Selección de Resúmenes de Menopausia

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Prevention of aromatase inhibitor-induced bone loss with anti-resorptive therapy in post-menopausal women with early-stage breast cancer

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Purpose: This study aimed to describe changes in femoral and lumbar bone mineral density (BMD) after 24 months of aromatase inhibitors (AIs) and antiresorptive treatment in postmenopausal women with estrogen receptor-positive breast cancer. Methods: Prospective, longitudinal study in a real-life setting with a 2-year follow-up. Patients underwent a complete baseline bone assessment including clinical assessment, biological evaluation, BMD measurement, and spine X-ray. Antiresorptive treatment was prescribed to patients with a T-score < - 2 or a T-score < - 1.5 SD with additional osteoporosis risk factors. A follow-up bone assessment was carried out after 24 months. Results: Among 328 patients referred to our center, 168 patients (67.7 ± 10.6 years) were included in our study, and 144 were eligible for antiresorptive treatment. After 24 months, patients receiving antiresorptive treatment experienced a significant increase of + 6.28% in femoral-BMD (F-BMD) and + 7.79% in lumbar-BMD (L-BMD). This increase was not significantly different between osteoporotic and osteopenic patients. Conversely, patients not receiving antiresorptive treatment presented significant F-BMD and L-BMD loss regardless of the baseline BMD. In the multivariate logistic model, the lack of antiresorptive treatment was the only predictive factor for major femoral bone loss with a 20.83 odds ratio (CI95%:4.2-100, p < 0.001). Conclusion: This real-life study confirmed that antiresorptive treatment significantly increases femoral and lumbar BMD regardless of the baseline BMD in postmenopausal patients receiving AIs for early breast cancer. Patients who did not receive antiresorptive treatment had a 20.8-fold increased risk of major bone loss. Nevertheless, the best threshold to adopt for starting antiresorptive agents remains undetermined.

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Long-term effects of premenopausal risk-reducing salpingo-oophorectomy on cognition in women with high familial risk of ovarian cancer: A cross-sectional study

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Objective: To examine the effect of a premenopausal risk-reducing salpingo-oophorectomy (RRSO) in women at increased risk of ovarian cancer on objective and subjective cognition at least 10 years after RRSO. Design: A cross-sectional study with prospective follow-up, nested in a nationwide cohort SETTING: Multicenter in the Netherlands POPULATION OR SAMPLE: 641 women (66% BRCA1/2 pathogenic variant carriers) who underwent either a premenopausal RRSO ≤ age 45 (n=436) or a postmenopausal RRSO ≥ age 54 (n=205). All participants were older than 55 years at recruitment. Methods: Participants completed an online cognitive test battery and a questionnaire on subjective cognition. We used multivariable regression analyses, adjusting for age, education, breast cancer, hormone replacement therapy, cardiovascular risk factors and depression. Main outcome measures: The influence of RRSO on objective and subjective cognition of women with a premenopausal RRSO compared with women with a postmenopausal RRSO RESULTS: After adjustment, women with a premenopausal RRSO (mean time since RRSO 18.2 years) performed similarly on objective cognitive tests as women with a postmenopausal RRSO (mean time since RRSO 11.9 years). However, they more frequently reported problems with reasoning (odds ratio (OR) 1.8 (95% confidence interval (95%CI) 1.1-3.1)) and multitasking (OR 1.9 (95%CI 1.1-3.4)) than women with a postmenopausal RRSO. This difference between groups disappeared in an analysis restricted to women of comparable ages (60-70 years). Conclusions: Reassuringly, approximately 18 years after RRSO, we found no association between premenopausal RRSO and objective cognition.

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Muscle plays a more superior role than fat in bone homeostasis: A cross-sectional study of old Asian people

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Objectives: The aim of this study was to discover the role of fat and muscle in bone structures, as well as the relationship between obesity and sarcopenia on age-related osteoporosis. Methods: A total of 400 participants (65.0 ± 8.2 years old, 42.3% women) were recruited. Fat, muscle, bone parameters, basic demographics, medical history, physical performance and activity, and calcium intake of participants were obtained from datasets. The diagnosis of osteoporosis, sarcopenia, and obesity was based on current recommendations. Pearson correlation, non-linear regression models, and decision tree analyses were performed to study the relationship between fat, muscle, and bone. Logistic regression analyses were used to explore the risk of osteoporosis in old people with obesity or sarcopenia via Model 1 (unadjusted) and Model 2 (adjusted by age, physical activity, and calcium intake). Results: Correlation analysis showed that limb muscle mass and index, and age were best related to bone mineral density (BMD) ($|r| = 0.386$-0.632, $p < 0.001$). On the contrary, body mass index (BMI) and increased body fat percentage (BF%) were harmful for bone health. An increase of BMI and fat mass index slowed the increase of BMD in the spine, while skeletal muscle mass index accelerated the increase. People with sarcopenia had low muscle mass and strength. When separating subjects into sarcopenia and non-sarcopenia status, sarcopenia was independently related to higher risks of osteoporosis in both models ($OR > 1$, $p < 0.05$). BMI-defined obesity in Model 1 as well as BF%-defined obesity in both models did not reduce the risk of osteoporosis in both models ($p > 0.05$). The decision tree classification (85% accuracy) showed that greater body weight and larger lower limb muscle performance were negatively related to osteoporosis, while fat mass and percentage did not play roles in this prediction. Conclusion: Low muscle mass and function were harmful to bone health. Obesity defined by both BMI and BF% had limited protective roles in osteoporosis. The benefits for bone from increased muscle mass and function play a more superior role than increased fat mass in old people. Sarcopenia prevention and treatment instead of controlling obesity should be recommended as an approach to reduce the risks of age-related osteoporosis and fragility fracture for elderly people.

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Mechanisms of action of vitamin D in delaying aging and preventing disease by inhibiting oxidative stress

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Although several recent studies have shown that vitamin D supplementation beneficially decreases oxidative stress parameters, there is no consensus on this subject in humans. Thus the role of vitamin D supplementation has recently become a controversial topic because large intervention studies in humans have not shown significant benefits. These studies have indicated that supplementation with precursor forms of active vitamin D has no effect on all-cause mortality, cannot reduce the fracture risk of the elderly, cannot reduce the incidence of cancer or cardiovascular disease in the elderly, and cannot significantly reduce the incidence risk of diabetes in the elderly. However, a link between several age-related diseases and enhanced oxidative stress has been found in mice with insufficient or deficient 1,25-dihydroxyvitamin D (1,25(OH)2D), the active form of vitamin D, which indicates that reduced active vitamin D accelerates aging and age-related diseases by increasing oxidative stress. Furthermore, supplementation of exogenous 1,25(OH)2D3, or antioxidants, could dramatically postpone aging, prevent osteoporosis and spontaneous tumor development induced by 1,25(OH)2D insufficiency or deficiency, by inhibiting oxidative stress. Mechanistically, the antioxidative effects of 1,25(OH)2D3 are carried out via the vitamin D receptor (VDR) by activation of the Nrf2 oxidative stress response pathway though transcriptional or posttranscriptional activation of Nrf2 or transcriptional upregulation of Sirt1 and Bmi1 expression. Whether discrepancies between studies in humans and in mice reflect the different forms of vitamin D examined remains to be determined.

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Calcium and vitamin D for increasing bone mineral density in premenopausal women

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Background: Osteoporosis is a condition where bones become fragile due to low bone density and impaired bone quality. This results in fractures that lead to higher morbidity and reduced quality of life. Osteoporosis is considered a major public health concern worldwide. For this reason, preventive measurements need to be addressed throughout the life course. Exercise and a healthy diet are among the lifestyle factors that can help prevent the disease, the latter including intake of key micronutrients for bone, such as calcium and vitamin D. The evidence on whether supplementation with calcium and vitamin D improves bone mineral density (BMD) in premenopausal women is still inconclusive. In this age group, bone accrual is considered to be the goal of supplementation, so BMD is relevant for the future stages of life.

Objectives: To evaluate the benefits and harms of calcium and vitamin D supplementation, alone or in combination, to increase the BMD, reduce fractures, and report the potential adverse events in healthy premenopausal women compared to

placebo. Search methods: We used standard, extensive Cochrane search methods. The latest search was 12 April 2022. Selection criteria: We included randomised controlled trials in healthy premenopausal women (with or without calcium or vitamin D deficiency) comparing supplementation of calcium or vitamin D (or both) at any dose and by any route of administration versus placebo for at least three months. Vitamin D could have been administered as cholecalciferol (vitamin D3) or ergocalciferol (vitamin D2). Data collection and analysis: We used standard Cochrane methods. Outcomes included total hip bone mineral density (BMD), lumbar spine BMD, quality of life, new symptomatic vertebral fractures, new symptomatic non-vertebral fractures, withdrawals due to adverse events, serious adverse events, all reported adverse events and additional withdrawals for any reason. Main results: We included seven RCTs with 941 participants, of whom 138 were randomised to calcium supplementation, 110 to vitamin D supplementation, 271 to vitamin D plus calcium supplementation, and 422 to placebo. Mean age ranged from 18.1 to 42.1 years. Studies reported results for total hip or lumbar spine BMD (or both) and withdrawals for various reasons, but none reported fractures or withdrawals for adverse events or serious adverse events. Results for the reported outcomes are presented for the three comparisons: calcium versus placebo, vitamin D versus placebo, and calcium plus vitamin D versus placebo. In all comparisons, there was no clinical difference in outcomes, and the certainty of the evidence was moderate to low. Most studies were at risk of selection, performance, detection, and reporting biases. Calcium versus placebo Four studies compared calcium versus placebo (138 participants in the calcium group and 123 in the placebo group) with mean ages from 18.0 to 47.3 years. Calcium supplementation may have little to no effect on total hip or lumbar spine BMD after 12 months in three studies and after six months in one study (total hip BMD: mean difference (MD) -0.04 g/cm2, 95% confidence interval (CI) -0.11 to 0.03; I2 = 71%; 3 studies, 174 participants; low-certainty evidence; lumbar spine BMD: MD 0 g/cm2, 95% CI -0.06 to 0.06; I2 = 71%; 4 studies, 202 participants; low-certainty evidence). Calcium alone supplementation does not reduce or increase the withdrawals in the trials (risk ratio (RR) 0.78, 95% CI 0.52 to 1.16; I2 = 0%; 4 studies, 261 participants: moderate-certainty evidence). Vitamin D versus placebo Two studies compared vitamin D versus placebo (110 participants in the vitamin D group and 79 in the placebo group), with mean ages from 18.0 to 32.7 years. These studies reported lumbar spine BMD as a mixture of MDs and percent of change and we were unable to pool the results. In the original studies, there were no differences in lumbar BMD between groups. Vitamin D alone supplementation does not reduce or increase withdrawals for any reason between groups (RR 0.74, 95% CI 0.46 to 1.19; moderate-certainty evidence). Calcium plus vitamin D versus placebo Two studies compared calcium plus vitamin D versus placebo (271 participants in the calcium plus vitamin D group and 270 in the placebo group; 220 participants from Woo 2007 and 50 participants from Islam 2010). The mean age range was 18.0 to 36 years. These studies measured different anatomic areas, one study reported total hip BMD and the other study reported lumbar spine BMD; therefore, data were not pooled for this outcome. The individual studies found no difference between groups in percent of change on total hip BMD (-0.03, 95% CI -0.06 to 0; moderate-certainty evidence), and lumbar spine BMD (MD 0.01, 95% CI -0.01 to 0.03; moderate-certainty evidence). Calcium plus vitamin D supplementation may not reduce or increase withdrawals for any reason (RR 0.82, 95% CI 0.29 to 2.35; I2 = 72%; 2 studies, 541 participants; low-certainty evidence). Authors' conclusions: Our results do not support the isolated or combined use of calcium and vitamin D supplementation in healthy premenopausal women as a public health intervention to improve BMD in the total hip or lumbar spine, and therefore it is unlikely to have a benefit for the prevention of fractures (vertebral and non-vertebral). The evidence found suggests that there is no need for future studies in the general population of premenopausal women; however, studies focused on populations with a predisposition to diseases related to bone metabolism, or with low bone mass or osteoporosis diagnosed BMD would be useful.

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Association of age at menopause with type 2 diabetes mellitus in postmenopausal women in the United States: National Health and Nutrition Examination Survey 2011-2018

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Introduction: The present study aimed to examine the impact of age at menopause on the type 2 diabetes mellitus (T2DM) risk in postmenopausal women. Material and methods: We included 4,968 postmenopausal women from the National Health and Nutrition Examination Survey 2011-2018. Age at menopause was measured by single year and categorically (< 40 years, 40-44 years, 45-54 years, 55 years and above). The outcome variable T2DM was measured with self-report and fasting blood glucose level. We performed logistic regression to estimate the odds ratio (OR) (95% confidence interval [CI]). Linear regression was used to examine the correlation between age at menopause and age at T2DM. Results: Of the 4,968 postmenopausal women, 796 (16.0%) had T2DM after menopause. The mean age at menopause was 44.2 years. The mean age at T2DM was 57.2 years. Adjusting for potential confounders, the ORs for the association between age at menopause of < 40 years, 40-44 years and ≥ 55 years and T2DM were 1.97 (95% CI: 1.47-2.63), 1.27 (95% CI: 0.90-1.79) and 0.98 (95% CI: 0.66-1.45), respectively, compared to women having menopause at age 45 to 54 years. Each increase by

1 year in age at menopause was associated with a 3% reduction in the prevalence of T2DM (95% CI: 2-5). Age at menopause was significantly correlated with age at T2DM. Each 1-year increase in age at menopause might lead to a decrease of 0.39 years in age at T2DM. Conclusions: Premature menopause was associated with increased T2DM risk in women. The earlier menopause occurs, the younger is the age at which T2DM may occur.

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Sex Differences in Dementia

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BackgroundWomen in many cohorts have a higher risk for Alzheimer's disease (AD), the most common form of dementia. Sex is a biological construct whereby differences in disease manifestation and prevalence are rooted in genetic differences between XX and XY combinations of chromosomes. This chapter focuses specifically on sex-driven differences in dementia, as opposed to differences driven by gender - a social construct referring to the societal norms that influence people's roles, relationships, and positional power throughout their lifetime.MethodsUsing a narrative review, this chapter explored the characteristics and risk factors for the dementias, alongside a discussion of sex differences including loss of sex steroid hormones in middle-aged women, differences in the prevalence of cardiovascular diseases and engagement in lifestyle protective factors for dementia.ResultsThe sex difference in AD prevalence may exist because of systematic and historic differences in risk and protective factors for dementia, including level of education obtained and socioeconomic status differences, which can impact on health and dementia risk.Levels of sex steroids decline significantly after menopause in women, whereas this is more gradual in men with age. Animal and cell culture studies show strong biological plausibility for sex steroids to protect the ageing brain against dementia. Sex steroid hormone replacement therapy has in some observational studies shown to protect against AD, but treatment studies in humans have mainly shown disappointing results. Cardiovascular disease (CVD) shares midlife medical risk (e.g. hypertension, hyperlipidaemia, obesity etc.) factors with AD and other forms of dementia, but also with related lifestyle risk - and protective factors (e.g. exercise, not smoking etc.). Men tend to die earlier of CVD, so fewer survive to develop AD at an older age. Those who do survive may have healthier lifestyles and fewer risk factors for both CVD and AD. An earlier age at menopause also confers great risk for both without hormone treatment.DiscussionIt could be the case that the decline in sex steroids around the menopause make women more susceptible to lifestyle-related risk factors associated with dementia and CVD, but this remains to be further investigated. Combining hormone treatment with lifestyle changes in midlife (e.g. exercise) could be an important preventative treatment for dementia and CVD in later life, but this also requires further research.

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Loss of muscle mass in women with premature ovarian insufficiency as compared with healthy controls

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Objective: Menopausal transition has been known to be associated with the loss of muscle mass. However, muscle health in women with premature menopause, that is, premature ovarian insufficiency (POI), remains unclear. We aimed to investigate and compare muscle mass parameters and the prevalence of low muscle mass between patients with spontaneous POI and healthy controls. Methods: In this cross-sectional study, 59 women with spontaneous POI and 57 premenopausal controls with normal ovarian function were enrolled at the Women's Hospital, Zhejiang University School of Medicine (Hangzhou, China) from June 17, 2020, to August 20, 2021. Muscle mass parameters were measured by dual-energy x-ray absorptiometry, and low muscle mass was diagnosed using the Asian Working Group for Sarcopenia criteria. In addition, participants provided their sociodemographic data, menstrual and reproductive history, lifestyle factors, and medical history. Multivariate linear regression analysis was conducted. Results: Muscle mass parameters, including appendicular skeletal muscle mass (ASM), ASM/height2, ASM/weight, ASM/body mass index, total skeletal muscle mass (TSM), and TSM/weight, were significantly lower in women with POI as compared with healthy controls (ASM: 14.62 ± 2.08 vs 15.97 ± 1.78, $P < 0.001$; ASM/height2: 5.71 ± 0.64 vs 6.15 ± 0.62, $P < 0.001$; ASM/weight: 0.27 [0.25, 0.28] vs 0.28 [0.27, 0.29], $P = 0.002$; ASM/BMI: 0.68 ± 0.07 vs 0.73 ± 0.06, $P = 0.001$; TSM: 33.85 ± 4.08 vs 36.43 ± 3.56, $P < 0.001$; TSM/weight: 0.63 [0.59, 0.65] vs 0.64 [0.61, 0.67], $P = 0.02$). The prevalence of low muscle mass in POI patients was significantly higher than that in controls (32.20% vs 8.77%, $\chi 2 = 9.70$, $P = 0.002$). Furthermore, multivariate linear regression analyses demonstrated that POI status was an independent risk factor for ASM ($\beta = -1.13$; 95% CI, -1.62 to -0.65), ASM/height2 (-0.35, -0.47 to -0.22), ASM/weight (-0.01, -0.02 to -0.009), ASM/BMI (-0.05, -0.07 to -0.02), TSM (-2.16, -3.14 to -1.17), and TSM/weight (-0.03, -0.04 to -0.02). Conclusions: Women with POI exhibit significant loss of muscle mass as compared with healthy controls. Early diagnosis and long-term health management in POI patients are important.