Selección de Resúmenes de Menopausia

Semana del 22 al 28 de Febrero de 2017

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Eur J Cancer. 2017 Feb 28;75:299-307. doi: 10.1016/j.ejca.2017.01.014. [Epub ahead of print]

DNA methylome analysis identifies accelerated epigenetic ageing associated with postmenopausal breast cancer susceptibility.

Ambatipudi S, Horvath S, Perrier F, Cuenin C, Hernandez-Vargas H, Le Calvez-Kelm F, Durand G, et al.

AIM OF THE STUDY: A vast majority of human malignancies are associated with ageing, and age is a strong predictor of cancer risk. Recently, DNA methylation-based marker of ageing, known as 'epigenetic clock', has been linked with cancer risk factors. This study aimed to evaluate whether the epigenetic clock is associated with breast cancer risk susceptibility and to identify potential epigenetics-based biomarkers for risk stratification. METHODS: Here, we profiled DNA methylation changes in a nested case-control study embedded in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort (n = 960) using the Illumina HumanMethylation 450K BeadChip arrays and used the Horvath age estimation method to calculate epigenetic age for these samples. Intrinsic epigenetic age acceleration (IEAA) was estimated as the residuals by regressing epigenetic age on chronological age. RESULTS: We observed an association between IEAA and breast cancer risk (OR, 1.04; 95% CI, 1.007-1.076, P = 0.016). One unit increase in IEAA was associated with a 4% increased odds of developing breast cancer (OR, 1.04; 95% CI, 1.007-1.076). Stratified analysis based on menopausal status revealed that IEAA was associated with development of postmenopausal breast cancers (OR, 1.07; 95% CI, 1.020-1.11, P = 0.003). In addition, methylome-wide analyses revealed that a higher mean DNA methylation at cytosine-phosphate-guanine (CpG) islands was associated with increased risk of breast cancer development (OR per 1 SD = 1.20; 95 %CI: 1.03-1.40, P = 0.02) whereas mean methylation levels at non-island CpGs were indistinguishable between cancer cases and controls. CONCLUSION: Epigenetic age acceleration and CpG island methylation have a weak, but statistically significant, association with breast cancer susceptibility.

J Orthop Sci. 2017 Feb 28. pii: S0949-2658(17)30031-3. doi: 10.1016/j.jos.2017.02.001. [Epub ahead of print]

Alendronate inhibits hyperalgesia and suppresses neuropeptide markers of pain in a mouse model of osteoporosis.

Naito Y, Wakabayashi H, Kato S, Nakagawa T, Iino T, Sudo A.

BACKGROUND: Chronic back pain is one of the most important complications of postmenopausal osteoporosis. The aim of this study was to evaluate skeletal pain associated with osteoporosis and to examine the inhibitory effect of bisphosphonates (BPs) on pain in ovariectomized (OVX) mice. The mechanism of osteoporotic pain in OVX mice was evaluated through an examination of pain-related behavior, as well as immunohistochemical findings. In addition, the effects of alendronate (ALN), a potent osteoclast inhibitor, on these parameters were assessed. METHODS: 8-week-old female ddY mice were ovariectomized and assigned to 3 groups: SHAM-operated mice treated with vehicle (SHAM; n = 8); OVX mice treated with vehicle (OVX-V; n = 8); and OVX mice treated with ALN (OVX-ALN; n = 8). Starting immediately after surgery, vehicle or 40 μg/kg ALN was injected subcutaneously twice a week for 4 weeks. The bilateral distal femoral metaphyses and proximal tibial metaphyses were analyzed three-dimensionally by μCT. Mechanical sensitivity was tested using von Frey filaments. Transient receptor potential channel vanilloid 1 (TRPV1) and calcitonin gene-related peptide (CGRP) expressions in L3-5 dorsal root ganglion (DRG) neurons were examined immunohistochemically. RESULTS: Ovariectomy induced bone loss and mechanical hyperalgesia in hindlimbs with upregulation of TRPV1 and CGRP expressions in DRG neurons innervating hindlimbs. ALN prevented bone loss and mechanical hyperalgesia in ovariectomized mouse hindlimbs, and it suppressed upregulation of pain markers.

Eur J Ophthalmol. 2003 May;13(4):337-342. doi: 10.5301/EJO.2008.4330.

Tear function tests and conjunctival impression cytology before and after hormone replacement therapy in postmenopausal women.

Pelit A, Bagis T, Kayaseluk F, Dursun D, Akova YA, Aydin P.

PURPOSE: To investigate the effect of hormone replacement therapy (HRT) on postmenopausal tear function and the conjunctival epithelium. METHODS: Schirmer I-Jones test, tear film break-up time (BUT), and impression cytology findings were analyzed in 34 eyes of 17 women who were at least two years postmenopausal and not taking HRT. This series of tests was repeated after three months on HRT. RESULTS: The patients average age was 53.82 3.6 years, and the mean time postmenopause was 35.29 11.59 months. There was no significant difference in the Schirmer I-Jones test results before and after three months of HRT ($p > 0.05$). However, the BUT ($p < 0.05$) and impression cytology ($p < 0.05$) findings were significantly affected by HRT. CONCLUSIONS: HRT may alleviate postmenopausal dry eye symptoms by increasing goblet cell density.

J Nutr. 2017 Mar 1. pii: jn240390. doi: 10.3945/jn.116.240390. [Epub ahead of print]

Dairy Intake Is Protective against Bone Loss in Older Vitamin D Supplement Users: The Framingham Study.

Sahni S, Mangano KM, Kiel DP, Tucker KL, Hannan MT.

Background: Previous studies showed beneficial effects of specific dairy foods on bone health in middle-aged adults.Objective: We examined the association of milk, yogurt, cheese, cream, fluid dairy (milk + yogurt), and milk + yogurt + cheese intakes with bone mineral density (BMD) and 4-y percentage of change in BMD [▵%BMD; femoral neck, trochanter, and lumbar spine (LS)]. We further assessed whether these associations were modified by vitamin D supplement use in this cohort of older adults. Methods: Food-frequency questionnaire responses, baseline BMD (hip and spine, n = 862 in 1988-1989), and follow-up BMD (n = 628 in 1992-1993) were measured in the Framingham study, a prospective cohort study of older Caucasian men and women aged 67-93 y. Outcomes included baseline BMD and ▵%BMD. Dairy-food intakes (servings per week) were converted to energy-adjusted residuals, and linear regression was used, adjusting for covariates. These associations were further examined by vitamin D supplement use. Results: The mean age of the participants was 75 y. In the full sample, dairy-food items were not associated with BMD (P = 0.11-0.99) or with ▵%BMD (P = 0.29-0.96). Among vitamin D supplement users, but not among nonusers, higher milk, fluid dairy, and milk + yogurt + cheese intakes were associated with higher LS BMD (P = 0.011-0.009). Among vitamin D supplement users, but not among nonusers, higher milk + yogurt + cheese intakes were protective against trochanter BMD loss (P = 0.009). Conclusions: In this population of older adults, higher intakes of milk, fluid dairy, and milk + yogurt + cheese were associated with higher LS BMD, and a higher intake of milk + yogurt + cheese was protective against trochanter BMD loss among vitamin D supplement users but not among nonusers. These findings underscore that the benefits of dairy intake on the skeleton may be dependent on vitamin D intake.

J Frailty Aging. 2017;6(1):18-23. doi: 10.14283/jfa.2016.111.

Prevalence of Concomitant Bone and Muscle Wasting in Elderly Women from the SarcoPhAge Cohort: Preliminary Results.

Locquet M, Beaudart C, Reginster JY, Petermans J, Gillain S, Quabron A, Slomian J, Buckinx F, Bruyère O.

BACKGROUND: Recent studies suggest that bone and muscle wasting are closely interconnected. OBJECTIVE: The aim was of this study is to assess the prevalence of osteoporosis in a population of women diagnosed with sarcopenia. Participants, setting and design: We analyzed cross-sectional data of women, aged 65 years and above, for whom bone mineral density was available at the time of inclusion in the SarcoPhAge (Sarcopenia and Physical impairment with advancing Age) cohort, an ongoing prospective study with the aim to assess consequences of sarcopenia. MEASUREMENTS: Muscle strength was evaluated with a hydraulic hand-dynamometer, appendicular lean mass and bone mineral density by Dual-Energy X-Ray Absorptiometry and physical performance by the Short Physical Performance Battery test (SPPB). Sarcopenia was diagnosed according to the European Working Group on Sarcopenia in Older People definition, i.e. a low muscle mass plus either low muscle strength or low physical performance. A bone mineral density T-score equal to or below -2.5SD at the lumbar spine, at the total hip or at the femoral neck was used to define osteoporosis (World Health Organization definition). RESULTS: A total of 126 women aged 74.38±6.32 years were included. Among them, 26 were assessed with sarcopenia (20.6%) and 34 (27.0%) with osteoporosis. There were more osteoporotic women among sarcopenic subjects (46.1%) than among non-sarcopenic subjects (22.0%) (p-value=0.011). A significant lower appendicular lean mass index was observed in osteoporotic women (p-value=0.025). We also observed, in osteoporotic subjects, a lower muscle strength (p-

value=0.023). Numerical values of bone mineral density were lower in the sarcopenic population but the differences did not reach the level of statistical significance. CONCLUSION: Our study demonstrated that muscle mass and strength are lower in patients with osteoporosis. Prospective changes in bone and muscle mass will be investigated during the follow-up of our cohort.

Osteoporos Int. 2017 Feb 27. doi: 10.1007/s00198-017-3967-6. [Epub ahead of print]

Total 25-hydroxyvitamin D levels predict fracture risk: results from the 15-year follow-up of the Japanese Population-based Osteoporosis (JPOS) Cohort Study.

Tamaki J, Iki M, Sato Y, Kajita E, Nishino H, Akiba T, Matsumoto T, Kagamimori S; JPOS Study Group.

INTRODUCTION: We examined whether total 25-hydroxyvitamin D (25[OH]D) levels are associated with fracture risk over 15 years in a Japanese female cohort. METHODS: Of 1437 community-dwelling women aged ≥50 years in the baseline survey, 1236 provided information regarding fractures during a 15-year follow-up period. The analysis included 1211 women without early menopause or diseases affecting bone metabolism. RESULTS: Over 15 years, 269 clinical (224 non-vertebral, 149 fragility) fracture events were confirmed. Incidence rates categorized by 25(OH)D levels (<10, 10-20, 20-30, and ≥30 ng/mL) indicated a significant divergence for any clinical fractures in 5 years (log rank test p = 0.016) and for non-vertebral fractures in 5, 10, and 15 years (p < 0.001, p = 0.001, p = 0.017, respectively). Hazard ratios (HRs) for 25(OH)D levels <10 and 10-20 ng/mL compared to levels ≥30 ng/mL during 5 years indicated significances for clinical fractures (HR 4.93 with p = 0.009, HR 3.00 with p = 0.034) and for non-vertebral fractures (HR 6.55 with p = 0.005, HR 3.49 with p = 0.036). Those with levels <20 ng/mL compared to those with levels ≥20 ng/mL indicated significant increased risks for clinical fractures (HR 1.72 with p = 0.010), non-vertebral fractures (HR 2.45 with p < 0.001), and fragility fractures (HR 2.00 with p = 0.032) in 5 years. The HR of non-vertebral fractures for levels <20 ng/mL remained significant during 15 years (HR 1.42 with p = 0.012) after adjustment for age and femoral neck bone mineral density. CONCLUSIONS: Low 25(OH)D levels, especially <20 ng/mL, were associated with elevated fracture risks in Japanese women.

JCI Insight. 2017 Feb 23;2(4):e89703. doi: 10.1172/jci.insight.89703.

Estrogens regulate glycosylation of IgG in women and men.

Ercan A, Kohrt WM, Cui J, Deane KD, Pezer M, Yu EW, Hausmann JS, Campbell H, Kaiser UB, Rudd PM0, et al.

The immunologic potency of IgG is modulated by glycosylation, but mechanisms regulating this process are undefined. A role for sex hormones is suggested by differences in IgG glycans between women and men, most prominently with respect to galactose. We therefore assessed IgG galactosylation in 713 healthy adults from 2 cohorts as well as in 159 subjects from 4 randomized controlled studies of endocrine manipulation: postmenopausal women receiving conjugated estrogens, raloxifene, or placebo; premenopausal women deprived of gonadal hormones with leuprolide and treated with estradiol or placebo; men deprived of gonadal hormones with goserelin and given testosterone or placebo; and men deprived of gonadal hormones with goserelin and given testosterone or placebo together with anastrozole to block conversion of testosterone to estradiol. Menopause was associated with an increase in agalactosylated IgG glycans, particularly in the most abundant fucosylated nonbisected (G0F) glycoform. Conjugated estrogens and raloxifene reduced G0F glycans in postmenopausal women, while in premenopausal women leuprolide increased G0F glycans in a manner reversed by estradiol. Among men, goserelin increased G0F glycans, an effect blocked by testosterone through conversion to estradiol. These results establish estrogens as an in vivo modulator of IgG galactosylation in both women and men, defining a pathway by which sex modulates immunity.

Acta Obstet Gynecol Scand. 2017 Feb 25. doi: 10.1111/aogs.13120. [Epub ahead of print]

Use of hormone replacement therapy after risk-reducing salpingo-oophorectomy.

Johansen N, Liavaag AH, Iversen OE, Dørum A, Braaten T, Michelsen TM.

INTRODUCTION: After premenopausal risk-reducing salpingo-oophorectomy (RRSO) to prevent ovarian cancer, the non-cancer related morbidity and mortality may be increased if sex hormones are not replaced. Several guidelines recommend systemic hormone replacement therapy (HRT) to these women until the expected age of menopause. We

aimed to study the use of HRT after RRSO MATERIAL AND METHODS: Participants were 324 women after RRSO and 11 160 postmenopausal controls. A subsample of 950 controls had undergone bilateral salpingo-oophorectomy (BSO). All participants completed the same questionnaire regarding HRT use. We compared HRT use in the RRSO group with the BSO controls by use of logistic regression RESULTS: Among the women aged ≤ 52 years without a history of breast cancer, 51.7% of the RRSO group and 48.7% of the BSO controls reported current use of systemic HRT (odds ratio 1.13, 95% confidence interval 0.72, 1.76). Among the HRT users, systemic estrogen was used by 35.1% and 58.7% in the RRSO and BSO control groups, respectively (P = 0.001). Among the women aged > 52 years, 16.8% of the RRSO group and 38.4% of the BSO controls (P < 0.001) used systemic HRT CONCLUSIONS: Among the RRSO women and BSO controls ≤ 52 years without a history of breast cancer, relatively few were current users. If no contraindications, these women would benefit from systemic HRT. Additionally, almost 40% of the BSO controls > 52 years used systemic HRT. Doctors should be aware of this practice, and prescribe systemic HRT when indicated.

Curr Urol Rep. 2017 Mar;18(3):17. doi: 10.1007/s11934-017-0668-9.

Do Calcium Supplements Predispose to Urolithiasis?

Kozyrakis D, Paridis D, Karatzas A, Soukias G, Dailiana Z.

PURPOSE OF REVIEW: The purpose of this study was to investigate the role of calcium supplements, with or without vitamin D, in urinary stone formation in healthy population and in osteoporotic patients as well. Moreover, this review aims to clarify whether or not, and above which dose, they are associated with the risk of lithiasis. RECENT FINDINGS: A research in Medline, Embase, and Scopus databases up to September 2015 was conducted using the following keywords: calcium, supplements, vitamin D, complications, lithiasis, and urinary stone. All types of studies were taken into account (cohort studies, reviews, meta-analyses), and in case they fulfilled the inclusion criteria, they were included in our review. The analysis of the data showed that calcium supplements, probably in association with anti osteoporotic treatment, do not create a predisposition towards lithiasis formation among women suffering from osteoporosis, neither among non-osteoporotic older men. In healthy postmenopausal as well as younger women, the supplements might increase susceptibility to urinary stone formation in long-term basis. The consumption of calcium supplements with the meals could play a protective role in women and younger males. There is certain evidence that supplements containing citrate may be more beneficial over the rest of calcium supplements, particularly when consumed during the meal. Osteoporotic women and healthy men are not at risk of stone formation. On the contrary, healthy women should be aware of the potential risk of developing urinary lithiasis in long-term basis.