Selección de Resúmenes de Menopausia

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Crosstalk between skeletal and neural tissues is critical for skeletal health

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Emerging evidence in the literature describes a physical and functional association between the neural and skeletal systems that forms a neuro-osteogenic network. This communication between bone cells and neural tissues within the skeleton is important in facilitating bone skeletal growth, homeostasis and repair. The growth and repair of the skeleton is dependent on correct neural innervation for correct skeletal developmental growth and fracture repair, while pathological conditions such as osteoporosis are accelerated by disruptions to sympathetic innervation. To date, different molecular mechanisms have been reported to mediate communication between bone and neural populations. This review highlights the important role of various cell surface receptors, cytokines and associated ligands as potential regulators of skeletal development, homeostasis, and repair, by mediating interactions between the skeletal and nervous systems. Specifically, this review describes how Bone Morphogenetic Proteins (BMPs), Eph/ephrin, Chemokine CXCL12, Calcitonin Gene-related Peptide (CGRP), Netrins, Neurotrophins (NTs), Slit/Robo and the Semaphorins (Semas) contribute to the cross talk between bone cells and peripheral nerves, and the importance of these interactions in maintaining skeletal health.

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Early ovarian ageing: is a low number of oocytes harvested in young women associated with an earlier and increased risk of age-related diseases?

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Study question: Do young women with early ovarian ageing (EOA), defined as unexplained, and repeatedly few oocytes harvested in ART have an increased risk of age-related events? Summary answer: At follow-up, women with idiopathic EOA had an increased risk of age-related events compared to women with normal ovarian ageing (NOA). What is known already: Early and premature menopause is associated with an increased risk of cardiovascular diseases (CVDs), osteoporosis and death. In young women, repeated harvest of few oocytes in well-stimulated ART cycles is a likely predictor of advanced menopausal age and may thus serve as an early marker of accelerated general ageing.Study design, size, duration: A register-based national, historical cohort study. Young women (≤37 years) having their first ART treatment in a public or private fertility clinic during the period 1995-2014 were divided into two grou ps depending on ovarian reserve status: EOA (n = 1222) and NOA (n = 16 385). Several national registers were applied to assess morbidity and mortality. Participants/materials, setting, methods: EOA was defined as ≤5 oocytes harvested in a minimum of two FSH-stimulated cycles and NOA as ≥8 oocytes in at least one cycle. Cases with known causes influencing the ovarian reserve (endometriosis, ovarian surgery, polycystic ovary syndrome, chemotherapy etc.) were excluded. To investigate for early signs of ageing, primary outcome was an overall risk of ageing-related events, defined as a diagnosis of either CVD, osteoporosis, type 2 diabetes, cancer, cataract, Alzheimer's or Parkinson's disease, by death of any-cause as well as a Charlson comorbidity index score of ≥1 or by registration of early retirement benefit. Cox regression models were used to assess the risk of these events. Exposure status was defined 1 year after the first ART cycle to assure reliable classification, and time-to-event was measured from that time point. Main results and the role of chance: Median follow-up time from baseline to first event was 4.9 years (10/90 percentile 0.7/11.8) and 6.4 years (1.1/13.3) in the EOA and NOA group, respectively. Women with EOA had an increased risk of ageing-related events when compared to women with a normal oocyte yield (adjusted hazard ratio 1.24, 95% CI 1.08 to 1.43). Stratifying on categories, the EOA group had a significantly increased risk for CVD (1.44, 1.19 to 1.75) and osteoporosis (2.45, 1.59 to 3.90). Charlson comorbidity index (1.15, 0.93 to 1.41) and early retirement benefit (1.21, 0.80 to 1.83) was also increased, although not reaching statistical significance. Limitations, reasons for caution: Cycles never reaching oocyte aspiration were left out of account in the inclusion process and we may therefore have missed women with the most severe forms of EOA. We had no information on the total doses of gonadotrophin administered in each cycle. Wider implications of the findings: These findings indicate that oocyte yield may serve as marker of later accelerated ageing when, unexpectedly, repeatedly few oocytes are harvested in young women. Counselling on life-style factors as a prophylactic effort against cardiovascular and other age-related diseases may be essential for this group of women.

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The association between low lean mass and osteoporosis increases the risk of weakness, poor physical performance and frailty in Brazilian older adults: data from SARCOS study

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Purpose: To characterize the phenotypes of older adults with low lean mass and osteoporosis, concomitantly or isolated, in regards to poor physical performance and frailty status. Design: Cross-sectional analysis of the SARCopenia and OSteoporosis in Older Adults with Cardiovascular Diseases Study (SARCOS). Setting: Outpatient geriatric cardiology clinic. Participants and method: 385 older adults underwent DXA analysis. Low lean mass was diagnosed according to FNIH and low BMD by a T-score ≤ -2.5 SD. Subjects were grouped into: I-Low lean mass and Osteoporosis (LLMO); II-Low lean mass (LLM); III-Osteoporosis (OP), and IV-Controls. Poor physical performance was diagnosed by weakness or slow walking speed or impaired mobility. Frailty was diagnosed by CHS criteria. Results: The mean age was 78.22 ± 7.16 years. The prevalence of LLMO, LLM, and OP were 14.8%, 39.5%, and 19.2%, respectively. LLMO subjects were older, predominantly women, with a high percentage of body fat (HTBF). LLM was represented by obese men, while individuals with OP were preferably women, older and leaner. In a regression analyses, LLMO presented an OR: 6.42 (2.63–15.65; p < 0.001) for weakness, OR: 2.55 (1.09–5.95; p = 0.030) for impaired mobility, and OR: 14.75 (2.72–79.94; p = 0.002) for frailty. After adjusting for HTBF, the OR for frailty, decreased to 7.25 (1.11-47.21; p = 0.038). LLM and OP were associated only with weakness with an OR: 3.06 (1.36-6.84; p = 0.006) and OR: 3.14 (1.29-7.62; p = 0.011), respectively. Conclusion: In Brazilian older community-dwelling outpatient adults, the phenotype characterized by low lean mass and osteoporosis presents a higher association with impaired mobility, weakness and frailty status compared to the others phenotyeps and controls. A high percentage of body fat presents a synergistic effect with low lean mass and osteoporosis phenotype in regards to frailty.

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Total Antioxidant Capacity and Frailty in Older Men

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Frailty, a clinical syndrome characterized by multisystem dysregulation, has been associated with high levels of oxidative stress. We investigated the association between serum total antioxidant capacity (TAC) and frailty in older men. This cross-sectional study included 581 men (age 60-90 years) enrolled in the Geelong Osteoporosis Study. Frailty comprised at least three of unintentional weight loss, exhaustion, low physical activity, slowness, and weakness. Serum TAC was measured by quantitative colorimetric determination and expressed as uric acid equivalents (mM). Relationships between TAC (in SD units) and frailty were explored using multivariable logistic regression models. Sociodemographic, anthropometric, and lifestyle variables were tested as potential confounders and effect modifiers. A sensitivity analysis excluded participants (n = 145) in the upper quartile of TAC, who were likely to have hyperuricemia. Fifty (8.6%) men were frail. There was evidence that higher TAC levels were associated with increased likelihood of frailty (OR 1.34, 95% confidence interval [CI; 0.99, 1.80]), and this was attenuated after adjustment for age and body mass index (BMI; OR 1.26, 95% CI [0.93,1.71]). No effect modifiers or other confounders were identified. The sensitivity analysis revealed a positive association between TAC and frailty, before and after accounting for age and BMI (adjusted OR 1.79, 95% CI [1.01, 3.17] p = .038). These results suggest a positive association between TAC levels and frailty, supporting the hypothesis that this biomarker could be useful in identifying individuals at risk of frailty. We speculate that a milieu of heightened oxidative stress in frailty may elevate the oxidative stress regulatory set point, raising antioxidant activity. This warrants further investigation.

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Association of Adverse Pregnancy Outcomes With Risk of Atherosclerotic Cardiovascular Disease in Postmenopausal Women

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Importance: Atherosclerotic cardiovascular disease (ASCVD) may have unique risk factors in women. Most women have a history of pregnancy; com on adverse pregnancy outcomes (APOs) appear to be associated with ASCVD, but prior studies have limitations. Objective: To assess whether APOs are associated with increased ASCVD risk independently of traditional risk factors. Design, setting, and participants: The APO history among participants in the Women's Health Initiative, a large multiethnic cohort of postmenopausal women, was assessed. The associations of 5

self-reported APOs (gestational diabetes, hypertensive disorders of pregnancy, low birth weight [ie, birth weight less than 2.49 kg], high birth weight [ie, birth weight greater than 4.08 kg], and preterm delivery by 3 weeks or more) with ASCVD were analyzed, adjusting for traditional ASCVD risk factors. Data were collected and analyzed in 2017. Exposures: APOs (gestational diabetes, hypertensive disorders of pregnancy, low birth weight, high birth weight, and preterm delivery). Main outcomes and measures: Adjudicated ASCVD. Results: A total of 48 113 Women's Health Initiative participants responded to the survey; the median (interquartile range) age at time of enrollment was 60.0 (55.0-64.0) years. A total of 13 482 participants (28.8%) reported 1 or more APOs. Atherosclerotic cardiovascular disease was more frequent in women who reported an APO compared with those without APOs (1028 of 13 482 [7.6%] vs 1758 of 30 522 [5.8%]). Each APO, analyzed separately, was significantly associated with ASCVD, and gestational diabetes, hypertensive disorders of pregnancy, low birth weight, and preterm delivery remained significant after adjustment for traditional ASCVD risk factors. When all APOs were analyzed together, hypertensive disorders of pregnancy (odds ratio, 1.27; 95% CI, 1.15-1.40) and low birth weight (odds ratio, 1.12; 95% CI, 1.00-1.26) remained independently associated with ASCVD. All findings were materially unchanged by additional adjustment for parity, body mass index, and socioeconomic factors. Conclusions and relevance: In this large multiethnic cohort of women, hypertensive disorders of pregnancy and low birth weight were independently associated with ASCVD after adjustment for risk factors and other APOs.

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Association Between Reproductive Life Span and Incident Nonfatal Cardiovascular Disease: A Pooled Analysis of Individual Patient Data From 12 Studies

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Importance: Early menarche and early menopause are associated with increased risk of cardiovascular disease (CVD) in midlife, but little is known about the association between reproductive life span and the risk of CVD. Objective: To investigate the association between the length of reproductive life span and risk of incident CVD events, while also considering the timing of menarche and menopause. Design, setting, and participants: Individual-level data were pooled from 12 studies participating in the International Collaboration for a Life Course Approach to Reproductive Health and Chronic Disease Events consortium. Women provided complete information on the timing of menarche and menopause, nonfatal CVD events, and covariates. Cox proportional hazards models were used to estimate hazard ratios and 95% CIs, adjusted for covariates. The association between reproductive life span and CVD was adjusted for age at menarche and age at menopause separately. Analysis began March 2018 and ended December 2019. Exposures: Reproductive life span was calculated by subtracting age at menarche from age at menopause and categorized as younger than 30, 30 to 32, 33 to 35, 36 to 38 (reference group), 39 to 41, 42 to 44, and 45 years or older. Main outcomes and measures: First nonfatal CVD event, including coronary heart disease and stroke events. Results: A total of 307 855 women were included. Overall, the mean (SD) ages at menarche, menopause, and reproductive life span were 13.0 (1.5) years, 50.2 (4.4) years, and 37.2 (4.6) years, respectively. Pooled analyses showed that women with a very short reproductive life span (<30 years) were at 1.71 (95% CI, 1.58-1.84) times higher risk of incident CVD events than women with a reproductive life span of 36 to 38 years after adjustment for covariates. This association remained unchanged when adjusted for age at menarche but was attenuated to 1.26 (95% CI, 1.09-1.46) when adjusted for age at menopause. There was a significant interaction between reproductive life span and age at menarche associated with CVD risk (P < .001). Women who had both short reproductive life span (<33 years) and early menarche (age ≤11 years) had the highest risk of CVD (hazard ratio, 2.06; 95% CI, 1.76-2.41) compared with those with a reproductive life span of 36 to 38 years and menarche at age 13 years. Conclusions and relevance: Short reproductive life span was associated with an increased risk of nonfatal CVD events in midlife, and the risk was significantly higher for women with early age at menarche.

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Effects of Combined 17β-estradiol and progesterone on weight and blood pressure in postmenopausal women of the REPLENISH trial

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Objective: To examine the impact of a single-capsule 17β-estradiol (E2)/progesterone (P4) on weight and blood pressure (BP) when treating moderate to severe vasomotor symptoms in postmenopausal women with a uterus. Methods: Healthy postmenopausal women with a uterus (aged 40-65, body mass index ≤34 kg/m, BP ≤140/90 mm Hg) were randomized

to daily E2/P4 (mg/mg; 1/100, 0.5/100, 0.5/50, 0.25/50) or placebo in the phase 3 REPLENISH trial (NCT01942668). Changes in weight and BP from baseline to month 12 were evaluated. Potentially clinically important changes were defined as increases or decreases from baseline in weight by ≥15% and ≥11.3 kg, systolic BP by ≥20 mm Hg (absolute value ≥160 or ≤90 mm Hg), and diastolic BP by ≥15 mm Hg (absolute value ≥90 or ≤60 mm Hg). Results: Overall mean changes in weight and BP from baseline to month 12 with E2/P4 were modest and generally not statistically or clinically significant versus placebo. Incidence of potentially clinically important changes was low for weight (E2/P4 vs placebo: 1.1-2.6% vs 2.2%), systolic BP (0.3-1.1% vs 1.1%), and diastolic BP (1.4-4.2% vs 3.2%). A small number of women had treatment-related, treatment-emergent adverse events of weight gain (1.4-2.6% vs 1.3%) or hypertension (0.2-1.2% vs 0%). Few women who discontinued E2/P4 had weight gain (1.6%) or hypertension (0.6%) as a primary reason. Efficacy profile on VMS was consistent with previous findings and not modified by body mass index. Conclusions: Twelve-month use of E2/P4 had no clinically meaningful impact on weight or BP in postmenopausal women of the REPLENISH study.

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Dairy intake and bone health across the lifespan: a systematic review and expert narrative

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Over the past 30-years, the U.S. Dietary Guidelines for Americans have included recommendations around dairy consumption, largely based on meeting recommendations for calcium intake with the intended purpose of osteoporosis prevention. Although dairy products provide more bone-beneficial nutrients (e.g., calcium, magnesium, potassium, zinc, phosphorus, and protein) per unit of energy than any other food group, the relevance of dairy products for long-term bone health and fracture prevention has resurged as some observational studies have suggested consumption to be associated with a greater risk of fractures. Given this controversy, we sought to synthesize the evidence on dairy consumption and bone health across the lifespan. We searched the PubMed, EMBASE, Web of Science, and Cochrane Central Register of Controlled Trials databases for English-language publications through June 2, 2020. Case-controlled, cross-sectional, prospective cohort or nestled case-control (or case cohort), and clinical trials reporting the effect of dairy products on bone mineral density, bone mineral content, and/or fractures were included in the systematic review. Two reviewers independently performed data extractions. Data from 91 publications, including 30 RCTs, 28 prospective cohorts, 23 cross-sectional studies, and 10 case-control studies were included in the systematic review. We assigned a "D" grade or "insufficient evidence" for the effect of dairy in infants and toddlers (0- to <36-months), children (3- to <10-years), and young adults (19- to <50-years). A "C" grade or "limited evidence" was assigned for the effect of dairy in adolescents (10- to <19-years). A "B" grade or "moderate" evidence was assigned for the effect of dairy in middle aged to older adults (≥50-years). Research on bone mass in adults between the ages of 20- to 50-years and individuals from other ethnic groups apart from Chinese females and Caucasians is greatly needed. Daily intake of low or nonfat dairy products as part of a healthy habitual dietary pattern may be associated with improved BMD of the total body and at some sites and associated with fewer fractures in older adults.

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Postmenopausal Hormone Therapy and Colorectal Cancer Risk by Molecularly Defined Subtypes and Tumor Location

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Background: Postmenopausal hormone therapy (HT) is associated with a decreased colorectal cancer (CRC) risk. As CRC is a heterogeneous disease, we evaluated whether the association of HT and CRC differs across etiologically relevant, molecularly defined tumor subtypes and tumor location. Methods: We pooled data on tumor subtypes (microsatellite instability status, CpG island methylator phenotype status, BRAF and KRAS mutations, pathway: adenoma-carcinoma, alternate, serrated), tumor location (proximal colon, distal colon, rectum), and HT use among 8220 postmenopausal women (3898 CRC cases and 4322 controls) from 8 observational studies. We used multinomial logistic regression to estimate odds ratios (OR) and 95% confidence intervals (CIs) for the association of ever vs never HT use with each tumor subtype compared with controls. Models were adjusted for study, age, body mass index, smoking status, and CRC family history. All statistical tests were 2-sided. Results: Among postmenopausal women, ever HT use was associated with a 38% reduction in overall CRC risk (OR =0.62, 95% CI = 0.56 to 0.69). This association was similar according to microsatellite instability, CpG island methylator phenotype and BRAF or KRAS status. However, the

association was attenuated for tumors arising through the serrated pathway (OR = 0.81, 95% CI = 0.66 to 1.01) compared with the adenoma-carcinoma pathway (OR = 0.63, 95% CI = 0.55 to 0.73; P het =.04) and alternate pathway (OR = 0.61, 95% CI = 0.51 to 0.72). Additionally, proximal colon tumors had a weaker association (OR = 0.71, 95% CI = 0.62 to 0.80) compared with rectal (OR = 0.54, 95% CI = 0.46 to 0.63) and distal colon (OR = 0.57, 95% CI = 0.49 to 0.66; P het =.01) tumors. Conclusions: We observed a strong inverse association between HT use and overall CRC risk, which may predominantly reflect a benefit of HT use for tumors arising through the adenoma-carcinoma and alternate pathways as well as distal colon and rectal tumors.

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Osteosarcopenia Predicts Falls, Fractures, and Mortality in Chilean Community-Dwelling Older Adults

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Objectives: The objective of this study was to describe the prevalence of osteosarcopenia and its association with falls, fractures, and mortality in community-dwelling older adults. Design: Follow-up of ALEXANDROS cohorts designed to study disability associated with obesity in older adults. Setting and participants: Community-dwelling people aged 60 years and older living in Chile.Measures: At baseline, 1119 of 2372 participants had a dual-energy X-ray absorptiometry scan and the measurements for the diagnosis of sarcopenia. World Health Organization standards for bone mineral density were used to classify them as normal, osteopenia, and osteoporosis. Sarcopenia was identified using the algorithm from the European Working Group on Sarcopenia in Older People 1, validated for the Chilean population. Osteosarcopenia was defined as having sarcopenia plus osteoporosis or osteopenia. Results: The sample of 1119 participants (68.5% female) had a mean age of 72 years. At baseline, osteoporosis was identified in 23.2%, osteopenia in 49.8%, sarcopenia in 19.5%, and osteosarcopenia in 16.4% of the sample. The prevalence of osteosarcopenia increases with age, reaching 33.7% for those older than 80 years. Sarcopenia was found in 34.4% of osteoporotic people and osteoporosis in 40.8% of those with sarcopenia. After 5640 person-years of follow-up, 86 people died. The mortality was significantly higher for the group with osteosarcopenia (15.9%) compared with those without the condition (6.1%). After an adjusted Cox Regression analysis, the hazard ratio for death in people with osteosarcopenia was 2.48. Falls, fractures, and functional impairment were significantly more frequent in osteosarcopenic patients. Conclusions and implications: Osteosarcopenia is a common condition among older adults and is associated with an increased risk of falls, fractures, functional impairment, and mortality. Considering the high proportion of sarcopenia among osteoporotic patients and vice versa, screening for the second condition when the first is suspected should be advised.

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A later menopausal age is associated with a lower prevalence of physical frailty in community-dwelling older adults: The Korean Frailty and Aging Cohort Study (KFACS)

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Objectives: The aim of this study was to determine whether age at menopause is associated with physical frailty. Methods: This was a cross-sectional study that included 1264 women (70-84 years) from the Korean and Aging Cohort Study (KFACS) who had records of their ages at menarche and their ages at menopause and had experienced a natural menopause. We used Fried criteria to assess physical frailty status. The ages at menopause and menarche were collected using self-reported questionnaires. Results: The prevalence of physical frailty decreased by 5.3 % with each year of increase in age at menopause after adjusting for age, marital status, years of education, diabetes mellitus, hypertension, polypharmacy, hospitalizations, falls, and hormone replacement therapy (p = 0.005). The prevalence of frailty significantly decreased by 4.1 % when the reproductive span increased by a year (p = 0.019). Conclusions: This study found that a later menopausal age was associated with a lower risk of frailty using Fried criteria. In addition, it showed that a longer reproductive span was associated with a lower prevalence of frailty.