

Selección de Resúmenes de Menopausia

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María Soledad Vallejo. Obstetricia Ginecología. Hospital Clínico. Universidad de Chile

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The contribution of age and sex hormones to female neuromuscular function across the adult lifespan

Steven J O'Bryan 1, Annabel Critchlow 2, Cas J Fuchs 3, Danielle Hiam 2, Séverine Lamon 2

Neuromuscular ageing is characterized by neural and/or skeletal muscle degeneration that decreases maximal force and power. Female neuromuscular ageing occurs earlier in life compared to males, potentially due to sex hormone changes during the menopausal transition. We quantified neuromuscular function in 88 females represented equally over each decade from 18 to 80 years of age and investigated the role of decreased ovarian hormone concentrations following menopause. Neuromuscular assessment included quadriceps maximal voluntary and evoked isometric torque and surface electromyography measurements, plus one-repetition maximum leg press. Voluntary and evoked torques and one-repetition maximum decreased non-linearly with age, with accelerated reductions starting during the fourth decade. An absence of changes in volitional recruitment of existing quadriceps motor units and Ia afferent facilitation of spinal motoneurons suggests that functional decline was largely mediated by impairment in intrinsic peripheral muscle function and/or neuromuscular transmission. Maximal muscle compound action potential amplitude decreased with increasing age for rectus femoris muscle only, indicating increased vulnerability to neuromuscular degeneration compared to vastus lateralis and medialis. In postmenopausal females, some variance was explained by inter-individual differences in quadriceps tissue composition and lifestyle factors, but changes in total or free concentrations of oestradiol, progesterone and/or testosterone were included in all correlations with age-related decreases in isometric voluntary and evoked torques. We demonstrate an accelerated onset of neuromuscular degeneration of peripheral muscular origin around menopause onset associated with changes in sex hormone concentrations. Interventions aimed at mitigating declines in ovarian hormones and their subsequent effects on neuromuscular function after menopause should be further explored. **KEY POINTS:** Neuromuscular deterioration with age is associated with poor physical function and quality of life in older adults, but female-specific trajectories and mechanisms remain unclear. This study is the first to map neuromuscular function across each decade of the adult lifespan in 88 females from 18 to 80 years old and to examine the potential role of hormonal changes after menopause. We show an accelerated reduction in neuromuscular function, primarily of peripheral muscular origin, that occurs during the fourth decade and coincides with menopause onset. In postmenopausal females, age-related reductions in neuromuscular function can in part be explained by quadriceps lean and intramuscular fat composition, physical activity and protein intake, and sex hormone concentrations. These findings help us better understand the factors that contribute to the loss of neuromuscular function with age in females, enabling the identification of potential therapeutic interventions to prolong female health span.

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Association between lower urinary tract symptoms and female sexual function: results from the GENitourinary syndrome of menopause in Japanese women (GENJA) study

Yumi Ozaki 1, Hikaru Tomoe 2, Mayuka Shimomura 3, Noriko Ninomiya 4, Yuki Sekiguchi 5, Yoshikazu Sato, et al. **Background:** Female sexual dysfunction (FSD) is highly prevalent in women with lower urinary tract symptoms (LUTS); however, few studies have assessed the association between specific LUTS and FSD. **Aim:** To identify which specific LUTS are associated with which domains of female sexual function in Japanese women. **Methods:** Data from 1337 sexually active women aged 40-79 years who participated in the GENitourinary syndrome of menopause in Japanese women (GENJA) study were analyzed. All participants answered web-based questionnaires including the Core Lower Urinary Tract Symptom Score, Female Sexual Function Index (FSFI), and Vulvovaginal Symptoms Questionnaire. We used multivariable regression to assess the association between LUTS and FSFI domain scores, adjusted for age, menstrual status, hormone therapy, hypertension, dyslipidemia, diabetes mellitus, and depression. **Outcomes:** FSFI domain and total scores associated with LUTS. **Results:** The mean age of participants was 54.0 ± 10.7

years. Women with LUTS were more likely to have lower total FSFI scores than those without, except for increased daytime urinary frequency. The multivariate analysis revealed that nocturia was associated with lower orgasm scores (coefficient: -0.23; 95% confidence interval [CI]: -0.45 to -0.01; $P = .044$), urgency with lower pain scores (coefficient: -0.62; CI: -1.09 to -0.14; $P = .011$), stress urinary incontinence (coefficient: -0.51; CI: -0.90 to -0.12; $P = .011$), and vaginal bulge/lump sensations (coefficient: -0.42; CI: -0.81 to -0.04; $P = .031$) with lower satisfaction scores. Clinical implications: This study highlights the need to include routine assessments of sexual function in women with LUTS. Strengths and limitations: This is the first study to comprehensively examine the association between specific LUTS and FSFI domain scores using validated questionnaires in a nationwide epidemiological survey among sexually active Japanese women. Limitations include non-random participant selection and reliance on self-reported data, which represent subjective symptoms. Conclusion: LUTS, including nocturia, urgency, stress urinary incontinence, as well as vaginal bulge/lump sensations, were associated with FSD regardless of age, menstrual status, lifestyle-related diseases, or depression.

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Changes in Sleep Quality after Hormone Replacement Therapy with Micronized Progesterone in Japanese Menopausal Women: A Pilot Study

Mariko Ogawa 1 2 3, Kazuya Makita 4, Kiyoshi Takamatsu 2 5, Toshifumi Takahashi 1

Sleep disturbances are common among women during menopause. Hormone replacement therapy (HRT) using micronized progesterone (MP) may improve sleep, owing to its neurosteroid effects. Studies on the impact of oral MP on sleep quality in Japanese women are limited, given the recent introduction of MP in Japan. We conducted a single-arm, open-label study to examine the effects of HRT with estradiol (E2) and oral MP on sleep quality in 15 peri- and postmenopausal Japanese women who chose HRT to address their menopausal symptoms. The participants completed the Pittsburgh Sleep Quality Index (PSQI) and menopausal symptoms questionnaires at baseline, 1 month, and 3 months after HRT. The changes in PSQI scores were evaluated. Responders were defined as those with a $\geq 25\%$ reduction in the PSQI global score at 1 month. The PSQI components and menopausal symptoms at baseline were compared between responders and non-responders. Initially, 86.7% of the participants were categorized as poor sleepers. The PSQI global score and sleep quality significantly improved at 1 and 3 months after HRT (baseline to 3rd month mean scores: from 7.8 to 6.1 to 6.5 and from 1.7 to 1.0 to 1.2, respectively). Responders ($n = 5$) exhibited poorer habitual sleep efficiency before treatment than the non-responders. However, menopausal symptoms did not differ significantly between the groups at baseline. The results indicate that HRT with E2 and MP is a promising treatment option for peri- and postmenopausal Japanese women experiencing sleep disturbances, especially those with poor sleep efficiency.

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A cohort study on the associations between age at natural menopause and rheumatoid arthritis in postmenopausal women from the Canadian Longitudinal Study on Aging

Durmalouk Kesibi 1, Michael Rotondi 2, Heather Edgell 3, Hala Tamim 4

Menopause represents a significant phase in a woman's life, marked by profound physiological changes. An early onset of menopause has been associated with a variety of negative outcomes. Estrogen has been shown to be protective of bone and joint health. Hormonal links to rheumatoid arthritis have been found; previous studies exploring age at natural menopause (ANM) and Rheumatoid arthritis have produced conflicting results. This study investigated the association between ANM and incidence of rheumatoid arthritis among postmenopausal Canadian women. The study included women between the ages of 45-85 years from the Canadian Longitudinal Study on Aging followed over a 10-year period. Analysis was restricted to naturally postmenopausal women that did not have rheumatoid arthritis prior to menopause. ANM was examined using the following categories ≤ 44 (reference), 45-49, and ≥ 50 . Survival analysis was used to determine time to onset of rheumatoid arthritis. Unadjusted and adjusted multivariable Cox regression models were used to examine the relationship between ANM and incidence of rheumatoid arthritis. The adjusted multivariable Cox regression model showed significantly lower risk of rheumatoid arthritis in women with an older ANM of ≥ 50 years and who have been on hormone replacement therapy for ≥ 8 years with a hazard ratio of 0.2 (95 % CI: 0.1-0.7) compared to women with an ANM ≤ 44 who have never used hormone replacement therapy. Our findings suggest a potential beneficial effect of longer estrogen exposure on the risk of developing rheumatoid arthritis.

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Climacteric women's perspectives on menopause and hormone therapy: Knowledge gaps, fears, and the role of healthcare advice

Marcio Alexandre H Rodrigues 1, Zilma Silveira Nogueira Reis 1, Ana Paula de Andrade Verona 2, et al.

Objective: This study aims to evaluate the knowledge, attitudes, and practices of Brazilian women regarding menopause, related symptoms, and the use of hormone therapy, including indications and contraindications. **Methods:** A cross-sectional study was conducted between 2022/07/18 and 2023/10/01, involving women aged 40-65 years from various cities in Minas Gerais, São Paulo, and other regions of Brazil. A structured KAP (Knowledge, Attitudes, and Practices) Survey was used to assess sociodemographic characteristics, the prevalence of menopausal symptoms, and the participants' knowledge and practices concerning Menopause Hormone Therapy (MHT). **Results:** The median age of the women surveyed was 50 years; 55.4% were postmenopausal (median age 55), and 44.6% were premenopausal (median age 45). The data indicate limited knowledge about menopause among Brazilian women. Less than one-third (30.3%) expressed satisfaction with the information they had received regarding menopause and available treatment options. Furthermore, 92.97% of participants demonstrated little or no knowledge of hormone therapy. Nearly 27% were unaware of MHT, and 22% opposed its use. Only 29% reported current use of MHT, with common reasons for discontinuation including fear of side effects and contraindications advised by gynecologists. **Conclusion:** The findings indicate that many Brazilian women have insufficient knowledge about menopause and hormone therapy. Furthermore, a lack of information and training among healthcare providers may lead to the low utilization of menopausal hormone therapy (MHT). To effectively address menopausal symptoms and empower women to make informed choices about hormone therapy, it is crucial to improve access to accurate information and enhance the training of healthcare providers.

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Cardiovascular Disease After Hysterectomy in the Nurses' Health Study and Nurses' Health Study II

Viengneese Thao 1, Bijan Borah, Elizabeth A Stewart, Leslie V Farland, Shannon K Laughlin-Tommaso, et al.

Objective: To examine long-term risk of cardiovascular disease (CVD) after undergoing hysterectomy with or without oophorectomy. **Methods:** Participants in the Nurses' Health Study (NHS) and the Nurses' Health Study II (NHS II) (N=239,907) were grouped based on history of no surgery, hysterectomy alone, or hysterectomy with bilateral oophorectomy, and further categorized by use or nonuse of estrogen. The primary outcome was the risk of CVD (combined incidence of fatal and nonfatal myocardial infarction, coronary artery bypass graft and stroke) among the groups. Data were analyzed by multivariable Cox proportional hazards model, stratified by age to estimate adjusted hazard ratios (aHRs). Models controlled for menopausal hormone therapy as well as race, marital status, family income, personal and family history of relevant health conditions, alcohol consumption, physical activity, healthy eating index, body mass index (BMI), and parity. **Results:** After pooling the NHS and NHS II participants, the risk of CVD was higher among all participants who had hysterectomy before age 50 years compared with no surgery. Specifically, those who underwent hysterectomy before age 46 years and did not use estrogen had a 21.0% increased risk of CVD compared with no surgery (aHR 1.21, 95% CI, 1.04-1.40). Furthermore, among estrogen users who had hysterectomy and bilateral oophorectomy, those from the youngest two age groups (younger than 46 years and 46-50 years) had higher risk of CVD (aHR 1.26, 95% CI, 1.16-1.37; aHR 1.11, 95% CI, 1.01-1.22, respectively) compared with no surgery. Non-estrogen users who had hysterectomy with bilateral oophorectomy from all but the oldest age group (older than 60 years) experienced higher risk of CVD compared with no surgery. **Conclusion:** Younger age at time of hysterectomy, with or without oophorectomy, is associated with higher risk of CVD. Notably, use of estrogen does not appear to mitigate deleterious effects of hysterectomy with oophorectomy before age 50 years.

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Cardiovascular outcomes of menopause hormone therapy initiated in women aged ≥ 60 years or ≥ 10 years post-menopause: A systematic review of the literature

Nancy Yaneth Contreras Garza 1, José Antonio Dávila Rivas, Carlos Félix Arce, María Elizabeth Fraustro Avila, et al.

3Master Internacional de Climaterio y Menopausia. Universidad de Madrid (UDIMA), España.

Introduction Menopause hormone therapy (MHT) is the most effective treatment for climacteric syndrome. However, its cardiovascular effects remain complex. The 'timing hypothesis' suggests these effects depend on the timing of initiation, but this has been increasingly questioned. This study evaluates evidence on cardiovascular risks associated with late MHT initiation in healthy women aged ≥ 60 years or ≥ 10 years post-menopause. **Methods** A comprehensive literature search was conducted from the inception of each database until November 2023. The databases searched included PubMed, SciELO, Embase, and Cochrane. RCTs of human studies examining the cardiovascular effects of MHT in healthy women aged ≥ 60 years or those ≥ 10 years post-menopause were included. Eligibility screening, data extraction, risk of bias assessment were performed independently and in duplicate. **Results** Nine RCTs comprising 36,051 participants were included. We focus on results from participants aged ≥ 60 years. The mean follow-up was 7.2 years. Six studies were sub-analyses of the Women's Health Initiative (WHI) trial, while three studies originated from other trials. Results from the WHI indicated no significant increase in cardiovascular risks with either CEE + MPA or Estrogen-only therapy. Non-WHI studies showed an elevated stroke risk with tibolone and higher doses of combined MHT, but no cardiovascular complications were observed with low doses. **Conclusion** The increased risk of cardiovascular events in our target population is not statistically significant. There is a lack of high-quality evidence to suggest an increased risk of adverse cardiovascular outcomes in healthy women who initiate MHT at age ≥ 60 years or ≥ 10 years post-menopause.