Selección de Resúmenes de Menopausia

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The Effect of Tobacco Smoking on Bone Mass: An Overview of Pathophysiologic Mechanisms.

Al-Bashaireh AM, Haddad LG, Weaver M, Chengguo X, Kelly DL, Yoon S.

Recent evidence demonstrates that tobacco smoking causes an imbalance in bone turnover, leading to lower bone mass and making bone vulnerable to osteoporosis and fracture. Tobacco smoke influences bone mass indirectly through alteration of body weight, parathyroid hormone-vitamin D axis, adrenal hormones, sex hormones, and increased oxidative stress on bony tissues. Also, tobacco smoke influences bone mass through a direct effect on osteogenesis and angiogenesis of bone. A RANKL-RANK-OPG pathway is an essential regulatory pathway for bone metabolism and its importance lies in its interaction with most of the pathophysiologic mechanisms by which smoking influences bone mass. Both first- and secondhand smoke adversely affect bone mass; smoking cessation seems to reverse the effect of smoking and improve bone health. Recent advances in research on bone turnover markers could advance scientific knowledge regarding the mechanisms by which smoking may influence bone mass.

BMJ. 2019 Jan 9;364:k4810. doi: 10.1136/bmj.k4810.

Use of hormone replacement therapy and risk of venous thromboembolism: nested case-control studies using the QResearch and CPRD databases.

Vinogradova Y, Coupland C, Hippisley-Cox J.

OBJECTIVE: To assess the association between risk of venous thromboembolism and use of different types of hormone replacement therapy. DESIGN: Two nested case-control studies. SETTING: UK general practices contributing to the QResearch or Clinical Practice Research Datalink (CPRD) databases, and linked to hospital, mortality, and social deprivation data. PARTICIPANTS: 80 396 women aged 40-79 with a primary diagnosis of venous thromboembolism between 1998 and 2017, matched by age, general practice, and index date to 391 494 female controls. MAIN OUTCOME MEASURES: Venous thromboembolism recorded on general practice, mortality, or hospital records. Odds ratios were adjusted for demographics, smoking status, alcohol consumption, comorbidities, recent medical events, and other prescribed drugs. RESULTS: Overall, 5795 (7.2%) women who had venous thromboembolism and 21 670 (5.5%) controls had been exposed to hormone replacement therapy within 90 days before the index date. Of these two groups, 4915 (85%) and 16 938 (78%) women used oral therapy, respectively, which was associated with a significantly increased risk of venous thromboembolism compared with no exposure (adjusted odds ratio 1.58, 95% confidence interval 1.52 to 1.64), for both oestrogen only preparations (1.40, 1.32 to 1.48) and combined preparations (1.73, 1.65 to 1.81). Estradiolhad a lower risk than conjugated equine oestrogen for oestrogen only preparations (0.85, 0.76 to 0.95) and combined preparations (0.83, 0.76 to 0.91). Compared with no exposure, conjugated equine oestrogen with medroxyprogesterone acetate had the highest risk (2.10, 1.92 to 2.31), and estradiol with dydrogesterone had the lowest risk (1.18, 0.98 to 1.42). Transdermal preparations were not associated with risk of venous thromboembolism, which was consistent for different regimens (overall adjusted odds ratio 0.93, 95% confidence interval 0.87 to 1.01). CONCLUSIONS: In the present study, transdermal treatment was the safest type of hormone replacement therapy when risk of venous thromboembolism was assessed. Transdermal treatment appears to be underused, with the overwhelming preference still for oral preparations.

Climacteric. 2019 Jan 10:1-4. doi: 10.1080/13697137.2018.1551347. [Epub ahead of print]

Hormone replacement therapy and prevention of chronic conditions.

Gambacciani M, Cagnacci A, Lello S.

Nowadays, postmenopausal women are largely undertreated. Analysis of conflicting results among different studies suggests that hormone replacement therapy (HRT) can prevent osteoporosis and cardiovascular disease in symptomatic, early postmenopausal women. In fact, climacteric symptoms are related to an increased risk of chronic conditions, including hypertension and cardiovascular disease. Different scientific societies have pointed out that patient selection, timing of initiation, and the choice of the type and dose of HRT used are the major determinants of the ultimate effect of

HRT on women's health and quality of life in selected women. HRT may prevent chronic conditions when started in symptomatic women before the age of 60 years or within 10 years of the onset of the menopause, taking into consideration the characteristics and risk profiles of each given woman. The bulk of scientific evidence from preclinical, clinical, epidemiological, and also randomized studies indicates that wisely selected HRT is generally useful and rarely dangerous. Following simple and well-established rules, HRT benefits outweigh all of the possible risks. Progestogen choice can make the difference in terms of cardiovascular disease benefits.

Arch Endocrinol Metab. 2018;62(6):615-622. doi: 10.20945/2359-3997000000087.

Sex effects on the association between sarcopenia EWGSOP and osteoporosis in outpatient older adults: data from the SARCOS study.

Frisoli A Jr, Martin FG, Carvalho ACC, Borges J, Paes AT, Ingham SJM.

OBJECTIVE: The objective was to evaluate the association between sarcopenia (EWGSOP) and osteoporosis in older adults. SUBJECTS AND METHODS: This is a cross sectional analysis of a baseline evaluation of the SARCopenia and OSteoporosis in Older Adults with Cardiovascular Diseases Study (SARCOS). Three hundred and thirty-two subjects over 65 years of age were evaluated. Sarcopenia was determined by EWGSOP flowchart and Osteoporosis was established by WHO's criteria. Physical function, comorbidities and medications were evaluated. RESULTS: Women were older (79.8 ± 7.2 years) than men (78.21 ± 6.7 years) ($p = 0.042$). Osteoporosis occurred in 24.8% of men, and in 42.7% of women ($p < 0.001$); sarcopenia occurred in 25.5% of men and in 17.7%, of women ($p = 0.103$). Osteoporosis was diagnosed in 68% of sarcopenic women, however only 20.7% ($p = 0.009$) of women with osteoporosis had sarcopenia; in older men, 44.7% of individuals with sarcopenia presented osteoporosis and 42.9% ($p = 0.013$) of men with osteoporosis showed sarcopenia. In an adjusted logistic regression analyses for sarcopenia, osteoporosis presented a statistically significant association with sarcopenia in men [OR: 2.930 (95% CI: 1.044-8.237; $p = 0.041$)] but not in women [OR: 2.081 (0.787-5.5; $p = 0.142$)]; in the adjusted logistic regression analyses for osteoporosis, a statistically significant association occurred in men [OR: 2.984 (95% CI: 1.144-7.809; $p = 0.025$)], but not in women [OR: 2.093 (0.962-3.714; $p = 0.137$)]. CONCLUSION: According to sex, there are significant differences in the association between sarcopenia EWGSOP and osteoporosis in outpatient older adults. It is strong and significant in males; in females, despite showing a positive trend, it was not statistically significant.

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Assessment and hormonal management of osteoporosis.

Trémollieres F.

Postmenopausal osteoporosis is a frequent health issue in women. Because osteoporosis-related fractures cause a significant increase in mortality and morbidity, it is clinically important to identify as soon as possible women at increased risk for future fracture so that preventive measures can be instituted. At the beginning of menopause, evaluation of the subsequent risk of fracture is not so easy. Most screening tools fail to accurately identify those women who will fracture within the next 10 years. A history of a prior fracture and low bone mineral density are the only major consistently found predictors for the risk of fracture. On the other hand, it is no longer a question whether menopause hormone therapy (MHT) is efficient not only to prevent postmenopausal bone loss but also the incidence of fragility fracture. Over the last years, utility of menopause hormone therapy for the prevention of osteoporosis has been questioned due to safety concerns. In light of the most recent reports on a more favorable benefit/risk balance than was initially claimed in early postmenopausal women, this needs to be reconsidered. Prevention of bone loss in those women with a moderate or slightly high risk of fracture is likely a strategy to reduce fracture risk in older women. MHT must be considered as a true primary preventive therapy more than an anti-fracture therapy at an age when the risk of fracture is likely much lower than later in life. Only thereafter should other anti-osteoporotic medications be discussed in women still at high risk for fracture.

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Postmenopausal androgen-secreting ovarian tumors: challenging differential diagnosis in two cases.

Arteaga E, Martinez A, Jaramilo J, Villaseca P, Cuello M, Valenzuela P, Gejman R, Blumel JE.

Postmenopausal hyperandrogenism constitutes a very rare condition of tumoral or non-tumoral origin primarily residing either in the ovary or in the adrenal glands. We present herein two cases with this condition; one with abnormal

postmenopausal genital bleeding and mild increase in facial hair, and the second with slow-developing hirsutism and virilization. Both cases shared a notorious increase in libido. The laboratory tests showed high levels of testosterone (>100 ng/ml). A normal value of dehydroepiandrosterone sulfate and a normal cortisol level at 9 am after 1 mg of dexamethasone administered at midnight (Nugent test) made an adrenal etiology very unlikely. On the other hand, a high level of inhibine B oriented to an ovarian source. Transvaginal sonography failed to demonstrate an ovarian tumor, but an abdominal and pelvic computed tomography scan or magnetic resonance imaging detected an ovarian tumor and normal adrenal glands. A laparoscopic oophorectomy was performed, and the histological study demonstrated a steroidal cell tumor in the first case and a Leydig cell tumor in the second.

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A systematic review and meta-analysis of the effect of bisphosphonate drug holidays on bone mineral density and osteoporotic fracture risk.

Nayak S, Greenspan SL.

INTRODUCTION: We performed a systematic review and meta-analysis on the effect of drug holidays (discontinuation) on BMD and fracture risk. METHODS: We searched PubMed, Embase, and Cochrane Library databases to locate controlled clinical trials and cohort studies evaluating the effect of drug holidays/discontinuation versus osteoporosis treatment continuation. We performed random-effects meta-analyses of hazard ratios of hip and any clinical osteoporotic fracture for individuals who discontinued bisphosphonates compared to persistent users. RESULTS: Thirteen records reporting results from eight different studies met inclusion criteria. The FLEX study found a reduced clinical vertebral fracture risk with 10 years of alendronate therapy compared to 5 (RR 0.45, 95% CI 0.24-0.85), and the HORIZON extension studies found a reduced risk of morphometric vertebral fracture with 6 years of zoledronic acid therapy compared to 3 (OR = 0.51, 95% CI 0.26-0.95); subgroup analyses showed that women with low hip BMD T-scores after the initial treatment period benefitted from continued treatment in terms of reduced vertebral fracture risk. Meta-analysis of adjusted hazard ratios of hip and any clinical osteoporotic fracture for women who discontinued bisphosphonates revealed no significant differences in the risk of hip fracture (summary estimate of HR 1.09, 95% CI 0.87-1.37) or any clinical fracture (summary estimate of HR 1.13, 95% CI 0.75-1.70) compared to persistent users. CONCLUSIONS: Bisphosphonate discontinuation may be considered for women who do not have low hip BMD after 3 to 5 years of initial treatment, while women who have low hip BMD may benefit from treatment continuation.

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Hormone Replacement Therapy in Cancer Survivors - Review of the Literature.

Deli T, Orosz M, Jakab A.

Rapid advance in oncology leads to increasing survival of oncologic patients. More and more of them live long enough to reach either the natural age of menopause or, as a side effect of their oncotherapy, experience the cessation of gonadal function, leading to premature ovarian insufficiency, with disturbing vasomotor symtoms and long-term negative cardiovascular and skeletal effects. Thus, an ever increasing number of cancer survivors search endocrinologic help in the form of hormone replacement therapy (HRT). The misinterpretation of the Women's Health Initiative Study has lead to an irrational fear of female hormone replacement, both by the general population and medical professionals. It has seemed the logical and safe conclusion to many physicians to avoid HRT, supposing that this attitude definitely causes no harm, whereas the decision of prescribing estrogen alone or with progestins might bear oncologic and thromboembolic risks and may even lead to litigation in case of a potentially related complication. However, it was known even before the WHI results that premature menopause and hypogonadism decreases the life expectancy of women by years through its skeletal and cardiovascular effects, and this negative effect correlates with the length of the hypoestrogenaemic period. Therefore, the denial of HRT also needs to be supported by evidence and should be weighed againts the risks of HRT. Yet, the oncologic risk of HRT is extremely difficult to assess. In this work we review the latest evidence from in vitro experiments to clinical studies, regarding HRT in survivors of gynecologic and non-gynecologic cancers. Based on our literature research, we group tumours regarding the oncologic risk of properly chosen female hormone replacement therapy in cancer survivors as follows: 'HRT is advanageous' (e.g. endometrial cancer type I, cervical adenocarcinoma, haematologic malignancies, local cutaneous malignant melanoma, colorectal cancer, hepatocellular cancer); 'HRT is neutral' (e.g. BRCA 1/2 mutation carriers without cancer, endometrial cancer type II, uterinal carcinosarcoma and adenosarcoma, certain types of ovarian cancer, cervical, vaginal and vulvar squamous cell carcinoma, prolactinoma, kidney cancer, pancreatic cancer, thyroid cancer); 'HRT is relatively contraindicated' for various reasons (e.g. leiomyosarcoma, certain types of ovarian tumours, brain tumours, advanced metastatic malignant

melanoma, lung cancer, gastric cancer, bladder cancer); 'HRT is diasadvantageous and thus contraindicated' (e.g. breast cancer, endometrial stroma sarcoma, meningioma, glioma, hormone receptor positive gastric and bladder cancer).

PLoS One. 2019 Jan 7;14(1):e0209175. doi: 10.1371/journal.pone.0209175. eCollection 2019.

Carotid artery plaque screening using abdominal aortic calcification on lumbar radiographs.

Kobayashi K, Ando K, Seki T, Hamada T, Suzuki K, Ishiguro N, Hasegawa Y, Imagama S.

AIM: Arteriosclerotic disease is increasing due to aging of the population, and is associated with diabetes, hypertension, hyperlipidemia, obesity, and smoking. This disease may result in fatal cerebrovascular disease, and especially cardiogenic cerebral embolism caused by artery plaque-based atherothrombotic cerebral infarction. The study was performed to examine the relationship of abdominal aortic calcification (AAC) on lumbar radiographs with carotid intima-media complex thickness (IMT), factors associated with carotid artery plaque, and cutoff values in middle-aged and elderly people. PATIENTS AND METHODS: The subjects were 309 healthy volunteers (average age 63 years) who attended a health checkup supported by a local government in 2015. The AAC-24 score was determined on lumbar lateral standing radiographs and was categorized as 0 (54% of subjects),1-4 (31%), and ≥5 (severe, 15%). Carotid ultrasonography was used to evaluate IMT of the common carotid artery. Carotid artery plaque was defined as IMT >1.1 mm. Body mass index (BMI), hypertension, diabetes mellitus (DM), dyslipidemia, smoking, alcohol intake, and osteoporosis were examined. RESULTS: Of 309 cases, 142 (46%) had AAC and 104 (34%) had carotid artery plaque. Thus, 15% (n = 45) had severe AAC. Age, prevalence of DM and carotid artery plaque increased with severity of AAC. In patients with carotid artery plaque (n = 104), age (67.8±7.5 vs. 61.0±10.1 years), % male (56% vs. 39%), BMI (22.9±2.8 vs. 23.7±3.5), AAC rate (58% vs. 40%) and AAC-24 score (3 (0, 8) vs. 0 (0, 2)) were all significantly higher than in those (n = 205) without carotid artery plaque. In multivariate analysis, age (OR 1.172), male gender (OR 1.654), AAC (OR 1.352), and AAC-24 ≥5 (OR 4.191) were significantly associated with carotid artery plaque. Combining AAC-24 with age significantly increased the AUC from 0.632 to 0.834 ($p<0.05$). CONCLUSION: There was a significant relationship between AAC on lumbar radiographs and carotid IMT.

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Adolescent Use of Combined Hormonal Contraception and Peak Bone Mineral Density Accrual: a meta-analysis of international prospective controlled studies.

Goshtasebi A, Subotic Brajic T, Scholes D, Beres Lederer Goldberg T, Berenson A, Prior JC.

Objective: Many women use combined hormonal contraceptives (CHC) during adolescence during which they are accruing peak areal bone mineral density (BMD) that relates to lifetime fracture risk. To build BMD requires formation with which CHC-related exogenous estrogen may interfere. We compared peak BMD accrual in adolescents using and not using CHC. Design/participants: We performed literature searches for prospective published peer-reviewed articles providing 12-24 month BMD change in adolescent (12-19-year-old) women using CHC versus CHC-unexposed control women. Methods: Meta-analyses used random-effects models to assess BMD change rate at lumbar spine (LS) and other sites in adolescent CHC-users versus non-CHC users. Results: Literature searches yielded 84 publications of which nine were eligible. Adolescent-only data were sought from cohorts with wider age inclusions. The 12-month LS meta-analysis with eight paired comparisons in 1535 adolescents showed a weighted mean BMD difference in CHC-exposed of -0.02 (95% Confidence Interval [CI]: -0.05 to 0.00) g/cm2 (P = 0.04). The 24-month LS meta-analysis with five paired comparisons in 885 adolescents showed a highly significant weighted mean BMD difference of -0.02 (95% CI: -0.03 to -0.01) g/cm2 in CHC exposed adolescents (P = 0.0006). Heterogeneities by I2 were 96 and 85% respectively. Insufficient data for other bone sites precluded quantitative analysis. Conclusion: Given that adolescent exposure to CHC appears to be increasing, this evidence for potential impairment of peak spinal BMD accrual is of concern and suggests a potential public health problem. Randomized controlled trial data are needed to determine CHC effects on adolescent bone health.

Aging Clin Exp Res. 2019 Jan 5. doi: 10.1007/s40520-018-1109-4. [Epub ahead of print]

Executive summary of European guidance for the diagnosis and management of osteoporosis in postmenopausal women.

Kanis JA, Cooper C, Rizzoli R, Reginster JY; Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) and the Committees of Scientific Advisors and National Societies of the International Osteoporosis Foundation (IOF). **Ver archivo adjunto**