



Selección de Resúmenes de Menopausia

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Menopausal Status and Abdominal Obesity Are Significant Determinants of Hepatic Lipid Metabolism in Women.

Hodson L, Banerjee R, Rial B, Arlt W, Adiels M, Boren J et al

BACKGROUND: Android fat distribution (abdominal obesity) is associated with insulin resistance, hepatic steatosis, and greater secretion of large very low-density lipoprotein (VLDL) particles in men. Since abdominal obesity is becoming increasingly prevalent in women, we aimed to investigate the relationship between android fat and hepatic lipid metabolism in pre- and postmenopausal women. **METHODS AND RESULTS:** We used a combination of stable isotope tracer techniques to investigate intrahepatic fatty acid synthesis and partitioning in 29 lean and 29 abdominally obese women (android fat/total fat 0.065 [0.02 to 0.08] and 0.095 [0.08 to 0.11], respectively). Thirty women were premenopausal aged 35 to 45 and they were matched for abdominal obesity with 28 postmenopausal women aged 55 to 65. As anticipated, abdominal obese women were more insulin resistant with enhanced hepatic secretion of large (404 ± 30 versus 268 ± 26 mg/kg lean mass, $P < 0.001$) but not small VLDL (160 ± 11 versus 142 ± 13). However, postmenopausal status had a pronounced effect on the characteristics of small VLDL particles, which were considerably triglyceride-enriched (production ratio of VLDL2- triglyceride: apolipoprotein B 30 ± 5.3 versus 19 ± 1.6 , $P < 0.05$). In contrast to postmenopausal women, there was a tight control of hepatic fatty acid metabolism and triglyceride production in premenopausal women, whereby oxidation ($r_s = -0.49$, $P = 0.006$), de novo lipogenesis ($r_s = 0.55$, $P = 0.003$), and desaturation ($r_s = 0.48$, $P = 0.012$) were closely correlated with abdominal obesity-driven large VLDL-triglyceride secretion rate. **CONCLUSIONS:** In women, abdominal obesity is a major driver of hepatic large VLDL particle secretion, whereas postmenopausal status was characterized by increased small VLDL particle size. These data provide a mechanistic basis for the hyperlipidemia observed in postmenopausal obesity.

Nota Editor: Partículas grandes de VLDL son aterogénicas

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Hormone Replacement Therapy and Risk of Breast Cancer in Korean Women: A Quantitative Systematic Review.

Bae JM, Kim EH.

OBJECTIVES: The epidemiological characteristics of breast cancer incidence by age group in Korean women are unique. This systematic review aimed to investigate the association between hormone replacement therapy (HRT) and breast cancer risk in Korean women. **METHODS:** We searched electronic databases such as KoreaMed, KMBase, KISS, and RISS4U as well as PubMed for publications on Korean breast cancer patients. We also conducted manual searching based on references and citations in potential papers. All of the analytically epidemiologic studies that obtained individual data on HRT exposure and breast cancer occurrence in Korean women were selected. We restricted the inclusion of case-control studies to those that included age-matched controls. Estimates of summary odds ratio (SOR) with 95% confidence intervals (CIs) were calculated using random effect models. **RESULTS:** One cohort and five case-control studies were finally selected. Based on the heterogeneity that existed among the six studies ($I^2 = 70.2\%$), a random effect model was applied. The summary effect size of HRT history from the six articles indicated no statistical significance in breast cancer risk (SOR, 0.983; 95% CI, 0.620 to 1.556). **CONCLUSIONS:** These facts support no significant effect of HRT history in the risk of breast cancer in Korean women. It is necessary to conduct a pooled analysis.

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Timing of estradiol treatment after menopause may determine benefit or harm to insulin action.

Pereira RI, Casey BA, Swibas TA, Erickson CB, Wolfe P, Van Pelt RE.

CONTEXT: Type 2 diabetes (T2D) is reduced in postmenopausal women randomized to estrogen-based hormone therapy (HT) compared with placebo. Insulin sensitivity is a key determinant of T2D risk and overall cardiometabolic health and studies indicate that estradiol (E2) directly impacts insulin action. OBJECTIVE: We hypothesized that the timing of E2 administration after menopause is an important determinant of its effect on insulin action. DESIGN: Randomized, cross-over, placebo-controlled Participants: Early postmenopausal (EPM; ≤ 6 yr of final menses; $n=22$) and late postmenopausal (LPM; ≥ 10 yr since last menses; $n=24$) women naïve to HT. INTERVENTION: Short-term (1 week) transdermal E2 and placebo Main Outcome: Insulin-mediated glucose disposal (GDR) via hyperinsulinemic-euglycemic clamp Results: Compared to EPM, LPM were older (mean \pm SD; 63 ± 3 vs 56 ± 4 yr, $p<0.05$) and more years past menopause (12 ± 2 vs 3 ± 2 yr, $p<0.05$). Body mass index (24 ± 3 vs 25 ± 7 kg/m²) and fat mass (25 ± 7 vs 23 ± 6 kg) did not differ between groups, but fat-free mass (FFM) was lower in LPM compared to EPM (40 ± 4 vs 43 ± 5 kg, $p<0.05$). Baseline GDR did not differ between groups (11.7 ± 2.8 vs. 11.5 ± 2.9 mg/kg FFM/min). In support of our hypothesis, 1 week of E2 decreased GDR in LPM compared to an increase in EPM ($+0.44 \pm 1.7$ vs -0.76 ± 2.1 mg/kg FFM/min, $p<0.05$). CONCLUSIONS: There was not an apparent decline in GDR with age or time since menopause per se. However, E2 action on GDR was dependent on time since menopause, such that there was an apparent benefit early (≤ 6 yr) compared to harm later (≥ 10 yr) in menopause. E2-mediated effects on insulin action may be one mechanism by which HT reduces the incidence of T2D in early postmenopausal women.

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The Influence of Hormone Therapies on Type I and II Endometrial Cancer A Nationwide Cohort Study.

Mørch LS, Kjaer SK, Keiding N, Løkkegaard E, Lidegaard Ø.

The influence of hormone therapy (HT) on risk for endometrial cancer is still casting which type of hormone therapy the clinicians recommend. It is unrevealed if HT has a differential influence on Type I versus Type II endometrial tumors, and little is known about the influence of e.g. different routes of administration and about the influence of tibolone. We followed all Danish women 50-79 years old without previous cancer or hysterectomy ($n=914,595$) 1995-2009. From the National Prescription Register we computed HT exposures as time-dependent covariates. Incident endometrial cancers ($n=6,202$) were identified from the National Cancer Registry; 4,972 Type I tumors and 500 Type II tumors. Incidence rate ratios (RR) and 95% confidence intervals (CIs) were estimated by Poisson regression. Compared with women never on HT, the RR of endometrial cancer was increased with conjugated estrogen; 4.27 (1.92-9.52), non-conjugated estrogen: 2.00 (1.87-2.13), long cycle combined therapy: 2.89 (2.27-3.67), cyclic combined therapy: 2.06 (1.88-2.27), tibolone 3.56 (2.94-4.32), transdermal estrogen: 2.77 (2.12-3.62), and vaginal estrogen: 1.96 (1.77-2.17), but not with continuous combined therapy: 1.02 (0.87-1.20). In contrast, the risk of Type II tumors seemed decreased with continuous combined therapy: 0.45 (0.20-1.01), and estrogen therapy implied a non-significantly altered risk of 1.43 (0.85-2.41). Our findings support that continuous combined therapy is risk free for Type I tumors, while all other hormone therapies increase risk. In contrast, Type II endometrial cancer was less convincingly associated with hormone use, and continuous combined therapy seemed to decrease the risk.

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Vaginal atrophy of women in postmenopause. Results from a multicentric observational study: The AGATA study.

Palma F, Volpe A, Villa P, Cagnacci A; as the writing group of the AGATA study.

OBJECTIVES: Prevalence of vulvar-vaginal atrophy (VVA) has been always investigated by phone or web interview without any objective evaluation. Objective signs associated with symptoms of VVA are now termed genitourinary syndrome of menopause (GSM). This multi-centric study was performed in order to provide nationwide data on the prevalence and management of GSM. METHODS: Nine hundred thirteen females, 59.3 ± 7.4 years old asking for a routine gynecological examination were recruited. Diagnosis of GSM was based on patient sensation of vaginal dryness, any objective sign of VVA and a pH >5 . RESULTS: A 722/913 (79.1%) women were diagnosed with GSM with a prevalence ranging from 64.7% to 84.2%, starting from 1 to 6 years after menopause. Sedentary women were at higher risk of GSM (OR 1.8, 95% CI: 1.3-2.5; $p=0.0005$). Recent vaginal infection was more likely

in women with GSM (OR 2.48, 95% CI: 1.33-4.62; p=0.0041). Symptoms reported by women with GSM were vaginal dryness (100%), dyspareunia (77.6%), burning (56.9%), itching (56.6%) and dysuria (36.1%). Signs detected by gynecologists were mucosal dryness (99%), thinning of vaginal rugae (92.1%), pallor of the mucosa (90.7%), mucosal fragility (71.9%) and petechiae (46.7%). Only 274 (30%) of women had had a previous diagnosis of VVA/GSM. These were treated either with no therapy (9.8%), systemic hormone (9.2%), local hormone (44.5%) or local non-hormonal (36.5%) therapy. At the time of our investigation 266 of them (97.1%) still had the disorder. CONCLUSIONS: GSM is a common, under-diagnosed and under-treated disorder. Measures to improve its early detection and its appropriate management are needed.

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Increased cardiovascular mortality risk in women discontinuing postmenopausal hormone therapy.

Mikkola TS, Tuomikoski P, Lyytinen H, Korhonen P, Hoti F, Vattulainen P, Gissler M, Ylikorkala O.

CONTEXT: Current guidelines recommend annual discontinuation of postmenopausal hormone therapy (HT) to evaluate whether a woman could manage without the treatment. The impact of HT on cardiovascular health has been widely studied, but it is not known how withdrawal of HT affects cardiovascular risk. OBJECTIVE: We evaluated the risk of cardiac or stroke death after the discontinuation of HT. Design, Patients, Interventions and Main Outcome Measures: Altogether 332 202 Finnish women discontinuing HT between 1994-2009 (data from National Reimbursement register) were followed from the discontinuation date to death due to cardiac cause (n=3 177) or stroke (n=1 952), or to the end of 2009. The deaths, retrieved from the national Cause of Death Register, were compared with the expected number of deaths in the age-standardized background population. In a sub-analysis we also compared HT stoppers with HT users. RESULTS: Within the first post-treatment year, the risk of cardiac death was significantly elevated (standardized mortality ratio; 95% confidence interval 1.26; 1.16-1.37), whereas follow-up >1 year was accompanied with reduction (0.75; 0.72-0.78). The risk of stroke death in the first post-treatment year was increased (1.63; 1.47-1.79), but follow-up >1 year accompanied with a reduced risk (0.89; 0.85-0.94). The cardiac (2.30; 2.12-2.50) and stroke (2.52; 2.28-2.77) death risk elevations were even higher when compared to HT users. In women who discontinued HT at <60, but not in women aged ≥60 years, cardiac mortality risk was elevated (1.94; 1.51-2.48). CONCLUSIONS: Increased cardiovascular death risks question the safety of annual HT discontinuation practice to evaluate whether a woman could manage without HT.