

## Selección de Resúmenes de Menopausia

Semana del 28 de diciembre 2022 al 3 de enero de 2023  
María Soledad Vallejo. Clínica Quilín. Universidad de Chile

**Sci Rep. 2022 Dec 30;12(1):22596. doi: 10.1038/s41598-022-27240-5.**

### **Effect of hormonal therapy on the otoconial changes caused by estrogen deficiency**

Takahiro Nakata 1 2, Masahiro Okada 3, Eriko Nishihara 3, Aoi Ikeda 4, Sawa Asoh 3, Taro Takagi 3, et al.

Benign paroxysmal positional vertigo (BPPV) is associated with menopause and/or osteopenia. Morphological changes in the otoconial layer have been reported after ovariectomy (OVX). Moreover, hormone replacement therapy decreases BPPV risk. However, knowledge concerning the effect of hormonal therapy on the otoconial changes caused by estrogen deficiency is limited. We aimed to examine the effect of hormonal therapy on otoconial changes caused by estrogen deficiency. We hypothesized that hormonal therapy could reduce otoconial changes caused by OVX. Eight-week-old C57BL/6 mice were divided into four groups: sham operation with implantation of vehicle (sham + v), OVX with implantation of vehicle (OVX + v), OVX with implantation of estradiol (E2) (OVX + E2), and OVX with implantation of raloxifene (RAL) (OVX + RAL) groups. Otoconial layer volume was measured by micro-CT at 4 weeks after OVX or the sham operation. The otic bullae were removed; immunohistochemistry was performed for estrogen receptor alpha and 4-hydroxynonenal. Otoconial layer volume was significantly higher in the OVX + v than in the sham + v group. E2 and RAL significantly reduced these changes in the endometrial layer. The staining of estrogen receptor alpha and 4-hydroxynonenal were stronger in the OVX + v than in the sham + v group but equal in the sham + v, OVX + E2, and OVX + RAL groups. These results indicate that E2 and RAL are effective against morphological changes of the otoconial layer caused by estrogen deficiency via oxidative stress reduction.

**Eur J Appl Physiol. 2022 Dec 31. doi: 10.1007/s00421-022-05093-0. Online ahead of print.**

### **Effects of transdermal estrogen therapy on satellite cell number and molecular markers for muscle hypertrophy in response to resistance training in early postmenopausal women**

Tine Vrist Dam 1, Line Barner Dalgaard 1, Frank Ted Johansen 1, Mads Bisgaard Bengtsen 2, Maike Mose 2, et al.

Purpose: To investigate the effects of resistance training with or without transdermal estrogen therapy (ET) on satellite cell (SC) number and molecular markers for muscle hypertrophy in early postmenopausal women. Methods: Using a double-blinded randomized controlled design, we allocated healthy, untrained postmenopausal women to perform 12 weeks of resistance training with placebo (PLC, n = 16) or ET (n = 15). Muscle biopsies obtained before and after the intervention, and two hours after the last training session were analyzed for fiber type, SC number and molecular markers for muscle hypertrophy and degradation (real-time PCR, western blotting). Results: The analysis of SCs per Type I fiber showed a time x treatment interaction caused by a 47% decrease in PLC, and a 26% increase after ET after the training period. Also, SCs per Type II fiber area was lower after the intervention driven by a 57% decrease in PLC. Most molecular markers changed similarly in the two groups. Conclusion: A decline in SC per muscle fiber was observed after the 12-week training period in postmenopausal women, which was counteracted when combined with use of transdermal ET.

**Clin Endocrinol (Oxf). 2022 Dec 30. doi: 10.1111/cen.14874. Online ahead of print.**

### **Endogenous testosterone concentrations and muscle mass, strength and performance in women, a systematic review of observational studies**

Sasha Taylor 1, Rakibul M Islam 1, Robin J Bell 1, Chandima Hemachandra 1 2, Susan R Davis 1 3

Objective: To explore the associations between endogenous testosterone blood concentrations and muscle mass, strength and performance in community dwelling women. Design, patients, and measurements: Online databases, including Ovid MEDLINE, EMBASE and Web of Science, were searched for observational studies, with at least 100 female participants, reporting associations between endogenous testosterone blood concentrations and muscle mass, strength and performance. The findings were synthesised in a narrative review. Heterogeneity in study design and analysis precluded a meta-analysis. Results: Of the 36 articles retrieved for full-text review, 10 met the inclusion criteria. Eight studies were cross-sectional, one longitudinal, and one provided both cross-sectional and longitudinal data. Testosterone was measured by liquid chromatography-tandem mass spectrometry in two studies and by immunoassay in eight. An association between total

testosterone and muscle mass, strength or performance in women was not found. The studies of calculated free or bioavailable testosterone and lean muscle mass reported a positive association, but no association was reported for muscle strength or performance. Each included study was limited by a high risk of bias in at least one assessed domain. Conclusions: This review does not support an association between testosterone and muscle mass, strength or performance in women. This, together with the reported associations between free or bioavailable testosterone and muscle mass should be interpreted cautiously due to the predominant use of immunoassay and the inaccuracy of calculated variables. Additionally, biological significance of nonprotein bound testosterone has not been established. Further studies examining the relationship between precisely measured testosterone and muscle mass and function in women are required.

**PLoS One. 2022 Dec 30;17(12):e0270242. doi: 10.1371/journal.pone.0270242. eCollection 2022.**

### **Evaluation of the efficacy of Lactobacillus-containing feminine hygiene products on vaginal microbiome and genitourinary symptoms in pre- and postmenopausal women: A pilot randomized controlled trial**

Remi Yoshikata 1 2, Michiko Yamaguchi 1, Yuri Mase 1 2, Ayano Tatsuyuki 1 2, Khin Zay Yar Myint 2, et al.

As estrogen level decreases with aging, the vaginal mucosa gets thinner, and collagen amount decreases. In addition, the population of Lactobacillus in the vagina declines, increasing the risk of atrophic vaginitis, bacterial vaginosis, and genitourinary symptoms in the postmenopausal women. In this study, we evaluated the effects of Lactobacillus-containing feminine hygiene products on vaginal microbiome and genitourinary symptoms in pre- and postmenopausal women. This was a pilot randomized controlled trial in 35 premenopausal and 35 postmenopausal healthy women. For 4 weeks, treatment 1 group (14 premenopausal and 16 postmenopausal women) used the Lactobacillus-containing feminine soap and cream, and treatment 2 group (15 premenopausal and 14 postmenopausal women) used Lactobacillus-containing feminine gel in addition to soap and cream. The remaining 6 premenopausal and 5 postmenopausal women served as controls without using any products. We then compared the changes in the vaginal microbiota, genitourinary symptoms, and other related biomarkers after completion of treatment. Vaginal pH and pathogenic flora were reduced in both treatment groups compared to control group, which was more significant in the treatment 2 group of postmenopausal women. Genitourinary symptoms significantly improved in 60% of premenopausal women in treatment 1 group and 81.3% of postmenopausal women in treatment 2 group, compared to control group (0%,  $p = 0.043$  and  $p < 0.01$  respectively). Overactive bladder symptom scores were significantly improved after using the products in eleven out of twelve postmenopausal women suspected of having overactive bladder. The use of Lactobacillus-containing feminine products was associated with improved vaginal ecosystem and urogenital health compared to control group, especially in those women using feminine gel.

**Diabetes Metab Res Rev. 2022 Dec 29;e3603. doi: 10.1002/dmrr.3603. Online ahead of print.**

### **Statin use in patients with type 2 diabetes has lower risk of hip fractures: A Taiwan national population-based study**

Tien-Ching Lee 1 2 3 4 5, Jian-Chih Chen 4 5, Sung-Yen Lin 2 3 4 5, Pei-Shan Ho 6, Chung-Hwan Chen, et al.

Introduction: Type 2 diabetes mellitus (T2DM) frequently co-exists with osteoporosis and dyslipidemia. Statins have been commonly used in the treatment of dyslipidemia. Recent studies have indicated a therapeutic role of statins in decreasing the risk of osteoporosis and fractures, but conflicting results have been reported. This study investigated the association between statin use and hip fracture (HFX) risk among T2DM patients. Methods: A retrospective Taiwan population-based propensity-matched cohort study was performed using the Diabetes Mellitus Health Database from Taiwan National Health Insurance Research Database. Patients newly diagnosed with T2DM between 2010 and 2014 were identified. Patients who previously used statins and ever suffered HFX before the index date were excluded. HFX that occurred from 2010 to 2019 were collected to compute the cumulative rate of HFX. Hazard ratios (HRs) were calculated for the HFX risk according to the use or non-use of statins. To evaluate the dose-effect relationship of statins, sensitivity analyses were conducted. Results: After propensity score matching for age and sex, 188,588 patients were identified as statin users and non-statin users. Statin use after T2DM diagnosis was associated with a decreased HFX risk with an adjusted HR (aHR) of 0.69 ( $P < 0.001$ ). A dose-effect relationship was identified. The aHRs for developing HFX were 1.29, 0.67, and 0.36 for patients who used 28-174, 175-447, and  $>447$  cumulative defined daily doses of statins, respectively ( $P < 0.001$ ). Conclusions: Statin use in adults with T2DM showed lower risk of HFX with demonstrating a dose-response relationship.

**J Ovarian Res. 2022 Dec 28;15(1):139. doi: 10.1186/s13048-022-01083-0.**

## Ovarian tissue transplantation ameliorates osteoporosis and dyslipidaemia in ovariectomised mice

Encheng Zhou 1, Du Xiang 1, Bin Yu 1, Hanlin Yao 1, Chao Sun 1, Yanfeng Wang 2

Background: Ovarian insufficiency frequently renders postmenopausal women susceptible to osteoporosis and dyslipidaemia. Postmenopausal transplant women are at a higher risk developing osteoporosis and dyslipidaemia due to the concomitant application of glucocorticoids and immunosuppressants after solid organ transplantation. Thus, this study aimed to explore the feasibility of ovarian tissue transplantation (OTT) as an alternative to Hormone replacement therapy (HRT) for postmenopausal women with solid organ transplant needs. Results: Sixty mice were randomly divided into four groups: sham operation, ovariectomised (OVX group), ovariectomy plus oestrogen (E2 group), and ovariectomy plus OTT (OTT group). The inhibin levels in the OTT group were increased and the follicle stimulating hormone and luteinizing hormone were suppressed to normal levels, which could not be achieved in the E2 group. The femoral bone mineral density in the OTT group was significantly increased than the E2 group ( $P < 0.05$ ), and the probability of fracture was reduced by 1.4-2.6 times. Additionally, the high-density lipoprotein cholesterol levels were higher in the OTT group than in the E2 group and the triglyceride levels were lower in the OTT group than in the E2 group ( $P < 0.05$ ). Conclusion: OTT not only achieves certain endocrine effects by participating in the regulation of the hypothalamic-pituitary-ovarian feedback control loop, but also ameliorates osteoporosis and dyslipidaemia, which may be an alternative to traditional HRT for postmenopausal women with solid organ transplant needs.

**J Obstet Gynaecol. 2022 Dec 28;2160928. doi: 10.1080/01443615.2022.2160928. Online ahead of print.**

## Asymptomatic endometrial thickening in postmenopausal women: predictor of malignant pathology?

Alba María Cruz García 1, Elena Pérez Morales 1, Ludmila Ocón Padrón 1, Cristina Pérez Matos 1, et al.

It is not standardised what is the endometrial thickness that discriminates between normal and potentially malignant. The objective of this study was to determine the endometrial thickness cut-off point from which the risk of endometrial cancer (EC) increases in asymptomatic postmenopausal women; and to evaluate the risk factors linked to malignant endometrial pathology as well as other associated ultrasound findings. This was a retrospective observational study that included hysteroscopies performed at the Hospital Materno-Infantil on 267 asymptomatic menopausal women with an increase in endometrial thickness (AET)  $> 5$  mm, from 2015 to 2019. The results show that the prevalence of malignant pathology in asymptomatic postmenopausal women with a casual finding of endometrial thickening was 3.7%. This percentage was 16.3% when the cut-off point of AET was established at 10 mm. There was a significant association for the diagnosis of malignant pathology with this cut-off point. There is a significant association between the 10 mm endometrial thickness cut-off point from which the risk of EC increases in asymptomatic postmenopausal women. Impact statement What is already known on this subject? Several studies have established the cut-off point for asymptomatic endometrial thickening (AET) for atypical endometrial hyperplasia and endometrial cancer at 10 mm. Although no cut-off point has optimal accuracy for the diagnosis of malignant endometrial pathology, it has been found that with a cut-off value of AET  $> 10$  mm no cases are missed. Likewise, a cut-off point of AET  $> 11$  mm may provide a balance between cancer detection and histopathological workup extension. What do the results of this study add? A significant association was found at the cut-off point of AET  $> 10$  mm, which suggests that screening postmenopausal women at this thickness is acceptable and unlikely to miss cases of endometrial hyperplasia and endometrial cancer. What are the implications of these findings for clinical practice and/or further research? After analysing our results we can conclude, like other published studies, that by establishing a cut-off point of 10 mm we obtain a good discrimination between benign and malignant pathology, which would allow us to diagnose 100% of malignant pathology. Above this cut-off point, the risk of endometrial cancer increases, and it would therefore be advisable to extend the study. A multicentre study is needed to confirm the cut-off point at which the risk of endometrial cancer increases in postmenopausal women with asymptomatic endometrial thickening.

**Arch Osteoporos. 2022 Dec 27;18(1):15. doi: 10.1007/s11657-022-01202-w.**

## Decreasing incidence rates of osteoporotic hip fractures in Ecuador during the COVID-19 pandemic

Enrique Lopez Gavilanez, Manuel Navarro Chávez, Antonio W D Gavilanes, Roberto Cedeño German, Peter Chedraui

We aimed at comparing the incidence of hip fractures in older adults from Ecuador before and during the COVID-19 pandemic. There was a significant reduction in the number of hip fractures, with no change in the length of hospital stay, mortality, and case-fatality rate, during the period of social isolation. Introduction: The impact that the COVID-19 pandemic has had on fragility fractures is being recently evaluated in the literature. Despite this, data from Latin America

in this regard is scarce. Purpose: This study aims to compare the incidence rate of hip fractures before and during the COVID-19 pandemic in older adults who received care in the public and private health system of Ecuador. Methods: This was a descriptive and retrospective study that analyzed data of individuals aged 60 years and older who had hip fractures before and during the COVID-19 pandemic. The information was obtained from the National Hospital Discharge Yearbook. We calculated the incidence, average length of hospital stay, mortality, and case-fatality rate associated with hip fractures. Results: There was a significant reduction in the incidence of hip fractures in adults 60 or older during the period of social isolation due to COVID-19. Between March and December 2019, there was an incidence of 152 hip fractures per 100,000 inhabitants, whereas during the same period but in 2020 the incidence was 110 per 100,000 inhabitants ( $p < 0.0001$ ). The main decrease was observed in women aged 80 or more. The average length of hospital stay did not show significant changes. Mortality displayed a non-significant decrease ( $p = 0.14$ ), although this decrease was significant among women ( $p = 0.02$ ). Case-fatality rate showed a non-significant increase for the whole group ( $p = 0.68$ ) and for men ( $p = 0.09$ ). Conclusion: Hip fracture rates decreased significantly in adults aged 60 and older in 2020 compared to 2019. This decrease of hip fracture incidence rates was mainly due to the reductions observed in older people and women. The average length of hospital stay, mortality, and case-fatality rate associated with hip fractures did not show significant changes during the pandemic.

**Maturitas. 2022 Dec 21;169:2-9. doi: 10.1016/j.maturitas.2022.12.006. Online ahead of print.**

### **EMAS position statement: Vitamin D and menopausal health**

Panagiotis Anagnostis 1, Sarantis Livadas 2, Dimitrios G Goulis 3, Silvia Bretz 4, Iuliana Ceausu 5, et al

Introduction: There is increasing evidence that vitamin D has widespread tissue effects. In addition to osteoporosis, vitamin D deficiency has been associated with cardiovascular disease, diabetes, cancer, infections and neurodegenerative disease. However, the effect of vitamin D supplementation on non-skeletal outcomes requires clarification, especially in postmenopausal women. Aim: This position statement provides an evidence-based overview of the role of vitamin D in the health of postmenopausal women based on observational and interventional studies. Materials and methods: Literature review and consensus of expert opinion. Results and conclusions: Vitamin D status is determined by measuring serum 25-hydroxyvitamin D levels. Concentrations  $<20$  ng/ml ( $<50$  nmol/l) and  $<10$  ng/ml ( $<25$  nmol/l) are considered to constitute vitamin D deficiency and severe deficiency, respectively. Observational data suggest an association between vitamin D deficiency and adverse health outcomes in postmenopausal women, although they cannot establish causality. The evidence from randomized controlled trials concerning vitamin D supplementation is not robust, since many studies did not consider whether people were deficient at baseline. Moreover, high heterogeneity exists in terms of the population studied, vitamin D dosage, calcium co-administration and duration of intervention. Concerning skeletal health, vitamin D deficiency is associated with low bone mass and an increased risk of fractures. Vitamin D supplementation at maintenance doses of 800-2000 IU/day (20-50  $\mu$ g/day), after repletion of vitamin D status with higher weekly or daily doses, may be of benefit only when co-administered with calcium (1000-1200 mg/day), especially in the elderly populations and those with severe vitamin D deficiency. Concerning cardiovascular disease, vitamin D deficiency is associated with an increased prevalence of cardiovascular risk factors, mainly metabolic syndrome, type 2 diabetes mellitus and dyslipidemia. Vitamin D deficiency, especially its severe form, is associated with an increased risk of cardiovascular events (coronary heart disease, stroke, mortality), independently of traditional risk factors. Vitamin D supplementation may have a modestly beneficial effect on lipid profile and glucose homeostasis, especially in obese individuals or those  $\geq 60$  years old and at doses of  $\geq 2000$  IU/day ( $\geq 50$   $\mu$ g/day). However, it has no effect on the incidence of cardiovascular events. Concerning cancer, vitamin D deficiency is associated with increased incidence of and mortality from several types of cancer, such as colorectal, lung and breast cancer. However, the data on other types of gynecological cancer are inconsistent. Vitamin D supplementation has no effect on cancer incidence, although a modest reduction in cancer-related mortality has been observed. Concerning infections, vitamin D deficiency has been associated with acute respiratory tract infections, including coronavirus disease 2019 (COVID-19). Vitamin D supplementation may decrease the risk of acute respiratory tract infections and the severity of COVID-19 (not the risk of infection). Concerning menopausal symptomatology, vitamin D deficiency may have a negative impact on some aspects, such as sleep disturbances, depression, sexual function and joint pains. However, vitamin D supplementation has no effect on these, except for vulvovaginal atrophy, at relatively high doses, i.e., 40,000-60,000 IU/week (1000-1500 IU/week) orally or 1000 IU/day (25  $\mu$ g/day) as a vaginal suppository.