Selección de Resúmenes de Menopausia

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Vitamin D supplementation in the prevention and management of major chronic diseases not related to mineral homeostasis in adults: research for evidence and a scientific statement from the European society for clinical and economic aspects of osteoporosis and osteoarthritis (ESCEO).

Cianferotti L, Bertoldo F, Bischoff-Ferrari HA, Bruyere O, Cooper C, Cutolo M, Kanis JA, Kaufman JM, Reginster JY, Rizzoli R, Brandi ML.

INTRODUCTION: Optimal vitamin D status promotes skeletal health and is recommended with specific treatment in individuals at high risk for fragility fractures. A growing body of literature has provided indirect and some direct evidence for possible extraskeletal vitamin D-related effects. PURPOSE AND METHODS: Members of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis have reviewed the main evidence for possible proven benefits of vitamin D supplementation in adults at risk of or with overt chronic extra-skeletal diseases, providing recommendations and guidelines for future studies in this field. RESULTS AND CONCLUSIONS: Robust mechanistic evidence is available from in vitro studies and in vivo animal studies, usually employing cholecalciferol, calcidiol or calcitriol in pharmacologic rather than physiologic doses. Although many cross-sectional and prospective association studies in humans have shown that low 25-hydroxyvitamin D levels (i.e., <50 nmol/L) are consistently associated with chronic diseases, further strengthened by a dose-response relationship, several meta-analyses of clinical trials have shown contradictory results. Overall, large randomized controlled trials with sufficient doses of vitamin D are missing, and available small to moderate-size trials often included people with baseline levels of serum 25-hydroxyvitamin D levels >50 nmol/L, did not simultaneously assess multiple outcomes, and did not report overall safety (e.g., falls). Thus, no recommendations can be made to date for the use of vitamin D supplementation in general, parental compounds, or non-hypercalcemic vitamin D analogs in the prevention and treatment of extra-skeletal chronic diseases. Moreover, attainment of serum 25-hydroxyvitamin D levels well above the threshold desired for bone health cannot be recommended based on current evidence, since safety has yet to be confirmed. Finally, the promising findings from mechanistic studies, large cohort studies, and small clinical trials obtained for autoimmune diseases (including type 1 diabetes, multiple sclerosis, and systemic lupus erythematosus), cardiovascular disorders, and overall reduction in mortality require further confirmation.

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Is the oral contraceptive or hormone replacement therapy a risk factor for cholelithiasis: A systematic review and meta-analysis.

Wang S, Wang Y, Xu J, Chen Y.

BACKGROUND: Association between exogenous estrogen intake and cholelithiasis risk has been reported in several epidemiological studies, including oral contraceptive (OC) and hormone replacement therapy (HRT), while the results were controversial. This study aimed to perform a comprehensive meta-analysis of this issue. METHODS: PUBMED, EMBASE, and Cochrane library database were searched up to October 2016. Two reviewers independently extracted data from eligible studies, relative risks (RRs), and/or odds ratios (ORs) with 95% confidence intervals (95% CIs) for the highest versus lowest categories of intake were adopted. Either a fixed- or a random-effects model was adopted to estimate overall RRs or ORs. Besides, subgroup and publication bias analyses were applied to explain the heterogeneity. An original study was also conducted to verify our conclusion. RESULTS: A total of 19 studies with approximately 556,620 participants were included in this meta-analysis. The pooled RR of cholelithiasis for the highest versus the lowest categories was 1.59 (95% CI: 1.44-1.75), indicating that exogenous estrogen was positive associated with the intake of exogenous estrogen. However, the pooled RR of OC intake and cholelithiasis risk was 1.19 (95% CI: 0.97-1.45), and the RR for HRT was 1.79 (95% CI: 1.61-2.00). CONCLUSION: The HRT was positively associated with the cholelithiasis risk, and the OC will not increase the risk of cholelithiasis.

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Cholesterol, Cholesterol-Lowering Medication Use, and Breast Cancer Outcome in the BIG 1-98 Study.

Borgquist S, Giobbie-Hurder A, Ahern TP, Garber JE, Colleoni M, Láng I, Debled M, Ejlertsen B, von Moos R, et al.

Purpose Cholesterol-lowering medication (CLM) has been reported to have a role in preventing breast cancer recurrence. CLM may attenuate signaling through the estrogen receptor by reducing levels of the estrogenic cholesterol metabolite 27-hydroxycholesterol. The impact of endocrine treatment on cholesterol levels and hypercholesterolemia per se may counteract the intended effect of aromatase inhibitors. Patients and Methods The Breast International Group (BIG) conducted a randomized, phase III, double-blind trial, BIG 1-98, which enrolled 8,010 postmenopausal women with early-stage, hormone receptor-positive invasive breast cancer from 1998 to 2003. Systemic levels of total cholesterol and use of CLM were measured at study entry and every 6 months up to 5.5 years. Cumulative incidence functions were used to describe the initiation of CLM in the presence of competing risks. Marginal structural Cox proportional hazards modeling investigated the relationships between initiation of CLM during endocrine therapy and outcome. Three time-to-event end points were considered: disease-free-survival, breast cancer-free interval, and distant recurrence-free interval. Results Cholesterol levels were reduced during tamoxifen therapy. Of 789 patients who initiated CLM during endocrine therapy, the majority came from the letrozole monotherapy arm (n = 318), followed by sequential tamoxifen-letrozole (n = 189), letrozole-tamoxifen (n = 176), and tamoxifen monotherapy (n = 106). Initiation of CLM during endocrine therapy was related to improved disease-free-survival (hazard ratio [HR], 0.79; 95% CI, 0.66 to 0.95; P = .01), breast cancer-free interval (HR, 0.76; 95% CI, 0.60 to 0.97; P = .02), and distant recurrence-free interval (HR, 0.74; 95% CI, 0.56 to 0.97; P = .03). Conclusion Cholesterol-lowering medication during adjuvant endocrine therapy may have a role in preventing breast cancer recurrence in hormone receptor-positive early-stage breast cancer. We recommend that these observational results be addressed in prospective randomized trials.

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Mammographic Density Change with Estrogen and Progestin Therapy and Breast Cancer Risk.

Byrne C, Ursin G, Martin CF, Peck JD, Cole EB, Zeng D, Kim E, Yaffe MD, Boyd NF, Heiss G, McTiernan A, et al.

Background: Estrogen plus progestin therapy increases both mammographic density and breast cancer incidence. Whether mammographic density change associated with estrogen plus progestin initiation predicts breast cancer risk is unknown. Methods: We conducted an ancillary nested case-control study within the Women's Health Initiative trial that randomly assigned postmenopausal women to daily conjugated equine estrogen 0.625 mg plus medroxyprogesterone acetate 2.5 mg or placebo. Mammographic density was assessed from mammograms taken prior to and one year after random assignment for 174 women who later developed breast cancer (cases) and 733 healthy women (controls). Logistic regression analyses included adjustment for confounders and baseline mammographic density when appropriate. Results: Among women in the estrogen plus progestin arm (97 cases/378 controls), each 1% positive change in percent mammographic density increased breast cancer risk 3% (odds ratio [OR] = 1.03, 95% confidence interval [CI] = 1.01 to 1.06). For women in the highest quintile of mammographic density change (>19.3% increase), breast cancer risk increased 3.6-fold (95% CI = 1.52 to 8.56). The effect of estrogen plus progestin use on breast cancer risk (OR = 1.28, 95% CI = 0.90 to 1.82) was eliminated in this study, after adjusting for change in mammographic density (OR = 1.00, 95% CI = 0.66 to 1.51). Conclusions: We found the one-year change in mammographic density after estrogen plus progestin initiation predicted subsequent increase in breast cancer risk. All of the increased risk from estrogen plus progestin use was mediated through mammographic density change. Doctors should evaluate changes in mammographic density with women who initiate estrogen plus progestin therapy and discuss the breast cancer risk implications.

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Exposure to statins is associated to fracture risk reduction in elderly people with cardiovascular disease: evidence from the AIFA-I-GrADE observational project.

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PURPOSE: Conflicting findings were observed from clinical trials and observational studies evaluating the association between the use of statins and the risk of fracture. A case-control study nested into a cohort of elderly patients on treatment with statins for cardiovascular secondary prevention was performed on this issue. METHODS: The cohort was formed by 13 875 individuals aged ≥65 years from several Italian health units receiving statins after hospital discharge for cardiovascular outcomes. From this cohort, 964 patients who experienced fracture were identified (i.e., cases). Up to five controls were randomly selected for each case from the underlying cohort. Conditional logistic regression was used to model the risk of fracture associated with adherence to statins, which was measured from the proportion of days covered (PDC) by treatment. A set of sensitivity analyses was performed in order to account for sources of systematic uncertainty. RESULTS: Compared with patients with low adherence (PDC ≤ 40%), those on intermediate (PDC 41-80%) and high (PDC > 80%) adherence exhibited a risk reduction of 21% (95% confidence interval 6% to 23%) and 25% (7% to 40%). Similar effects were observed among patients younger and older than 80 years, as well as among men, while there was no evidence that adherence to statins affected the risk of fracture among women. Sensitivity analyses revealed that the associations were consistent and robust. CONCLUSIONS: Use of statins for secondary cardiovascular prevention is associated with fracture risk reduction in elderly people. Further studies are required to better clarify the statin-fracture association in postmenopausal women.

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Menstrual Cycle Hormone Changes in Women Traversing the Menopause: Study of Women's Health Across the Nation.

Santoro N, Crawford SL, El Khoudary SR, Allshouse AA, Burnett-Bowie SA, Finkelstein J, Derby C, et al.

Context: Menstrual cycle hormone patterns in women approaching menopause are inadequately studied. Objective: To describe day-to-day menstrual cycle hormones in women as they approach menopause from the Study of Women's Health Across the Nation (SWAN) Daily Hormone Study (DHS). Design: DHS enrollees collected daily urine for one entire menstrual cycle or up to 50 days, whichever came first, annually, up to the final menstrual period (FMP) or for up to 10 years. Setting: 7 sites across the US. Participants: 511 premenopausal or early perimenopausal women at enrollment, within 10 years before menopause. Intervention: time-to-FMP measurement. Main Outcome Measures: Evidence of luteal activity (ELA), determined using objective algorithms. Menstrual cycle/segment length; whole cycle and segment integrated urinary LH, FSH, estrone conjugates (E1c) and pregnanediol glucuronide (Pdg) for each year, organized around the FMP. Results: Mean menstrual cycle length was remarkably preserved at 26-27 days in ELA cycles; non-ELA cycles had greater variability. The % cycles that were ELA remained high until 5 years before the FMP (87.9%); only 22.8% of cycles within 1 year of the FMP were ELA. Whole cycle hormones remained relatively stable up to 3 years before the FMP, when gonadotropins began to increase. Pdg excretion declined slowly with progress to the FMP, but Pdg patterns of ELA cycles remained distinguishable from non-ELA. Conclusions: Menstrual cycle hormone patterns in perimenopausal women resemble those of midreproductive aged women until 5 years before menopause and presumably ovulatory cycles retain a potentially fertile pattern up to the end of reproductive life.

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Functional Hypothalamic Amenorrhea: An Endocrine Society Clinical Practice Guideline.

Gordon CM, Ackerman KE, Berga SL, Kaplan JR, Mastorakos G, Misra M, Murad MH, Santoro NF, Warren MP.

Objective: To formulate clinical practice guidelines for the diagnosis and treatment of functional hypothalamic amenorrhea (FHA). Participants: The participants include an Endocrine Society-appointed task force of eight experts, a methodologist, and a medical writer. Evidence: This evidence-based guideline was developed using the Grading of Recommendations, Assessment, Development, and Evaluation approach to describe the strength of recommendations and the quality of evidence. The task force commissioned two systematic reviews and used the best available evidence from other published systematic reviews and individual studies. Consensus Process: One group meeting,

several conference calls, and e-mail communications enabled consensus. Endocrine Society committees and members and cosponsoring organizations reviewed and commented on preliminary drafts of this guideline. Conclusions: FHA is a form of chronic anovulation, not due to identifiable organic causes, but often associated with stress, weight loss, excessive exercise, or a combination thereof. Investigations should include assessment of systemic and endocrinologic etiologies, as FHA is a diagnosis of exclusion. A multidisciplinary treatment approach is necessary, including medical, dietary, and mental health support. Medical complications include, among others, bone loss and infertility, and appropriate therapies are under debate and investigation.