



Selección de Resúmenes de Menopausia

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Association of Estrogen Metabolism with Breast Cancer Risk in Different Cohorts of Postmenopausal Women.

Sampson JN, Falk RT, Schairer C, Moore SC, Fuhrman BJ, Dallal CM, et al.

Endogenous estradiol and estrone are linked causally to increased risks of breast cancer. In this study, we evaluated multiple competing hypotheses for how metabolism of these parent estrogens may influence risk. Prediagnostic concentrations of estradiol, estrone, and 13 metabolites were measured in 1298 postmenopausal cases of breast cancer and 1524 matched controls in four separate patient cohorts. Median time between sample collection and diagnosis was 4.4-12.7 years across the cohorts. Estrogen analytes were measured in serum or urine by liquid chromatographic-tandem mass spectrometry. Total estrogen levels (summing all 15 estrogens/estrogen metabolites) were associated strongly and positively with breast cancer risk. Normalizing total estrogen levels, we also found that a relative increase in levels of 2-hydroxylation pathway metabolites, or in the ratio of 2-hydroxylation:16-hydroxylation pathway metabolites, were associated inversely with breast cancer risk. These associations varied by total estrogen levels, with the largest risk reductions occurring in women in the highest tertile. With appropriate validation, these findings suggest opportunities for breast cancer prevention by modifying individual estrogen metabolism profiles through either lifestyle alterations or chemopreventive strategies.

Arch Osteoporos. 2017 Dec;12(1):5. doi: 10.1007/s11657-016-0303-2. Epub 2016 Dec 21.

Evaluation of sarcopenia in patients with distal radius fractures.

Roh YH, Koh YD, Noh JH, Gong HS, Baek GH.

Sarcopenia is more prevalent in patients with distal radius fracture (DRF) than in age- and sex-matched controls. Lower appendicular mass index in men and weaker grip strength in both men and women increase the likelihood of DRF. INTRODUCTION: Sarcopenia is a core component of physical frailty that predisposes older people to falls and negatively impacts the activities of daily living. The objectives of this study were to compare the prevalence of sarcopenia in patients with DRF with that in age- and sex-matched controls without DRF; and evaluate the association between sarcopenia and the occurrence of DRF. METHODS: We prospectively recruited 132 patients over 50 years of age who sustained DRF due to fall and 132 age- and sex-matched controls without DRF. A definition of sarcopenia was based on the consensus of the Asian Working Group for Sarcopenia. Sarcopenic components including appendicular lean body mass, grip strength, and gait speed were compared between the two groups. Other factors assessed for the occurrence of DRF were age, gender, body mass index (BMI), lumbar, and hip bone mineral density (BMD) values. A conditional logistic regression analysis was conducted to evaluate the associations between sarcopenia and the occurrence of DRF. RESULTS: A total of 39 (30%) of 132 DRF patients were sarcopenic, whereas 23 (17%) of the 132 controls were within the sarcopenic criteria ($p = 0.048$). The patient group had significantly lower lean body mass and weaker grip strength than those of the control group. However, there was no significant difference in gait speed between the two groups. According to regression analysis, lower appendicular mass index in men was associated with an increased incidence of DRF (odds ratio [OR] = 0.84, 95% confidence interval [CI] = 0.72, 0.95) while weaker grip strength and lower total hip BMD values were associated with the occurrence of DRF in both men (OR = 0.77, 95% CI = 0.63, 0.92; and OR = 0.79, 95% CI = 0.64, 0.94, respectively) and women (OR = 0.78, 95% CI = 0.64, 0.93, and OR = 0.73, 95% CI = 0.52, 0.92, respectively). CONCLUSIONS: Sarcopenia is more prevalent in patients with DRF than in age- and sex-matched controls. Lower appendicular mass in men, weaker grip strength, and lower hip BMD in both men and women increase the likelihood of DRF.

J Gerontol A Biol Sci Med Sci. 2016 Dec 21. pii: glw240. doi: 10.1093/gerona/glw240. [Epub ahead of print]

Chronic Inflammation: Accelerator of Biological Aging.

Fougère B, Boulanger E, Nourhashémi F4, Guyonnet S, Cesari M.

Biological aging is characterized by a chronic low-grade inflammation level. This chronic phenomenon has been named "inflamm-aging" and is a highly significant risk factor for morbidity and mortality in the older persons. The most common theories of inflamm-aging include redox stress, mitochondrial dysfunction, glycation, deregulation of the immune system, hormonal changes, epigenetic modifications, and dysfunction telomere attrition. Inflamm-aging plays a role in the initiation and progression of age-related diseases such as type II diabetes, Alzheimer's disease, cardiovascular disease, frailty,

sarcopenia, osteoporosis, and cancer. This review will cover the identification of pathways that control age-related inflammation across multiple systems and its potential causal role in contributing to adverse health outcomes.

Nutr Metab Cardiovasc Dis. 2016 Nov 20. pii: S0939-4753(16)30193-4. [Epub ahead of print]

Influence of the degree of adherence to the Mediterranean diet on the cardiometabolic risk in peri and menopausal women. The Flamenco project.

Ruiz-Cabello P, Coll-Risco I, Acosta-Manzano P, Borges-Cosic M, Gallo-Vallejo FJ, Aranda P, et al.

BACKGROUND AND AIMS: The Mediterranean diet (MD) has been associated with reduced morbidity from cardiovascular diseases in the general population. The aim of this study was to assess whether different degrees of adherence to the MD were associated with the cardiometabolic risk in peri and menopausal women. **METHODS AND RESULTS:** This cross-sectional study included 198 peri and menopausal women participating in the Flamenco project. Validated questionnaires were used to assess menopause health-related quality of life and degree of adherence to the MD (low, medium and high). The following cardiometabolic risk factors were assessed: fat mass percentage, waist circumference, blood pressure and resting heart rate, plasma markers (total cholesterol, high and low-density lipoprotein cholesterol [HDL-C and LDL-C, respectively], total cholesterol/HDL ratio, triglycerides, C-reactive protein and fasting glucose), Physical activity levels and smoking status. The degree of adherence to the MD among the study sample was 27%, 40% and 30% for low, medium and high adherence, respectively. After controlling for potential confounders, women with a high adherence to the MD showed lower plasma total cholesterol ($p = 0.025$), resting heart rate ($p = 0.005$), LDL-C ($p = 0.019$), triglycerides ($p = 0.046$) and C-reactive protein ($p = 0.009$) compared to those with a low adherence. Likewise women with high adherence to the MD showed lower total cholesterol/HDL-C ratio ($p = 0.020$) compared to those with a medium adherence. The high MD adherence group also showed lower clustered cardiometabolic risk ($p = 0.004$). Moreover, when analysing specific MD components, whole grain cereals, pulses (both $p < 0.05$) and red wine ($p < 0.01$) consumption were inversely associated with the clustered cardiometabolic risk. **CONCLUSION:** The present findings suggest that a high but not medium adherence to the MD is associated with a cardioprotective effect in peri and menopausal women. As a low percentage of the sample showed a high adherence to the MD, future research aimed at increasing the adherence to this dietary pattern for a better cardiometabolic status during peri and menopause is warranted.

Horm Mol Biol Clin Investig. 2016 Dec 20. doi: 10.1515/hmbci-2016-0042. [Epub ahead of print]

A low dose (6.5 mg) of intravaginal DHEA permits a strictly local action while maintaining all serum estrogens or androgens as well as their metabolites within normal values.

Labrie F, Martel C.

OBJECTIVE: Serum concentrations of estradiol (E2) and testosterone (testo) measured by mass spectrometry-based assays should remain below the 95th centile measured at 9.3 pg/mL for E2 and 0.26 ng/mL for testo in normal postmenopausal women in order to avoid the risk of non-physiological systemic exposure to elevated serum concentrations of these two sex steroids. **METHODS:** Serum E2 and testo, as well as dehydroepiandrosterone (DHEA) and nine of its other metabolites, were measured at 10 time intervals over 24 h on the first and seventh days of daily intravaginal administration of 0.50% (6.5 mg) DHEA by validated mass spectrometry-based assays. **RESULTS:** No biologically significant change in the individual serum concentrations of E2, testo or DHEA was observed. Most importantly, estrone sulfate (E1-S) and the glucuronidated androgen metabolites also remained within normal values, thus confirming the absence of biologically significant systemic exposure in line with intracrinology. Using data from the literature, comparison is made with serum E2 above normal postmenopausal values following administration of 10- μ g E2 tablets. **CONCLUSION:** While the clinical program on vulvovaginal atrophy has shown the efficacy and safety of intravaginal 6.5 mg of DHEA (prasterone), the present data illustrate in detail the serum levels of the individual sex steroids and their metabolites derived from DHEA. The data obtained are in line with the physiology of intracrinology and confirm an action limited to the vagina as the serum concentrations of all sex steroids are maintained within the normal values of menopause, thus protecting the uterus and most likely other tissues.

J Am Geriatr Soc. 2016 Dec;64(12):2448-2456. doi: 10.1111/jgs.14658. Epub 2016 Nov 7.

Effect of Reproductive History and Exogenous Hormone Use on Cognitive Function in Mid- and Late Life.

Karim R, Dang H, Henderson VW, Hodis HN, St John J, Brinton RD, Mack WJ.

OBJECTIVES: To investigate the association between reproductive history indicators of hormonal exposure, including reproductive period, pregnancy, and use of hormonal contraceptives, and mid- and late-life cognition in postmenopausal women. **DESIGN:** Analysis of baseline data from two randomized clinical trials: the Women's Isoflavone Soy Health and the Early vs Late Intervention Trial of Estradiol. **SETTING:** University academic research center. **PARTICIPANTS:** Naturally menopausal women (N = 830). **MEASUREMENTS:** Participants were uniformly evaluated using a cognitive battery and a structured reproductive history questionnaire. Outcomes were composite scores for verbal episodic memory, executive function, and global cognition. Reproductive variables included ages at pregnancies, menarche, and menopause; reproductive period; number of pregnancies; and use of hormones for contraception and menopausal symptoms. Multivariable linear regression was used to evaluate associations between cognitive scores (dependent variable) and reproductive factors (independent variables), adjusting for age, race and ethnicity, income, and education. **RESULTS:** On multivariable modeling, age at menarche of 13 and older was inversely associated with global cognition (P = .05). Last pregnancy after age 35 was positively associated with verbal memory (P = .03). Use of hormonal contraceptives was positively associated with global cognition (P trend = .04), and verbal memory (P trend = .007). The association between hormonal contraceptive use and verbal memory and executive function was strongest for more than 10 years of use. Reproductive period was positively associated with global cognition (P = .04) and executive function (P = .04). **CONCLUSION:** In this sample of healthy postmenopausal women, reproductive life events related to sex hormones, including earlier age at menarche, later age at last pregnancy, longer reproductive period, and use of oral contraceptives are positively related to aspects of cognition in later life.

Bone. 2016 Oct 27. pii: S8756-3282(16)30320-9. doi: 10.1016/j.bone.2016.10.024. [Epub ahead of print]

Muscle mass is associated with incident fracture in postmenopausal women: The OFELY study.

Sornay-Rendu E, Duboeuf F, Boutroy S, Chapurlat RD.

The relationships between body composition and bone mineral density are well established but the contribution of body composition to the risk of fracture (Fx) has rarely been evaluated prospectively. We analyzed the risk of Fx by body composition in 595 postmenopausal women (mean age 66±8years) from a longitudinal cohort study (Os des Femmes de Lyon). We assessed the risk of the first incident fragility Fx according to body composition obtained from whole-body DXA: abdominal visceral (VFAT) and subcutaneous fat mass (SFAT), total body fat mass (FM), lean mass index (LMI) and appendicular skeletal muscle mass index (ASMI). During a median [IQ] follow-up of 13.1years [1.9], 138 women sustained a first incident Fx, including 85 women with a major osteoporotic Fx (MOP Fx: hip, clinical spine, humerus or wrist). After adjustment for age, women who sustained Fx had lower BMI (-4%, p=0.01), LMI (-6%, p=0.002) and ASMI (-3%, p=0.003), compared with women without Fx. After adjustment for age, prevalent Fx, physical activity, incident falls and FN BMD, each SD increase of baseline values of LMI and ASMI was associated with decreased Fx risk with adjusted hazard ratios of 0.76 for both of p≤0.02. Those associations were similar after accounting for the competing risk of death. VFAT and SFAT were associated with Fx risk in the multivariate model only for MOP Fx and the association did not persist after consideration of competing mortality. We conclude that lean mass and appendicular muscle mass indexes are associated with the risk of fracture in postmenopausal women independently of BMD and clinical risk factors.

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Association of use of bisphosphonates with risk of colorectal cancer.

Rennert G, Pinchev M, Rennert HS, Gruber SB.

371 **Background:** Bisphosphonates are commonly used for the treatment of osteoporosis and of bone metastases due to breast cancer and were recently reported to be associated with reduced risk of breast cancer, but their association with risk of other cancers is unknown. **METHODS:** The Molecular Epidemiology of Colorectal Cancer (MECC) study is a population-based case-control study in northern Israel of colorectal cancer cases and age/sex/clinic/ethnic-group matched controls. Use of bisphosphonates prior to diagnosis was assessed in a subset of 933 pairs of post-menopausal female cases and controls, enrolled in Clalit Health Services (CHS), using computerized pharmacy records. **RESULTS:** The use of bisphosphonates for more than one year prior to diagnosis, but not for less than a year, was associated with a significantly reduced relative risk of colorectal cancer (odds ratio=0.50, 95% CI: 0.35-0.71). This association remained statistically significant after adjustment for, vegetable consumption, sports activity, family history of colorectal cancer, , BMI, use of low-dose aspirin, statins, vitamin D and post-menopausal hormones (OR=0.40, 0.24-0.64). Concomitant use of bisphosphonates and statins did not further reduce the risk. **CONCLUSIONS:** The use of oral bisphosphonates for more than 1 year was associated with a 60% relative reduction in the risk of colorectal cancer similar to the recently reported association of this drug class with reduction in breast cancer risk. No significant financial relationships to disclose.