Selección de Resúmenes de Menopausia

Semana del 3 al 9 de Mayo de 2017

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Energy Metabolism of the Osteoblast: Implications for Osteoporosis.

Lee WC, Guntur AR, Long F, Rosen CJ.

Osteoblasts, the bone forming cells of the remodeling unit, are essential for growth and maintenance of the skeleton. Clinical disorders of substrate availability (e.g. diabetes mellitus, anorexia nervosa and aging) cause osteoblast dysfunction ultimately leading to skeletal fragility and osteoporotic fractures. Conversely, anabolic treatments for osteoporosis enhance the work of the osteoblast by altering osteoblast metabolism. Emerging evidence supports glycolysis as the major metabolic pathway to meet ATP demand during osteoblast differentiation. Glut1 and Glut3 are the principal transporters of glucose in osteoblasts, although Glut 4has also been implicated. Wnt signaling induces osteoblast differentiation and activates glycolysis through mTOR, while PTH stimulates glycolysis through induction of IGF-I. Glutamine is an alternate fuel source for osteogenesis via the TCA cycle, and fatty acids can be metabolized to generate ATP via oxidative phosphorylation although temporal specificity has not been established. More studies with new model systems are needed to fully understand how the osteoblast utilizes fuel substrates in health and disease and how that impacts metabolic bone diseases.

Gynecol Endocrinol. 2017 May 3:1-5. doi: 10.1080/09513590.2017.1320379. [Epub ahead of print]

Higher level of circulating estradiol is associated with lower frequency of cognitive impairment in Southeast China.

Hu J, Chu K, Song Y, Chatooah ND, Ying Q, Ma L, Zhou J, Qu F, Zhou J.

BACKGROUND: Estrogen has been proved to have positive effects on the brain cognitive function. However, many clinical studies investigating the associations between cognitive functions and circulating estrogen levels in perimenopausal and postmenopausal women demonstrated controversial results. METHOD: Circulating estradiol and follicle stimulating hormone (FSH) levels were obtained from 199 perimenopausal and postmenopausal women (mean age: 49.61 years). The cognitive function has been assessed using the Beijing version of the Montreal Cognitive Assessment. RESULTS: Results revealed that higher estradiol levels were associated with better cognitive function ($p < 0.05$) both in perimenopausal and postmenopausal women and levels of FSH were unrelated to cognitive performance. CONCLUSIONS: In perimenopausal and postmenopausal women, higher levels of circulating estradiol are associated with lower risk of cognitive impairment.

J Clin Hypertens (Greenwich). 2017 May 2. doi: 10.1111/jch.13010. [Epub ahead of print]

Calcium supplementation and cardiovascular risk: A rising concern.

Tankeu AT, Ndip Agbor V, Noubiap JJ.

Over the past decade, the number of individuals taking calcium supplementation worldwide has been on the rise, especially with the emergence of new pharmaceutical companies specialized in the marketing of dietary supplements; with calcium supplementation being their main business axis. This is mostly because of the established role of calcium in the prevention and treatment of osteoporosis and, to a lesser extent, its role in the prevention of fractures. Recently, a rising body of evidence on the adverse effect of calcium supplementation on nonskeletal, especially cardiovascular, health has been a cause for concern. In fact, a significant number of studies have reported an association between calcium supplementation and adverse cardiovascular events, even though high dietary calcium intake was shown to have a protective effect. The mechanism by which calcium supplementation could cause a cardiovascular event was still unclear until a recent study published in the Journal of the American Heart Association. Combining this recent finding with available data associating calcium supplementation with cardiovascular mortality and all-cause mortality, we call on the need for an evidence-based approach to calcium supplementation, while stressing on the safety of dietary calcium intake over the former on cardiovascular health.

J Bone Miner Res. 2017 Apr 29. doi: 10.1002/jbmr.3161. [Epub ahead of print]

Leisure-time physical activity and risk of fracture: a cohort study of 66,940 men and women.

Stattin K, Michaëlsson K, Larsson SC, Wolk A, Byberg L.

Physical activity has been associated with reduced risk of fracture, but it is not known how the intensity or frequency of physical activity influences this risk reduction. We aim to compare the risk of hip fracture and fracture of any locale between men and women with different levels of leisure-time walking/bicycling and exercise. A total of 37,238 women (born 1914-1948) from the Swedish Mammography Cohort and 45,906 men (born 1918-1952) from the Cohort of Swedish Men were followed for a maximum of 17 years. Exposure and covariate information was collected through a self-administered questionnaire in 1997. Incident fractures (5,153 individuals with hip fracture and 15,043 with any type of fracture) and comorbidities were gathered from national and local patient registries. Hazard ratios (HRs) were calculated using Cox proportional hazards regression. Individuals who walked/bicycled less than 20 minutes per day had a lower rate of hip fracture (multivariable adjusted HR 0.77; 95% confidence interval [CI], 0.70 to 0.85) and any fracture (HR 0.87; 95% CI, 0.82 to 0.92), compared with those who hardly ever walked/bicycled. These reduced rates were also evident in both sexes, in different age categories, for vertebral fractures and for non-hip non-vertebral fractures. Those who reported exercise one hour per week had a lower rate of hip fracture (HR 0.87; 95% CI, 0.80 to 0.96) and any fracture (HR 0.94; 95% CI, 0.89 to 0.99) compared with those who exercised less than one hour per week. Only minor differences in HRs were observed in individuals with moderate compared to higher levels of walking/bicycling or exercise. Walking/bicycling and exercise showed almost equal reductions in rate of fracture when compared to those in a joint category with lowest activity. In conclusion, both moderate and high self-reported frequency of physical activity is associated with reduced future risk of fracture.

PLoS One. 2017 May 1;12(5):e0176685. doi: 10.1371/journal.pone.0176685. eCollection 2017.

Poor sleep quality and later sleep timing are risk factors for osteopenia and sarcopenia in middle-aged men and women: The NEO study.

Lucassen EA, de Mutsert R, le Cessie S, Appelman-Dijkstra NM, Rosendaal FR, van Heemst D, et al.

CONTEXT: Sleep deprivation has detrimental metabolic consequences. Osteopenia and sarcopenia usually occur together and increase risk of fractures and disease. Results from studies linking sleep parameters to osteopenia or sarcopenia are scarce and inconsistent. OBJECTIVE: To examine the associations of sleep parameters with osteopenia and sarcopenia, considering the influence of sex and menopause. DESIGN, SETTING AND PARTICIPANTS: Cross-sectional analysis of 915 participants (45-65 years, 56% women, BMI 26 (range: 18-56) kg/m2) in the Netherlands Epidemiology of Obesity (NEO) study, a population-based cohort study. Sleep duration, quality, and timing were assessed with the Pittsburgh Sleep Quality Index (PSQI); bone mineral density and relative appendicular muscle mass were measured by DXA scans. Linear and logistic regressions were performed to associate sleep parameters to bone mineral density, relative appendicular muscle mass, osteopenia (t-score between -1 and -2.5) and sarcopenia (1 SD below average muscle mass). RESULTS: After adjustment for confounding factors, one unit increase in PSQI score (OR and 95% CI, 1.09, 1.03-1.14), declined self-rated sleep quality (1.76, 1.03-3.01), sleep latency (1.18, 1.06-1.31), and a one hour later sleep timing (1.51, 1.08-2.11), but not sleep duration (1.05, 0.90-1.23), were associated with osteopenia. PSQI score (1.10, 1.02-1.19) was also associated with sarcopenia; OR's of sleep latency and later mid-sleep time with sarcopenia were 1.14 (0.99-1.31) and 1.54 (0.91-2.61), respectively. Associations were somewhat stronger in women and varied per menopausal status. CONCLUSIONS: These results suggest that decreased sleep quality and a later sleep timing are risk factors for osteopenia and sarcopenia in middle aged individuals.

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HDL and the menopause.

El Khoudary SR.

PURPOSE OF REVIEW: To summarize recent provocative findings on conventional and novel metrics of HDL including HDL-C, HDL subclasses and HDL cholesterol efflux capacity as related to menopause. RECENT FINDINGS: Pattern of menopause-related changes in HDL-C are not consistent, suggesting a complex relationship between HDL and menopause. Growing body of literature indicates that higher levels of HDL-C may not be consistently cardio-protective in midlife women, suggesting a potential change in other metrics of HDL that could not be captured by the static metric HDL-C. It is also possible that higher HDL-C at certain conditions could be a marker

of HDL metabolism dysfunctionality. Significant alterations in other metrics of HDL have been reported after menopause and found to be related to estradiol. SUMMARY: The impact of changes in novel metrics of HDL over the menopausal transition on cardiovascular disease (CVD) risk later in life is not clear in women. Much of our understanding of how the menopausal transition may impact HDL metrics comes from cross-sectional studies. Future longitudinal studies are needed to evaluate other metrics of HDL shown to better reflect the cardio-protective capacities of HDL, so that the complex association of menopause, HDL and CVD risk could be characterized.

Ther Adv Musculoskelet Dis. 2017 May;9(5):107-114. doi: 10.1177/1759720X16685547. Epub 2017 Mar 26.

The calcium and vitamin D controversy.

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Areas of the world where vitamin D levels are low for months of the year and intakes of calcium are high have a high prevalence of osteoporosis and cardiovascular disease. This suggests a public health message of avoiding calcium supplements and increasing vitamin D intake. No message could be more welcome as vitamin D can be given as a bolus while calcium must be taken daily and may be poorly tolerated. This approach is based on no evidence from intervention studies. Randomized controlled trials (RCTs) suggest that vitamin D given with calcium elicits a small reduction in fracture risk and deaths. This has not been demonstrated for D given alone. The cardiovascular safety of calcium and vitamin D (CaD) supplements is difficult to ascertain due to weaknesses in RCT designs and adjudication that cannot be remedied by subanalysis. Moreover, no major new RCTs are in process to provide better evidence. It remains unclear that calcium from dietary sources has health advantages over supplements. Benefits may be confined to patients with poor nutritional intake and the small effects at societal levels may be derived from large effects in a small number of patients. This has been impossible to confirm given the limited information about baseline vitamin D and calcium status at entry into trials. Future intervention studies should carefully capture baseline characteristics as these may determine the strength of the response, and make more efficient use of randomization strategies allowing subsequent disassembly or subanalyses while maintaining balancing. Though large clinical RCTs currently evaluate the effects of higher vitamin D doses (equivalent to 50-83 µg/d) there is no current research effort regarding the calcium controversy. In the absence of such studies it is not possible to provide clinicians with evidence-based recommendations regarding the best use of CaD supplementation.

J Midlife Health. 2017 Jan-Mar;8(1):11-16. doi: 10.4103/0976-7800.201967.

Hormone replacement therapy reduces lipid oxidation directly at the arterial wall: A possible link to estrogens' cardioprotective effect through atherosclerosis prevention.

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BACKGROUND: The first step in atherosclerosis formation is the ingurgitation of an oxidized low-density lipid (LDL) molecule by a macrophage which then turns into a foam cell within the vascular wall and initiates a cascade of inflammatory responses. Could it be that the potential cardioprotective effect observed in women receiving hormone replacement therapy (HRT) is modulated by estrogen's capacity to decrease LDL oxidation in the vascular wall and thus decrease atherosclerotic foam cells? MATERIALS AND METHODS: Thirty-four adult female Wistar rats were divided into three groups. All were double oophorectomized. After recovery, Group 1 received Estradiol Valerate subcutaneous (SC) (2.5 mg/kg/week), Group 2 Estradiol Valerate SC (2.5 mg/kg/week) + Progesterone SC (10 mg/kg/48 h), and Group 3 Placebo SC. After 10 weeks, all rats were sacrificed and a vascular dissection performed. Malondialdehyde (MDA) was measured directly on the vascular extract to determine lipid oxidative levels and HRTs' effect. Renal and hepatic tissue was also studied. Total antioxidant status (TAS) was measured to determine overall oxidative behavior. RESULTS: Vascular MDA levels for Group 1 = 80.80 (±16.8) µmol/ml/g, Group 2 = 107.69 (±24.9) µmol/ml/g, and Group 3 = 140.96 (±32.4) µmol/ml/g. ANOVA ($P < 0.05$), with a post hoc Bonferroni corrective t-test, showed that both Group 1 and 2 have statistically significant lower levels of MDA than Group 3. Renal tissue showed less oxidative damage in the HRT groups, while hepatic tissue showed an inverse behavior with less lipid oxidation in the placebo group. TAS decreased with oophorectomy in all groups but decreased less in both groups that received HRT compared to placebo ($P < 0.05$).

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Are women with polycystic ovary syndrome at increased cardiovascular disease risk later in life?

Gunning MN, Fauser BCJM.

To date, the world's leading cause of death amongst women is cardiovascular disease. Polycystic ovary syndrome (PCOS) is associated with an unfavorable cardiometabolic profile in early life. Apart from dyslipidemia, obesity and onset of type 2 diabetes mellitus, androgens are thought to influence cardiovascular health. The question rises whether women with PCOS are truly at risk for cardiovascular disease in later life. In this review paper, we aim to reflect on this assumed relation based on studies in different stages of life in women with PCOS. Cardiovascular risk factors (type 2 diabetes mellitus, obesity and metabolic syndrome), surrogate outcomes (flow-mediated dilation, carotid intima-media thickness and coronary artery calcium) and clinical long-term outcomes (cardiovascular disease and mortality) will be summarized. Data on cardiovascular disease and mortality in peri- and postmenopausal women with PCOS appear to be controversial. Whether androgens have a protective or unfavorable influence on the manifestation of cardiovascular disease remains uncertain. The need for large, prospective, well-phenotyped cohort studies of women with PCOS is high. Only then will we be able to answer this research question.

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Vasomotor symptoms in menopause: a biomarker of cardiovascular disease risk and other chronic diseases?

Biglia N, Cagnacci A, Gambacciani M, Lello S, Maffei S, Nappi RE.

Menopausal disorders may include shorter-term symptoms, such as hot flushes and night sweats (vasomotor symptoms, VMS) and longer-term chronic conditions such as cardiovascular disease (CVD), osteoporosis, and cognitive impairment. Initially, no clear link between the shorter-term symptoms and longer-term chronic conditions was evident and these disorders seemed to occur independently from each other. However, there is a growing body of evidence demonstrating that VMS may be a biomarker for chronic disease. In this review, the association between VMS and a range of chronic postmenopausal conditions including CVD, osteoporosis, and cognitive decline is discussed. Prevention of CVD in women, as for men, should be started early, and effective management of chronic disease in postmenopausal women has to start with the awareness that VMS during menopause are harbingers of things to come and should be treated accordingly.