# Selección de Resúmenes de Menopausia

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## Quality of life assessment in women with sponaneous premature insufficiency: A comparative cross-sectional study -11

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Objective: Premature ovarian insufficiency is cessation of ovarian function prior to 40 years of age. It is known to have varied short and long-term implications on the health of the women. The quality of life is affected in various domanins. The objective of this study is to evaluate QOL of women with POI and the factors associated with it, using WHO QOL-BREF scale. Methods: This is a cross sectional comparative study. Women with premature ovarian insufficiency with normal karyotype were included before initiation of hormone replacement therapy as cases and age matched women without any menstrual irregularity, infertility or any chronic illness were included as controls. Written informed consent was obtained from all patients. The pre-validated Tamil version of the WHOQOL-BREF (26 items, 4 domains) was filled through face-to-face interview. The score of each domain was transformed into 0-100 as per the guideline provided by WHOQOL-BREF. Statistical analysis was done using SPSS version 19. Results: A total of 100 (50 women with POI and 50 control women) completed the WHOQOL-BREF questionnaire. The mean age of the women who participated in the study was 29.6 ± 6.5 years. Among the cases, 72% were nulliparous. There was statistically significant difference in the median scores of overall QOL, physical, psychological and social domains between the two groups. Univariate analysis showed that nulliparity and infertility were the factors responsible for poor QOL, however, these were not independently associated with poor QOL after applying bivariate linear regression analysis. Conclusion: The scores of overall QOL, physical, psychological and social domains were poorer in women with POI as compared to healthy controls.

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## Medroxyprogesterone acetate positively modulates specific GABA A-receptor subtypes - affecting memory and cognition

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Medroxyprogesterone acetate (MPA) is a progestin widely used in humans as hormone replacement therapy and at other indications. Many progestin metabolites, as the progesterone metabolite allopregnanolone, have GABAA-receptor modulatory effects and are known to affect memory, learning, appetite, and mood. In women, 4 years chronic treatment with MPA doubles the frequency of dementia and in rats, MPA causes cognitive impairment related to the GABAergic system. Activation of the membrane bound GABAA receptor results in a chloride ion flux that can be studied by whole-cell patch-clamp electrophysiological recordings. The purpose of this study was to clarify the modulatory effects of MPA and specific MPA metabolites, with structures like known GABAA-receptor modulators, on different GABAA-receptor subtypes. An additional aim was to verify the results as steroid effects on GABA response in single cells taken from rat hypothalamus. HEK-293 cell-lines permanently expressing the recombinant human GABAA-receptor subtype α1β2γ2L or α5β3γ2L or α2β3γ2S were created. The MPA metabolites 3α5α-MPA,3β5α-MPA and 3β5β-MPA were synthesised and purified for electrophysiological patch-clamp measurements with a Dynaflow system. The effects of MPA and tetrahydrodeoxycorticosterone were also studied. None of the studied MPA metabolites affected the responses mediated by α1β2γ2L or α5β3γ2L GABAA receptors. Contrary, MPA clearly acted both as a positive modulator and as a direct activator of the α5β3γ2L and α2β3γ2S GABAA receptors. However, in concentrations up to 10 μM, MPA was inactive at the α1β2γ2L GABAA receptor. In the patch-clamp recordings from dissociated cells of the preoptic area in rats, MPA increased the amplitude of responses to GABA. In addition, MPA alone without added GABA, evoked a current response. In conclusion, MPA acts as a positive modulator of specific GABAA receptor subtypes expressed in HEK cells and at native GABA receptors in single cells from the hypothalamic preoptic area.

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## The Function of Metformin in Aging-Related Musculoskeletal Disorders

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Metformin is a widely accepted first-line hypoglycemic agent in current clinical practice, and it has been applied to the clinic for more than 60 years. Recently, researchers have identified that metformin not only has an efficient capacity to lower glucose but also exerts anti-aging effects by regulating intracellular signaling molecules. With the accelerating aging process and mankind's desire for a long and healthy life, studies on aging have witnessed an unprecedented boom. Osteoporosis, sarcopenia, degenerative osteoarthropathy, and frailty are age-related diseases of the musculoskeletal system. The decline in motor function is a problem that many elderly people have to face, and in serious cases, they may even fail to self-care, and their quality of life will be seriously reduced. Therefore, exploring potential treatments to effectively prevent or delay the progression of aging-related diseases is essential to promote healthy aging. In this review, we first briefly describe the origin of metformin and the aging of the movement system, and next review the evidence associated with its ability to extend lifespan. Furthermore, we discuss the mechanisms related to the modulation of aging in the musculoskeletal system by metformin, mainly its contribution to bone homeostasis, muscle aging, and joint degeneration. Finally, we analyze the protective benefits of metformin in aging-related diseases of the musculoskeletal system.

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## Reproductive factors and the risk of incident dementia: A cohort study of UK Biobank participants

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Background: Women's reproductive factors have been associated with the risk of dementia; however, these findings remain uncertain. This study aimed to examine the risk of incident all-cause dementia associated with reproductive factors in women and the number of children in both sexes and whether the associations vary by age, socioeconomic status (SES), smoking status, and body mass index (BMI) in the UK Biobank. Methods and findings: A total of 273,240 women and 228,957 men without prevalent dementia from the UK Biobank were included in the analyses. Cox proportional hazard regressions estimated hazard ratios (HRs) for reproductive factors with incident all-cause dementia. Multiple adjusted models included age at study entry, SES, ethnicity, smoking status, systolic blood pressure, BMI, history of diabetes mellitus, total cholesterol, antihypertensive drugs, and lipid-lowering drugs. Over a median of 11.8 years follow-up, 1,866 dementia cases were recorded in women and 2,202 in men. Multiple adjusted HRs ((95% confidence intervals (CIs)), p-value) for dementia were 1.20 (1.08, 1.34) (p = 0.016) for menarche <12 years and 1.19 (1.07, 1.34) (p = 0.024) for menarche >14 years compared to 13 years; 0.85 (0.74, 0.98) (p = 0.026) for ever been pregnant; 1.43 (1.26, 1.62) (p < 0.001) for age at first live birth <21 compared to 25 to 26 years; 0.82 (0.71, 0.94) (p = 0.006) for each abortion; 1.32 (1.15, 1.51) (p = 0.008) for natural menopause at <47 compared to 50 years; 1.12 (1.01, 1.25) (p = 0.039) for hysterectomy; 2.35 (1.06, 5.23) (p = 0.037) for hysterectomy with previous oophorectomy; and 0.80 (0.72, 0.88) (p < 0.001) for oral contraceptive pills use. The U-shaped associations between the number of children and the risk of dementia were similar for both sexes: Compared with those with 2 children, for those without children, the multiple adjusted HR ((95% CIs), p-value) was 1.18 (1.04, 1.33) (p = 0.027) for women and 1.10 (0.98, 1.23) (p = 0.164) for men, and the women-to-men ratio of HRs was 1.09 (0.92, 1.28) (p = 0.403); for those with 4 or more children, the HR was 1.14 (0.98, 1.33) (p = 0.132) for women and 1.26 (1.10, 1.45) (p = 0.003) for men, and the women-to-men ratio of HRs was 0.93 (0.76, 1.14) (p = 0.530). There was evidence that hysterectomy (HR, 1.31 (1.09, 1.59), p = 0.013) and oophorectomy (HR, 1.39 (1.08, 1.78), p = 0.002) were associated with a higher risk of dementia among women of relatively lower SES only. Limitations of the study include potential residual confounding and self-reported measures of reproductive factors, as well as the limited representativeness of the UK Biobank population. Conclusions: In this study, we observed that some reproductive events related to shorter cumulative endogenous estrogen exposure in women were associated with higher dementia risk, and there was a similar association between the number of children and dementia risk between women and men.

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## Skin, hair and beyond: the impact of menopause

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The skin is an endocrine organ and a major target of hormones such as estrogens, androgens and cortisol. Besides vasomotor symptoms (VMS), skin and hair symptoms often receive less attention than other menopausal symptoms

despite having a significant negative effect on quality of life. Skin and mucosal menopausal symptoms include dryness and pruritus, thinning and atrophy, wrinkles and sagging, poor wound healing and reduced vascularity, whereas skin premalignant and malignant lesions and skin aging signs are almost exclusively caused by environmental factors, especially solar radiation. Hair menopausal symptoms include reduced hair growth and density on the scalp (diffuse effluvium due to follicular rarefication and/or androgenetic alopecia of female pattern), altered hair quality and structure, and increased unwanted hair growth on facial areas. Hormone replacement therapy (HRT) is not indicated for skin and hair symptoms alone due to the risk-benefit balance, but wider potential benefits of HRT (beyond estrogen's effect on VMS, bone, breast, heart and blood vessels) to include skin, hair and mucosal benefits should be discussed with women so that they will be able to make the best possible informed decisions on how to prevent or manage their menopausal symptoms.

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## Early Menopause May Associate with a Higher Risk of CKD and All-Cause Mortality in Postmenopausal Women: An Analysis of NHANES, 1999-2014

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Background: Chronic kidney disease (CKD) in women is often accompanied by hormone disorders such as sex hormones, and most women with CKD are in the post-menopausal age group. Due to the close relationship between menopause and sex hormones, we aimed to explore the association between early menopause and CKD in post-menopausal women, and the influence of early menopause on longevity in the CKD population. Methods: Information regarding 4,945 post-menopausal women was extracted from the database of the National Health and Nutrition Examination Survey (NHANES) 1999-2014, and then divided into 4 groups according to the type of menopause (natural or surgical) and early menopause (menopause at age <45) or not. The association between early menopause and CKD prevalence was examined using multivariable logistic regression, while we used multivariable Cox proportional hazards models to investigate the possible relationship between early menopause and all-cause mortality in CKD and non-CKD populations. The differences in the levels of sex hormones between women with and without CKD were also explored. Results: Compared with women with natural menopause at age ≥45, women experiencing early natural menopause had a higher risk of CKD [OR = 1.26 (1.01-1.56)]. Similarly, as compared to women with surgical menopause at age ≥ 45, women in the early surgical menopause group were more likely to have CKD [OR = 1.38 (1.05-1.81)]. In addition, early surgical menopause was associated with higher mortality in the non-CKD group [HR = 1.62 (1.06-2.49)], but not in the CKD group. Women with CKD had a higher level of luteinizing hormone and follicle-stimulating hormone, combined with a lower level of testosterone and estradiol than the non-CKD women. Conclusion: Both early natural and surgical menopause were associated with a higher risk of CKD. Early surgical menopause was a hazard factor for survival in the non-CKD group, but not in the CKD group. Further research is required to understand the mechanisms.