



Selección de Resúmenes de Menopausia

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La asociación entre la edad en el momento del diagnóstico de la complicación de la diabetes, con la edad de la menopausia natural en mujeres con diabetes tipo 1: Estudio de Pittsburgh Epidemiology of Diabetes Complications (EDC)

Association of age at diabetes complication diagnosis with age at natural menopause in women with type 1 diabetes: The Pittsburgh Epidemiology of Diabetes Complications (EDC) Study

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Objective: Vascular damage is thought to have a role in premature ovarian aging. We thus assessed the association between the presence, and age at onset of, vascular diabetes complications and age at natural menopause in women with type 1 diabetes. Methods: Female participants of the Epidemiology of Diabetes Complications study with type 1 diabetes who experienced natural menopause and who never received hormone therapy during their menopausal transition were included in the analysis (n=105). Microalbuminuria (MA), overt nephropathy, proliferative retinopathy, confirmed distal symmetric polyneuropathy, and coronary artery disease, were assessed during biennial clinical examinations for the first 10 years of follow-up and at year 18, 25 and 30. Menopausal status was determined via self-report and sex hormone data. For each complication, separate linear regression models were used to assess whether, compared with women without the complication of interest, an earlier age at complication development (i.e., <30 years of age) was associated with an earlier age at natural menopause. Results: Although results from multivariable linear regression models suggested a similar age at menopause between women with normo-albuminuria and those diagnosed with MA after 30 years of age, menopause occurred 2.06 years earlier ($\beta \pm SE = -2.06 \pm 1.08$) among women diagnosed with MA before age 30 ($p=0.06$). No significant association was observed for other complications. Conclusion: Among women with type 1 diabetes, menopause appears to occur earlier in those diagnosed with MA before age 30 compared to those with normo-albuminuria, suggesting that vascular dysfunction associated with early microvascular disease may affect ovarian aging.

Food Funct. 2021 Jan 14. doi: 10.1039/d0fo02664f. Online ahead of print.

El impacto de una dieta alta en grasas sobre los huesos: posibles mecanismos

The impact of a high fat diet on bones: potential mechanisms

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A high-fat diet (HFD) is defined as a diet that contains lipids that account for more than 30% of the total energy intake, and current research has documented cases with intakes as high as 45% and 60%. There is a view that patients who have a tendency to consume a HFD are more susceptible to various kinds of diseases, including osteoporosis, metabolic syndrome, coronary heart disease, and cancer. Thus, hypotheses have been proposed that a HFD may serve as a significant risk factor for bone loss and osteoporosis. A plethora of studies has suggested a relationship between a HFD and bone health. Moreover, high fat has a vital effect on the bone structure and bone health, and intestinal flora imbalances and intestine barrier deterioration, inflammation, oxidative stress, adipokine changes, and bone marrow fat tissue (BMFT) accumulation are thought to be potential mechanisms. Most research has demonstrated that a HFD diminishes bone mineral density and bone microstructure. Some studies, however, showed that a HFD contributes to achieving peak bone mass, which is associated with weight gain. As diet is modifiable, lifestyle changes and medication can help bone improvement, as well as alleviating bone loss associated with a HFD. This review aims to give a comprehensive understanding of the relationship between a HFD and bone health, which might provide strategies to improve bone health by varying daily dietary components and building a healthy lifestyle. We also hope that further treatments for diet-related bone loss can be put forward.

BMC Med. 2021 Jan 14;19(1):10.doi: 10.1186/s12916-020-01877-3.

El índice de masa corporal y el perímetro de la cintura en relación con el riesgo de 26 tipos de cáncer: un estudio de cohorte prospectivo de 3,5 millones de adultos en España

Body mass index and waist circumference in relation to the risk of 26 types of cancer: a prospective cohort study of 3.5 million adults in Spain

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Background: A high body mass index (BMI) has been associated with increased risk of several cancers; however, whether BMI is related to a larger number of cancers than currently recognized is unclear. Moreover, whether waist circumference (WC) is more strongly associated with specific cancers than BMI is not well established. We aimed to investigate the associations between BMI and 26 cancers accounting for non-linearity and residual confounding by smoking status as well as to compare cancer risk estimates between BMI and WC. **Methods:** Prospective cohort study with population-based electronic health records from Catalonia, Spain. We included 3,658,417 adults aged ≥ 18 years and free of cancer at baseline between 2006 and 2017. Our main outcome measures were cause-specific hazard ratios (HRs) with 99% confidence intervals (CIs) for incident cancer at 26 anatomical sites. **Results:** After a median follow-up time of 8.3 years, 202,837 participants were diagnosed with cancer. A higher BMI was positively associated with risk of nine cancers (corpus uteri, kidney, gallbladder, thyroid, colorectal, breast post-menopausal, multiple myeloma, leukemia, non-Hodgkin lymphoma) and was positively associated with three additional cancers among never smokers (head and neck, brain and central nervous system, Hodgkin lymphoma). The respective HRs (per 5 kg/m² increment) ranged from 1.04 (99%CI 1.01 to 1.08) for non-Hodgkin lymphoma to 1.49 (1.45 to 1.53) for corpus uteri cancer. While BMI was negatively associated to five cancer types in the linear analyses of the overall population, accounting for non-linearity revealed that BMI was associated to prostate cancer in a U-shaped manner and to head and neck, esophagus, larynx, and trachea, bronchus and lung cancers in an L-shaped fashion, suggesting that low BMIs are an approximation of heavy smoking. Of the 291,305 participants with a WC measurement, 27,837 were diagnosed with cancer. The 99%CIs of the BMI and WC point estimates (per 1 standard deviation increment) overlapped for all cancers. **Conclusions:** In this large Southern European study, a higher BMI was associated with increased risk of twelve cancers, including four hematological and head and neck (only among never smokers) cancers. Furthermore, BMI and WC showed comparable estimates of cancer risk associated with adiposity.

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Los estrógenos previenen la aterosclerosis al atenuar la piroptosis de las células endoteliales mediante la activación de la autofagia mediada por el receptor de estrógenos α

Estrogen prevent atherosclerosis by attenuating endothelial cell pyroptosis via activation of estrogen receptor α -mediated autophagy

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Excessive inflammation and the pyroptosis of vascular endothelial cells caused by estrogen deficiency is one cause of atherosclerosis in post-menopausal women. Because autophagy is highly regulated by estrogen, we hypothesized that estrogen can reduce vascular endothelial cell pyroptosis through estrogen receptor alpha (ER α)-mediated activation of autophagy to improve atherosclerosis in post-menopausal stage. Aortic samples from pro-menopausal and post-menopausal women with ascending aortic arteriosclerosis were analyzed, and bilateral ovariectomized (OVX) female ApoE^{-/-} mice and homocysteine (Hcy)-treated HUVECs were used to analyze the effect of estrogen supplementation therapy. The aortic endothelium showed a decrease in ER α expression and autophagy, but presented an increase in inflammation and pyroptosis in female post-menopausal patients. Estrogen treatment accelerated autophagy and ameliorated cell pyroptosis in the cardiac aortas of OVX ApoE^{-/-} mice and Hcy-treated HUVECs. Estrogen had therapeutic effect on atherosclerosis and improved the symptoms associated with lipid metabolism disorders in OVX ApoE^{-/-} mice. Inhibition and silencing of ER α led to a reduction in the autophagy promoting ability of estrogen and aggravated pyroptosis. Moreover, the inhibition of autophagy promoted pyroptosis and abolished the protective effect of estrogen, but had no influence on ER α expression. Thus, the results of the present study demonstrated that post-menopausal women present decreased autophagy and ER α expression and excessive damage to the ascending aorta. In

addition, in vitro and in vivo assay results demonstrated that estrogen prevents atherosclerosis by upregulating ER α expression and subsequently induces autophagy to reduce inflammation and pyroptosis.

Nota Editoria. Piroposis: Ésta vía de muerte celular es dependiente únicamente de la caspasa 1. Esta caspasa no está involucrada en la muerte celular apoptótica y su función es procesar los precursores de las citoquinas inflamatorias, activándolos.

Menopause. 2021 Jan 11; Publish Ahead of Print. doi: 10.1097/GME.0000000000001731. Online ahead of print.

Cambio en las tasas de infección y mortalidad por Covid-19 en mujeres posmenopáusicas

Change in Covid-19 infection and mortality rates in postmenopausal women

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Objective: To evaluate whether the rates of COVID-19 infection and death in women versus men differ with age. **Methods:** From data provided by the Italian National Institute of Statistics, we calculated the respective proportions of women among COVID-infected versus noninfected populations and male versus female infection and death rates, stratifying the results into 10-year age groups. **Results:** The prevalence of COVID-19 infection was 3.6% higher in women than in the general population from 20 to 59 years of age, then decreased to -13.3% below that of the general population between 60 and 89 years of age. Death rates among infected women showed the opposite age-related trend. In infected women, the mortality rate was -77.4% lower than that of men aged 20 to 59 years. Between 60 and 89 years of age, the difference in women decreases to -34.5% below that of men. **Conclusions:** Our results indicate opposing age-related trends among women in infection and death rates due to COVID-19. Further studies are needed to examine the contribution of the phases of the female reproductive cycle to the observed variations.

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La hormona antimülleriana en el diagnóstico y predicción de la insuficiencia ovárica prematura

Anti-Müllerian Hormone in the Diagnosis and Prediction of Premature Ovarian Insufficiency

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The menopause and its pathological version, premature ovarian insufficiency (POI), are characterized by the cessation of follicle growth in the ovary, with consequent lack of estrogen production and amenorrhea. The measurement of a specific product of ovarian follicles would therefore be expected to be a valuable biomarker in women with POI, and to be of likely clinical value in the diagnosis and perhaps prediction of POI. Anti-Müllerian hormone (AMH) is produced by the granulosa cells of growing follicles and is therefore likely to be of value in this context. Current data indicate that measurement of AMH is an accurate indicator of POI in many situations and has diagnostic validity and may facilitate more timely diagnosis. AMH seems to be of limited value in predicting age at natural menopause, even with multiple measurements, and there are scarce data regarding prediction of POI, other than when it is imminent, and in some contexts where there is an immediate iatrogenic threat to ovarian function. AMH therefore appears to have considerable value as a diagnostic test for POI, but apart from highlighting broadly those at increased risk, it has inadequate precision to be able to predict accurately the timing of onset of impending POI.

Tissue Eng Part B Rev. 2021 Jan 10. doi: 10.1089/ten.TEB.2020.0205. Online ahead of print.

Terapia con células madre adultas para la falla ovárica prematura: del laboratorio a la práctica.

Adult stem cell therapy for premature ovarian failure: from bench to bedside

Premature ovarian failure (POF) is a devastating condition for women of childbearing age with serious health consequences including distress, infertility, osteoporosis, autoimmune disorders, ischemic heart disease, and increased mortality. In addition to the mainstay estrogen therapy, stem cell therapy has been tested as the result of rapid progress in stem cell biology and cell reprogramming. We hereby provide a review for recent research and issues related with stem-cell-based therapy for POF, and provide a commentary on various methods for enhancing the effect of stem cell therapy for POF. Large amount of animal studies have demonstrated an extensive benefit of stem cells for failed ovarian

recovering. As shown by such studies, stem cell therapy can result in recovery of hormone levels, follicle activation, ovarian angiogenesis and function restoration. Meanwhile, study of molecular pathways revealed that the function of stem cells mainly depends on their paracrine actions, which may produce multiple factors for the promotion of ovarian angiogenesis and regulation of cellular functions. Nevertheless, study of the disease model also revealed certain drawbacks. Clinical trials have shown that menstrual cycle and even pregnancy may occur following transplantation of stem cells in POF cases, albeit the limitations including inadequate number of cases and space for the improvement of transplantation methodology. Only with the improvement of safety and function assessment and expansion of clinical trials, can stem cell therapy bring benefits to more women with POF. Additionally, effective pre-treatments and appropriate transplantation methods for stem cells are also required. Taken together, stem cell therapy has shown a great potential for POF recovery and is promising to step from bench to bedside.

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Asociación de seis marcadores relacionados con la adiposidad, la incidencia y la mortalidad de 24 cánceres: resultados del estudio de cohorte prospectivo del Biobanco del Reino Unido

Associations of six adiposity-related markers with incidence and mortality from 24 cancers-findings from the UK Biobank prospective cohort study

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Background: Adiposity is a strong risk factor for cancer incidence and mortality. However, most of the evidence available has focused on body mass index (BMI) as a marker of adiposity. There is limited evidence on relationships of cancer with other adiposity markers, and if these associations are linear or not. The aim of this study was to investigate the associations of six adiposity markers with incidence and mortality from 24 cancers by accounting for potential non-linear associations. **Methods:** A total of 437,393 participants (53.8% women; mean age 56.3 years) from the UK Biobank prospective cohort study were included in this study. The median follow-up was 8.8 years (interquartile range 7.9 to 9.6) for mortality and 9.3 years (IQR 8.6 to 9.9) for cancer incidence. Adiposity-related exposures were BMI, body fat percentage, waist-hip ratio, waist-height ratio, and waist and hip circumference. Incidence and mortality of 24 cancer sites were the outcomes. Cox proportional hazard models were used with each of the exposure variables fitted separately on penalised cubic splines. **Results:** During follow-up, 47,882 individuals developed cancer and 11,265 died due to cancer during the follow-up period. All adiposity markers had similar associations with overall cancer incidence. BMI was associated with a higher incidence of 10 cancers (stomach cardia (hazard ratio per 1 SD increment 1.35, (95% CI 1.23; 1.47)), gallbladder (1.33 (1.12; 1.58)), liver (1.27 (1.19; 1.36)), kidney (1.26 (1.20; 1.33)), pancreas (1.12 (1.06; 1.19)), bladder (1.09 (1.04; 1.14)), colorectal (1.10 (1.06; 1.13)), endometrial (1.73 (1.65; 1.82)), uterine (1.68 (1.60; 1.75)), and breast cancer (1.08 (1.05; 1.11))) and overall cancer (1.03 (1.02; 1.04)). All these associations were linear except for breast cancer in postmenopausal women. Similar results were observed when other markers of central and overall adiposity were used. For mortality, nine cancer sites were linearly associated with BMI and eight with waist circumference and body fat percentage. **Conclusion:** Adiposity, regardless of the marker used, was associated with an increased risk in 10 cancer sites.