



Selección de Resúmenes de Menopausia

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Noninvasive Predictor for Premalignant and Cancerous Lesions in Endometrial Polyps Diagnosed by Ultrasound

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Background: There was no consensus for management of asymptomatic endometrial polyps (EPs) up to date. **Objective:** The aim of present study was to determine the risk factors of malignant lesions in EPs diagnosed by ultrasound and establish a noninvasive predictor to decrease unnecessary hysteroscopy for EPs. **Study design:** We reviewed the records of all consecutive patients who underwent hysteroscopy for EPs in the Women's Hospital School of Medicine Zhejiang University between January 1, 2001 and December 31, 2018. The patients with histological diagnoses of atypical hyperplasia or cancer were defined as malignancy, while the patients with histological diagnoses of benign lesions were randomly selected as benign group according to the ratio of 1:4 (malignancy:benign), matching by age and year of hospitalization. Logistic regression analysis was used to analyze the clinical parameters for predicting malignancy of EPs. A Chi-squared automatic interaction detection (CHAID) decision tree analysis was performed to find a noninvasive predictor. The sensitivity, specificity, and the receiver operating characteristic curve (ROC) were used for assess the efficacy of the noninvasive predictor. New diagnosed EPs patients received in 2019 were used for verifying the accuracy of the noninvasive predictor. **Results:** The age in 15,790 cases of benign lesions was significantly younger than that in 230 malignancy cases (41.97 ± 11.53 year vs 53.31 ± 11.61 years, $p < 0.001$). AUB (OR 7.306, 95%CI 4.927-10.835), large EPs (OR 2.595, 95%CI 1.662-4.052), and blood flow signal in EPs (OR 2.690, 95%CI 1.872-3.866) were independent predictive factors of malignancy in all enrolled patients. A noninvasive predictor for malignancy of EPs was established, through combining with AUB, large polyps and blood flow signal. This predictor presented excellent sensitivity and NPV (91.3 and 95.8%), with acceptable specificity and AUC (0.801). Further validation in new diagnosed EPs also suggested excellent sensitivity and reasonable specificity (100 and 58.5%) of the predictor. Factors such as thickened endometrial thickness, menopause shorter than 10 years, hypertension, obesity and nulliparous were also validated as independent predictors of malignancy in different subgroup analysis. **Conclusions:** The noninvasive predictor combined with other risk factors from subgroup analysis would be reliable to distinguish the benign lesions from malignancy for EPs diagnosed by ultrasound.

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Estimation of fracture risk by the FRAX tool in patients with systemic lupus erythematosus: a 10-year longitudinal validation study

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Background: The fracture risk assessment tool has been widely used to stratify the 10-year fracture risk to guide therapy. Using the actual fracture data of a 10-year longitudinal cohort of older patients with systemic lupus erythematosus, we reported an underestimation of the tool in predicting major symptomatic osteoporotic fractures. Treatment of osteoporosis in systemic lupus erythematosus should not be based on fracture risk estimation alone. Relevant time-dependent risk factors should be taken into account for an individualized decision. **Objective:** To compare the observed fracture incidence in a 10-year longitudinal cohort of patients with systemic lupus erythematosus (SLE) with the fracture risk prediction from the fracture risk assessment (FRAX) tool. **Methods:** Adult patients (≥ 40 years) with SLE who had a first DEXA scan performed in 2005-2009 were studied. The 10-year rates of major osteoporotic and hip fractures were estimated by FRAX using clinical data at DEXA with adjustment for prednisolone dosage. The actual incidence of clinical fractures at 10 years was compared with the estimated rates. Factors associated with new fractures were studied by logistic regression. **Results:** A total of 229 SLE patients were studied (age: 50.2 ± 6.6 years, 93% women). Glucocorticoid was used in 148 (65%) patients at baseline (mean dose: 7.3 ± 6.9 mg/day; 34% ≥ 7.5 mg/day). Osteoporosis (bone mineral density T score ≤ -2.5) at the hip, femoral neck, or spine was present in 61 (27%) patients. The estimated 10-year risk of major osteoporotic and hip fractures by FRAX was $3.4 \pm 4.5\%$ and $0.95 \pm 2.3\%$, respectively. After 10 years, three patients developed hip fracture, 6 patients had limb fractures and 20 patients had symptomatic vertebral fractures (major osteoporotic fracture 12.7%, hip fracture 1.3%). The actual major osteoporotic

fracture rate was significantly higher than the FRAX estimation (12.7% vs 3.4%; $p < 0.001$). Logistic regression revealed that osteoporosis (odds ratio (OR): 4.07 [1.51-10.9]), previous fragility fracture (OR: 3.18 [1.02-9.90]), and a parental history of fracture (OR: 4.44 [1.16-17.0]) were independently associated with new clinical fractures at 10 years. Conclusion: The FRAX tool underestimates the major clinical fracture risk at 10 years in patients with SLE.

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The Efficacy of Alendronate Versus Denosumab on Major Osteoporotic Fracture Risk in Elderly Patients With Diabetes Mellitus: A Danish Retrospective Cohort Study

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Objective: Patients with diabetes mellitus have an increased risk of fractures; however, the underlying mechanism is largely unknown. We aimed to investigate whether the risk of major osteoporotic fractures in diabetes patients differs between subjects initiated with alendronate and denosumab, respectively. Methods and research design: We conducted a retrospective nationwide cohort study through access to all discharge diagnoses (ICD-10 system) from the National Danish Patient Registry along with all redeemed drug prescriptions (ATC classification system) from the Health Service Prescription Registry. We identified all subjects with a diabetes diagnosis between 2000 and 2018 and collected data on the first new prescription of anti-osteoporotic treatment between 2011 and 2018. Exposure was defined as either alendronate or denosumab treatment initiated after diabetes diagnosis. Outcome information was collected by identification of all major osteoporotic fracture (MOF) diagnoses, i.e., hip, spine, forearm, and humerus, from exposure until 2018 or censoring by emigration or death. The risk of fracture was calculated as hazard ratios (HR) using multiply adjusted Cox proportional models with death as a competing risk. Results: We included 8,745 subjects initiated with either alendronate ($n = 8,255$) or denosumab ($n = 490$). The cohort consisted of subjects with a mean age of 73.62 (SD ± 9.27) years, primarily females (69%) and suffering mainly from type 2 diabetes (98.22%) with a median diabetes duration at baseline of 5.45 years (IQR 2.41-9.19). Those in the denosumab group were older (mean 75.60 [SD ± 9.72] versus 73.51 [SD ± 9.23] years), had a higher proportion of women (81% versus 68%, RR 1.18 [95% CI 1.13-1.24], and were more comorbid (mean CCI 2.68 [95% CI 2.47-2.88] versus 1.98 [95% CI 1.93-2.02]) compared to alendronate initiators. In addition, denosumab users had a higher prevalence of previous fractures (64% versus 46%, RR 1.38 [95% CI 1.28-1.48]). The adjusted HR for any MOF after treatment initiation with denosumab was 0.89 (95% CI 0.78-1.02) compared to initiation with alendronate. Conclusion: The risk of incident MOF among subjects with diabetes was similar between those initially treated with alendronate and denosumab. These findings indicate that the two treatment strategies are equally effective in preventing osteoporotic fractures in subjects with diabetes.

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Metabolic bone disease and fracture risk after gastric bypass and sleeve gastrectomy: comparative analysis of a multi-institutional research network

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Background: Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG) are the two most performed bariatric procedures. Multiple studies have investigated the metabolic bone complications after bariatric surgery, but there is a paucity of data comparing bone health after RYGB and SG. Objectives: To compare the rates of major fractures and osteoporosis after Roux-en-Y gastric bypass and sleeve gastrectomy. Setting: Data from TriNetX multi-institutional research network that includes data from multiple health care organizations in the USA was analyzed at West Virginia University. Methods: We conducted a retrospective cohort study using TriNetX, a federated multi-institutional research network. We identified patients who underwent RYGB or SG. Primary outcome was the rate of major fractures at 3 years after the procedure. Other outcomes included the rate of spine fracture, femur fracture, osteoporosis, and vitamin D deficiency at follow-up. Results: In unmatched analysis, patients with SG were less likely to have major fractures or an osteoporosis diagnosis than RYGB patients at 3 years after the procedure ($P < .05$). After propensity-score matching, similar results were noted; patients with SG were less likely to have major fractures than RYGB patients at 3 years after procedure (2.85% versus 3.66%, risk ratio [RR]: .78, 95% confidence interval [CI]: .71-.85), and a lower rate of osteoporosis diagnosis was noted in the SG group. High rates of vitamin D deficiency were noted in both cohorts. The incidence of spine fractures was significantly lower in the SG group than in the RYGB group (.76% versus 1.18%, RR: .65, 95% CI: .54-.77). Similarly, the incidence of femur fracture was significantly lower after SG (RR: .62, 95% CI: .44-.88). Female sex, higher age, smoking history, and diabetes were independently associated with osteoporosis

diagnosis during follow-up (all P values <.05). Conclusion: Our analyses showed that RYGB is associated with a higher risk of osteoporosis, vitamin D deficiency, and osteoporotic fractures. Thus, in patients with a higher baseline osteoporotic risk, SG may be preferred option; however, further studies are needed.

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Menopausal hormone therapy: why we should no longer be afraid of the breast cancer risk

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The threat that women may develop breast cancer is the major reason why both physicians and women are afraid to use menopausal hormone therapy (MHT). The fear pertains to estrogen-progestin replacement therapy (EPRT) as estrogen-alone replacement therapy has no, or even a reduced, breast cancer risk. We reviewed the way breast cancer risk with EPRT was reported in some major publications since 2002 and tried to put the use-risk association in context. We hope this will make it easier for the physician and the menopausal woman to understand the risk involved and allow more confident and more informed decision-making regarding MHT use. We conclude that there are five interrelated reasons why physicians and women should no longer be afraid of the breast cancer risk with EPRT. We submit that breast cancer related to EPRT use is rare because the risk is very low; the reported increase in breast cancer risk with EPRT is not relevant to current practice; modifiable lifestyle factors, not EPRT, are the real risks for breast cancer; breast cancer-specific mortality is reduced in women who develop breast cancer while on EPRT; and avoiding MHT use when indicated puts a woman in harm's way.

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Fat Mass Has Negative Effects on Bone, Especially in Men: A Cross-Sectional Analysis of NHANES 2011-2018

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Context: The effect of high levels of obesity on bone health are not clear. Objective: We aimed to examine the associations of body composition and bone mineral density (BMD) in a large, nationally representative population with a wide range of body mass index. Methods: We analyzed 10,814 subjects aged 20-59 from NHANES 2011-2018 who had total body BMD and body composition data. Body composition was examined as lean mass index (LMI) and fat mass index (FMI). Linear regression models were created with BMD as the outcome, while examining LMI and FMI and controlling for age, gender, race/ethnicity, height, and smoking status. Results: In multivariable modeling, every 1 kg/m² additional LMI was associated with 0.19 higher T-score, while every additional 1 kg/m² in FMI was associated with 0.10 lower T-score (p<0.001 for both). The negative association of FMI with BMD was mainly seen when adjusting for LMI. Effects of LMI were similar in men and women, but the effect of FMI was more negative in men (0.13 lower T-score per additional 1 kg/m² of FMI in men vs. 0.08 lower BMD T-score in women, p-for-interaction<0.001). Conclusions: In subjects under 60 years old, lean mass had a strong positive association with BMD. Conversely, fat mass had a moderate, negative association with BMD that was most notable in men at high levels of fat. Our results emphasize the importance of bone health in obesity and may explain site-specific increases in fracture rates in some studies of obese subjects.

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Comparative risk of acute myocardial infarction for anti-osteoporosis drugs in primary care: a meta-analysis of propensity-matched cohort findings from the UK Clinical Practice Research Database and the Catalan SIDIAP Database

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The aim of this study was to evaluate the risk of acute myocardial infarction in patients taking osteoporosis medication. Patients were taken from the SIDIAP or CPRD database and were matched using propensity scores. Patients with diabetes and chronic kidney disease taking SERMs were at an increased risk. The results favour the cardiovascular safety of alendronate as a first-line choice for osteoporosis treatment. Introduction: This study aims to evaluate the comparative safety of anti-osteoporosis drugs based on the observed risk of acute myocardial infarction while on treatment in a primary care setting. Methods: This is a propensity-matched cohort study and meta-analysis. This study

was conducted in two primary care record databases covering UK NHS (CPRD) and Catalan healthcare (SIDIAP) patients during 1995-2014 and 2006-2014, respectively. The outcome was acute myocardial infarction while on treatment. Users of alendronate (reference group) were compared to those of (1) other oral bisphosphonates (OBP), (2) strontium ranelate (SR), and (3) selective oestrogen receptor modulator (SERM), after matching on baseline characteristics (socio-demographics, fracture risk factors, comorbidities, and concomitant drug use) using propensity scores. Multiple imputation was used to handle missing data on confounders and competing risk modelling for the calculation of relative risk (sub-distribution hazard ratios (SHR)) according to therapy. Country-specific data were analysed individually and meta-analysed. Results: A 10% increased risk of acute myocardial infarction was found in users of other bisphosphonates as compared to alendronate users within CPRD. The meta-analysis of CPRD and SIDIAP results showed a 9% increased risk in users of other bisphosphonate as compared to alendronate users. Sensitivity analysis showed SERMS users with diabetes and chronic kidney disease were at an elevated risk. Conclusions: This study provides additional data on the risk of acute myocardial infarction in patients receiving osteoporosis treatment. The results favour the cardiovascular safety of alendronate as a first-line choice for osteoporosis treatment.

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Incidence and familial risk of premature ovarian insufficiency in the Finnish female population

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 Study question: What is the incidence of premature ovarian insufficiency (POI), has the incidence of POI changed over time, and what is the risk of POI among relatives of POI women? Summary answer: The incidence of POI increased among females aged 15-19 years from 2007 onwards and decreased in older age groups, and among relatives of women with POI the risk of POI is significantly increased. What is known already: So far, there has been no good quality, nationwide studies of the incidence of POI. Early menopause has been associated with the elevated risk of early menopause among relatives, but the knowledge of the familial risk of POI is scarce. Lower socioeconomic status has been associated with lower age at natural menopause. Study design, size, duration: Population-based study with 5011 women diagnosed with POI in 1988-2017. The data were collected from national registries and covers POI subjects in entire Finland. Participants/materials, setting, methods: Women with hormone replacement therapy reimbursement for POI were identified from Social Insurance Institution (SII). We calculated POI incidence in different age groups and studied the changes in the incidence rate over time in 5-year segments. Four population-based controls were selected from the Digital and Population Data Services Agency (DVV) for each POI woman. Family members of the POI cases and controls were identified from the DVV and linked to SII reimbursement data to identify POI diagnoses among them. The familial risk of POI was estimated with a logistical regression model. Main results and the role of chance: The incidence was highest in the 35-39 age group, ranging from 73.8/100 000 women-years in 1993-1997 to 39.9/100 000 women-years in 2013-2017. From 2007, the incidence among 15- to 19-year-olds rose from 7.0 to 10.0/100 000 women-years in 2015-2017. Cumulative incidence of POI for women under 40 years in 1988-2017 was 478/100 000 women. The relative risk of POI among relatives of women with POI was 4.6 (95% CI 3.3-6.5) compared to relatives of women without POI. POI women tended to have slightly lower socioeconomic status and level of education compared to controls. Limitations, reasons for caution: For some women with POI, diagnosis or reimbursement may be lacking. However, we presume that these women represent a minority due to the nature of the disease and the economic benefits of reimbursement. Some changes in the incidence of POI can reflect changes in clinical practice and changing treatments and reimbursement criteria. Wider implications of the findings: The risk of developing POI is significantly higher in women who have first-degree relatives diagnosed with POI. Raising awareness of the increased risk might lead to earlier diagnosis and initiation of hormonal replacement therapy, possibly preventing adverse effects of low oestrogen levels, such as osteoporosis.