Selección de Resúmenes de Menopausia

Semana del 31 de diciembre de 2019 al 7 de enero 2020

María Soledad Vallejo. Clínica Quilín. Universidad de Chile

J Clin Endocrinol Metab. 2020 Jan 3. pii: dgz322. doi: 10.1210/clinem/dgz322. [Epub ahead of print]

Risk for Infections During Treatment with Denosumab for Osteoporosis: a Systematic Review and Meta-analysis.

Diker-Cohen T1,2,3, Rosenberg D1,3, Avni T1,3, Shepshelovich D1,3, Tsvetov G2,3, Gafter-Gvili A1,3.

CONTEXT: Denosumab inhibits the receptor activator of nuclear factor κ-B ligand, an immune system modulator. Safety endpoints including risk for infections were assessed as secondary outcomes in randomized controlled trials (RCTs) of the drug. OBJECTIVE: To assess the risk of serious adverse events of infections (SAEI) in denosumab-treated patients. DATA SOURCES: PubMed and Cochrane Central Register of Controlled Trials were searched up to May 27, 2019. STUDY SELECTION: All RCTs of denosumab (60 mg every 6 months) versus any comparator were included. We excluded trials in cancer patients for prevention of skeletal-related events. DATA EXTRACTION: Two reviewers independently applied selection criteria and extracted the data. Risk ratios (RR) with 95% confidence intervals (CI) were pooled using a fixed effect model. Sensitivity analysis was based on risk of bias. DATA SYNTHESIS: Thirty-three studies (22,253 patients) were included. There was a higher incidence of SAEI during denosumab treatment versus any comparator (RR, 1.21; 95% CI, 1.04-1.40; I2 = 0%), mainly of ear, nose and throat (RR ,2.66; 95% CI, 1.20-5.91) and gastrointestinal origin (RR, 1.43; 95% CI, 1.02-2.01). Risk ratio was similar in a sensitivity analysis based on adequate allocation concealment. The risk ratio of any infection (RR, 1.03; 95% CI, 0.99-1.06) and infection-related mortality (RR, 0.50; 95% CI, 0.20-1.23) was comparable between groups. CONCLUSIONS: A higher incidence of SAEI is demonstrated during treatment with denosumab in an osteoporosis dose. Nevertheless, the overall risk for any infection or related mortality is similar to comparator groups. These findings merit consideration before therapy initiation.

J Natl Cancer Inst. 2020 Jan 3. pii: djz241. doi: 10.1093/jnci/djz241. [Epub ahead of print]

Genetic factors, adherence to healthy lifestyle behavior, and risk of invasive breast cancer among women in the UK Biobank.

Arthur RS1, Wang T1, Xue X1, Kamensky V1, Rohan TE1.

BACKGROUND: Breast cancer is considered to result from a combination of genetic and lifestyle-related factors, but the degree to which an overall healthy lifestyle may attenuate the impact of multiple genetic variants on invasive breast cancer risk remains equivocal. METHODS: Using Cox proportional hazards regression models, we examined the association of a modified healthy lifestyle index (HLI) with risk of invasive breast cancer by genetic risk group among 146,326 women from the UK Biobank. We generated an HLI score based on a combination of diet, physical activity, smoking, alcohol consumption and anthropometry, and a polygenic risk score (PRS) using 304 breast cancer-associated genetic loci. RESULTS: Among premenopausal and postmenopausal women, a favorable lifestyle (highest tertile) was associated with 22% and 31% reductions in invasive breast cancer risk, respectively (HRhigh vs low: 0.78, 95% CI = 0.64 to 0.94 and 0.69, 0.63 to 0.77), while a high PRS (highest tertile) was associated with more than a doubling in the risk in both groups. For premenopausal women, the greatest risk reduction in association with the HLI was seen among those with a high PRS (HRhigh vs low: 0.73, 95% CI = 0.75 to 0.95). In postmenopausal women, those with a favorable lifestyle had 30%, 29% and 32% reductions in risk of invasive breast cancer in the low, intermediate and high PRS groups, respectively (HRhigh vs low: 0.70, 95% CI = 0.56 to 0.88, 0.71, 0.59 to 0.84 and 0.68, 0.59 to 0.78, respectively). There was an additive but not multiplicative interaction between the HLI score and PRS for postmenopausal and, to a lesser extent, premenopausal women. CONCLUSION: Our findings support the view that an overall healthy lifestyle may attenuate the impact of genetic factors on invasive breast cancer risk among women of European ancestry.

Breast Cancer Res Treat. 2020 Jan 2. doi: 10.1007/s10549-019-05516-1. [Epub ahead of print]

Uterine cancer in breast cancer survivors: a systematic review.

Wijayabahu AT1, Egan KM2, Yaghjyan L3.

PURPOSE: Epidemiological evidence on the risk factors for uterine/endometrial cancer in breast cancer (BCa) survivors is limited and inconsistent. Therefore, we critically reviewed and summarized available evidence related to the risk factors for uterine/endometrial cancer in BCa survivors. METHODS: We conducted a literature search through PubMed, Web of Science Core Collection/Cited Reference Search, as well as through manual searches of the bibliographies of the articles identified in electronic searches. We included in this review studies that were published up to November 30, 2018 that were accessible in full-text format and were published in English. RESULTS: Of the 27 eligible studies, 96% had > 700 participants, 74% were prospective cohorts, 70% originated outside of the US, 44% reported as having pre-/postmenopausal women, and 26% reported having racially heterogeneous populations. Risk factors positively associated with uterine/endometrial cancer risk among BCa survivors included age at BCa diagnosis > 50 years, African American race, greater BMI/weight gain, and Tamoxifen treatment. For other lifestyle, reproductive and clinical factors, associations were either not significant (parity) or inconsistent (HRT use, menopausal status, smoking status) or had limited evidence (alcohol intake, family history of cancer, age at first birth, oral contraceptive use, age at menopause, comorbidities). CONCLUSION: We identified several methodological concerns and limitations across epidemiological studies on potential risk factors for uterine/endometrial cancer in BCa survivors, including lack of details on uterine/endometrial cancer case ascertainment, varying and imprecise definitions of important covariates, insufficient adjustment for potential confounders, and small numbers of uterine/endometrial cancer cases in the overall as well as stratified analyses. Based on the available evidence, older age and higher body weight measures appear to be a shared risk factor for uterine/endometrial cancer in the general population as well as in BCa survivors. In addition, there is suggestive evidence that African American BCa survivors have a higher risk of uterine/endometrial cancer as compared to their White counterparts. There is also evidence that Tamoxifen contributes to uterine/endometrial cancer in BCa survivors. Given limitations of existing studies, more thorough investigation of these associations is warranted to identify additional preventive strategies needed for BCa survivors to reduce uterine/endometrial cancer risk and improve overall survival.

Arch Osteoporos. 2020 Jan 2;15(1):6. doi: 10.1007/s11657-019-0673-3.

Common errors in dual-energy X-ray absorptiometry scans in imaging centers in Ecuador.

Maldonado G1, Intriago M2, Larroude M3, Aguilar G4, Moreno M5, Gonzalez J, Vargas S, Vera C, Rios K, Rios C.

Dual-energy X-ray absorptiometry is recognized for measuring bone mineral density. The lack of knowledge can lead to errors both in the acquisition of information and in its analysis and subsequent interpretation. The main errors in Ecuadorian Centers were positioning of the patient to the equipment and incorrect analyzed area. PURPOSE/INTRODUCTION: Dual-energy X-ray absorptiometry (DXA) is recognized as the gold standard for measuring bone mineral density (BMD) with acceptable errors, good precision, and reproducibility. However, the training of operators in different centers and countries is not standardized, and the lack of knowledge can lead to errors both in the acquisition of information and in its analysis and subsequent interpretation. The purpose was to determine the most common errors in the performance of bone densitometry from different imaging centers in Ecuador. METHODS: Cross-sectional descriptive study. We collected DXA scans from different imaging centers in Ecuador. Data from the DXA scan included city of origin, type of specialist that requested it, and densitometry diagnosis. The DXA images provided were analyzed double blind by experts in the field from Argentina. RESULTS: From a total of 141 patients with a mean age of 61 ± 10 years, 93.6% were women. About 78% of the DXA scans came from private imaging centers and 22% from public centers, 95% of all came from the city of Guayaquil. The machines used were Hologic 50.4% and Lunar 49.6%. The densitometric diagnosis was 16.3% normal, 46.1% osteoporosis, and 37.6% osteopenia. A total of 112 left hip and 49 right hip scans were analyzed from which 31.2% and 22.4% had errors in patient positioning, respectively, mainly internal or external rotation. About 140 lumbar scans were analyzed from which 21.4% had patient positioning errors (not centered or not straight). Also in 38.5% the vertebral area did not correspond to L1-L4. About 3.5% had artifacts such as a metal bar or implant. The region of interest was misplaced in 24.1% of the lumbar scans and 19.9% of the femur. CONCLUSIONS: DXA quality standards exist but are often not implemented in clinical practice. When studies are performed incorrectly, it can lead to important errors in diagnosis and therapy. Physicians interested in the management of osteoporosis, although not directly involved in the performance and interpretation of DXA, should be familiar with the protocols to minimize errors and allow the proper use of bone densitometry.

Alzheimers Dement (N Y). 2019 Dec 9;5:906-917. doi: 10.1016/j.trci.2019.09.004. eCollection 2019.

Estrogen activates Alzheimer's disease genes.

Ratnakumar A1, Zimmerman SE1, Jordan BA2,3, Mar JC1,4.

Introduction: Women are at increased risk for Alzheimer's disease (AD), but the reason why remains unknown. One hypothesis is that low estrogen levels at menopause increases vulnerability to AD, but this remains unproven. Methods: We compared neuronal genes upregulated by estrogen in ovariectomized female rhesus macaques with a database of >17,000 diverse gene sets and applied a rare variant burden test to exome sequencing data from 1208 female AD patients with the age of onset < 75 years and 2162 female AD controls. Results: We found a striking overlap between genes upregulated by estrogen in macaques and genes downregulated in the human postmortem AD brain, and we found that estrogen upregulates the APOE gene and that progesterone acts antagonistically to estrogen genome-wide. We also found that female patients with AD have excess rare mutations in the early menopause gene MCM8. Discussion: We show with genomic data that the menopausal loss of estrogen could underlie the increased risk for AD in women.