endometrial hyperplasia or malignancy was evaluated according to U.S. Food and Drug Administration guidance (point estimate of 1% or less with an upper bound of one-sided 95% CI of 4% or less). Secondary endpoints included change in bone mineral density (BMD) and trabecular bone score. A sample size of 1,740 was calculated to enable observation of one or more events (≈80% probability for events with background rate of less than 1%). Results: A total of 1,830 participants were randomized and took one or more medication dose (July 2019-January 2022). Treatment-emergent adverse events occurred in 64.1% (391/610) of the placebo group, 67.9% (415/611) of the fezolinetant 30-mg group, and 63.9% (389/609) of the fezolinetant 45-mg group. Treatment-emergent adverse events leading to discontinuation were similar across groups (placebo, 26/610 [4.3%]; fezolinetant 30 mg, 34/611 [5.6%]; fezolinetant 45 mg, 28/609 [4.6%]). Endometrial safety was assessed in 599 participants. In the fezolinetant 45-mg group, 1 of 203 participants had endometrial hyperplasia (0.5%; upper limit of one-sided 95% CI 2.3%); there were no cases in the placebo (0/186) or fezolinetant 30 mg (0/210) group. Endometrial malignancy occurred in 1 of 210 in the fezolinetant 30-mg group (0.5%; 95% CI 2.2%) with no cases in the other groups. Liver enzyme elevations more than three times the upper limit of normal occurred in 6 of 583 placebo, 8 of 590 fezolinetant 30 mg, and 12 of 589 fezolinetant 45 mg participants; no Hy's law cases were reported (ie, no severe drug-induced liver injury with alanine aminotransferase or aspartate aminotransferase more than three times the upper limit of normal and total bilirubin more than two times the upper limit of normal, with no elevation of alkaline phosphatase and no other reason to explain the combination). Changes

in BMD and trabecular bone score were similar across groups. Conclusion: Results from SKYLIGHT 4 confirm the 52-week safety and tolerability of fezolinetant and support its continued development.

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Fat mass, weight and body shape changes at menopause - causes and consequences: a narrative review

A Fenton 1, C Smart 1, L Goldschmidt 1, V Price 1, J Scott 1

In addition to age-related weight gain, menopause adds additional challenges for women with the occurrence of significant metabolic alterations and central and visceral fat redistribution. The changes in body composition then influence risks of cardiovascular disease, metabolic disruption, cancer, fracture, lung disease, sexual dysfunction, mental health disorders and dementia. They may also heighten the severity of vasomotor symptoms. Treatment of these changes requires a flexible long-term strategy. This narrative review explores the pathogenesis of the metabolic changes at menopause and effective management options.

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Menopause Transition - A Cross-Sectional Evaluation on Muscle Size and Quality

Abbie E Smith-Ryan, Katie R Hirsch 1, Hannah E Cabre, Lacey M Gould 2, Amanda N Gordon 2, Arny A Ferrando

Introduction: The menopause transition yields significant physiologic alterations. The purpose was to characterize lean soft tissue (LST), muscle size (muscle cross-sectional area; mCSA), muscle quality (echo intensity; EI), and strength across the menopause transition. A secondary aim was to evaluate whole body protein turnover in a subsample of women. Methods: Seventy-two healthy women were enrolled in this cross-sectional study based on menopause stage (PRE: n = 24; PERI: n = 24; POST: n = 24). Whole-body LST was measured via dual-energy x-ray absorptiometry and muscle characteristics (mCSA and EI) were measured via B-mode ultrasound of the vastus lateralis. Maximal voluntary contractions (MVC; Nm) of the knee extensors were evaluated. Physical activity (min per day) was accounted for using the International Physical Activity Questionnaire. A sub-sample of women (n = 27) ingested 2.0 g of 15N-alanine to determine whole-body net protein balance (NB; g/kg BM/day).R esults: Significant differences were evident in LST (p = 0.022), leg LST (p = 0.05) and EI (p = 0.018) between menopause stages. Bonferroni post-hoc comparisons revealed greater LST in PRE vs PERI (mean difference [MD] ± SE: 3.8 ± 1.5 kg; p = 0.048) and POST (3.9 ± 1.5 lbs; p = 0.049). Similarly, EI was significantly higher in PERI PRE (MD: 18.3 ± 7.1 a.u.; p = 0.036.). There was no significant difference in mCSA (p = 0.082) or in MVC (p = 0.167). NB was significantly different across groups (p = 0.026); NB was greater in PRE compared to PERI (MD: 0.39 ± 0.17 g/kg; p = 0.090), and from PRE to POST (MD: 0.46 ± 0.17 g/kg; p = 0.042). Physical activity was not significantly different across groups but demonstrated a linear increase from PRE to POST. Conclusions: The current findings suggest that LST, muscle quality, and protein balance may be negatively influenced by the menopause transition.