



Selección de Resúmenes de Menopausia

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María Soledad Vallejo. Clínica Quilín. Universidad de Chile

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Musculoskeletal exercise: Its role in promoting health and longevity

Gerard D'Onofrio 1, Jonathan Kirschner 1, Heidi Prather 1, David Goldman 2, Alan Rozanski 3

Resistance training (RT) is an often ignored but essential component of physical health.. The functioning of the musculoskeletal system declines with age, resulting in sarcopenia, loss of muscle strength and power, decrease in muscle flexibility and balance. Other pertinent age-related changes include decline in basal metabolic rate, increase in fat mass, and decrease in bone mineral density. Such primary aging can be accentuated by the concomitant presence of comorbid conditions, such as insulin resistance and diabetes, obesity, inflammatory conditions, and physical inactivity (PI). The latter is often promoted by the presence of musculoskeletal conditions, such as osteoarthritis, back pain, and osteoporosis, which are quite common in society. RT can diminish long-term joint stress, "resist" age-related physiological deterioration and improve health outcomes through its ability to increase muscle strength and mass, balance the distribution of forces within a joint, increase basal metabolic rate and bone density, reduce body fat and cardiac risk factors, enhance endothelial function, and promote cognitive function and psychological well-being. Accordingly, health providers should screen for PI, lack of RT, and mobility risks using short screening questions, and employ simple functional tests, when indicated, to evaluate patients for impairment in gait, muscle strength, flexibility, and balance. This review also provides general principles for initiating and conducting RT and provides general and specific examples of resistance training programs, which should be individualized for patients through the evaluation and guidance by appropriate health providers, physical therapists, and certified trainers.

Neurourol Urodyn. 2023 Feb 25. doi: 10.1002/nau.25165. Online ahead of print.

The effect of 12 weeks of estriol cream on stress urinary incontinence post-menopause: A prospective multinational observational study

Nevine I D Te West 1, Katie Harris 2, Steven Jeffrey 3, Iris de Nie, Katrina Parkin, Jan-Paul Roovers, Kate H Moore

Objective: To quantitate the changes in stress urinary incontinence (SUI) outcome measures after 12 weeks of vaginal estriol cream in women with stress incontinence. Methods: A prospective multicentre observational study conducted in tertiary urogynaecology centers. Postmenopausal women with pure SUI or stress predominant mixed urinary incontinence (MUI), not receiving any other treatment for their incontinence were given written instructions regarding digital application of a standard dose of vaginal estriol cream. Outcomes were measured at baseline and 12 weeks. The primary objective outcome was vaginal pH. The primary subjective outcome was the stress domain of the Urogenital Distress Inventory-6 (UDI-6). The secondary objective outcome used was the erect cough stress test. Two quality of life questionnaires and two patient reported outcomes were also included. Results: The 46 postmenopausal recruits had a median age of 62.1 interquartile range (IQR 56.2-65.4). At follow up, the primary subjective outcome SUI domain [UDI-6] significantly improved from 83.3 (IQR 50-100) to 33.3 (33.3-66.7, $p \leq 0.001$) as did vaginal pH [from 5.1 (4.9-5.9) to 4.9 (4.6-5.0)] $p \leq 0.001$; 18/43 patients (42%) were dry on cough stress test. Conclusions: Twelve weeks of vaginal estriol cream significantly reduced symptoms of stress urinary incontinence in this sample of postmenopausal women.

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Risk-Reducing Breast and Gynecological Surgery for BRCA Mutation Carriers: A Narrative Review

Serena Bertozzi 1 2, Ambrogio P Londero 2 3, Anjeza Xholli 4, Guglielmo Azioni 4, Roberta Di Vora 1, et al.

This narrative review aims to clarify the role of breast and gynecological risk-reduction surgery in BRCA mutation carriers. We examine the indications, contraindications, complications, technical aspects, timing, economic impact, ethical issues, and prognostic benefits of the most common prophylactic surgical options from the perspectives of a breast surgeon and a gynecologist. A comprehensive literature review was conducted using the PubMed/Medline,

Scopus, and EMBASE databases. The databases were explored from their inception to August 2022. Three independent reviewers screened the items and selected those most relevant to this review's scope. BRCA1/2 mutation carriers are significantly more likely to develop breast, ovarian, and serous endometrial cancer. Because of the Angelina effect, there has been a significant increase in bilateral risk-reducing mastectomy (BRRM) since 2013. BRRM and risk-reducing salpingo-oophorectomy (RRSO) significantly reduce the risk of developing breast and ovarian cancer. RRSO has significant side effects, including an impact on fertility and early menopause (i.e., vasomotor symptoms, cardiovascular disease, osteoporosis, cognitive impairment, and sexual dysfunction). Hormonal therapy can help with these symptoms. Because of the lower risk of developing breast cancer in the residual mammary gland tissue after BRRM, estrogen-only treatments have an advantage over an estrogen/progesterone combined treatment. Risk-reducing hysterectomy allows for estrogen-only treatments and lowers the risk of endometrial cancer. Although prophylactic surgery reduces the cancer risk, it has disadvantages associated with early menopause. A multidisciplinary team must carefully inform the woman who chooses this path of the broad spectrum of implications, from cancer risk reduction to hormonal therapies.

Int J Mol Sci. 2023 Feb 18;24(4):4123. doi: 10.3390/ijms24044123.

Effects of Estradiol/Micronized Progesterone vs. Conjugated Equine Estrogens/Medroxyprogesterone Acetate on Breast Cancer Gene Expression in Healthy Postmenopausal Women

Parameswaran Grace Luther Lalitkumar 1, Eva Lundström 1, Birgitta Byström, Dorina Ujvari, Daniel Murkes, et al. Recent studies suggest estradiol (E2)/natural progesterone (P) confers less breast cancer risk compared with conjugated equine estrogens (CEE)/synthetic progestogens. We investigate if differences in the regulation of breast cancer-related gene expression could provide some explanation. This study is a subset of a monocentric, 2-way, open observer-blinded, phase 4 randomized controlled trial on healthy postmenopausal women with climacteric symptoms (ClinicalTrials.gov; EUCTR-2005/001016-51). Study medication was two 28-day cycles of sequential hormone treatment with oral 0.625 mg CEE and 5 mg of oral medroxyprogesterone acetate (MPA) or 1.5 mg E2 as percutaneous gel/day with the addition of 200 mg oral micronized P. MPA and P were added days 15-28/cycle. Material from two core-needle breast biopsies in 15 women in each group was subject to quantitative PCR (Q-PCR). The primary endpoint was a change in breast carcinoma development gene expression. In the first eight consecutive women, RNA was extracted at baseline and after two months of treatment and subjected to microarray for 28856 genes and Ingenuity Pathways Analysis (IPA) to identify risk factor genes. Microarray analysis showed 3272 genes regulated with a fold-change of $>\pm 1.4$. IPA showed 225 genes belonging to mammary-tumor development function: 198 for CEE/MPA vs. 34 for E2/P. Sixteen genes involved in mammary tumor inclination were subject to Q-PCR, inclining the CEE/MPA group towards an increased risk for breast carcinoma compared to the E2/P group at a very high significance level ($p = 3.1 \times 10^{-8}$, z-score 1.94). The combination of E2/P affected breast cancer-related genes much less than CEE/MPA.

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Use of menopausal hormone therapy and ovarian cancer risk in a French cohort study

Agnès Fournier 1, Manon Cairat 1, Gianluca Severi 1 2, Marc J Gunter 3, Sabina Rinaldi 3, Laure Dossus 3
Background: Epidemiological studies have found that menopausal hormone therapy (MHT) use is associated with an increased ovarian cancer risk. However, whether different MHT types confer the same level of risk is unclear. We estimated the associations between different MHT types and the risk of ovarian cancer in a prospective cohort. Methods: The study population included 75,606 postmenopausal women from the E3N cohort. Exposure to MHT was identified from self-reports in biennial questionnaires between 1992 and 2004 and from drug claim data matched to the cohort between 2004 and 2014. Hazard ratios (HR) and 95% confidence intervals (CI) of ovarian cancer were estimated using multivariable Cox proportional hazards models with MHT as a time-varying exposure. Tests of statistical significance were 2-sided. Results: Over an average 15.3 years follow-up, 416 ovarian cancers were diagnosed. HRs of ovarian cancer associated with ever use of estrogens combined with progesterone or dydrogesterone and ever use of estrogens combined with other progestagen were equal to 1.28 (95%CI 1.04 to 1.57) and 0.81 (0.65 to 1.00), respectively (p -homogeneity = 0.003), compared with never use. The HR for unopposed estrogen use was 1.09 (0.82 to 1.46). We found no trend according to duration of use or time since last use except for estrogens combined with progesterone/dydrogesterone which showed decreasing risk with increasing time since last use. Conclusion:

Different MHT types may impact ovarian cancer risk differentially. The possibility that MHT containing progestagens other than progesterone or dydrogesterone may confer some protection should be evaluated in other epidemiological studies.

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A multicenter, randomized, placebo-controlled study to select the minimum effective dose of estetrol in postmenopausal participants (E4Relief): part 2- vaginal cytology, genitourinary syndrome of menopause, and health-related quality of life

Ulysse Gaspard, Mélanie Taziaux, Maud Jost, Herjan J T, Coelingh Bennink, Wulf Utian, Rogerio Lobo, JM Foidart. Objective: A phase 2 study showed that 15 mg estetrol (E4) alleviates vasomotor symptoms (VMS). Here, we present the effects of E4 15 mg on vaginal cytology, genitourinary syndrome of menopause, and health-related quality of life. Methods: In a double-blind, placebo-controlled study, postmenopausal participants (n = 257, 40-65 y) were randomized to receive E4 2.5, 5, 10, or 15 mg or placebo once daily for 12 weeks. Outcomes were the vaginal maturation index and maturation value, genitourinary syndrome of menopause score, and the Menopause Rating Scale to assess health-related quality of life. We focused on E4 15 mg, the dose studied in ongoing phase 3 trials, and tested its effect versus placebo at 12 weeks using analysis of covariance. Results: Least square (LS) mean percentages of parabasal and intermediate cells decreased, whereas superficial cells increased across E4 doses; for E4 15 mg, the respective changes were -10.81% (P = 0.0017), -20.96% (P = 0.0037), and +34.17% (P < 0.0001). E4 15 mg decreased LS mean intensity score for vaginal dryness and dyspareunia (-0.40, P = 0.03, and -0.47, P = 0.0006, respectively); symptom reporting decreased by 41% and 50%, respectively, and shifted to milder intensity categories. The overall Menopause Rating Scale score decreased with E4 15 mg (LS mean, -3.1; P = 0.069) and across doses was associated with a decreasing frequency and severity of VMS (r = 0.34 and r = 0.31, P < 0.001). Conclusions: E4 demonstrated estrogenic effects in the vagina and decreased signs of atrophy. E4 15 mg is a promising treatment option also for important menopausal symptoms other than VMS.

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The Impact of Persistent Low Weight Status on the Occurrence of Vertebral Fractures: A Nationwide Population-Based Cohort Study

Sang-Min Park, Jiwon Park, Sangsoo Han, Hae-Dong Jang, Jae-Young Hong, Kyungdo Han, Ho-Joong Kim, et al. Background: Although, being underweight is commonly associated with osteoporosis and sarcopenia, its association with vertebral fractures (VFs), is less well researched. We investigated the influence of cumulative, chronic periods of low weight and changes in body weight on VF development. Methods: We used a nationwide, population-based database with data on people (> 40 years) who attended three health screenings between January 1, 2007, and December 31, 2009 to assess the incidence of new VFs. Cox proportional hazard analyses were used to establish the hazard ratios (HRs) for new VFs based on the degree of body mass index (BMI), the cumulative numbers of underweight participants, and temporal change in weight. Results: Of the 561,779 individuals in this analysis, 5,354 (1.0%) people were diagnosed three times, 3,672 (0.7%) were diagnosed twice, and 6,929 (1.2%) were diagnosed once. The fully adjusted HR for VFs in underweight individuals was 1.213. Underweight individuals diagnosed only once, twice, or three times had an adjusted HR of 0.904, 1.443, and 1.256, respectively. Although the adjusted HR was higher in adults who were consistently underweight, there was no difference in those who experienced a temporal change in body weight. BMI, age, sex, and household income were significantly associated with VF incidence. Conclusion: Low weight is a risk factor for VFs in the general population. Given the significant correlation between cumulative periods of low weight and the risk of VFs, it is necessary to treat underweight patients before a VF to prevent its development and other osteoporotic fractures.

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Associations of reproductive factors with incidence of myocardial infarction and ischemic stroke in postmenopausal women: a cohort study

Su-Min Jeong, Jung Eun Yoo, Keun Hye Jeon, Kyungdo Han, Heesun Lee, Dong-Yun Lee, Dong Wook Shin

Background: To assess the association between the reproductive factors of age at menarche, age at menopause, and reproductive span and the incidence of myocardial infarction (MI) and ischemic stroke (IS). **Methods:** We used a population-based retrospective cohort study from the National Health Insurance Service database of Korea including a total of 1,224,547 postmenopausal women. Associations between age at menarche (≤ 12 , 13-14 [reference], 15, 16, and ≥ 17 years), age at menopause (< 40 , 40-45, 46-50, 51-54 [reference], and ≥ 55 years), and reproductive span (< 30 , 30-33, 34-36, 37-40 [reference], and ≥ 41 years) and the incidence of MI and IS were assessed by Cox proportional hazard models with adjustment for traditional cardiovascular risk factors and various reproductive factors. **Results:** During a median follow-up of 8.4 years, 25,181 MI and 38,996 IS cases were identified. Late menarche (≥ 16 years), early menopause (≤ 50 years), and short reproductive span (≤ 36 years) were linearly associated with a 6%, 12-40%, and 12-32% higher risk of MI, respectively. Meanwhile, a U-shaped association between age at menarche and risk of IS was found, with a 16% higher risk in early menarche (≤ 12 years) and a 7-9% higher risk in late menarche (≥ 16 years). Short reproductive span was linearly associated with an increased risk of MI, whereas both shorter and longer reproductive spans were associated with an increased risk of IS. **Conclusions:** This study demonstrated different patterns of association between age at menarche and incidence of MI and IS: a linear association for MI versus a U-shaped association for IS. Female reproductive factors in addition to traditional cardiovascular risk factors should be considered when assessing overall cardiovascular risk in postmenopausal women.