



Selección de Resúmenes de Menopausia

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 María Soledad Vallejo. Clínica Quilín. Universidad de Chile

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Bone Marrow and Muscle Fat Infiltration are Correlated Among Postmenopausal Women with Osteoporosis: the AMBERS Cohort Study.

Wong AK^{1,2,3}, Chandrakumar A¹, Whyte R^{1,3}, Reitsma S⁴, Gillick H⁴, Pokhoy A¹, Papaioannou A⁵, Adachi J^{D4}. Bone and muscle have shown to interact, but little is known about fat within bone and muscle. Clinical studies have isolated fat within bone and muscle using MRI. In this cross-sectional study, we hypothesized that bone marrow adiposity and muscle adiposity are related, and that this relationship is associated with osteoporosis. Postmenopausal women 60-85 years of age were recruited as part of the Appendicular Muscle and Bone Extension Research Study (AMBERS). Participants completed DXA of the hip and spine to diagnose osteoporosis. Muscle adiposity was measured with MRI at the 66% site of the leg. Fat segmentation was achieved using a semi-automated iterative threshold-optimizing algorithm (error<5%). Peripheral quantitative computed tomography measured marrow density of the 4% distal tibia (surrogate for marrow fat) by threshold-based, edge-detection segmentations and by examining residuals from trabecular bone density regressed on trabecular tissue mineral density. Muscle adiposity from MRI was regressed on marrow density using linear regression. Models were further examined with an interaction with osteoporosis status. Among 312 women (age: 75.4±5.9yrs, BMI: 29.5±5.7kg/m²), a larger amount of muscle fat was associated with lower marrow density at the 66% mid-tibia (B: 84.08(27.56), p=0.002) and at the 4% distal tibia (B: 129.17(55.96), p=0.022) after accounting for age, height, weight, average daily energy expenditure, hypertension and diabetes. Interactions of this relationship with osteoporosis status were also significant. Upon probing these interactions, the relationships were significant only in women with osteoporosis, but not in those without osteoporosis. Fat from bone marrow and muscle may be related to one another through the same phenomenon, which is likely also responsible for osteoporosis, but independent of hypertension and diabetes. More research should focus on the potential abnormalities in muscle and bone fat metabolism and mesenchymal cell commitment to fat within patients with osteoporosis.

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Effect of Abaloparatide Versus Alendronate on Fracture Risk Reduction in Postmenopausal Women With Osteoporosis.

Leder B^{Z1}, Mitlak B², Hu M^{Y2}, Hattersley G², Bockman R^{S3}.

CONTEXT: The ACTIVE study demonstrated the antifracture efficacy of abaloparatide in postmenopausal women with osteoporosis. ACTIVEExtend demonstrated sustained fracture risk reduction with alendronate in abaloparatide-treated participants from ACTIVE. A direct comparison of the efficacy of abaloparatide and antiresorptive therapies has not been done. **OBJECTIVE:** To compare the antifracture efficacy of abaloparatide in ACTIVE with that of alendronate in ACTIVEExtend. **DESIGN:** In this post hoc analysis, the rate of new vertebral fractures for women in ACTIVEExtend (N=1139) was calculated based on baseline and endpoint radiographs for placebo or abaloparatide in ACTIVE and alendronate in ACTIVEExtend. Vertebral fracture rates between abaloparatide and alendronate were compared in a Poisson regression model. Fracture rates for nonvertebral and clinical fractures were compared based on Poisson model during 18 months of abaloparatide or placebo treatment in ACTIVE and 18 months of alendronate treatment in ACTIVEExtend. **RESULTS:** The vertebral fracture rate was lower during abaloparatide treatment in ACTIVE (0.47 fractures/100 patient-years) than alendronate treatment in ACTIVEExtend (1.66 fractures/100 patient-years) (relative risk reduction [RRR] 71%; P=0.027). Although the comparisons did not meet statistical significance, after switching from placebo (ACTIVE) to alendronate (ACTIVEExtend), the rate of new vertebral fractures decreased from 2.49 to 1.66 fractures/100 patient-years, and after switching from abaloparatide to alendronate from 0.47 to 0.19 fractures/100 patient-years. The rate of nonvertebral fractures and clinical fractures were not significantly different. **CONCLUSION:** Initial treatment with abaloparatide may result in greater vertebral fracture reduction compared with alendronate in postmenopausal women with osteoporosis.

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Clinical Role of Aspirin in Mood Disorders: A Systematic Review.

Ng QX^{1,2}, Ramamoorthy K^{3,4}, Loke W⁵, Lee MWL⁶, Yeo WS^{7,8}, Lim DY^{9,10}, Sivalingam V¹¹.

Worldwide, depression and bipolar disorder affect a large and growing number of people. However, current pharmacotherapy options remain limited. Despite adequate treatment, many patients continue to have subsyndromal symptoms, which predict relapse in bipolar illness and often result in functional impairments. Aspirin, a common nonsteroidal anti-inflammatory drug (NSAID), has purported beneficial effects on mood symptoms, showing protective effects against depression in early cohort studies. This systematic review thus aimed to investigate the role of aspirin in mood disorders. Using the keywords (aspirin or acetylsalicy* or asa) and (mood or depress* or bipolar or mania or suicid*), a comprehensive search of PubMed, EMBASE, Medline, PsycINFO, Clinical Trials Register of the Cochrane Collaboration Depression, Anxiety and Neurosis Group (CCDANTR), Clinicaltrials.gov and Google Scholar databases found 13,952 papers published in English between 1 January 1988 and 1 May 2019. A total of six clinical studies were reviewed. There were two randomized, placebo-controlled, double-blind trials and populations drawn from two main cohort studies (i.e., the Geelong Osteoporosis Study and the Osteoarthritis Initiative study). Using a random-effects model, the pooled hazard ratio of the three cohort studies was 0.624 (95% confidence interval: 0.0503 to 1.198, $p = 0.033$), supporting a reduced risk of depression with aspirin exposure. Overall, the dropout rates were low, and aspirin appears to be well-tolerated with minimal risk of affective switch. In terms of methodological quality, most studies had a generally low risk of bias. Low-dose aspirin (80 to 100 mg/day) is safe, well-tolerated and potentially efficacious for improving depressive symptoms in both unipolar and bipolar depression. Due to its ability to modulate neuroinflammation and central nervous system processes, aspirin may also have valuable neuroprotective and pro-cognitive effects that deserve further exploration. Further randomized, controlled trials involving the adjunctive use of aspirin should be encouraged to confirm its therapeutic benefits.

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Sex Differences in the Association Between Bone Mineral Density and Coronary Artery Disease in Patients Referred for Cardiac Computed Tomography.

Therkildsen J¹, Winther S², Nissen L³, Jørgensen HS⁴, Thygesen J⁵, Ivarsen P⁶, Frost L⁷, Isaksen C⁸, Langdahl BL⁹, Hauge EM¹⁰, Böttcher M³.

Atherosclerosis and osteoporosis are both common and preventable diseases. Evidence supports a link between coronary artery disease (CAD) and low bone mineral density (BMD). This study aimed to assess the association between thoracic spine BMD and CAD in men and women with symptoms suggestive of CAD. This cross-sectional study included 1487 (mean age 57 years (range 40-80), 47% men) patients referred for cardiac computed tomography (CT). Agatston coronary artery calcium score (CACS), CAD severity (no, mild, moderate, and severe), vessel involvement (no, 1-, 2-, and 3/left main disease), and invasive measurements were evaluated. BMD of three thoracic vertebrae was measured using quantitative CT. We used the American college of radiology cut-off values for lumbar spine BMD to categorize patients into very low (<80 mg/cm³), low (80-120 mg/cm³), or normal BMD (>120 mg/cm³). BMD as a continuous variable was included in the linear regression analyses to assess associations between CACS (CACS=0, CACS 1- 399, and CACS \geq 400) and BMD, and CAD severity and BMD. Significant lower BMD was present with increasing CACS and stenosis degree unadjusted. Multivariate linear regression analyses in women revealed a significant correlation between BMD and CACS groups ($\beta = -4.06$, $p < 0.05$), but no correlation between BMD and CAD severity ($\beta = -1.59$, $p = 0.14$). No association was found between BMD and CACS ($\beta = -1.50$, $p = 0.36$) and CAD severity ($\beta = 0.07$, $p = 0.94$) in men. BMD is significantly correlated to CACS after adjusting for confounders in women, but not in men, suggesting a possible sex difference in pathophysiology.

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Effect of continuous long-term treatment for 10 years with bisphosphonate on Japanese osteoporosis patients.

Iba K¹, Takada J², Sonoda T³, Yamashita T⁴.

INTRODUCTION: In terms of the balance between benefits and risks of long-term treatment with bisphosphonate, uncertainties remain regarding the optimal treatment duration. We investigated effects of continuous long-term

treatment for 10 years with bisphosphonate in postmenopausal osteoporosis patients. MATERIALS AND METHODS:

Fifty five patients in the outpatient clinic of our hospital have been continuously treated with alendronate or risedronate for 10 years. All data were retrospectively collected. The age, height, weight, total muscle volume, total fat volume, and BMD at the lumbar spine, total hip and distal 1/3 radius, alkaline phosphatase (ALP), urinary type I collagen cross-linked N-telopeptide (uNTX) and tartrate-resistant acid phosphatase-5b (TRAP5b), calcium (Ca) and phosphate (P) levels were measured pre- and after the start of 10-year continuous treatment. RESULTS: BMD at the lumbar spine increased continuously over the 10-year period, while BMD at the total hip slightly but significantly decreased, and that at the 1/3 radius did not show any significant change over the 10 years. Serum Ca value was significantly decreased after the start of treatment, and became stable within the reference range from the second year. Bone resorption markers such as uNTX and TRAP5b significantly decreased from the second year after the start of treatment and no significant changes were observed thereafter. There were no serious medical adverse events including atypical femoral fractures and osteonecrosis of the jaw. CONCLUSION: We believe that the continuous use of alendronate and risedronate for 10 years could be an option for the treatment of postmenopausal osteoporosis patients.

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Molecular Links between Central Obesity and Breast Cancer.

Zimta AA1, Tigu AB2,3, Muntean M4, Cenariu D5, Slaby O6,7, Berindan-Neagoe I8,9,10.

Worldwide, breast cancer (BC) is the most common malignancy in women, in regard to incidence and mortality. In recent years, the negative role of obesity during BC development and progression has been made abundantly clear in several studies. However, the distribution of body fat may be more important to analyze than the overall body weight. In our review of literature, we reported some key findings regarding the role of obesity in BC development, but focused more on central adiposity. Firstly, the adipose microenvironment in obese people bears many similarities with the tumor microenvironment, in respect to associated cellular composition, chronic low-grade inflammation, and high ratio of reactive oxygen species to antioxidants. Secondly, the adipose tissue functions as an endocrine organ, which in obese people produces a high level of tumor-promoting hormones, such as leptin and estrogen, and a low level of the tumor suppressor hormone, adiponectin. As follows, in BC this leads to the activation of oncogenic signaling pathways: NFκB, JAK, STAT3, AKT. Moreover, overall obesity, but especially central obesity, promotes a systemic and local low grade chronic inflammation that further stimulates the increase of tumor-promoting oxidative stress. Lastly, there is a constant exchange of information between BC cells and adipocytes, mediated especially by extracellular vesicles, and which changes the transcription profile of both cell types to an oncogenic one with the help of regulatory non-coding RNAs.

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Vertebral Fractures in Individuals With Type 2 Diabetes: More Than Skeletal Complications Alone.

Koromani F1,2, Oei L1, Shevroja E3, Trajanoska K1, Schoufour J1,4, Muka T4,5, Franco OH4,5, Ikram , et al.

OBJECTIVE: We aimed to assess whether individuals with type 2 diabetes (T2D) have increased risk of vertebral fractures (VFs) and to estimate nonvertebral fracture and mortality risk among individuals with both prevalent T2D and VFs. RESEARCH DESIGN AND METHODS: A systematic PubMed search was performed to identify studies that investigated the relationship between T2D and VFs. Cohorts providing individual-participant data (IPD) were also included. Estimates from published summary data and IPD cohorts were pooled in a random-effects meta-analysis. Multivariate Cox-regression models were used to estimate nonvertebral fracture and mortality risk among individuals with T2D and VFs. RESULTS: Across 15 studies comprising 852,705 men and women, individuals with T2D had lower risk of prevalent (odds ratio [OR] 0.84 [95% CI 0.74-0.95]; I² = 0.0%; P_{het} = 0.54) but increased risk of incident VFs (OR 1.35 [95% CI 1.27-1.44]; I² = 0.6%; P_{het} = 0.43). In the IPD cohorts (N = 19,820), risk of nonvertebral fractures was higher in those with both T2D and VFs compared with those without T2D or VFs (hazard ratio [HR] 2.42 [95% CI 1.86-3.15]), with VFs (HR 1.73 [95% CI 1.32-2.27]), or T2D (HR 1.94 [95% CI 1.46-2.59]) alone. Individuals with both T2D and VFs had increased mortality compared with individuals without T2D and VFs (HR 2.11 [95% CI 1.72-2.59]) or with VFs alone (HR 1.84 [95% CI 1.49-2.28]) and borderline increased compared with individuals with T2D alone (HR 1.23 [95% CI 0.99-1.52]). CONCLUSIONS: Based on our findings,

individuals with T2D should be systematically assessed for presence of VFs, and, as in individuals without T2D, their presence constitutes an indication to start osteoporosis treatment for the prevention of future fractures.