Selección de Resúmenes de Menopausia

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Knee loading repairs osteoporotic osteoarthritis by relieving abnormal remodeling of subchondral bone via Wnt/β-catenin signaling.

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Osteoporotic osteoarthritis (OPOA) is a common bone disease mostly in the elderly, but the relationship between Osteoporotic (OP) and osteoarthritis (OA) is complex. It has been shown that knee loading can mitigate OA symptoms. However, its effects on OPOA remain unclear. In this study, we characterized pathological linkage of OP to OA, and evaluated the effect of knee loading on OPOA. We employed two mouse models (OA and OPOA), and conducted histology, cytology, and molecular analyses. In the OA and OPOA groups, articular cartilage was degenerated and Osteoarthritis Research Society International score was increased. Subchondral bone underwent abnormal remodeling, the differentiation of bone marrow mesenchymal stem cells (BMSCs) to osteoblasts and chondrocytes was reduced, and migration and adhesion of pre-osteoclasts were enhanced. Compared to the OA group, the pathological changes of OA in the OPOA group were considerably aggravated. After knee loading, however, cartilage degradation was effectively prevented, and the abnormal remodeling of subchondral bone was significantly inhibited. The differentiation of BMSCs was also improved, and the expression of Wnt/β-catenin was elevated. Collectively, this study demonstrates that osteoporosis aggravates OA symptoms. Knee loading restores OPOA by regulating subchondral bone remodeling, and may provide an effective method for repairing OPOA.

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Effects of Supplemental Vitamin D on Bone Health Outcomes in Women and Men in the VITamin D and OmegA-3 TriaL (VITAL).

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Although supplemental vitamin D is used to promote bone health in the general population, data from randomized controlled trials (RCTs) have been inconsistent. We determined whether daily, vitamin D3 supplementation improves bone mineral density (BMD) and/or structure. VITamin D and OmegA-3 TriaL (VITAL) is a double-blind, placebo-controlled RCT of supplemental vitamin D3 (2,000 IU/day) and/or omega-3 fatty acids (1 g/day) in 25,871 adults nationwide. This ancillary study included a subcohort of 771 participants (men ≥50 and women ≥55 years; not taking bone active medications) evaluated at baseline and 2-years follow-up (89% retention). Total 25(OH)D levels were measured by liquid chromatography tandem mass spectrometry (Quest Diagnostics, CA). Free 25(OH)D (FVD) levels were measured using the ELISA assay by Future Diagnostics Solutions B.V. (Wijchen Netherlands). Primary endpoints were 2-year changes in areal (a)BMD at the spine, hip, and whole body determined by dual-energy X-ray absorptiometry. Secondary endpoints were 2-year changes in volumetric (v)BMD and cortical thickness at the radius and tibia assessed by peripheral quantitative computed tomography. Supplemental vitamin D3 vs. placebo had no effect on 2-year changes in aBMD at the spine (0.33% vs. 0.17%; p = 0.55), femoral neck (-0.27% vs. -0.68%; p = 0.16), total hip (-0.76% vs. -0.95%; p = 0.23), or whole body (-0.22% vs. -0.15%; p = 0.60), or on measures of bone structure. Effects did not vary by sex, race/ethnicity, BMI, or 25(OH)D levels. Among participants with baseline FVD levels below the median (<14.2 pmol/L), there was a slight increase in spine aBMD (0.75% vs. 0%; p = 0.043) and attenuation in loss of total hip aBMD (-0.42% vs. -0.98%; p = 0.044) with vitamin D3 . Whether baseline FVD levels help to identify those more likely to benefit from supplementation warrants further study. Supplemental vitamin D3 vs. placebo for two years in general healthy adults not selected for vitamin D insufficiency did not improve BMD or structure.

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Lung cancer incidence and mortality in relationship to hormone replacement therapy use among women participating in the PLCO trial: a post hoc analysis.

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OBJECTIVE: To evaluate the impact of hormone replacement therapy (HRT) on the incidence and mortality of lung cancer among female participants in the prostate, lung, colorectal, and ovary (PLCO) trial. METHODS: All women participating in the PLCO trial with complete information about HRT exposure were included in the current analysis. All study population were aged 55-74 years without prior history of lung cancer at the time of study enrollment. Multivariate Cox regression analysis was used to evaluate the impact of HRT exposure on lung cancer incidence and mortality. For both end points, the model was adjusted for: age, body mass index, study arm, race, cigarette smoking and family history of lung cancer. RESULTS: A total of 77,911 female participants were included in the current analysis, including 27,663 participants who never used HRT before inclusion into the PLCO trial and 50,248 participants who used some form of HRT before inclusion into the PLCO trial. Prior exposure to HRT seems to be protective against the development of lung cancer in a multivariate analysis (hazard ratio for ever exposure versus never exposure 0.876; 95% CI 0.783-0.981; P = 0.022). Similarly, prior exposure to HRT seems also to be protective against death from lung cancer in a multivariate analysis (hazard ratio for ever exposure versus never exposure 0.814; 0.709-0.934; P = 0.003). Further multivariate Cox regression analysis showed that current HRT usage at the time of PLCO trial entry (and not former HRT usage) seemed to be protective against lung cancer development (hazard ratio for current versus never users 0.842; 0.743-0.954; P = 0.007) and lung cancer-specific mortality (hazard ratio for current versus never users 0.800; 0.686-0.932; P = 0.004). CONCLUSION: HRT use at the time of PLCO trial entry seems to be associated with lower probability of lung cancer development and death. Further studies are needed to elucidate the biological mechanisms behind this observation.

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Physical activity and breast cancer risk: results from the UK Biobank prospective cohort.

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BACKGROUND: Previous studies suggest a protective role of physical activity in breast cancer risk, largely based on self-reported activity. We aimed to clarify this association by examining breast cancer risk in relation to self-reported physical activity, informed by accelerometer-based measures in a large subset of participants. METHODS: We analysed data from 47,456 premenopausal and 126,704 postmenopausal women in UK Biobank followed from 2006 to 2014. Physical activity was self-reported at baseline, and at resurvey in a subsample of 6443 participants. Accelerometer data, measured from 2013 to 2015, were available in 20,785 women. Relative risks (RRs) and 95% confidence intervals (CIs) were calculated by using multivariable-adjusted Cox regression. RESULTS: A total of 3189 cases were diagnosed during follow-up (mean = 5.7 years). Women in the top compared with the bottom quartile of self-reported physical activity had a reduced risk of both premenopausal (RR 0.75; 95% CI 0.60-0.93) and postmenopausal breast cancer (RR 0.87; 95% CI 0.78-0.98), after adjusting for adiposity. In analyses utilising physical activity values assigned from accelerometer measurements, an increase of 5 milli-gravity was associated with a 21% (RR 0.79; 95% CI 0.66-0.95) reduction in premenopausal and a 16% (RR 0.84; 95% CI 0.73-0.96) reduction in postmenopausal breast cancer risk. CONCLUSIONS: Greater physical activity is associated with a reduction in breast cancer risk, which appears to be independent of any association it may have on risk through its effects on adiposity.

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Endometrial safety and bleeding profile of a 17β-estradiol/progesterone oral softgel capsule (TX-001HR).

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OBJECTIVE: The aim of the study was to evaluate the effect of a single-capsule 17β-estradiol/progesterone (E2/P4), TX-001HR, on endometrial safety, to report on amenorrhea and bleeding patterns of users, and to identify predictors of amenorrhea. METHODS: The REPLENISH trial (NCT01942668) evaluated use of TX-001HR in menopausal women (40-65 y) with vasomotor symptoms (VMS) and a uterus. Women were randomized to daily E2/P4 (mg/mg: 1/100, 0.5/100, 0.5/50, or 0.25/50), or placebo for 12 months. Incidence rate of endometrial hyperplasia was calculated from endometrial biopsies conducted at screening and study completion. Women reported bleeding and spotting in daily diaries. The number of bleeding and/or spotting days and the proportion of women with no bleeding or amenorrhea were compared between treatment and placebo using the Fisher exact test. Predictors of cumulative amenorrhea were assessed by univariate analyses. RESULTS:Women (n=1,835) who took at least one study dose comprised the safety

population; 1,255 had baseline and 12-month biopsies and comprised the endometrial safety population. Incidence of endometrial hyperplasia was ≤0.36% with any dose of TX-001HR after 1 year of use (one-sided upper 95% confidence interval ≤4%). Cumulative amenorrhea (no bleeding/spotting) rates increased over time and were relatively high from cycle 1 to 13 with TX-001HR (56%-73%; placebo 79%; P<0.05 except with 0.25/50 dose). Few vaginal bleeding adverse events (1.0%-4.6% TX-001HR vs 0.7% placebo) were reported and discontinuations due to bleeding were low (0.4%-1.4% vs 0%). Cumulative amenorrhea was significantly more frequent in older women, those further from their last menstrual period, and those with lower baseline E2 concentrations (all; P<0.01). CONCLUSIONS: All doses of TX-001HR provided endometrial protection and were associated with an improved bleeding profile over time; older age, further last menstrual period, or lower baseline E2 may predict amenorrhea with TX-001HR.

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Hospital-diagnosed overweight and obesity related to cancer risk: a 40-year Danish cohort study.

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BACKGROUND: Obesity is associated with metabolic abnormalities that predispose patients to increased cancer risk. Contemporary data on the long-term risk of specific cancers are sparse among patients with hospital-diagnosed overweight and obesity. OBJECTIVES: To examine the overall cancer incidence and specific site-related cancer incidences among patients with overweight and obesity, compared to the general Danish population. METHODS: For this 40-year (1977-2016), nationwide, Danish cohort study, we reviewed medical databases to identify individuals with hospital-based overweight and obesity diagnoses. We computed age- and gender-standardized incidence ratios (SIRs) for subsequent cancer compared to the general population. RESULTS: We observed 20 706 cancers among 313 321 patients diagnosed with overweight and obesity (median age 43 years; median follow-up 6.7 years, range 1-40 years) compared to the 18 480 cancers expected; thus, the SIR was 1.12 [95% confidence interval (95% CI): 1.11-1.14]. The SIR associated with overweight and obesity was increased with concomitant comorbidities, like type 2 diabetes (SIR: 1.18; 95% CI: 1.13-1.23) and alcoholism-related diseases (SIR: 1.62; 95% CI: 1.45-1.82). The SIR was 1.31 (95% CI: 1.28-1.34) for cancers previously identified as obesity-related, including pancreatic (SIR: 1.38; 95% CI; 1.27-1.49) and postmenopausal breast cancer (SIR: 1.14; 95% CI: 1.09-1.19). Obesity/overweight status also elevated the SIRs for haematological (SIR: 1.24; 95% CI: 1.18-1.29) and neurological cancers (SIR: 1.19; 95% CI: 1.11-1.27]. In contrast, SIRs were 1.01 (95% CI: 0.97-1.05) for immune-related cancers, 0.88 (95% CI: 0.82-0.95) for malignant melanoma, and 0.88 (95% CI: 0.85-0.92) for hormone-related cancers, other than postmenopausal breast cancer. CONCLUSION: In this large cohort study, overweight and obesity was associated with increased risk of several common cancers.