



Selección de Resúmenes de Menopausia

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Pelvic floor disorders in women with premature ovarian insufficiency: a cross-sectional study.

Fante JF1, da Costa Machado H, Teatin Juliato CR, Benetti-Pinto CL, Oliveira Brito LG.

OBJECTIVES: This study aimed to investigate the prevalence of self-reported main pelvic floor disorders (PFD) (urinary incontinence [UI], pelvic organ prolapse [POP], and fecal incontinence [FI]) and its associated factors in women with premature ovarian insufficiency (POI) and a control group. **METHODS:** This was a cross-sectional study wherein two groups were interviewed from August, 2017 to November, 2018-women with POI (n=150) and a control group matched for age and body weight (n=150). Sociodemographic variables and two questionnaires validated in Brazilian Portuguese language for PFD (Kings Health Questionnaire [KHQ] and Pelvic Floor Distress Inventory-20 [PFDI-20]) were used. Laycock's power, endurance, repetitions, fast contractions, every contraction timed (PERFECT) scale for pelvic floor muscle assessment was used in both groups. **RESULTS:** The prevalence of self-reported UI was 27.33% and 37.33% for POI and control groups ($P>0.05$), respectively. There was no perceived difference regarding the prevalence of POP (9.33% POI group vs 8% control group; $P=0.682$) and FI (8% POI vs 4% control group; $P=0.145$). The P (power) ($P=0.46$), E (endurance) ($P=0.91$), R (repetitions) ($P=0.88$), and F (fast contractions) ($P=0.19$) values were statistically similar in both the groups. Multivariate analysis (n=141) showed that higher weight (odds ratio [OR] 1.047 [1.018-1.076]; $P<0.001$) and gravidity rates (OR 1.627 [1.169-2.266]; $P<0.01$) were risk factors for UI and higher weight (OR 1.046 [1.010-1.084]; $P=0.01$), and presence of comorbidities (OR 8.75 [1.07-71.44]; $P<0.01$) were risk factors for POP in the POI group; there was no variable that was associated with FI. **CONCLUSIONS:** Women with POI did not have significant differences when compared with the control group regarding the prevalence of PFD and pelvic floor muscle assessment. Having higher weight and gravidity rates were associated with self-reported UI, while the presence of comorbidities and higher weight were risk factors for POP in the POI group.

J Bone Miner Res. 2020 Mar 12. doi: 10.1002/jbmr.3989. [Epub ahead of print]

The Effect of Plasma Lipids and Lipid-Lowering Interventions on Bone Mineral Density: A Mendelian Randomization Study.

Zheng J1,2, Brion MJ3, Kemp JP1,3, Warrington NM3, Borges MC1,2, Hemani G1,2, Richardson TG1,2, et al..

Several epidemiological studies have reported a relationship between statin treatment and increased bone mineral density (BMD) and reduced fracture risk, but the mechanism underlying the purported relationship is unclear. We used Mendelian randomization (MR) to assess whether this relationship is explained by a specific effect in response to statin use or by a general effect of lipid lowering. We utilized 400 single-nucleotide polymorphisms (SNPs) robustly associated with plasma lipid levels as exposure. The outcome results were obtained from a heel estimated BMD (eBMD) genomewide association study (GWAS) from the UK Biobank and dual-energy X-ray absorptiometry (DXA) BMD at four body sites and fracture GWAS from the GEFOS consortium. We performed univariate and multivariable MR analyses of low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride levels on BMD and fracture. Univariate MR analyses suggested a causal effect of LDL-C on eBMD ($\beta = -0.06$; standard deviation change in eBMD per standard deviation change in LDL-C, 95% confidence interval [CI] = -0.08 to -0.04; $p = 4 \times 10^{-6}$), total body BMD ($\beta = -0.05$, 95% CI = -0.08 to -0.01, $p = 6 \times 10^{-3}$) and potentially on lumbar spine BMD. Multivariable MR suggested that the effects of LDL-C on eBMD and total body BMD were independent of HDL-C and triglycerides. Sensitivity MR analyses suggested that the LDL-C results were robust to pleiotropy. MR analyses of LDL-C restricted to SNPs in the HMGCR region showed similar effects on eBMD ($\beta = -0.083$; -0.132 to -0.034; $p = 0.001$) to those excluding these SNPs ($\beta = -0.063$; -0.090 to -0.036; $p = 8 \times 10^{-6}$). Bidirectional MR analyses provided some evidence for a causal effect of eBMD on plasma LDL-C levels. Our results suggest that effects of statins on eBMD and total body BMD are at least partly due to their LDL-C lowering effect. Further studies are required to examine the potential role of modifying plasma lipid levels in treating osteoporosis.

Nat Rev Endocrinol. 2020 Mar 11. doi: 10.1038/s41574-020-0335-y. [Epub ahead of print]

The role of cellular senescence in ageing and endocrine disease.

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With the ageing of the global population, interest is growing in the 'geroscience hypothesis', which posits that manipulation of fundamental ageing mechanisms will delay (in parallel) the appearance or severity of multiple chronic, non-communicable diseases, as these diseases share the same underlying risk factor - namely, ageing. In this context, cellular senescence has received considerable attention as a potential target in preventing or treating multiple age-related diseases and increasing healthspan. Here we review mechanisms of cellular senescence and approaches to target this pathway therapeutically using 'senolytic' drugs that kill senescent cells or inhibitors of the senescence-associated secretory phenotype (SASP). Furthermore, we highlight the evidence that cellular senescence has a causative role in multiple diseases associated with ageing. Finally, we focus on the role of cellular senescence in a number of endocrine diseases, including osteoporosis, metabolic syndrome and type 2 diabetes mellitus, as well as other endocrine conditions. Although much remains to be done, considerable preclinical evidence is now leading to the initiation of proof-of-concept clinical trials using senolytics for several endocrine and non-endocrine diseases.

Psychol Med. 2020 Mar 11:1-9. doi: 10.1017/S0033291720000483. [Epub ahead of print]

Mood sensitivity to estradiol predicts depressive symptoms in the menopause transition.

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BACKGROUND: The risk for depression markedly rises during the 5-6 years leading up to the cessation of menstruation, known as the menopause transition. Exposure to extreme estradiol levels may help explain this increase but few studies have examined individual sensitivity to estradiol in predicting perimenopausal depression. **METHOD:** The current study recruited 101 perimenopausal women. During Phase 1, we quantified each woman's sensitivity to changes in estradiol using 12 weekly measures of estrone-3-glucuronide (E1G), a urinary metabolite of estradiol, and concurrent depressive symptoms. The weekly cortisol awakening response was measured to examine the hypothalamic-pituitary-adrenal (HPA) axis in mediating mood sensitivity to estradiol. In Phase 2, depressive symptoms and major depression diagnoses were assessed monthly for 9 months. The relationship between Phase 1 E1G sensitivity and Phase 2 depressive symptoms and major depressive episodes was examined. Several baseline characteristics were examined as potential moderators of this relationship. **RESULTS:** The within-person correlation between weekly E1G and mood varied greatly from woman to woman, both in strength and direction. Phase 1 E1G mood sensitivity predicted the occurrence of clinically significant depressive symptoms in Phase 2 among certain subsets of women: those without a prior history of depression, reporting a low number of baseline stressful life events, and reporting fewer months since their last menstrual period. HPA axis sensitivity to estradiol fluctuation did not predict Phase 2 outcomes. **CONCLUSION:** Mood sensitivity to estradiol predicts risk for perimenopausal depression, particularly among women who are otherwise at low risk and among those who are early in the transition.

Diagnostics (Basel). 2020 Mar 7;10(3). pii: E149. doi: 10.3390/diagnostics10030149.

The Influence of Thyroid Pathology on Osteoporosis and Fracture Risk: A Review.

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Thyroid hormones are important factors that regulate metabolism and cell differentiation throughout the human body. A complication of thyroid pathology is represented by an alteration of the bone metabolism which can lead to osteoporosis and fragility fractures, known to have a high mortality rate. Although there is a consensus on the negative impact of hyperthyroidism on bone metabolism, when referring to hypothyroidism, subclinical hypothyroidism, or subclinical hyperthyroidism, there is no general agreement. The aim of our review was to update clinicians and researchers about the current data regarding the bone health in hypothyroidism, subclinical hypothyroidism, and subclinical hyperthyroidism patients. Thyroid disorders have an important impact on bone metabolism and fracture risk, such that hyperthyroidism, hypothyroidism, and subclinical hyperthyroidism are associated with a decreased bone mineral density (BMD) and increased risk of fracture. Subclinical hypothyroidism, on the other hand, is not associated with osteoporosis or fragility fractures, and subclinical hyperthyroidism treatment with radioiodine could improve bone health.

Biomed Res Int. 2020 Feb 19;2020:6910312. doi: 10.1155/2020/6910312. eCollection 2020.

RANKL/RANK/OPG Pathway: A Mechanism Involved in Exercise-Induced Bone Remodeling.

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Bones as an alive organ consist of about 70% mineral and 30% organic component. About 200 million people are suffering from osteopenia and osteoporosis around the world. There are multiple ways of protecting bone from endogenous and exogenous risk factors. Planned physical activity is another useful way for protecting bone health. It has been investigated that arranged exercise would effectively regulate bone metabolism. Until now, a number of systems have discovered how exercise could help bone health. Previous studies reported different mechanisms of the effect of exercise on bone health by modulation of bone remodeling. However, the regulation of RANKL/RANK/OPG pathway in exercise and physical performance as one of the most important remodeling systems is not considered comprehensive in previous evidence. Therefore, the aim of this review is to clarify exercise influence on bone modeling and remodeling, with a concentration on its role in regulating RANKL/RANK/OPG pathway.

Diabetes Care. 2020 Mar 6. pii: dc191807. doi: 10.2337/dc19-1807. [Epub ahead of print]

Trends in Bone Mineral Density, Osteoporosis, and Osteopenia Among U.S. Adults With Prediabetes, 2005-2014.

Chen C1, Chen Q2, Nie B3, Zhang H1, Zhai H1, Zhao L1,4, Xia P5, Lu Y1, Wang N6.

OBJECTIVE: We aimed to evaluate trends in bone mineral density (BMD) and the prevalence of osteoporosis/osteopenia in U.S. adults with prediabetes and normal glucose regulation (NGR) and further investigate the association among prediabetes, osteopenia/osteoporosis, and fracture. **RESEARCH DESIGN AND METHODS:** We collected and analyzed data from the U.S. National Health and Nutrition Examination Surveys during the period from 2005 to 2014. Femoral neck and lumbar spine BMD data were available for 5,310 adults with prediabetes and 5,162 adults with NGR >40 years old. **RESULTS:** A shift was observed toward a lower BMD and a higher prevalence of osteopenia/osteoporosis at the femoral neck and lumbar spine in U.S. adults >40 years old with prediabetes since 2005, especially in men <60 and women ≥60 years old. A shift toward a higher prevalence of osteopenia/osteoporosis at the femoral neck was also observed in adults >40 years old with NGR. Moreover, prediabetes was associated with a higher prevalence of hip fracture, although participants with prediabetes had higher BMD and a lower prevalence of osteopenia/osteoporosis at the femoral neck. **CONCLUSIONS:** There was a declining trend in BMD from 2005 to 2014 in U.S. adults >40 years old with prediabetes and NGR, and this trend was more significant in men <60 years old. Populations with prediabetes may be exposed to relatively higher BMD but a higher prevalence of fracture.

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Is hormonal therapy after risk-reducing salpingo-oophorectomy associated with an increased risk of malignancy in pathogenic variant carriers?

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OBJECTIVES: This study aimed to assess the association between hormone replacement therapy and the incidence of subsequent malignancies in patients who underwent risk-reducing salpingo-oophorectomy and had mutations predisposing them to Müllerian cancers. **METHODS:** This Institutional Review Board-approved retrospective study was performed at five academic institutions. Women were included if they were age 18-51 years, had one or more confirmed germline highly penetrant pathogenic variants, and underwent risk-reducing salpingo-oophorectomy. Patients with a prior malignancy were excluded. Clinicodemographic data were collected by chart review. Patients with no documented contact for one year prior to study termination were called to confirm duration of hormone use and occurrence of secondary outcomes. Hormone replacement therapy included any combination of estrogen or progesterone. **RESULTS:** Data were analyzed for 159 women, of which 82 received hormone replacement therapy and 77 did not. In both groups an average of 6 years since risk reduction had passed. The patients treated with hormone replacement therapy did not have a higher risk of subsequent malignancy than those not treated with hormone replacement therapy (6 out of 82 vs. 7 out of 77, $P = .68$). Patients who received hormone replacement therapy were younger than those who did not receive hormone replacement therapy (39.0 vs. 43.9 years, $P < .01$) and were more likely to have undergone other risk reductive procedures including mastectomy and/or hysterectomy, though this difference was not statistically significant (69.5% vs. 55.8%, $P = .07$). **CONCLUSIONS:** In this multi-institution retrospective study of data from patients with high-risk variant carriers who underwent risk-reducing salpingo-oophorectomy, there was no statistically significant difference in the incidence of malignancy between women who did and did not receive hormone replacement therapy.

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Serum anti-Mullerian hormone (AMH) concentration has limited prognostic value for density of primordial and primary follicles, questioning it as an accurate parameter for the ovarian reserve.

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OBJECTIVES: To evaluate the prognostic value of anti-Mullerian hormone (AMH) levels in estimating the ovarian density of primordial and primary follicles, which can be assumed to reflect the real ovarian reserve. **STUDY DESIGN:** A total of 537 women, average age 30.4 years (range 8.0-43.7 years), underwent ovarian tissue cryopreservation prior to gonadotoxic therapies due to malignant diseases which do not affect ovarian reserve parameters. Standardized ovarian biopsies were obtained, and follicular density was analysed. The prognostic accuracy of serum AMH in estimating ovarian follicle density was evaluated. **MAIN OUTCOME MEASURES:** Histologically determined follicle density, AMH serum concentration and their correlation. **RESULTS:** In children, follicle density was high but AMH concentration was low. AMH concentration was predicted to be maximum at the age of 15.5 years. In women aged over 15.5 years, the relationship between AMH concentration and follicle density was evaluated. Crude analysis revealed that serum AMH levels and follicular density were moderately correlated ($r=0.34$, $p<0.001$). From the adjusted regression model the predicted value of follicle density of women aged 20, 30 and 40 years as well as the associated 50 % and 95 % prediction intervals (50 % PI and 95 % PI, respectively) were calculated. For example, for women aged 40 years with a serum AMH level of 1 ng/ml, a follicle density of 2.3/mm³ (50 %PI: [1.1, 4.6]; 95 %PI: [0.3, 18]) was predicted. These large prediction intervals demonstrate the low predictive value of serum AMH for the ovarian follicle density. **CONCLUSIONS:** Serum AMH levels have limited prognostic value for the follicle density and therefore for the real ovarian reserve.