

### Selección de Resúmenes de Menopausia

Semana del 26 de Noviembre al 2 de Diciembre de 2014 Juan Enrique Blümel. Departamento Medicina Sur. Universidad de Chile

#### Calcif Tissue Int. 2014 Nov 29. [Epub ahead of print]

### Analysis of the Bone MicroRNome in Osteoporotic Fractures.

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Osteoporosis causes important morbidity among elderly individuals. Fragility fractures, and especially hip fractures, have a particularly negative impact on the patients' quality of life. The role of epigenetic mechanisms in the pathogenesis of many disorders is increasingly recognized, yet little is known about their role in non-malignant bone disorders such as osteoporosis. The aim of this study was to explore the expression of miRNAs in patients with osteoporotic hip fractures. Trabecular bone samples were obtained from the femoral heads of patients undergoing replacement surgery for osteoporotic hip fractures and non-fracture controls with hip osteoarthritis. Levels of 760 miRNA were analyzed by real-time PCR. Thirteen miRNAs showed nominally significant (p < 0.05) differences between both groups. Six miRNAs (miR-187, miR-193a-3p, miR-214, miR518f, miR-636, and miR-210) were selected for the replication stage. These miRNAs were individually analyzed in a larger group of 38 bone samples. At this stage, we confirmed statistically significant differences across groups for mir-187 and miR-518f. The median relative expression levels of miR-187 were 5.3-fold higher in the non-fracture group (p = 0.002). On the contrary, miR-518f was preferentially expressed in bones from osteoporotic patients (8.6-fold higher in fractures; p = 0.046). In this first hypothesis-free study of the bone microRNome we found two miRNAs, miR-187, and miR-518f, differentially regulated in osteoporotic bone. Further studies are needed to elucidate the mechanisms involved in the association of these miRNAs with fractures.

Nota de Editor. Un microRNA (miRNA, abreviado) es un pequeño molécula de RNA (que contiene alrededor de 22 nucleótidos) que puede actuar en múltiples genes, modificando la lectura del RNA mensajero y por lo tanto, alterar la síntesis proteica.

## Neurobiol Aging. 2014 Nov 1. pii: S0197-4580(14)00688-5. doi: 10.1016/j.neurobiolaging.2014.10.028. [Epub ahead of print]

## Critical period for dopaminergic neuroprotection by hormonal replacement in menopausal rats.

Rodriguez-Perez AI1, Borrajo A1, Valenzuela R1, Lanciego JL2, Labandeira-Garcia JL3.

The neuroprotective effects of menopausal hormonal therapy in Parkinson's disease have not yet been clarified, and it is not known whether there is a critical period. Estrogen induced significant protection against 6-hydroxydopamine-induced dopaminergic degeneration when administered immediately or 6 weeks, but not 20 weeks after ovariectomy. In the substantia nigra, ovariectomy induced a decrease in levels of estrogen receptor- $\alpha$  and increased angiotensin activity, NADPH-oxidase activity, and expression of neuroinflammatory markers, which were regulated by estrogen administered immediately or 6 weeks but not 20 weeks after ovariectomy. Interestingly, treatment with angiotensin receptor antagonists after the critical period induced a significant level of neuroprotection. In cultures, treatment with 1-methyl-4-phenylpyridinium induced an increase in astrocyte-derived angiotensinogen and dopaminergic neuron death, which were inhibited by estrogen receptor  $\alpha$  agonists. In microglial cells, estrogen receptor  $\beta$  agonists inhibited the angiotensin-induced increase in inflammatory markers. The results suggest that there is a critical period for the neuroprotective effect of estrogen against dopaminergic cell death, and local estrogen receptor  $\alpha$  and reninangiotensin system play a major role.

#### Am J Lifestyle Med. 2007 May;1(3):220-235.

### The Anti-Inflammatory Actions of Exercise Training.

Flynn MG, McFarlin BK, Markofski MM.

The list of diseases with a known inflammatory etiology is growing. Cardiovascular disease, osteoporosis, diabetes, geriatric cachexia, and Alzheimer's disease have all been shown to be linked to or exacerbated by aberrantly regulated inflammatory processes. Nevertheless, there is mounting evidence that those who are physically active, or

who become physically active, have a reduction in biomarkers associated with chronic inflammation. There was strong early consensus that exercise-induced reductions in inflammation were explained by body mass index or body fatness, but recent studies provide support for the contention that exercise has body fat-independent anti-inflammatory effects. With few exceptions, the anti-inflammatory effects of exercise appear to occur regardless of age or the presence of chronic diseases. What remains unclear are the mechanisms by which exercise training induces these anti-inflammatory effects, but there are several intriguing possibilities, including release of endogenous products, such as heat shock proteins; selective reduction of visceral adipose tissue mass or reducing infiltration of adipocytes by macrophages; shift in immune cell phenotype; cross-tolerizing effects; or exercise-induced shifts in accessory proteins of toll-like receptor signaling. However, future research endeavors are likely to uncover additional potential mechanisms, and it could be some time before functional mechanisms are made clear. In summary, the potential anti-inflammatory influences of exercise training may provide a low-cost, readily available, and effective treatment for low-grade systemic inflammation and could contribute significantly to the positive effects of exercise training on chronic disease.

## Cochrane Database Syst Rev. 2014 Nov 28;11:CD006108. [Epub ahead of print] Exercise for vasomotor menopausal symptoms.

Daley A1, Stokes-Lampard H, Thomas A, MacArthur C.

BACKGROUND: Evidence suggests that many perimenopausal and early postmenopausal women will experience menopausal symptoms; hot flushes are the most common. Symptoms caused by fluctuating levels of oestrogen may be alleviated by hormone therapy (HT), but a marked global decline in its use has resulted from concerns about the risks and benefits of HT. Consequently, many women are seeking alternatives. As large numbers of women are choosing not to take HT, it is increasingly important to identify evidence-based lifestyle modifications that have the potential to reduce vasomotor menopausal symptoms, OBJECTIVES: To examine the effectiveness of any type of exercise intervention in the management of vasomotor symptoms in symptomatic perimenopausal and postmenopausal women. Searches include findings up to 3 March 2014. SELECTION CRITERIA: RCTs in which any type of exercise intervention was compared with no treatment/control or other treatments in the management of menopausal vasomotor symptoms in symptomatic perimenopausal/postmenopausal women. MAIN RESULTS: We included five RCTs (733 women) comparing exercise with no active treatment, exercise with yoga and exercise with HT. The evidence was of low quality: Limitations in study design were noted, along with inconsistency and imprecision. In the comparison of exercise versus no active treatment (three studies, n = 454 women), no evidence was found of a difference between groups in frequency or intensity of vasomotor symptoms (SMD -0.10, 95% CI -0.33 to 0.13, three RCTs, 454 women, I2 = 30%, low-quality evidence). Nor was any evidence found of a difference between groups in the frequency or intensity of vasomotor symptoms when exercise was compared with yoga (SMD -0.03, 95% CI -0.45 to 0.38, two studies, n = 279 women, I2 = 61%, low-quality evidence). It was not possible to include one of the trials in the meta-analyses; this trial compared three groups: exercise plus soy milk, soy milk only and control; results favoured exercise relative to the comparators, but study numbers were small. One trial compared exercise with HT, and the HT group reported significantly fewer flushes in 24 hours than the exercise group (mean difference 5.8, 95% CI 3.17 to 8.43, 14 participants). None of the trials found evidence of a difference between groups with respect to adverse effects, but data were very scanty. AUTHORS' CONCLUSIONS: Evidence was insufficient to show whether exercise is an effective treatment for vasomotor menopausal symptoms. One small study suggested that HT is more effective than exercise. Evidence was insufficient to show the relative effectiveness of exercise when compared with HT or yoga.

#### Ther Clin Risk Manag. 2014 Nov 18;10:937-948. eCollection 2014.

A systematic review of the outcomes of osteoporotic fracture patients after hospital discharge: morbidity, subsequent fractures, and mortality.

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PURPOSE: Osteoporotic fracture is the main complication of osteoporosis. The current management is to discharge patients as early as possible so they can get back to their daily activities. Once discharged, there are three main issues relating to morbidity, mortality, and risk of a subsequent fracture that need to be addressed and discussed. Therefore, the aim of this systematic review was to summarize and evaluate the evidence from published literature, to determine the outcome of osteoporotic fracture patients after their hospital discharge. METHODS: The MEDLINE and Cumulative Index to Nursing and Allied Health Literature (CINAHL) databases were searched, using the terms

"osteoporosis", "fracture", "osteoporotic fracture", "hip fracture", and "vertebral fracture". We included only human studies published in English between 2004 and 2014. The reference lists of included studies were thoroughly reviewed in search for other relevant studies. RESULTS: A total of 18 studies met the selection criteria. Most were observational and cohort studies. Out of all the studies, five studies looked into the morbidity, six studies looked into the risk of subsequent fractures, and seven studies looked into mortality. Vertebral fracture caused the greatest health burden, but hip fracture patients were the main users of informal care after hospital discharge. There was an increased risk of a subsequent fracture after a primary fracture compared with the control group, a cohort comparison, or the general population. Osteoporotic fractures, especially hip fractures, are associated with higher mortality rate despite the advances in the management of osteoporotic fracture cases. CONCLUSION: There is strong evidence to show that after hospital discharge, osteoporotic fracture patients are faced with higher morbidity, subsequent fractures, and mortality.

# Acta Obstet Gynecol Scand. 2014 Nov 24. doi: 10.1111/aogs.12546. [Epub ahead of print] Postmenopausal hot flushes and bone mineral density. A longitudinal study.

Tuomikoski P1. Ylikorkala O. Mikkola TS.

OBJECTIVE: To study the possible association between menopausal hot flushes and bone mineral density. DESIGN: Observational study. SETTING: University clinic. POPULATION: Healthy women (n=143) with or without hot flushes and 6-36 months postmenopausal of participating in a six month hormone therapy trial. METHODS: The women prospectively recorded the number and severity of hot flushes for two weeks. Bone mineral density in lumbar and hip bones was measured with dual-energy x-ray absorptiometry at recruitment and reassessed in 114 women approximately 6.2 years later. MAIN OUTCOME MEASURES: Hot flushes and bone mineral density. RESULTS: At recruitment hot flushes were absent in 22 women, mild in 32, moderate in 28, and severe in 61. Lumbar bone mineral densities in non-flushing women (1.130±0.022 g/cm2; mean±SEM), and in those with mild (1.088±0.024 g/cm<sup>2</sup>), moderate (1.082±0.030 g/cm<sup>2</sup>), or severe (1.102±0.019 g/cm<sup>2</sup>) hot flushes did not differ. Neither were there differences in hip bone mineral densities between the four study groups. During the followup lumbar bone mineral density decreased by a mean of 0.4±0.1 percent/year in women not using hormone therapy, and increased by  $0.1\pm0.2$  percent/year in hormone therapy users (p=0.019). The respective non-significant changes in left and right total hip bone mineral densities were -0.6±0.01 and -1.0±0.1 for the non-users, and -0.4±0.1 and -0.6±0.2 for hormone therapy users. These changes in bone mineral density bore no relation to the hot flush status at baseline. CONCLUSION: In recently menopausal women, hot flushes do not appear to determine bone mass density. This article is protected by copyright. All rights reserved.

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