



## Selección de Resúmenes de Menopausia

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### Cellular senescence in musculoskeletal homeostasis, diseases, and regeneration

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Emerging insights into cellular senescence highlight the relevance of senescence in musculoskeletal disorders, which represent the leading global cause of disability. Cellular senescence was initially described by Hayflick et al. in 1961 as an irreversible nondividing state in in vitro cell culture studies. We now know that cellular senescence can occur in vivo in response to various stressors as a heterogeneous and tissue-specific cell state with a secretome phenotype acquired after the initial growth arrest. In the past two decades, compelling evidence from preclinical models and human data show an accumulation of senescent cells in many components of the musculoskeletal system. Cellular senescence is therefore a defining feature of age-related musculoskeletal disorders, and targeted elimination of these cells has emerged recently as a promising therapeutic approach to ameliorate tissue damage and promote repair and regeneration of the skeleton and skeletal muscles. In this review, we summarize evidence of the role of senescent cells in the maintenance of bone homeostasis during childhood and their contribution to the pathogenesis of chronic musculoskeletal disorders, including osteoporosis, osteoarthritis, and sarcopenia. We highlight the diversity of the senescent cells in the microenvironment of bone, joint, and skeletal muscle tissue, as well as the mechanisms by which these senescent cells are involved in musculoskeletal diseases. In addition, we discuss how identifying and targeting senescent cells might positively affect pathologic progression and musculoskeletal system regeneration.

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### Progesterone eliminates 17 $\beta$ -estradiol-Mediated cardioprotection against diabetic cardiovascular dysfunction in ovariectomized rats

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Background: Type2 Diabetes (T2D) remains one of the most important causes of cardiovascular diseases (CVD). Menopause leads to an increase in CVD and metabolic syndrome, which indicates the role of sex steroids as a protective factor. In the present study, we surveyed the effects of 17 $\beta$ -estradiol (E2) alone and in combination with progesterone (P4) on cardiovascular dysfunction in T2D. Methods: Female ovariectomized (OVX) diabetic rats were divided into eight groups: Sham-Control, Diabetes (Dia), OVX + Dia, OVX + Dia + Vehicle, OVX + Dia + E2, OVX + Dia + P4, OVX + Dia + E2+P4, and OVX + Dia + E2+Vehicle. T2D was induced by a high-fat diet and streptozotocin. E2 and P4 were administered every four days for four weeks. The heart cytokines and angiotensin II, lipid profile, insulin, water, and food intake and cardiovascular indices were measured. Results: Results showed that single treatment with E2 decreased fasting blood glucose, water, and food intake, atherogenic and cardiac risk indices, and blood pressure. Also, P4 led to a decrease in atherogenic and cardiac risk indices. TNF $\alpha$  and IL-6 levels were increased and IL-10 was decreased in the Dia group, while E2 alone was able to inhibit these changes. The combined use of E2 and P4 eliminated the beneficial effects of E2 on these indices. Although diabetes results in an increment of cholesterol, LDL and triglyceride, hormone therapy with E2 was associated with improved dyslipidemia. Conclusion: The use of E2 alone, and not the individual use of P4, and its combination with E2 improved cardiovascular function in OVX diabetic animals, possibly by reducing the amount of inflammatory cytokines and improving metabolic parameters.

**Reumatol Clin. 2021 Sep 7;S1699-258X(21)00185-6.doi: 10.1016/j.reuma.2021.07.003. Online ahead of print.**

### Bone Health and Predictors of 15-Year Mortality in a Physically Active Population

Antonio Juan, Guillem Frontera, Ana Paula Cacheda, Mónica Ibáñez, Javier Narváez, Bartolomé Marí, et al.

Objective: To analyse determinants of mortality at 15years in a population over 60years of age and physically active. Methods: This is a prospective longitudinal study. After 15years of participating in an active aging programme, participants were contacted by telephone to verify their state of health and to determine whether in that time they had had any fractures. Results: A total of 561 individuals over 60years of age were included, 82% of whom were women.

Only differences in densitometric data, FRAX values and history of previous fracture at baseline characteristics were found between the group that died at 15years and the group that remained alive. The only variables that were related to mortality risk were the basal data of the densitometric T-score (OR=.50, P<.001) and history of fracture in any location (OR=2.44, P<.033). Conclusions: The value of bone mineral density could be considered as a useful biomarker to calculate the risk of mortality in people over 60years old with a physically active lifestyle.

**Rev Colomb Obstet Ginecol. 2021 Jun 30;72(2):162-170.doi: 10.18597/rcog.3662.**

## **Prevalencia de problemas de sueño en mujeres climatéricas colombianas durante la pandemia COVID-19**

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Objetivo: elaborar una aproximación a la prevalencia de los problemas de sueño (PDS) en mujeres climatéricas colombianas durante la pandemia COVID-19. Materiales y Métodos: estudio transversal que pertenece al proyecto de investigación Calidad de Vida en la Menopausia y Etnias Colombianas bajo condiciones de pandemia [CAVIMEC+COVID STUDY]. Se incluyeron mujeres naturales y residentes en Colombia entre 40 y 59 años, quienes en los primeros cinco días de junio del 2020 participaron de forma anónima y voluntaria, previo consentimiento informado en el diligenciamiento de un formulario alojado en una plataforma virtual. Los PDS fueron identificados con el tercer ítem de Menopause Rating Scale. Se exploraron características sociodemográficas, la presencia y severidad de los PDS y el estado menopáusico. Se hace estadística descriptiva. Resultados: participaron 984 mujeres, la mediana de edad fue 47,0 [RIC: 42,0-53,5] años. El 84,5% de las participantes eran mestizas, el 13,7% afrodescendientes y 1,7% indígenas. El 39,3% posmenopáusicas. El 70% residían en la región caribe colombiana. Informaron PDS 637 (64,7%) de las participantes y 112 (11,3%) tenían PDS severos. Las posmenopáusicas informaron un 65,1% de PDS, en forma severa el 10,1%, y las premenopáusicas informaron 64,5%, en forma severa el 12,2%. Conclusiones: los PDS podrían ser un problema frecuente en las mujeres en estado premenopáusico y postmenopáusico. Se debe explorar este problema en la consulta ginecológica para ofrecer soluciones. Se requieren estudios poblacionales que confirmen estas observaciones.

**Mech Ageing Dev. 2021 Sep 6;199:111565.doi: 10.1016/j.mad.2021.111565. Online ahead of print.**

## **The role of senolytics in osteoporosis and other skeletal pathologies**

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The skeletal system undergoes irreversible structural deterioration with aging, leading to increased fracture risk and detrimental changes in mobility, posture, and gait. This state of low bone mass and microarchitectural changes, diagnosed as osteoporosis, affects millions of individuals worldwide and has high clinical and economic burdens. Recently, pre-clinical studies have linked the onset of age-related bone loss with an accumulation of senescent cells in the bone microenvironment. These senescent cells appear to be causal to age-related bone loss, as targeted clearance of these cells leads to improved bone mass and microarchitecture in old mice. Additionally, other pathologies leading to bone loss that result from DNA damage, such as cancer treatments, have shown improvements after clearance of senescent cells. The development of new therapies that clear senescent cells, termed "senolytics", is currently underway and may allow for the modulation of bone loss that results from states of high senescent cell burden, such as aging.

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## **One leg standing time predicts fracture risk in older women independent of clinical risk factors and BMD**

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Introduction: Physical function and risk of falls are important risk factors for fracture. A few previous studies have suggested that a one leg standing time (OLST) less than 10 s predicts fracture risk, but the impact of OLST, in addition to known clinical risk factors, for fracture probability is unknown. The aim of this study was to determine the independent contribution of OLST to fracture probability in older women. Methods: The Sahlgrenska University Hospital Prospective Evaluation of Risk of Bone Fractures (SUPERB) is a prospective population-based study of 3028 women 75-80 years old, recruited from the greater Gothenburg area in Sweden. At baseline, information on risk factors was collected using questionnaires, bone mineral density was measured with dual-energy X-ray absorptiometry (DXA), and OLST was performed. Results: During a median follow-up of 3.6 years (IQR 1.5 years), X-ray-verified

incident fractures were identified using health records. OLST was available in 2405 women. OLST less than 10 s was associated with an increased risk for incident hip fracture (Hazard Ratio (HR) 3.02, 95% Confidence Interval (CI) [1.49-6.10]), major osteoporotic fracture (HR 95% CI 1.76 [1.34-1.46]), and nonvertebral fracture (HR 95% CI 1.61 [1.26-2.05]) in Cox regression analyses adjusted for age, height, and weight. Depending on BMD, the 4-year fracture probability increased by a factor of 1.3 to 1.5 in a 75-year-old woman with a low OLST (<10 s). Conclusion: A low OLST has a substantial impact on fracture probability and should be considered when evaluating fracture risk in older women.

**J Am Heart Assoc. 2021 Sep 6;e021362.doi: 10.1161/JAHA.121.021362. Online ahead of print.**

### **Age at Menopause in Relationship to Lipid Changes and Subclinical Carotid Disease Across 20 Years: Study of Women's Health Across the Nation**

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Background Younger age at final menstrual period (FMP) is associated with increased risk for cardiovascular disease events. This paper evaluated whether older age at FMP is associated with more favorable patterns of lipid changes during the menopause transition and whether these changes are associated with less subclinical carotid disease in the postmenopausal years. Methods and Results Lipids and lipoproteins were measured repeatedly among 1554 premenopausal women who had a natural menopause during follow-up years (median=18.8 years); a subset of 890 women also had measures of carotid intima media thickness, adventitial diameter, and plaque. Women who had an older FMP age had less adverse changes in cholesterol from 1 to 3 years after FMP, and in triglycerides from FMP to 3 years after FMP, but they had more adverse changes in ApoB and Apo A1 from 3 years before to 1 year after the FMP. Increasing cholesterol and ApoB from 1 to 3 years after FMP were associated with greater intima media thickness and adventitial diameter, and the greater likelihood of a plaque score >2 the older the age at FMP. Conclusions Despite the epidemiological literature showing early age at FMP is associated with elevated risk for cardiovascular disease events, older age at FMP had inconsistent associations with less adverse lipid changes in midlife, which did not translate into less risk for subclinical carotid disease and in some cases more risk. These findings are restricted to women who experience FMP in the normative age range for the menopausal transition.