Selección de Resúmenes de Menopausia

Semana del 3 al 9 de Abril de 2019

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Two-thirds of all fractures are not attributable to osteoporosis and advancing age: implication for fracture prevention.

Mai HT, Tran TS, Ho-Le TP, Center JR, Eisman JA, Nguyen TV.

CONTEXT: Although bone mineral density (BMD) is strongly associated with fracture and post-fracture mortality, the burden of fractures attributable to low BMD has not been investigated. OBJECTIVES: We sought to estimate the population attributable fraction (PAF) of fractures and fracture-related mortality that can be attributed to low BMD. DESIGN AND SETTING: This study is a part of an ongoing population-based prospective cohort study, Dubbo Osteoporosis Epidemiology study. In total, 3700 participants aged from 50 years and older had participated in the study. Low-trauma fracture was ascertained by X-ray reports, and mortality was ascertain from the Birth, Death and Marriage Registry. RESULTS: Overall, 21% of women and 11% of men had osteoporotic BMD. In univariable analysis, 21% and 16% of total fractures in women and men, respectively, were attributable to osteoporosis. Osteoporosis combined with advancing age (>70 yrs) accounted for 34% and 35% of fractures in women and men, respectively. However, these two factors accounted for ~60% of hip fractures. About 99% and 66% of postfracture mortality in women and men, respectively, were attributable to advancing age, osteoporosis and fracture; however, most of the attributable proportion was accounted for advancing age. CONCLUSIONS: A substantial health care burden of fracture is on individuals aged <70 years and/or non-osteoporosis, suggesting that treatment of individuals with osteoporosis is unlikely to reduce a large number of fractures in the general population.

J Gerontol A Biol Sci Med Sci. 2019 Feb 14. pii: glz041. doi: 10.1093/gerona/glz041. [Epub ahead of print]

Three Doses of Vitamin D and Cognitive Outcomes in Older Women: A Double-Blind Randomized Controlled Trial.

Castle M, Fiedler N, Pop LC, Schneider SJ, Schlussel Y, Sukumar D, Hao L, Shapses SA.

Vitamin D may affect cognitive performance, but previous studies are either short term or observational. We conducted a randomized controlled trial of vitamin D supplementation on domain-specific cognitive measures in postmenopausal women. Overweight/obese women with serum 25-hydroxyvitamin D (25OHD) levels less than 30 ng/mL were recruited. Vitamin D3 supplementation (600, 2,000, or 4,000 IU/d) was randomly assigned in a double-blinded manner for 1 year. Serum 25-hydroxyvitamin D, osteocalcin (total and undercarboxylated), amyloid beta, parathyroid hormone, and estradiol were analyzed before and after supplementation. Cognitive tests were administered after treatment. The women (58 ± 6 years; body mass index, 30.0 ± 3.5 kg/m2) had a baseline serum 25-hydroxyvitamin D level of 22.6 ± 5.8 ng/mL that increased to 30.2 ± 5.6, 36.0 ± 4.9, and 40.8 ± 7.0 ng/mL in the 600, 2,000, and 4,000 IU/d groups, respectively ($p < .001$). Participants taking 2,000 IU/d compared to other doses performed better in learning and memory tests ($p < .05$), yet the 4,000 IU/d group had a slower reaction time compared to the 600 IU/d group. Multiple regression indicated that serum undercarboxylated osteocalcin predicted tasks associated with reaction time and executive function, whereas body mass index and parathyroid hormone negatively predicted reaction time and executive function ($p \leq .01$). These data suggest that vitamin D has differential effects on domain-specific cognitive measures and that a higher dose may negatively affect reaction time.

Int J Epidemiol. 2019 Mar 3. pii: dyz053. doi: 10.1093/ije/dyz053. [Epub ahead of print]

The triglyceride-glucose index as a measure of insulin resistance and risk of obesity-related cancers.

Fritz J, Bjørge T, Nagel G, Manjer J, Engeland A, Häggström C, Concin H, Teleka S, Tretli S, Gylling B, et al.

BACKGROUND: The role of insulin resistance as a mediator in the association of body mass index (BMI) with site-specific cancer risk has, to our knowledge, never been systematically quantified. METHODS: Altogether 510 471 individuals from six European cohorts, with a mean age of 43.1 years, were included. We used the triglyceride glucose product (TyG index) as a surrogate measure for insulin resistance. We fitted Cox models, adjusted for

relevant confounders, to investigate associations of TyG index with 10 common obesity-related cancers, and quantified the proportion of the effect of BMI mediated through TyG index on the log-transformed hazard ratio (HR) scale. RESULTS: During a median follow-up of 17.2 years, 16 052 individuals developed obesity-related cancers. TyG index was associated with the risk of cancers of the kidney HR per one standard deviation increase 1.13, 95% confidence interval: 1.07 to 1.20], liver (1.13, 1.04 to 1.23), pancreas (1.12, 1.06 to 1.19), colon (1.07, 1.03 to 1.10) and rectum (1.09, 1.04 to 1.14). Substantial proportions of the effect of BMI were mediated by TyG index for cancers of the pancreas (42%), rectum (34%) and colon (20%); smaller proportions for kidney (15%) and liver (11%). Little or no mediation was observed for breast (postmenopausal), endometrial and ovarian cancer. Results were similar for males and females, except for pancreatic cancer where the proportions mediated were 20% and 91%, respectively. CONCLUSIONS: The TyG index was associated with increased risk of cancers of the digestive system and substantially mediated the effect of BMI, suggesting that insulin resistance plays a promoting role in the pathogenesis of gastrointestinal cancers.

Cancer Causes Control. 2019 Apr 2. doi: 10.1007/s10552-019-01164-4. [Epub ahead of print]

Diabetes, obesity, and subsequent risk of postmenopausal breast cancer among white and black women in the Southern Community Cohort Study.

Sanderson M, Lipworth L, Shrubsole MJ, Andersen SW, Shu XO, Zheng W, Hargreaves MK, Blot WJ.

PURPOSE: Meta-analyses have reported a small but positive association between diabetes and postmenopausal breast cancer risk, with summary relative risks of approximately 1.15. We analyzed data from the Southern Community Cohort Study (SCCS) following an underserved population with high diabetes prevalence to prospectively examine whether diabetes was associated with subsequent postmenopausal breast cancer risk and whether obesity modified this effect. METHODS: Women with incident breast cancer were identified through linkage with state cancer registries and the National Death Index (213 white, 418 black cases). Person-years were calculated from date of entry into the SCCS until the earliest of date of breast cancer diagnosis, date of death, or date of last follow-up (8,277 white, 16,458 black noncases). Data on diabetes diagnosis were obtained through baseline and follow-up surveys. Cox regression was applied to examine the association between diabetes and postmenopausal breast cancer risk. RESULTS: After adjustment for confounding, there was no association between self-reported diabetes and postmenopausal breast cancer risk among white (hazard ratio [HR] 1.02, 95% confidence interval [CI] 0.75-1.40) or black (HR 1.00, 95% CI 0.81-1.22) women. Nor was there evidence that obesity modified the effect of diabetes on postmenopausal breast cancer in women of either race. CONCLUSIONS: We found no evidence of the hypothesized increased risk of breast cancer among women with diabetes. The breast cancer risks among those with diabetes in this population suggest that the association between these two illnesses is complex.

Menopause. 2019 Apr 1. doi: 10.1097/GME.0000000000001326. [Epub ahead of print]

The Kronos Early Estrogen Prevention Study (KEEPS): what have we learned?

Miller VM, Naftolin F, Asthana S, Black DM, Brinton EA, Budoff MJ, Cedars M7, Dowling NM, et al.

OBJECTIVE: The Kronos Early Estrogen Prevention Study (KEEPS) was designed to address gaps in understanding the effects of timely menopausal hormone treatments (HT) on cardiovascular health and other effects of menopause after the premature termination of the Women's Health Initiative. METHOD: The KEEPS was a randomized, double-blinded, placebo-controlled trial to test the hypothesis that initiation of HT (oral conjugated equine estrogens [o-CEE] or transdermal 17β-estradiol [t-E2]) in healthy, recently postmenopausal women (n=727) would slow the progression of atherosclerosis as measured by changes in carotid artery intima-media thickness (CIMT). RESULTS: After 4 years, neither HT affected the rate of increase in CIMT. There was a trend for reduced accumulation of coronary artery calcium with o-CEE. There were no severe adverse effects, including venous thrombosis. Several ancillary studies demonstrated a positive effect on mood with o-CEE, and reduced hot flashes, improved sleep, and maintenance of bone mineral density with both treatments. Sexual function improved with t-E2. There were no significant effects of either treatment on cognition, breast pain, or skin wrinkling. Variants of genes associated with estrogen metabolism influenced the age of menopause and variability in effects of the HT on CIMT. Platelet activation associated with the development of white matter hyperintensities in the brain. CONCLUSIONS: KEEPS and its ancillary studies have supported the value and safety of the use of HT in recently postmenopausal women and

provide a perspective for future research to optimize HT and health of postmenopausal women. The KEEPS continuation study continues to pursue these issues.

Fertil Steril. 2019 Apr;111(4):780-786. doi: 10.1016/j.fertnstert.2018.12.017.

Effect of aging, menopause, and age at natural menopause on the trend in body mass index: a 15-year population-based cohort.

Montazeri SA, Ramezani Tehrani F, Bidhendi Yarandi R, Erfani H, Mansournia MA, Azizi 6.

OBJECTIVE: To observe the effects of menopause, age at natural menopause (ANM), and aging on the trend in body mass index (BMI). DESIGN: Prospective cohort with a 15-year follow-up of 929 women. Data obtained from the Tehran Lipid and Glucose Study. SETTING: Not applicable. INTERVENTION(S): none. PARTICIPANT(S): Of women participating in the Tehran Lipid and Glucose Study, 929 who were reproductive during the study and menopaused at the last follow-up were included. Anthropometric data were measured repeatedly every 3 years, and the trend in BMI, associated with menopause and ANM, was tested using the generalized estimating equation. MAIN OUTCOME MEASURE(S): Body mass index in each follow-up session. RESULT(S): The adjusted model of the generalized estimating equation illustrates that BMI increases by age (β = 0.16) and menopausal status (β = 1.11). It also shows that women with higher ANM experienced a decreasing BMI (β = -0.03) compared with women with lower ANM. The interaction term of menopause and time (menopause × time) has a negative effect on BMI; that is, the usual increase in BMI after menopause is attenuated by time. (β = -0.4, 95% confidence interval -0.6, -0.3). CONCLUSION(S): Menopause and aging are independently correlated with increasing BMI. The trend in BMI, however, depends on the ANM of study participants: women with higher ANM than mean ANM of our population (i.e., 49 years) face a decreasing BMI compared with those with lower ANM.

Psychoneuroendocrinology. 2019 Mar 19;106:9-19. doi: 10.1016/j.psyneuen.2019.03.013. [Epub ahead of print]

Surgical menopause in association with cognitive function and risk of dementia: A systematic review and meta-analysis.

Georgakis MK, Beskou-Kontou T, Theodoridis I, Skalkidou A, Petridou ET.

INTRODUCTION: Experimental and epidemiological studies suggest female sex hormones to have long-lasting neuroprotective and anti-ageing properties. Surgically-induced menopause leads to a premature cessation of exposure to female sex hormones and could thus impact late-life cognitive function. Yet, evidence remains controversial. METHODS: We systematically reviewed literature for articles investigating the association of surgical menopause (defined as bilateral oophorectomy before the onset of menopause) with risk of dementia, cognitive performance, cognitive decline, and Alzheimer's disease neuropathological indices later in life. We evaluated study quality with the Newcastle-Ottawa scale and performed random-effects meta-analyses. RESULTS: We identified 11 eligible studies (N = 18,867). Although surgical menopause at any age was not associated with risk of dementia (4 studies; HR: 1.16, 95%CI: 0.96-1.43), early surgical menopause (≤45 years of age) was associated with a statistically significantly higher risk (2 studies; HR: 1.70, 95%CI: 1.07-2.69). Surgical menopause at any age was associated with faster decline in verbal memory, semantic memory, and processing speed, whereas early surgical menopause was further associated with faster global cognitive decline. No heterogeneity was noted. Among women undergoing surgical menopause, a younger age at surgery was associated with faster decline in global cognition, semantic and episodic memory, worse performance in verbal fluency and executive function, and accumulation of Alzheimer's neuropathology. CONCLUSIONS: Current evidence is limited, but suggests surgical menopause induced by bilateral oophorectomy at ≤45 years of age to be associated with higher risk of dementia and cognitive decline. Additional large-scale cohort studies are necessary to replicate these findings.