

Selección de Resúmenes de Menopausia

Semana del 16 al 22 de octubre de 2019

María Soledad Vallejo. Clínica Quilín. Universidad de Chile

J Aging Phys Act. 2019 Oct 17;1-8. doi: 10.1123/japa.2019-0066. [Epub ahead of print]

Decreased Serum Levels of C-Terminal Agrin in Postmenopausal Women Following Resistance Training.

Willoughby DS, Beretich KN, Chen M, Funderburk LK.

Elevated circulating C-terminal agrin fragment (CAF) is a marker of neuromuscular junction degradation and sarcopenia. This study sought to determine if resistance training (RT) impacted the serum levels of CAF in perimenopausal (PERI-M) and postmenopausal (POST-M) women. A total of 35 women, either PERI-M or POST-M, participated in 10 weeks of RT. Body composition, muscle strength, and serum estradiol and CAF were determined before and after the RT. The data were analyzed with two-way analysis of variance ($p \leq .05$). Upper body and lower body strength was significantly increased, by 81% and 73% and 86% and 79% for the PERI-M and POST-M participants, respectively; however, there were no significant changes in body composition. Estradiol was significantly less for the POST-M participants at pretraining compared with the PERI-M participants. CAF moderately increased by 22% for the PERI-M participants in response to RT, whereas it significantly decreased by 49% for the POST-M participants. Ten weeks of RT reduced the circulating CAF in the POST-M women and might play a role in attenuating degenerative neuromuscular junction changes.

Drug Des Devel Ther. 2019 Aug 14;13:2843-2852. doi: 10.2147/DDDT.S148654. eCollection 2019.

Denosumab in the treatment of glucocorticoid-induced osteoporosis: a systematic review and meta-analysis.

Yanbey ZA1, Hansen KE1.

Objective: Glucocorticoid-induced osteoporosis (GIOP) is the most common form of secondary osteoporosis. In May 2018, denosumab was approved for the treatment of GIOP in men and women at high risk of fracture. We undertook a systematic review and meta-analysis to summarize the efficacy and safety of denosumab in the prevention and treatment of GIOP. **Methods:** We searched PubMed, CINAHL, American College of Rheumatology and American Society for Bone and Mineral Research meeting abstracts for relevant studies. We included studies in which subjects were taking systemic glucocorticoid therapy and were assigned to take denosumab or control therapy, and assessed the effect of treatment on areal bone mineral density (BMD), fractures and/or safety. **Results:** Three eligible studies were included in the primary meta-analysis. Denosumab significantly increased lumbar spine BMD (2.32%, 95% CI 1.73%, 2.91%, $P < 0.0001$) and hip BMD (1.52%, 95% CI 1.1%, 1.94%, $P < 0.0001$) compared to bisphosphonates. Adverse events, serious adverse events and fractures were similar between denosumab and bisphosphonate arms. **Conclusion:** Results suggest that denosumab is superior to bisphosphonates in its effects on lumbar spine and total hip BMD in patients with GIOP. There was no difference in the incidence of infections, adverse events or serious adverse events. Studies were underpowered to detect differences in the risk of fracture. Denosumab is a reasonable option for treatment of GIOP. However, further studies are needed to guide transitions off denosumab.

Kidney Blood Press Res. 2019 Oct 15;44(5):1285-1293. doi: 10.1159/000503066. [Epub ahead of print]

Follow-Up of Bone Mineral Density Changes in de novo Kidney Transplant Recipients Treated with Two Doses of the Receptor Activator of Nuclear Factor κ B Ligand Inhibitor Denosumab.

Kobel C1, Frey D2, Graf N3, Wüthrich RP1, Bonani M4.

BACKGROUND: Studies in women with post-menopausal osteoporosis have shown that discontinuation of treatment with denosumab leads to an increased risk of vertebral fractures because of rebound bone turnover and rapid loss of bone mineral density (BMD). **METHODS:** In a post hoc analysis of the Prolia for Osteoporosis of Transplant Operated Patient study, we analyzed the effect of denosumab withdrawal on BMD changes. Twenty-five de novo kidney transplant recipients (KTR) who were treated for 1 year with 2 six-monthly doses of denosumab on

top of standard treatment (daily calcium and vitamin D) were compared to a control group of 29 KTR who received standard treatment alone. BMD changes were analyzed by repeated dual-energy X-ray absorptiometry shortly after transplantation (baseline), after 6 and 12 months (active treatment phase) and after 2-6.5 years (follow-up phase). RESULTS: The average BMD at the lumbar spine declined markedly after discontinuation of treatment with denosumab but increased again thereafter. Thus, the average monthly change in lumbar spine BMD from month 12 onward was only $0.1 \pm 2.8\%$ in the denosumab group but $1.5 \pm 1.9\%$ in the control group ($p = 0.021$). The average monthly change in lumbar spine BMD from baseline to follow-up was similar in the control and denosumab group ($1.1 \pm 1.2\%$ vs. $1.5 \pm 2.4\%$, $p = 0.788$). Similar results were seen at the total hip. CONCLUSIONS: In de novo KTR treated with 2 doses of denosumab, we detect a marked decrease in lumbar spine and hip BMD when denosumab is discontinued. Denosumab treatment should therefore not be discontinued without considering an alternative antiresorptive treatment.

J Clin Endocrinol Metab. 2019 Oct 15. pii: dgz056. doi: 10.1210/clinem/dgz056. [Epub ahead of print]

Trabecular Bone Score Declines During the Menopause Transition: the Study of Women's Health Across the Nation (SWAN).

Greendale GA1, Huang M1, Cauley JA2, Liao D1, Harlow S2, Finkelstein JS3, Hans D4, Karlamangla AS5.

CONTEXT: Rapid bone density loss starts during the menopause transition (MT). Whether other components of bone strength deteriorate prior to the final menstrual period (FMP) remains uncertain. OBJECTIVE: To discern whether TBS declines during the MT. DESIGN: An 18-year longitudinal analysis from the Study of Women's Health Across Nation. SETTING: Community-based cohort. PARTICIPANTS: 243 Black, 164 Japanese, and 298 White, initially pre- or early perimenopausal women, who experienced their FMP. MAIN OUTCOME MEASURES: Trabecular bone score (TBS), an indicator of bone strength. RESULTS: Multivariable mixed effects regressions fitted piece-wise linear models to repeated measures of TBS as a function of time before or after the FMP; covariates were age at FMP, race/ethnicity and body mass index. Prior to 1.5 years before the FMP, in the referent individual (a White woman with age at FMP of 52.2 years and BMI of 28.0 kg/m²), TBS evidenced no change (slope 0.12% per year, $p=0.2991$). TBS loss began 1.5 years prior to the FMP, declining by 1.16% annually ($p<0.0001$). Starting 2 years after the FMP, annual rate of TBS loss lessened to 0.89% ($p<0.0001$). In the 5 years before through the 5 years after the FMP, in the referent individual, total TBS decline was 6.3% ($p<0.0001$), but Black participants' total TBS loss was 4.90% ($p=0.0008$, difference in Black and White 10-year change). Results for Japanese did not differ from those of White women. CONCLUSIONS: The occurrence of an MT-related decline in TBS supports the thesis that this period is particularly damaging to skeletal integrity.

Menopause. 2019 Oct 14. doi: 10.1097/GME.0000000000001405. [Epub ahead of print]

Lifetime estrogen exposure and cognition in late life: the Cache County Study.

Matyi JM1, Rattinger GB2, Schwartz S1, Buhusi M1, Tschanz JT1.

OBJECTIVE: Prevalence of Alzheimer's disease (AD) is higher for women, possibly influenced by sex-dependent effects of the estrogen. We examined the association between estrogen and cognitive decline in over 2,000 older adult women in a 12-year population-based study in Cache County, Utah. METHODS: The baseline sample included 2,114 women (mean age = 74.94 y, SD=6.71) who were dementia-free at baseline and completed a women's health questionnaire, asking questions regarding reproductive history and hormone therapy (HT). Endogenous estrogen exposure (EEE) was calculated taking the reproductive window (age at menarche to age at menopause), adjusted for pregnancy and breastfeeding. HT variables included duration of use, HT type (unopposed; opposed), and time of HT initiation. A modified version of the Mini-Mental State Examination (3MS) was administered at four triennial waves to assess cognitive status. Linear mixed-effects models examined the relationship between estrogen exposure and 3MS score over time. RESULTS: EEE was positively associated with cognitive status ($\beta=0.03$, $P=0.054$). In addition, longer duration of HT use was positively associated with cognitive status ($\beta=0.02$, $P=0.046$) and interacted with age; older women had greater benefit compared with younger women. The timing of HT initiation was significantly associated with 3MS ($\beta=0.55$, $P=0.048$), with higher scores for women who initiated HT within 5 years of menopause compared with those initiating HT 6-or-more years later. CONCLUSIONS: Our results suggest that longer EEE and HT use, especially in older women, are associated with higher cognitive status in late life.

Int J Rheum Dis. 2019 Oct 14. doi: 10.1111/1756-185X.13713. [Epub ahead of print]

Fibromyalgia, sleep disturbance and menopause: Is there a relationship? A literature review.

Dias RCA1, Kulak Junior J1, Ferreira da Costa EH2, Nisihara RM1,2,3.

INTRODUCTION: Fibromyalgia (FM) symptoms worsen in a significant portion of patients with the onset of menopause. Some patients report that their symptoms begin after menopause, suggesting a relationship between these entities. Sleep disturbance is a common condition in FM and menopause, and it is associated with chronic pain. **METHODS/OBJECTIVES:** Several electronic databases were searched, from the first available year to April 2018 to evaluate the publications that assessed the effects of menopause and sleep disturbance on the appearance or worsening of FM and the role of hormone therapy for these patients. **RESULTS:** The results are summarized in three tables. The objective sleep patterns of FM patients included high sleep latency, frequent arousals and intrusion of alpha wave sleep and NREM (non-rapid eye movement) sleep in delta sleep. Poor sleep during menopause is more frequent in late perimenopause and surgical menopause, and may be related to vasomotor symptoms or not. Hormone therapy exerted a positive effect on subjective sleep quality of symptomatic menopausal women. Studies have shown a high association between FM and early and surgical menopause. Raloxifene exerted a positive effect on pain and sleep in FM patients; however one study that analyzed the effects of transdermal estrogen therapy found no improvement in subjective and objective parameters of pain. **CONCLUSION:** Further studies are needed to elucidate the nature of the association between menopause, sleep and persistent pain syndromes, such as FM, showing the role of hormone therapy in prospective placebo-controlled trials.

EXCLI J. 2019 Aug 6;18:591-603. doi: 10.17179/excli2019-1386. eCollection 2019.

The effects of vitamin D supplementation on muscle function among postmenopausal women: a systematic review and meta-analysis of randomized controlled trials.

Tabrizi R1,2, Hallajzadeh J3, Mirhosseini N4, Lankarani KB1, Maharlouei N1, Akbari M1, Asemi Z5.

The loss of muscle mass and its strength is one of the most critical changes in aging which is associated with an increased risk of falls, osteoporotic fractures and mobility disability. Vitamin D, with its extra-skeletal benefits, might improve muscle function in elderly. The current systematic review and meta-analysis of randomized controlled trials (RCTs) was conducted to summarize available relevant data and determine the effect of vitamin D supplementation on muscle function among postmenopausal women. We reached databases including; Cochrane library, Embase, PubMed, and Web of Science database until the end of May 2018 to identify relevant published RCTs. Heterogeneity among included studies was assessed using Q-test and I² statistics. Random-effect model was applied to pool data and weighted mean difference (WMD) was calculated representing summary effect size. Outcomes of interest included the effects of vitamin D supplementation on hand grip strength (HGS), back muscle strength (BMS), and Timed Up and Go (TUG). Twelve RCTs out of 1739 potential reports were included in our meta-analysis. The pooled findings showed that vitamin D supplementation had no significant effect on HGS (WMD -0.03 kilogram (Kg); 95 % CI, -0.26, 0.20; P=0.78), BMS (WMD 7.21 newton (N); 95 % CI, -5.98, 20.40; P=0.28), and TUG (WMD 0.01 second (S); 95 % CI, -0.17, 0.18; P=0.93) in postmenopausal women. Overall, the current meta-analysis showed that taking vitamin D supplementation by postmenopausal women did not affect markers of muscle function. Further studies are required to confirm the effect of vitamin D supplementation on markers of muscle function.