Selección de Resúmenes de Menopausia

Semana del 20 a 26 abril 2022

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Stem Cell Rev Rep. 2022 Apr 23. doi: 10.1007/s12015-022-10370-8. Online ahead of print.

Telomeres and Mitochondrial Metabolism: Implications for Cellular Senescence and Age-related Diseases

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Cellular senescence is an irreversible cell arrest process, which is determined by a variety of complicated mechanisms, including telomere attrition, mitochondrial dysfunction, metabolic disorders, loss of protein homeostasis, epigenetic changes, etc. Cellular senescence is causally related to the occurrence and development of age-related disease. The elderly is liable to suffer from disorders such as neurodegenerative diseases, cancer, and diabetes. Therefore, it is increasingly imperative to explore specific countermeasures for the treatment of age-related diseases. Numerous studies on humans and mice emphasize the significance of metabolic imbalance caused by short telomeres and mitochondrial damages in the onset of age-related diseases. Although the experimental data are relatively independent, more and more evidences have shown that there is mutual crosstalk between telomeres and mitochondrial metabolism in the process of cellular senescence. This review systematically discusses the relationship between telomere length, mitochondrial metabolic disorder, as well as their underlying mechanisms for cellular senescence and age-related diseases. Future studies on telomere and mitochondrial metabolism may shed light on potential therapeutic strategies for age-related diseases. Graphical Abstract The characteristics of cellular senescence mainly include mitochondrial dysfunction and telomere attrition. Mitochondrial dysfunction will cause mitochondrial metabolic disorders, including decreased ATP production, increased ROS production, as well as enhanced cellular apoptosis. While oxidative stress reaction to produce ROS, leads to DNA damage, and eventually influences telomere length. Under the stimulation of oxidative stress, telomerase catalytic subunit TERT mainly plays an inhibitory role on oxidative stress, reduces the production of ROS and protects telomere function. Concurrently, mitochondrial dysfunction and telomere attrition eventually induce a range of age-related diseases, such as T2DM, osteoporosis, AD, etc.

Nutrients. 2022 Apr 13;14(8):1617. doi: 10.3390/nu14081617.

Influence of Obesity on Bone Turnover Markers and Fracture Risk in Postmenopausal Women

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Background and aims: The relationship between obesity and bone metabolism is controversial. In recent decades, the protective role of obesity in the development of osteoporosis is questioned. The aims of this study are the following: to evaluate the differences in bone turnover markers between postmenopausal women with and without obesity and to compare the risk of fracture at five years between these groups. Methods: An observational longitudinal prospective cohort study of postmenopausal women with obesity (O) (body mass index (BMI) > 30 kg/m2) and non-obesity (NoO) (BMI < 30 kg/m2) is designed. 250 postmenopausal women are included in the study (NoO: 124 (49.6%) and O: 126 (50.4%)). It measures epidemiological variables, dietary variables (calcium intake, vitamin D intake, smoking, alcohol consumption, and physical activity), biochemicals (β-crosslap, type I procollagen amino-terminal peptide (P1NP), 25OH-vitamin D, and parathyroid hormone (PTH)), anthropometric variables, and fracture data five years after the start of the study. The mean age is 56.17 (3.91) years. Women with obesity showed lower levels of vitamin D (O: 17.27 (7.85) ng/mL, NoO: 24.51 (9.60) ng/mL; p < 0.01), and higher levels of PTH (O: 53.24 (38.44-65.96) pg/mL, NoO: 35.24 (25.36-42.40) pg/mL; p < 0.01). Regarding the bone formation marker (P1NP), it was found to be high in women without obesity, O: 45.46 (34.39-55.16) ng/mL, NoO: 56.74 (45.34-70.74) ng/mL; p < 0.01; the bone resorption marker (β-crosslap) was found to be high in women with obesity, being significant in those older than 59 years (O: 0.39 (0.14) ng/mL, NoO 0.24 (0.09) ng/mL; p < 0.05). No differences are observed in the risk of fracture at 5 years based on BMI (OR = 0.90 (95%CI 0.30-2.72); p = 0.85). Conclusions: Postmenopausal women with obesity showed lower levels of bone formation markers; older women with obesity showed higher markers of bone resorption.

Cells. 2022 Apr 15;11(8):1355. doi: 10.3390/cells11081355.

Role of Estrogens in Menstrual Migraine

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Migraine is a major neurological disorder affecting one in nine adults worldwide with a significant impact on health care and socioeconomic systems. Migraine is more prevalent in women than in men, with 17% of all women meeting the diagnostic criteria for migraine. In women, the frequency of migraine attacks shows variations over the menstrual cycle and pregnancy, and the use of combined hormonal contraception (CHC) or hormone replacement therapy (HRT) can unveil or modify migraine disease. In the general population, 18-25% of female migraineurs display a menstrual association of their headache. Here we present an overview on the evidence supporting the role of reproductive hormones, in particular estrogens, in the pathophysiology of migraine. We also analyze the efficacy and safety of prescribing exogenous estrogens as a potential treatment for menstrual-related migraine. Finally, we point to controversial issues and future research areas in the field of reproductive hormones and migraine.

J Clin Endocrinol Metab. 2022 Apr 22;dgac241. doi: 10.1210/clinem/dgac241. Online ahead of print.

Obesity and breast cancer risk: the oncogenic implications of metabolic dysregulation

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Context: Breast cancer is increasing in prevalence in parallel with rising rates of obesity worldwide. Obesity is recognized as a leading modifiable risk factor for the development of breast cancer; however, this association varies considerably by clinicopathologic features, and the underlying mechanisms are complex.Evidence acquisition: Pubmed literature search using combinations of "obesity," "breast cancer risk," "diet," "exercise," "weight gain", "weight loss", "adipose tissue inflammation", "crown-like structure", "immune markers", "metformin", "gliflozins", "SGLT-2i", "GLP1-RA," and related terms. Evidence synthesis: Elevated body mass index and weight gain are associated with increased risk of postmenopausal, hormone receptor-positive breast cancer. Emerging evidence suggests that adverse measures of body composition in individuals of any weight can also confer increased breast cancer risk. Mechanistically, various factors including altered adipokine balance, dysfunctional adipose tissue, dysregulated insulin signaling, and chronic inflammation contribute to tumorigenesis. Weight loss and more specifically, fat mass loss through lifestyle and pharmacologic interventions improve serum metabolic and inflammatory markers, sex hormone levels, and measures of breast density, suggesting a link to decreased breast cancer risk. Conclusion: Incorporating markers of metabolic health and body composition measures with body mass index can capture breast cancer risk more comprehensively. Further studies of interventions targeting body fat levels are needed to curb the growing prevalence of obesity-related cancer.

Climacteric. 2022 Apr 19;1-7. doi: 10.1080/13697137.2022.2050205. Online ahead of print.

Hormone therapy effect on menopausal systemic lupus erythematosus patients: a systematic review

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Systemic lupus erythematosus (SLE) primarily affects women, who may need hormone therapy (HT) in menopause. There is, however, some concern as to its efficacy and safety. This systematic review aimed to determine the effect of HT on the activity of SLE and its safety. The study was a qualitative systematic review. Research was conducted with data retrieved from Embase, MEDLINE and Cochrane databases using MESH terms up to April 2021, with no bar on date or language. Sixteen studies were selected for analysis. Most of them showed HT to be effective in the treatment of menopausal symptoms with no impact in SLE activity, but one randomized clinical trial showed an increase in the number of thrombotic events. The present systematic review demonstrated the efficacy of HT for treating the menopausal symptoms of SLE patients. The risk of flare and thrombosis seems to be very low.

J Clin Endocrinol Metab. 2022 Apr 18;dgac238. doi: 10.1210/clinem/dgac238. Online ahead of print.

Serum follicle stimulating hormone and five-year change in adiposity in healthy postmenopausal women

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Background: Evidence from animal studies suggests that the gradual rise in follicle stimulating hormone (FSH) during reproductive senescence may contribute to the change in adiposity distribution characteristic of menopause. The potential independent role the interrelationships of FSH and estradiol may play in postmenopausal adiposity changes are not well studied. Methods: In a sample of 667 postmenopausal women from the Women's Health Initiative Buffalo OsteoPerio Ancillary Study, we studied the associations of serum FSH and estradiol levels with dual x-ray absorptiometry (DXA)-derived adiposity measures via cross-sectional and longitudinal analyses (5-year follow-up). Results: In cross-sectional analyses, FSH levels were inversely associated with all measures of adiposity in models adjusted for age, years since menopause, smoking status, pack years, and hormone therapy (HT) use; these associations were not influenced by adjustment for serum estradiol. In longitudinal analyses, the subset of women who discontinued HT over follow-up (n=242) experienced the largest increase in FSH (+33.9 mIU/mL) and decrease in estradiol (-44.3 pg/mL) and gains in all adiposity measures in unadjusted analyses. In adjusted analyses, an increase in FSH was associated with a gain in percent total body fat, total body fat mass, and subcutaneous adipose tissue. Conclusions: While cross-sectional findings suggest that FSH is inversely associated with adiposity, our longitudinal findings suggest that greater increases in FSH were associated with greater increases in percent total body fat, total body fat mass and subcutaneous adipose tissue. Future studies are needed to provide additional insight into FSH-adiposity mechanisms in larger samples.

Expert Opin Pharmacother. 2022 Apr 17. doi: 10.1080/14656566.2022.2066997.

Pharmacotherapy for female sexual dysfunctions (FSDs): What is on the market and where is this field heading?

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Introduction: Female sexual dysfunctions (FSDs) are common in women of any age and have a huge impact on quality of life and relationships. They have a multifaceted etiology limiting the development of pharmacotherapies with a high rate of effectiveness. Safety issues are also a concern across the reproductive life span. Areas covered: The authors report the most recent advances in pharmacotherapy for premenopausal and postmenopausal women with a main focus on hypoactive sexual desire disorders (HSDD) and associated sexual symptoms. Good levels of evidence have emerged for psychoactive agents, such as flibanserin and bremelanotide, as well as hormonal compounds (transdermal testosterone). The authors also report briefly intravaginal DHEA (prasterone), local estrogen therapy (LET) and ospemifene to manage effectively vulvovaginal atrophy/genitourinary syndrome of menopause (VVA/GSM). In addition, they discuss promising therapeutic options highlighting the main reasons that hamper the availability of new-labelled products. Finally, they include the importance of the multimodal approach to address FSDs. Expert opinion: Approved pharmacotherapies for FSD are limited. Validated multidimensional instruments and adequate objective measures of physical and mental responses to sexual external and internal incentives are mandatory to identify women suitable to chronic or on-demand treatments and to assess their pattern of response in research and practice.