Selección de Resúmenes de Menopausia

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Risk of dementia among postmenopausal breast cancer survivors treated with aromatase inhibitors versus tamoxifen: a cohort study using primary care data from the UK.

Bromley SE1,2, Matthews A3, Smeeth L3, Stanway S4, Bhaskaran K3.

PURPOSE: Among a cohort of postmenopausal breast cancer survivors, we aimed to compare the risk of dementia associated with aromatase inhibitor (AI) therapy versus tamoxifen. METHODS: Using UK primary care electronic health records, we identified 14,214 postmenopausal breast cancer survivors (aged ≥ 54 years) with a first AI or tamoxifen prescription between January 2002 and December 2015 and no previous dementia diagnosis. Women were followed-up to identify incident cases of dementia. Cox regression was used to calculate hazard ratios (HRs) with 95% confidence intervals (CIs) to quantify the association between AI exposure (vs. tamoxifen) and dementia, adjusted for confounders. RESULTS: A total of 368 incident dementia cases was identified over 57,102 person-years of follow-up. The crude incidence rate of dementia was 7.46 per 1000 person-years (95% CI 6.43-8.65) among women starting endocrine treatment on an AI, and 6.32 per 1000 person-years (95% CI 5.34-7.47) among women starting on tamoxifen. After accounting for age differences and assessing other potential confounders, there was no evidence of a difference in dementia risk between exposure groups (HR for AI vs tamoxifen 1.04, 95% CI 0.83-1.03). There was no evidence of effect modification by age. CONCLUSION: There was no evidence for a difference in dementia risk between AI and tamoxifen users among postmenopausal breast cancer survivors. IMPLICATIONS FOR CANCER SURVIVORS: Our findings suggest that there is no reason for concern about a difference in dementia risk with AI vs. tamoxifen, which is relevant to postmenopausal breast cancer patients recommended these treatments.

JNCI Cancer Spectr. 2019 Sep;3(3):pkz029. doi: 10.1093/jncics/pkz029. Epub 2019 Apr 25.

Postmenopausal Androgen Metabolism and Endometrial Cancer Risk in the Women's Health Initiative Observational Study.

Michels KA1, Brinton LA1, Wentzensen N1, Pan K2, Chen C3, Anderson GL3, Pfeiffer RM1, Xu X4, Rohan TE5, Background: After menopause, several androgens continue to be produced primarily by the adrenal glands; these can be converted into estrogens via aromatization or into androgen metabolites. It is unclear if androgens are associated with endometrial cancer risk independently of their being precursors to estrogens or if alternative metabolic pathways influence risk. Methods: We measured prediagnostic serum concentrations of 12 androgens and their metabolites using highly sensitive liquid chromatography-tandem mass spectrometry assays in a nested case-control study of postmenopausal women from the Women's Health Initiative Observational Study (313 endometrial cancer case subjects, 354 matched control subjects). Estrogens were previously assayed. We used conditional logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for endometrial cancer with adjustment for confounders. Results: Compared to the lowest concentrations, the highest levels of adrenal androgens were associated with increased endometrial cancer risk: dehydroepiandrosterone (5th vs 1st quintile: OR = 1.85, 95% CI = 1.06 to 3.25), androstenedione (OR = 2.36, 95% CI = 1.34 to 4.16), and testosterone (OR = 1.91, 95% CI = 1.12 to 3.24). Downstream androgen metabolites were not associated with endometrial cancer. Although increased risks for the parent androgens were still suggested after adjustment for unconjugated estradiol, the associations attenuated, and with the exception of androstenedione, were no longer statistically significant. We also evaluated ratios of estrogens relative to their androgenic precursors; both higher unconjugated estrone:androstenedione and higher unconjugated estradiol:testosterone were associated with increased endometrial cancer risk. Conclusions: We identified increased risks for endometrial cancer with the highest levels of adrenal androgens and high levels of estrogens relative to these androgens. As adrenal androgens can be aromatized to estrogens, this suggests androgens likely influence endometrial carcinogenesis via estrogen metabolism.

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Celiac Disease and Its Role in the Development of Metabolic Bone Disease.

Micic D1, Rao VL2, Semrad CE2.

Celiac disease (CD) is an immune-mediated enteropathy that occurs in genetically susceptible hosts with the ingestion of gluten-containing products. Ongoing gluten consumption leads to intestinal damage, characterized by villous blunting and increased intraepithelial lymphocytes, resulting in malabsorption. Pertinent to the development of bone disease, malabsorption of calcium and vitamin D leads to secondary hyperparathyroidism and metabolic bone disease among individuals with CD. In this article, we review the pathogenesis of CD and the effects of malabsorption on bone health. Imbalances in bone resorption and formation particularly in individuals with CD and persistent disease activity ultimately lead to a state of bone loss and impaired mineralization. Initiation of a gluten-free diet is critical in the management of CD-related metabolic bone disease, demonstrating improvements in bone mineral density within the first year of dietary adherence.

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Assessment and management of bone health in women with oestrogen receptor-positive breast cancer receiving endocrine therapy: position statement summary.

Grossmann M1,2, Ramchand SK1,2, Milat F3,4, Vincent A5, Lim E6, Kotowicz MA7,8, Hicks J9, Teede HJ10.

INTRODUCTION: Representatives appointed by relevant Australian medical societies used a systematic approach for adaptation of guidelines (ADAPTE) to formulate clinical consensus recommendations on assessment and management of bone health in women with oestrogen receptor-positive early breast cancer receiving endocrine therapy. The current evidence suggests that women receiving adjuvant aromatase inhibitors and pre-menopausal woman treated with tamoxifen have accelerated bone loss and that women receiving adjuvant aromatase inhibitors have increased fracture risk. Both bisphosphonates and denosumab prevent bone loss; additionally, denosumab has proven anti-fracture benefit in post-menopausal women receiving aromatase inhibitors for hormone receptor-positive breast cancer. MAIN RECOMMENDATIONS: Women considering endocrine therapy need fracture risk assessment, including clinical risk factors, biochemistry and bone mineral density measurement, with monitoring based on risk factors. Weight-bearing exercise and vitamin D and calcium sufficiency are recommended routinely. Anti-resorptive treatment is indicated in women with prevalent or incident clinical or morphometric fragility fractures, and should be considered in women with a T score (or Z score in women aged < 50 years) of < - 2.0 at any site, or if annual bone loss is ≥ 5%, considering baseline bone mineral density and other fracture risk factors. Duration of anti-resorptive treatment can be individualised based on absolute fracture risk. Relative to their skeletal benefits, risks of adverse events with anti-resorptive treatments are low. CHANGES IN MANAGEMENT AS RESULT OF THE POSITION STATEMENT: Skeletal health should be considered in the decision-making process regarding choice and duration of endocrine therapy. Before and during endocrine therapy, skeletal health should be assessed regularly, optimised by non-pharmacological intervention and, where indicated, anti-resorptive treatment, in an individualised, multidisciplinary approach.

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How well do the FRAX (Australia) and Garvan calculators predict incident fractures? Data from the Geelong Osteoporosis Study.

Holloway-Kew KL1, Zhang Y2, Betson AG3, Anderson KB3, Hans D4, Hyde NK3, Nicholson GC5, Pocock NA6, Kotowicz MA3,4,7, Pasco JA3,4,7.

INTRODUCTION: This study assessed the ability of the FRAX (Australia) and Garvan calculators to predict fractures in Australian women and men. METHODS: Women (n = 809) and men (n = 821) aged 50-90 years, enrolled in the Geelong Osteoporosis Study, were included. Fracture risk was estimated using FRAX and Garvan calculators with and without femoral neck bone mineral density (BMD) (FRAXBMD, FRAXnoBMD, GarvanBMD, GarvannoBMD). Incident major osteoporotic (MOF), fragility, and hip fractures over the following 10 years were verified radiologically. Differences between observed and predicted numbers of fractures were assessed using a chi-squared test. Diagnostics indexes were calculated. RESULTS: In women, 115 MOF, 184 fragility, and 42 hip fractures occurred. For men, there were 73, 109, and 17 fractures, respectively. FRAX underestimated MOFs, regardless of sex or inclusion of BMD.

FRAX accurately predicted hip fractures, except in women with BMD (20 predicted, $p = 0.004$). Garvan underestimated fragility fractures except in men using BMD (88 predicted, $p = 0.109$). Garvan accurately predicted hip fractures except for women without BMD (12 predicted, $p < 0.001$). Fractures were underestimated primarily in the osteopenia and osteoporosis groups; MOFs in the normal BMD group were only underestimated by FRAXBMD and fragility fractures by GarvannoBMD, both in men. AUROCs were not different between scores with and without BMD, except for fragility fractures predicted by Garvan in women (0.696, 95% CI 0.652-0.739 and 0.668, 0.623-0.712, respectively, $p = 0.008$) and men, which almost reached significance (0.683, 0.631-0.734, and 0.667, 0.615-0.719, respectively, $p = 0.051$). Analyses of sensitivity and specificity showed overall that MOFs and fragility fractures were poorly predicted by both FRAX and Garvan, while hip fractures were acceptably predicted. CONCLUSIONS: Overall, the FRAX and Garvan calculators underestimated MOF and fragility fractures, particularly in individuals with osteopenia or osteoporosis. Hip fractures were predicted better by both calculators. AUROC analyses suggest that GarvanBMD performed better than GarvannoBMD for prediction of fragility fractures.