Selección de Resúmenes de Menopausia

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The role of microRNAs in bone development

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Epigenetic regulation is critical for proper bone development. Evidence from a large body of published literature informs us that microRNAs (miRNAs) are important epigenetic factors that control many aspects of bone development, homeostasis, and repair processes. These small non-coding RNAs function at the post-transcriptional level to suppress expression of specific target genes. Many target genes may be affected by one miRNA resulting in alteration in cellular pathways and networks. Therefore, changes in levels or activity of a specific miRNA (e.g. via genetic mutations, disease scenarios, or by over-expression or inhibition strategies in vitro or in vivo) can lead to substantial changes in cell processes including proliferation, metabolism, apoptosis and differentiation. In this review, Section 1 briefly covers general background information on processes that control bone development as well as the biogenesis and function of miRNAs. In Section 2, we discuss the importance of miRNAs in skeletal development based on findings from in vivo mouse models and human clinical reports. Section 3 focuses on describing more recent data from the last three years related to miRNA regulation of osteoblast differentiation in vitro. Some of these studies also involve utilization of an in vivo rodent model to study the effects of miRNA modulation in scenarios of osteoporosis, bone repair or ectopic bone formation. In Section 4, we provide some recent information from studies analyzing the potential of miRNA-mediated crosstalk in bone and how exosomes containing miRNAs from one bone cell may affect the differentiation or function of another bone cell type. We then conclude by summarizing where the field currently stands with respect to miRNA-mediated regulation of osteogenesis and how information gained from developmental processes can be instructive in identifying potential therapeutic miRNA targets for the treatment of certain bone conditions.

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Osteoporosis after adjuvant treatment for early-stage breast cancer

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Introduction: Adjuvant treatment of early-stage breast cancer has been associated with bone loss in randomised trials, but evidence from unselected populations is needed. In a single-center study, we assessed the annual percentage change in bone mineral density (ΔBMDt) and risk of osteoporosis from two to five years after adjuvant chemotherapy in patients with oestrogen-receptor-positive and oestrogen-receptor-negative tumours. Methods: Dual energy X-ray absorptiometry (DXA) was performed in 241 recurrence-free Danish breast cancer patients, among whom 157 had a prior DXA scan within two years of chemotherapy ("early"). Linear regression was used to assess ΔBMDt in spine and hip according to age, different health-related variables and time since early DXA. Results: Based on 157 patients, we observed annual decreases in spine BMD of 1.73% (95% confidence interval (CI): -2.01--1.44, p less than 0.001) and hip BMD of 1.30% (95% CI: -1.51--1.09, p less than 0.001). Patients aged less than 50 years at diagnosis had a significant decrease in mean spine BMD of 2.23% (95% CI: -2.78--1.68), whereas the decline was more limited in patients aged 50-59 years and patients aged 60 years or older with a mean spine BMD of 1.70% (95% CI: -2.07--1.34) and 0.81% (95% CI: -1.42--0.20), respectively. The results persisted in multivariable analyses. Osteoporosis was diagnosed in 9% of patients, all postmenopausal. Conclusions: Adjuvant anthracycline-taxane-based chemotherapy followed by endocrine therapy caused bone loss, especially in younger compared with older patients with early-stage breast cancer, confirming the results from randomised trials.

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Open-label placebos for menopausal hot flushes: a randomized controlled trial

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This study investigated the efficacy of an open-label placebo (OLP) treatment for menopausal hot flushes. Women with at least five moderate or severe hot flushes per day were allocated to receive four weeks of OLP for twice a day or no-treatment. Intention-to-treat analyses included n = 100 women. In comparison to no-treatment, OLP reduced the log-transformed hot flush composite score (frequency × intensity) (mean difference in change: - 0.32, 95% CI [- 0.43; -

0.21], p < 0.001, Cohen's d = 0.86), hot flush frequency (- 1.12 [- 1.81; - 0.43], p = 0.02, Cohen's d = 0.51), and improved overall menopause-related quality of life (- 2.53 [- 4.17; - 0.89], p = 0.02, Cohen's d = 0.49). Twelve (24%) (vs. three [6%]) patients had 50% lesser hot flushes. Problem rating of hot flushes and subdomains of quality of life did not improve. After four weeks, the OLP group was further divided via randomization to continue or discontinue the treatment. Benefits were maintained at week 8 (log-transformed score: - 0.04 [- 0.06; 0.14], p = 0.45). There was no difference between taking placebos for 8 or 4 weeks (log-transformed score: 0.04 [- 0.17; 0.25], p = 0.73). Results indicate that open-label placebos may be an effective, safe alternative for menopausal hot flushes.

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Reproductive hormones and anthropometry: a follow-up of PCOS and controls from perimenopause to above 80 years of age

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Context: There is a lack of knowledge about hormonal and anthropometric changes in women with polycystic ovary syndrome (PCOS) after the menopause. Objective: To study reproductive hormones and anthropometry in women with PCOS up to an age above 80 years. Design: Prospective cohort study. Setting: University Hospital. Patients: A well-defined cohort of women with PCOS, previously examined in 1987 and 2008 (21 years period) was re-examined in 2019 (11 years period). Of the original cohort (n = 37), 22 women were still alive and 21 (age range 72-91 years) participated. Comparisons were made with age-matched controls (n = 55) from the original control cohort (BMI similar to PCOS women). The results were compared with results from 1987 and 2008. Interventions: Hormonal measurements and physical examination. Main outcome measures: FSH, LH, testosterone, SHBG, free androgen index (FAI), hirsutism score, BMI, and waist-hip ratio (WHR). Results: At mean age 81 years, FSH levels were lower in women with PCOS (50 vs. 70 IU/L) who were still more hirsute than controls (33% vs. 4%). No differences were found in FAI, testosterone, SHBG or LH levels, BMI or WHR.From perimenopausal age until the present age, levels of testosterone and FAI continued to decline in women with PCOS. SHBG levels continued to increase with age. FSH had not changed over time during the last eleven years. Conclusions: Women with PCOS at ages 72-91 had lower FSH levels, remained clinically hyperandrogenic and had similar FAI and body composition as controls.

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Pharmacologic intervention for prevention of fractures in osteopenic and osteoporotic postmenopausal women: Systemic review and meta-analysis

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Objectives: Emerging evidence has indicated a role for pharmacologic agents in the primary prevention of osteoporotic fracture, but have not yet been systematically reviewed for meta-analysis. We conducted a meta-analysis to evaluate the efficacy of pharmacologic interventions in reducing fracture risk and increasing bone mineral density (BMD) in postmenopausal women with osteopenia or osteoporosis but without prevalent fragility fracture .Method: The Medline, EMBASE, and CENTRAL databases were searched from inception to September 30, 2019. Only randomized placebo-controlled trials evaluating postmenopausal women with -1.0 > bone mineral density (BMD) T-score > -2.5 (low bone mass) and those with BMD T-score ≤ -2.5 (osteoporosis) but without baseline fractures, who were receiving anti-osteoporotic agents, providing quantitative outcomes data and evaluating risk of vertebral and/or non-vertebral fragility fracture at follow-up. The PRISMA guidelines were followed, applying a random-effects model. The primary endpoint was the effect of anti-osteoporotic regimens in reducing the incidence of vertebral fractures. Secondary endpoints were percentage changes in baseline BMD at the lumbar spine and total hip at 1 and 2 years follow up. Results: Full-text review of 144 articles yielded, 20 for meta-analysis. Bisphosphonates reduced the risk of vertebral fracture (pooled OR = 0.50, 95%CIs = 0.36-0.71) and significantly increased lumbar spine BMD after 1 year, by 4.42% vs placebo (95%CIs = 3.70%-5.14%). At the hip, this value was 2.94% (95%CIs = 2.13%-3.75%). Overall results of limited studies for non-bisphosphonate drugs showed increased BMD and raloxifene significantly decreases the risk of subsequent clinical vertebral fractures. Conclusion: The bisphosphonates are efficacious and most evident for the primary prevention of osteoporotic vertebral fractures, reducing their incidence and improving BMD in postmenopausal women with osteopenia or osteoporosis.

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Relationships Between Level and Change in Sarcopenia and Other Body Composition Components and Adverse Health Outcomes: Findings from the Health, Aging, and Body Composition Study

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We investigated how baseline values and rates of decline in components of sarcopenia and other body composition parameters relate to adverse clinical outcomes using the Health, Aging, and Body Composition Study. 2689 participants aged 70-79 years were studied. Appendicular lean mass, whole body fat mass, and total hip BMD were ascertained using DXA; muscle strength by grip dynamometry; and muscle function by gait speed. Baseline values and 2-3 year conditional changes (independent of baseline) in each characteristic were examined as predictors of mortality, hospital admission, low trauma fracture, and recurrent falls in the subsequent 10-14 years using Cox regression (generalized estimating equations used for recurrent falls) with adjustment for sex, ethnicity, age, and potential confounders. Lower levels and greater declines in all parameters (excluding hip BMD level) were associated ($p < 0.05$) with increased rates of mortality; fully-adjusted hazard ratios per SD lower gait speed and grip strength were 1.27 (95% CI 1.19, 1.36) and 1.14 (1.07, 1.21), respectively. Risk factors of hospital admission included lower levels and greater declines in gait speed and grip strength, and greater declines in hip BMD. Lower levels and greater declines in fat mass and hip BMD were associated with low trauma fracture. Lower gait speed, higher fat mass, and both lower levels and greater declines in grip strength were related to recurrent falls. Lower baseline levels and greater declines in musculoskeletal parameters were related to adverse outcomes. Interventions to maximize peak levels in earlier life and reduce rates of age-related decline may reduce the burden of disease in this age group.

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Trends in hip and distal femoral fracture rates in Italy from 2007 to 2017

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Osteoporosis-related fractures are a growing public health concern worldwide due to high societal and economic burden. The study aims to assess trends in incidence rates of hip and distal femoral fractures and in the use of anti-osteoporosis drugs in Italy between 2007 and 2017. Patients with hip and distal femoral fractures (ICD-9-CM codes 820.x and 821.x) were identified in the Italian National Hospital Discharge Database while anti-osteoporosis medication data were retrieved from the National Observatory on the Use of Medicines Database. A joinpoint regression analysis was performed to identify the years where the trends in incidence rates of hip and distal femoral fractures changed significantly; the average annual percentage change for the period of observation was estimated. Hospitalizations for femoral fractures were 991,059, of which 91.4% were hip fractures and 76.5% occurred in women. Age-standardized hip fractures rate per 100,000 person-years decreased both in women (-8.7%; from 789.9 in 2007 to 721.5 in 2017) and in men (-4.3%; from 423.9 to 405.6), while the rate of distal femoral fractures increased by 23.9% in women (from 67.78 to 83.95) and 22.7% in men (from 27.76 to 34.06). These changes were associated with an increment in the use of anti-osteoporosis drugs from 2007 to 2011 (from 9.1 to 12.4 DDD/1000 inhabitants/day), followed by a plateau in the period 2012-2017. The use of bisphosphonates increased progressively from 2007 to 2010 (from 8.2 to 10.5 DDD/1000 inhabitants/day), followed by a plateau and then decreased from 2015 onwards. The decreasing trend of hip fractures could be related to a major intake of anti-osteoporosis medications while the increment of distal femoral fractures might be due to population aging and to the use of bisphosphonates and denosumab. Further research is needed to identify and implement interventions to prevent hip and distal femoral fractures.