Selección de Resúmenes de Menopausia

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María Soledad Vallejo. Clínica Quilín. Universidad de Chile

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Risk of 16 cancers across the full glycemic spectrum: a population-based cohort study using the UK Biobank

Christopher T Rentsch # 1 , Ruth E Farmer # 2 , Sophie V Eastwood 3 , Rohini Mathur 2 ,

Introduction: Diabetes is observed to increase cancer risk, leading to hypothesized direct effects of either hyperglycemia or medication. We investigated associations between glycosylated hemoglobin (HbA1c) across the whole glycemic spectrum and incidence of 16 cancers in a population sample with comprehensive adjustment for risk factors and medication. Research design and methods: Linked data from the UK Biobank and UK cancer registry for all individuals with baseline HbA1c and no history of cancer at enrollment were used. Incident cancer was based on International Classification of Diseases - 10th Edition diagnostic codes. Age-standardized incidence rates were estimated by HbA1c category. Associations between HbA1c, modeled as a restricted cubic spline, and cancer risk were estimated using Cox proportional hazards models. Results: Among 378 253 individuals with average follow-up of 7.1 years, 21 172 incident cancers occurred. While incidence for many of the 16 cancers was associated with hyperglycemia in crude analyses, these associations disappeared after multivariable adjustment, except for pancreatic cancer (HR 1.55, 95% CI 1.22 to 1.98 for 55 vs 35 mmol/mol), and a novel finding of an inverse association between HbA1c and premenopausal breast cancer (HR 1.27, 95% CI 1.00 to 1.60 for 25 vs 35 mmol/mol; HR 0.71, 95% CI 0.54 to 0.94 for 45 vs 35 mmol/mol), not observed for postmenopausal breast cancer. Adjustment for diabetes medications had no appreciable impact on HRs for cancer. Conclusions: Apart from pancreatic cancer, we did not demonstrate any independent positive association between HbA1c and cancer risk. These findings suggest that the potential for a cancer-inducing, direct effect of hyperglycemia may be misplaced.

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Effect of menopausal hormone therapy on proteins associated with senescence and inflammation

Laura Faubion 1 , Thomas A White 2 , Brett J Peterson 3 , Jennifer R Geske 3 , Nathan K LeBrasseur et al.

Background: Estrogen may inhibit cell senescence that contributes to age-related disorders. This study determined the effects of menopausal hormone treatments on circulating levels of markers of cell senescence. Methods: Growth differentiation factor 15 (GDF15), tumor necrosis factor receptor 1 (TNFR1), FAS, and macrophage inflammatory protein 1α (MIP1α) were measured in serum using multiplexed bead-based assays and compared among menopausal women participating in the Kronos Early Estrogen Prevention Study randomized to either placebo (n = 38), oral conjugated equine estrogen (oCEE, n = 37), or transdermal 17β-estradiol (tE2, n = 34). Serum levels of the senescent markers for each treatment were compared to placebo 36 months after randomization using the Wilcoxon rank sum test. Results: Serum levels of GDF15, TNFR1, and FAS, but not MIP1α, were lower in both the oCEE and tE2 groups compared to placebo. The difference in levels between treatment and placebo for GDF15, TNFR1, and FAS were greater for oCEE [-108 pg/mL (p = .008), -234 pg/mL (p = .0006), and -1374 pg/mL (p < .0001), respectively] than for tE2 [-76 pg/mL (p = .072), -105 pg/mL (p = .076), and -695 pg/mL (p = .036), respectively]. Additionally, TNFR1 showed a positive association with time past menopause (correlation = 0.255, p = .019). Conclusions: Circulating levels of some markers of cell senescence were lower in menopausal women treated with oCEE and tE2 compared to placebo. Differences in the magnitude of effect of the two active treatments may reflect the differences in circulating levels of estrogen metabolites due to formulation and mode of delivery. These data generate new hypotheses with regard to the effects of menopause on the biology of aging.

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Vitamin D supplementation: upper limit for safety revisited?

René Rizzoli 1

Vitamin D overdosing includes hypercalcemia, hypercalciuria, and mineral deposits in soft tissues. A safety upper limit of 4000 IU/day, which is consistently accepted, has been challenged, since the risk of adverse events in other systems than calcium-phosphate homeostasis may depend not only on the dose, but on the outcome, the treatment regimen, and possibly the age, sex and vitamin D status. The therapeutic window of vitamin D supplementation may be narrower than hitherto recognized. The prevention and/or correction of vitamin D deficiency/insufficiency with 800-1000 IU/daily of vitamin D or 10 µg/day of calcifediol are safe. Because of their potential harm, larger doses given on the long term or in intermittent regimens should not be selected.

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Women's brain aging: Effects of sex-hormone exposure, pregnancies, and genetic risk for Alzheimer's disease

Ann-Marie G de Lange 1 2 3 , Claudia Barth 2 , Tobias Kaufmann 2 , Ivan I Maximov 1 2 , al.

Sex hormones such as estrogen fluctuate across the female lifespan, with high levels during reproductive years and natural decline during the transition to menopause. Women's exposure to estrogen may influence their heightened risk of Alzheimer's disease (AD) relative to men, but little is known about how it affects normal brain aging. Recent findings from the UK Biobank demonstrate less apparent brain aging in women with a history of multiple childbirths, highlighting a potential link between sex-hormone exposure and brain aging. We investigated endogenous and exogenous sex-hormone exposure, genetic risk for AD, and neuroimaging-derived biomarkers for brain aging in 16,854 middle to older-aged women. The results showed that as opposed to parity, higher cumulative sex-hormone exposure was associated with more evident brain aging, indicating that i) high levels of cumulative exposure to sex-hormones may have adverse effects on the brain, and ii) beneficial effects of pregnancies on the female brain are not solely attributable to modulations in sex-hormone exposure. In addition, for women using hormonal replacement therapy (HRT), starting treatment earlier was associated with less evident brain aging, but only in women with a genetic risk for AD. Genetic factors may thus contribute to how timing of HRT initiation influences women's brain aging trajectories.

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Loss of bone density and bone strength following premenopausal risk-reducing bilateral salpingo-oophorectomy: a prospective controlled study (WHAM Study)

H Jiang 1 , D L Robinson 2 , P V S Lee 2 , E O Krejany 3 , C J Yates 1 4 5 , M Hickey 3 , J D Wark 6 7 8

Prophylactic oophorectomy is recommended for women at high risk for ovarian cancer, but the associated impact on bone health is of clinical concern. This prospective, controlled study demonstrated substantial loss of bone density and bone strength following surgical menopause. Postoperative hormone therapy alleviated, but not fully prevented, spinal bone loss. Introduction: This prospective study investigated bone health in women following premenopausal oophorectomy. Methods: Dual-energy x-ray absorptiometry (DXA), peripheral quantitative computed tomography (pQCT), and pQCT-based finite element analysis (pQCT-FEA) were used to assess bone health between systemic hormone therapy (HT) users and non-users after premenopausal risk-reducing bilateral salpingo-oophorectomy (RRBSO) compared with premenopausal controls over 24-month follow-up. Results: Mean age was 42.4 ± 2.6 years (n = 30) for the surgery group and 40.2 ± 6.3 years for controls (n = 42), and baseline bone measures were similar between groups. Compromised bone variables were observed at 24 months after RRBSO, among which areal bone mineral density (aBMD) at the lumbar spine, tibial volumetric cortical density (Crt vBMD), and tibial bending stiffness (kbend) had decreased by 4.7%, 1.0%, and 12.1%, respectively (all $p < 0.01$). In non-HT users, significant losses in lumbar spine (5.8%), total hip (5.2%), femoral neck (6.0%) aBMD, tibial Crt vBMD (2.3%), and kbend (14.8%) were observed at 24 months (all $p < 0.01$). HT prevented losses in kbend, tibial Crt vBMD, and aBMD, except for modest 2.3% loss at the lumbar spine ($p = 0.01$). Conclusion: This prospective, controlled study of bone health following RRBSO or premenopausal oophorectomy demonstrated substantial loss of bone density and bone strength following RRBSO. HT prevented loss of bone density and bone stiffness, although there was still a modest decrease in lumbar spine aBMD in HT users. These findings may inform decision-making about RRBSO and clinical management following premenopausal oophorectomy.

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Influence of dietary habits and Mediterranean diet adherence on menopausal symptoms. The FLAMENCO project

Marta Flor-Alemany , Nuria Marín-Jiménez, Irene Coll-Risco, Pilar Aranda, Virginia Arianna Aparicio.

Objective: To explore the association of dietary habits and Mediterranean diet adherence with menopausal symptoms. Methods: The present study included 172 women recruited from the FLAMENCO project. Menopausal symptoms were assessed with the Kupperman Menopausal Index and the Cervantes Menopause and Health Subscale from the validated Cervantes Scale. A food frequency questionnaire was employed to evaluate dietary habits. Adherence to the Mediterranean diet was assessed with the Mediterranean diet score. Results: Intake of poultry and skimmed dairy products was associated with a worse Kupperman Menopausal Index score (β: 0.17, P = 0.03 and β: 0.18, P = 0.01, respectively). On the contrary, soy milk consumption was associated with a better Kupperman Menopausal Index score (β: -0.17, P = 0.02). Poultry and skimmed dairy were associated with worse scores in the total Cervantes Menopause and Health Subscale score (β: 0.22, P = <0.01 and β: 0.19, P = 0.01, respectively), whereas soy milk and vegetables were associated with a better total Cervantes Menopause and Health Subscale score (β: -0.20, P = 0.01 and β: -0.17, P = 0.03, respectively). Regarding vasomotor symptoms, a greater consumption of poultry was associated with worse symptomatology (β: 0.18, P = 0.02), and soy milk consumption was associated with fewer vasomotor symptoms (β: -0.15, P = 0.04). In addition, women with numerous or severe vasomotor symptoms showed a greater consumption of skimmed dairy products (P < 0.05).Conclusions: This study seems to indicate that some women with mild menopausal symptoms may derive benefit from lower consumption of poultry and skimmed dairy products and a greater consumption of vegetables and soy milk.

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Association between waist-hip ratio and coronary artery calcification in postmenopausal women

Youngmi Eun 1 , Su Nam Lee 2 , Jin Jung 2 , Min Sik Kim 2 , Keon-Woong Moon 2 , Ki-Dong Yoo 2

Objective: Many studies have reported that body composition might be associated with cardiovascular disease, but the issue has not been fully investigated in postmenopausal women.Methods: This retrospect ive study comprised 582 postmenopausal women without a history of cardiovascular disease who visited the Health Promotion Center between May 2008 and February 2018. All women were screened for body fat composition by bioelectrical impedance analysis and for degree of coronary artery calcification (CAC) by multidetector computed tomography. In addition, multivariate analysis, integrated discrimination improvement, and category-free net reclassification improvement were performed. Results: The level of triglycerides, and the waist-hip ratio (WHR) in participants with CAC (coronary artery calcium score [CACS] > 0) were higher than in participants with a CACS of zero points. When the participants were stratified into four groups according to WHR, participants with CAC (CACS > 0) increased significantly as WHR quartile increased. A multivariate analysis showed that older age (odds ratio [OR]: 2.539; 95% confidence interval [CI]: 1.524-4.230; P < 0.001), triglyceride level (OR: 1.005; 95% CI: 1.002-1.008; P = 0.003), WHR (OR: 1.103; 95% CI: 1.018-1.195; P = 0.017), and history of hypertension (OR: 2.701; 95% CI: 1.715-4.253; P < 0.001) were significantly associated with CAC. The Brier score upon adding WHR to a clinical model was lower than that of the clinical model without WHR. Adding WHR to a clinical model better predicted CAC than a clinical model without WHR (C index: 0.761, 95% CI: 0.724-0.795, P < 0.001; net reclassification improvement: 0.195, P = 0.037; integrated discrimination improvement: 1.02%, P = 0.043). Conclusions: In asymptomatic postmenopausal women, WHR as measured by bioelectrical impedance analysis was significantly associated with coronary atherosclerosis, supplementing information of usual clinical markers. Hence, WHR might be appropriate as a marker for early atherosclerosis.

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Prevalence of ocular surface disease symptoms in peri- and postmenopausal women

Pascual Garcia-Alfaro 1 , Luciana Bergamaschi, Celia Marcos, Sandra Garcia, Ignacio Rodríguez

Objective: The objective of the study was to determine the prevalence of ocular surface disease (OSD) symptoms and the possible existence of differences between peri- and postmenopausal women, based on the result of the Ocular Surface Disease Index (OSDI). Methods: A transversal observational study based on the results of an e-mail survey between October 2018 and January 2019 involving 1,947 women. The study was performed on a group of peri- and

postmenopausal women aged between 45 and 79 years. The personal data in the survey included age, menopause status, age at menopause, prediagnosis of dry eye, undergoing dry eye treatment, and the OSDI questionnaire. Student's t test and Chi squared test were used to compare means or percentages between results on the survey and peri- and postmenopausal women. Finally, a univariate logistic regression was carried out to estimate the prevalence of OSD. The OSDI score is assessed on a scale of 0 to 100. Results: The mean age of the entire sample was 54.2 ± 6.8 years, with a mean age at menopause of 49.45 ± 4.02 years. The mean OSDI score was 29.2 ± 19.4, considered as moderate dry eye. The global prevalence of OSD symptoms was 64% (1,247/1,947), which increased significantly in postmenopausal women, being 66.8% (820/1,228) (P = 0.001). The probability of OSD symptoms prevalence increases with age (odds ratio: 1.02; 95% CI [1.01-1.03]). The greater the age at menopause, the lower the probability of OSD symptoms prevalence (odds ratio: 0.96 95% CI [0.93-0.99]). Conclusions: Sixty-four percent of the pre- and postmenopausal women studied had OSD symptoms. There was a correlation between OSD symptoms and age, postmenopause, and earlier age at menopause, which was associated with an increased prevalence.

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Fundamental Concepts and Novel Aspects of Polycystic Ovarian Syndrome: Expert Consensus Resolutions

Antonio Aversa 1 , Sandro La Vignera 2 , Rocco Rago 3 , Alessandra Gambineri 4 , Rossella E Nappi 5 , et al.

Polycystic ovary syndrome (PCOS) is a very common endocrine and metabolic disorder with the involvement of both genetic and environmental factors. Although much has been clarified on its pathogenesis, diagnosis, clinical manifestations, and therapy, there are still areas of uncertainty. To address fundamental concepts, novel aspects and hypotheses, and future perspectives, including the possible additional benefits of treatment with nutraceuticals, an expert consensus panel formed by endocrinologists and gynecologists was established. After an independent review of the literature, the panel convened electronically on February 3, 2020, and six resolutions were created, debated, and agreed upon discussion, and finally approved in their final form in a consensus livestream meeting held on April 15. The summary of the resolutions are: (1) PCOS is a well-established medical condition that negatively affects reproduction, general health, sexual health, and quality of life; (2) the symptoms and signs of PCOS appear early in life especially in female newborns from PCOS carriers; (3) women with PCOS have significantly increased risk of pregnancy-related complications including gestational diabetes mellitus; (4) a male PCOS equivalent exists, and it may impact on metabolic health and probably on reproduction; (5) the evidence supports that medical therapy for PCOS is effective, rational, and evidence-based; (6) the evidence supports a major research initiative to explore possible benefits of nutraceutical therapy for PCOS. The proposed resolutions may be regarded as points of agreement based on the current scientific evidence available.

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Roux-en-Y gastric bypass and gastric sleeve surgery result in long term bone loss

Malgorzata M Brzozowska 1 2 3 , Thach Tran 1 3 , Dana Bliuc 1 3 , John Jorgensen 4 , Michael Talbot et al.

Objectives: Little is known about the long-term skeletal impact of bariatric procedures, particularly the increasingly commonly performed gastric sleeve surgery (GS). We examined bone density (BMD) change following three types of bariatric surgery Roux-en-Y gastric bypass (RYGB), GS and laparoscopic adjustable gastric banding (LAGB), compared with diet, over 36 months. Methods: Non-randomized, prospective study of participants with severe obesity (n = 52), undergoing weight-loss interventions: RYGB (n = 7), GS (n = 21), LAGB (n = 11) and diet (n = 13). Measurements of calciotropic indices, gut hormones (fasting and post prandial) peptide YY (PYY), glucagon-like peptide 1 (GLP1) and adiponectin together with dual-X-ray absorptiometry and quantitative computed tomography scans were performed thorough the study. Results: All groups lost weight during the first 12 months. Despite weight stability from 12 to 36 months and supplementation of calcium and vitamin D, there was progressive bone loss at the total hip (TH) over 36 months in RYGB -14% (95% CI: -12, -17) and GS -9% (95% CI: -7, -10). In RYGB forearm BMD also declined over 36 months -9% (95% CI: -6, -12) and LS BMD declined over the first 12 months -7% (95% CI: -3, -12). RYGB and GS groups experienced significantly greater bone loss until 36 months than LAGB and diet groups, which experienced no significant BMD loss. These bone losses remained significant after adjustment for weight loss and age. RYGB and GS procedures resulted in elevated postprandial PYY, adiponectin and bone turnover markers up to 36 months without such changes among LAGB and diet participants. Conclusions: RYGB and GS but

not LAGB resulted in ongoing TH bone loss for three postoperative years. For RYGB, bone loss was also observed at LS and non-weight-bearing forearms. These BMD changes were independent of weight and age differences. We, therefore, recommend close monitoring of bone health following RYGB and GS surgeries.

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Relation of Obesity with Breast Cancer among the Patients Attending at National Institute of Cancer Research & Hospital

M Asaduzzaman 1 , I A Zannat, P S Akhtar, A Shahi, F Sarker, M R Islam, S M Ahmed, S S Shakil

Breast cancer among women is gradually increasing in Bangladesh day by day. A number of breast cancer related etiological factors identified as age, reproductive factors, menarche, menopausal status, life style, hormone replacement therapy, genetics and alcohol intake. Obesity is an important factor for developing breast cancer in different countries. Obesity is one of the modifiable factors. The aim of the study was to find out the factors which might be associated with obesity among female breast cancer patients in Bangladesh. It was a case-control study conducted at the Department of Medical Oncology, National Institute of Cancer Research & Hospital (NICRH), Dhaka, Bangladesh from August 2014 to July 2015. Ninety one case and equal numbers of age matched controls were included in the study. The mean age of the case was 42.99 (±9.24) years and that of the control was 44.11±8.97 years. Majority of patients i.e. 59.3% (n=54) in case group was in pre-menopausal state where as 52.7% (n=48) of respondents in control group were in menopausal state. Increased waist to hip ratio (>0.85) was associated with increased risk of breast cancer (OR: 8.1). This was also true for increased BMI of ≥25kg/m² (OR: 4.57), increased waist circumference (OR: 3.52) and ever OCP use (OR: 2.11). However, para >3, education and moderate to heavy work were found to be protective against breast cancer (OR: <1). In clinical setting waist-to-hip ratio, body mass index (BMI) and waist circumference (WC) can be used effectively to identify women with an increased risk of breast cancer.

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Breast effects of oral, combined 17β-estradiol, and progesterone capsules in menopausal women: a randomized controlled trial

James H Liu 1 , Denise R Black 2 , Lisa Larkin 3 , Shelli Graham 4 , Brian Bernick 4 , Sebastian Mirkin 4

Objective: To evaluate the effect of a single-capsule, bioidentical 17β-estradiol (E2) and progesterone (P4) hormone therapy on mammograms and breasts in postmenopausal women after 1 year of use. Methods: In the 12-month, phase 3, randomized, double-blind, placebo-controlled, multicenter REPLENISH trial, postmenopausal women (40-65 y) with moderate to severe vasomotor symptoms and a uterus were randomized to four active daily dose groups of E2/P4 (TX-001HR) or a placebo group. Mammograms were performed and read locally at screening (or ≤6 months before first dose) and at study end using BI-RADS classification. Incidence of abnormal mammograms and breast adverse events was evaluated. Results: All but 8 (0.4%) mammograms at screening were normal (BI-RADS 1 or 2). At 1 year, 39 (2.9%) of the 1,340 study-end mammograms were abnormal (BI-RADS 3 or 4); incidence was 1.7% to3.7% with active doses and 3.1% with placebo. Breast cancer incidence was 0.36% with active doses and 0% with placebo. Breast tenderness was reported at frequencies of 2.4% to 10.8% with active doses versus 0.7% with placebo, and led to eight study discontinuations (1.6% of discontinuations in active groups). Conclusions: In this phase 3 trial of a combined E2/P4, results of secondary outcomes suggest that E2/P4 may not be associated with increased risk of abnormal mammograms versus placebo, and the incidence of breast tenderness was low relative to most of the rates reported in other studies using hormone therapy.