Selección de Resúmenes de Menopausia

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María Soledad Vallejo. Clínica Quilín. Universidad de Chile

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A clinical guide to the pathophysiology, diagnosis and treatment of osteosarcopenia

Ben Kirk, Sarah Miller, Jesse Zanker, Gustavo Duque.

Advances in medicine have paved the way for older persons to live longer, but with more years spent living with disability and dependency. Many older persons are living with comorbidities such as osteoporosis (loss of bone mass) and sarcopenia (loss of muscle mass and function), two diseases that, when concurrent, form osteosarcopenia, a newly identified musculoskeletal syndrome. Osteosarcopenia impedes mobility and diminishes independence and thus quality of life. Evidence suggests the pathology of this syndrome comprises genetic polymorphisms, alterations in mechanotransduction, and localized or systemic crosstalk between growth factors and other proteins (myokines, osteokines, adipokines). As a direct result of an aging society, health outcomes such as falls and fractures will rise as the prevalence of osteosarcopenia increases. Two major risk factors for osteosarcopenia (other than age itself) are physical inactivity and poor nutrition. Addressing these modifiable risk factors can prevent, or at least delay, the onset of osteosarcopenia. Pharmaceutical treatments for osteosarcopenia are currently unavailable, although research trials are underway. This review provides an update from basic and clinical sciences on the biology, epidemiology (prevalence, risk factors and diagnosis) and treatments for osteosarcopenia, and recommends future research priorities to improve health outcomes for those living with or at risk of osteosarcopenia.

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Bone tissue composition in post-menopausal women varies with glycemic control from normal glucose tolerance to type 2 diabetes mellitus

Heather B Hunt 1 , Nicholas A Miller 1 , Kimberly J Hemmerling 1 , Maho Koga 1 , Kelsie A Lopez 1 , Erik A

The risk of fragility fracture increases for people with type 2 diabetes mellitus (T2DM), even after controlling for bone mineral density, body mass index, visual impairment, and falls. We hypothesize that progressive glycemic derangement alters micro-scale bone tissue composition. We used Fourier-transform infrared (FTIR) imaging to analyze the composition of iliac crest biopsies from cohorts of post-menopausal women characterized by oral glucose tolerance testing: normal glucose tolerance (NGT; n=35, age=65±7, HbA1c=5.8±0.3%), impaired glucose tolerance (IGT; n=26, age=64±5, HbA1c=6.0±0.4%), and overt T2DM on insulin (n=25, age=64±6, HbA1c=9.13±0.6). The distributions of cortical bone mineral content had greater mean values (+7%) and were narrower (-10%) in T2DM vs. NGT groups ($p<0.05$). The distributions of acid phosphate, an indicator of new mineral, were narrower in cortical T2DM vs. NGT and IGT groups (-14% and -14%, respectively) and in trabecular NGT and IGT vs. T2DM groups (-11% and -10%, respectively) (all $p<0.05$). The distributions of crystallinity were wider in cortical NGT vs. T2DM groups (+16%) and in trabecular NGT vs. T2DM groups (+14%) (all $p<0.05$). Additionally, bone turnover was lower in T2DM vs. NGT groups (P1NP: -25%, CTx: -30%, ucOC: -24%). Serum pentosidine was similar across groups. The FTIR compositional and biochemical marker values of the IGT group typically fell between the NGT and T2DM group values, though the differences were not always statistically significant. In summary, worsening glycemic control was associated with greater mineral content and narrower distributions of acid phosphate, an indicator of new mineral, which together are consistent with observations of lower turnover; however, wider distributions of mineral crystallinity were also observed. A more mineralized, less heterogeneous tissue may affect tissue-level mechanical properties, and in turn degrade macroscale skeletal integrity. In conclusion, these data are the first evidence of progressive alteration of bone tissue composition with worsening glycemic control in humans.

Minerva Endocrino. 2020 Sep 24.doi: 10.23736/S0391-1977.20.03266-6. Online ahead of print.

Mediterranean diet and breast cancer risk: a narrative review

Daniela Laudisio, Bianca Castellucci, Luigi Barrea, Gabriella Pugliese, Silvia Savastano, Annamaria Colao, et al. Breast cancer is the second most frequent type of cancer worldwide and the most commonly occurring malignancy in women,

and its incidence is increasing in most developed and developing countries. There is growing evidence that lifestyle factors, in particular diet may be associated with higher Breast Cancer risk. Some evidence exists regarding the benefit of Mediterranean Diet on reduced risk of Breast Cancer in premenopausal and postmenopausal women. The protective effect of the Mediterranean Diet against the risk of Breast Cancer, is primarily due to principal foods of this nutritional pattern. The principal components of the Mediterranean Diet, such as fruits and vegetables, olive oil, fish and red wine have important antioxidants properties due to their high content of substances like polyphenols, flavonoids, carotenoids and fibers, along with a favourable fatty acid profile, that in turn could reduce the risk of Breast Cancer. Considering the severity of breast cancer and the increasing incidence in the world, there is an increasing interest in promoting prevention strategies in order to reduce the incidence. The aim of this paper is to provide a general overview of the current evidence on the relationship between Breast Cancer and Mediterranean Diet, in premenopausal and postmenopausal women, and to emphasize the potential role of Mediterranean Diet as an effective tool in primary prevention. The possible molecular mechanisms underlying this association will be also pointed out.

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Prevalence of Vertebral Fractures in CTPA's in Adults Aged 75 and Older and Their Association with Subsequent Fractures and Mortality

Llewelyn Jones 1 , Sukhdev Singh 2 , Chris Edwards 3 , Nimit Goyal 2 , Inder Singh 4

Identifying vertebral fractures is prudent in the management of osteoporosis and the current literature suggests that less than one-third of incidental vertebral fractures are reported. The aim of this study is to determine the prevalence of reported and unreported vertebral fractures in computerized tomography pulmonary angiograms (CTPA) and their relevance to clinical outcomes. All acutely unwell patients aged 75 or older who underwent CTPAs were reviewed retrospectively. 179 CTPAs were reviewed to identify any unreported vertebral fractures. A total of 161 were included for further analysis. Of which, 14.3% (23/161) were reported to have a vertebral fracture, however, only 8.7% (14/161) of reports used the correct terminology of 'fracture'. On subsequent review, an additional 19.3% (31/161) were noted to have vertebral fractures. Therefore, the overall prevalence of vertebral fractures was 33.5% (54/161). A total of 22.2% (12/54) of patients with a vertebral fracture on CTPA sustained a new fragility fracture during the follow-up period (4.5 years). In comparison, a significantly lower 10.3% (11/107) of patients without a vertebral fracture developed a subsequent fragility fracture during the same period ($p = 0.04$). Overall mortality during the follow-up period was significantly higher for patients with vertebral fractures (68.5%, 37/54) as compared to those without (45.8%, 49/107, $p = 0.006$). Vertebral fractures within the elderly population are underreported on CTPAs. The significance of detecting incidental vertebral fractures is clear given the increased rates of subsequent fractures and mortality. Radiologists and physicians alike must be made aware of the importance of identifying and treating incidental, vertebral fragility fractures.

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Duration of oestrogen exposure during reproductive years, age at menarche and age at menopause, and risk of cardiovascular disease events, all-cause and cardiovascular mortality: a systematic review and meta-analysis

Shiva R Mishra 1 , Hsin-Fang Chung 1 , Michael Waller 1 , Gita D Mishra 1

Background: Little is known about the oestrogen exposure measurement and mutual effect of age at menarche and age at menopause in the risk of cardiovascular disease (CVD) events. Objectives: To evaluate oestrogen exposure measurement and describe mutual effect of age at menarche and age at menopause in the risk of CVD events. Search strategy Systematic review of literature in PubMed, Embase and Web of Science for studies published up to June 28, 2020. Selection criteria Observational studies related to oestrogen exposure measurement, including mutual effect of age at menarche and age at menopause and risk of CVD events. Data collection and analysis Synthesis of evidence was conducted by reviewing individual estimates, followed by meta-analysis. The study received no external funding. Main results A total of 75 studies were included in synthesis of evidence, of which 17 studies were included in meta-analysis. Reproductive lifespan (age at menopause - age at menarche), endogenous oestrogen exposure and total oestrogen exposure were used for oestrogen exposure measurement. By far, reproductive lifespan was the most commonly used method for oestrogen exposure measurement. A shorter reproductive lifespan was associated with a higher risk of CVD events; the pooled relative risk (95% CI) was 1.31 (1.25, 1.36) for stroke events. Further, robust epidemiological studies with measurement of oestrogen exposure and associated health risk would strengthen the evidence. Conclusions:

Reproductive lifespan was the most commonly used method for oestrogen exposure measurement in epidemiological studies. A shorter reproductive lifespan was associated with a higher risk of CVD events particularly stroke.

Z Gerontol Geriatr. 2020 Sep 23.doi: 10.1007/s00391-020-01784-5. Online ahead of print.

Risk of falls in patients with low bone mineral density : Analysis of placebo arms from clinical trials

Luis Möckel 1

Background: Falls are a major risk factor for osteoporotic fractures. Therefore, the aim of this study was to analyze the risk of falls in patients with low bone mineral density (BMD) and osteoporosis. Methods: The risk of falls in patients with low BMD and/or osteoporosis was analyzed using data from placebo arms of clinical trials, indexed on clinicaltrials.gov. The risk was estimated using a single arm meta-analysis method and by applying a binary random effects model. In addition, meta-regression analyses were performed to identify associations between risk of falls and age, body mass index (BMI) and BMD. Results: A total of 8762 patients from placebo arms of clinical trials were included into the analysis. Risk of falls was 5.2% (0.052, 95% confidence interval [95% CI] 0.022-0.082; n = 8714; I2 = 97.3%, $p \leq 0.001$) in patients with low BMD and/or osteoporosis and 5.9% (0.059, 95% CI 0.036-0.083; n = 7819; I2 = 87.8%, $p \leq 0.001$) in patients with osteoporosis. A significant association with risk of falls was identified for age in patients with low BMD and/or osteoporosis. BMD at total hip (TH; coefficient -0.077, 95% CI: -0.113--0.040, $p \leq 0.001$; n = 7715) and femoral neck (FN; coefficient -0.044, 95% CI -0.065--0.023, $p \leq 0.001$; n = 7662) were significantly associated with risk of falls in patients with osteoporosis. Conclusion: This analysis identified the risk of falls in patients with low BMD and osteoporosis and an association of falls with age and BMD. Therefore, patients with osteoporosis need to receive mandatory fall risk mitigation measures, and the BMD at total hip or femoral neck could function as an indicator for the risk of falling.

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Onset of the climacteric phase by the mid-forties associated with impaired insulin sensitivity: a birth cohort study

Susanna M Savukoski 1 2 , Eila T J Suvanto 1 2 , Juha P Auvinen 2 3 4 , Paula R O Pesonen 5 , et al

Objective: To investigate whether the early-onset menopausal transition is associated with deteriorated glucose tolerance in women in their mid-forties. Methods: A cross-sectional analysis of a cohort study including 2,632 women of the Northern Finland Birth Cohort 1966. The participants were divided into two groups by their menstrual history and follicle-stimulating hormone values at age 46: climacteric and preclimacteric women. Glucose and insulin parameters, as well as mathematical indices derived from them to evaluate insulin sensitivity, were compared between the groups. The results were adjusted for measured body mass index and smoking. The possible effect of hormone therapy was investigated in subanalyses excluding hormone therapy users. Results: Climacteric women (n = 379) were more often current smokers at age 46 (P = 0.008), and their body mass indices increased more from 31 to 46 years (P = 0.013), compared to preclimacteric women (n = 2,253). In a multivariable generalized linear model, being climacteric at age 46 was associated with several findings suggesting decreased insulin sensitivity: increased glycated hemoglobin (P < 0.001), 2-hour oral glucose tolerance test 30- and 60-minute insulin (P = 0.040 and 0.006, respectively), and area under the insulin curve (P = 0.005). Being climacteric also was associated with a decreased the McAuley (P = 0.024) and Belfiore indices (P = 0.027) and glucose tolerance test 60-minute glucose (P = 0.015). In subanalyses excluding hormone therapy users (n = 94), the results did not change significantly. Conclusions: Earlier onset of climacteric transition is associated with impaired insulin sensitivity in middle-aged women.

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The Central Regulation of Bone Mass: Genetic Evidence and Molecular Bases

Gerard Karsenty 1

The alternation of resorption of preexisting bone by the osteoclasts followed by de novo bone formation by osteoblasts is called bone modeling during childhood and bone remodeling during adulthood. A central question raised by this physiological process that is fundamental to longitudinal growth during childhood and adolescence and that is attacked at the other end of life in the context of osteoporosis is to know how it is regulated. This question was rejuvenated in the late 1990s and early 2000s years when the application of mouse genetics made it feasible to test whether there were new

endocrine determinants of bone (re)modeling. Addressing this question, taking into account fundamental cell biology features of bone led to the hypothesis that there should be a coordinated control of bone growth/mass, energy metabolism, and reproduction. Testing genetically and molecularly, this hypothesis revealed that, in vivo, the adipocyte-derived hormone leptin is a powerful inhibitor of bone mass accrual following its signaling in the brain. This chapter details the molecular bases and biological relevance of this regulation of bone mass accrual by leptin.

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Micronized progesterone, progestins, and menopause hormone therapy

Marcio Alexandre Hipolito Rodrigues 1 , Anne Gompel 2

Treatment with estrogens alone in women without a uterus or in combination with progestins (PG) in women with a uterus is the most effective treatment for vasomotor symptoms in the peri or postmenopausal period. However, PGs differ by their biological activities, and it is likely that not all PGs will display a class effect. The type of PG is important regarding tolerance and cardiovascular and breast cancer risk. Some studies indicate that micronized progesterone (P) is safer than synthetic PGs with an acceptable metabolic profile. For that purpose, we conducted a narrative review on the balance between benefit/risk using P versus PGs in menopause hormone therapy (MHT) to aid clinician to choose the best regimens, specifically the PG component of hormone therapy, for women with bothersome menopausal symptoms and with a uterus.

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Aspirin might reduce the incidence of breast cancer: An updated meta-analysis of 38 observational studies

Yueqing Cao 1 , Aihua Tan

Background: Many epidemiologic studies were performed to clarify the protective effect of regular aspirin use on breast cancer risks, but the results remain inconsistent. Here, we conducted an updated meta-analysis of 38 studies to quantitatively assess the association of regular aspirin use with risk of breast cancer. Method: We performed a bibliographic database search in PubMed, Embase, Web of Science, Cochrane library, Scopus, and Google Scholar from January 1939 to December 2019. Relative risk (RR) estimates were extracted from eligible case-control and cohort studies and pooled using a random effects model. Subgroup analysis was conducted based on study design, aspirin exposure assessment, hormone receptor status, menopausal status, cancer stage as well as aspirin use duration or frequency. Furthermore, sensitivity and publication bias analyses performed. Results: Thirty eight studies of 1,926,742 participants involving 97,099 breast cancer cases contributed to this meta-analysis. Compared with nonusers, the aspirin users had a reduced risk of bre ast cancer (RR = 0.91, 95% confidence interval [CI]: 0.87-0.95, P value of significance [Psig] < .001) with heterogeneity (P value of heterogeneity [Phet] < .001, I = 82.6%). Subgroup analysis revealed a reduced risk in case-control studies (RR = 0.83, 95% CI: 0.78-0.89, Psig < .001), in hormone receptor positive tumors (RR = 0.91, 95% CI: 0.88-0.94, Psig < .001), in situ breast tumors (RR = 0.79, 95% CI: 0.71-0.88, Psig < .001), and in postmenopausal women (RR = 0.89, 95% CI: 0.83-0.96, Psig = .002). Furthermore, participants who use aspirin for >4 times/wk (RR = 0.88, 95% CI: 0.82-0.96, Psig = .003) or for >10 years (RR = 0.94, 95% CI: 0.89-0.99, Psig = .025) appeared to benefit more from the reduction in breast cancer caused by aspirin. Conclusions: Our study suggested that aspirin use might be associated with a reduced risk of breast cancer, particularly for reducing the risk of hormone receptor positive tumors or in situ breast tumors, and the risk of breast cancer in postmenopausal women.