Selección de Resúmenes de Menopausia

Semana del 11 al 17 de abril de 2018

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2018 Update of French Recommendations on the Management of Postmenopausal Osteoporosis.

Briot K, Roux C, Thomas T, Blain H, Buchon D, Chapurlat R, Debiais F, Feron JM, Gauvain JB, et al.

OBJECTIVES: To update the 2012 recommendations on pharmacotherapy for postmenopausal osteoporosis, under the aegis of the Bone Task Force of the French Society for Rheumatology (SFR) and of the Osteoporosis Research and Information Group (GRIO), in collaboration with scientific societies (Collège National des Généralistes Enseignants, Collège National des Gynécologues et Obstétriciens Français, Fédération Nationale des Collèges de Gynécologie Médicale, Groupe d'Étude de la Ménopause et du Vieillissement hormonal, Société Française de Chirurgie Orthopédique, Société Française d'Endocrinologie, and Société Française de Gériatrie et de Gérontologie) METHODS: Updated recommendations were developed by a task force whose members represented the medical specialties involved in the management of postmenopausal osteoporosis. The update was based on a literature review and developed using the method advocated by the French National Authority for Health (HAS). DISCUSSION AND CONCLUSION: The updated recommendations place strong emphasis on the treatment of women with severe fractures, in whom the use of osteoporosis medications is recommended. All the available osteoporosis medications are suitable in patients with severe fractures; zoledronic acid deserves preference as the fist-line drug after a hip fracture. In patients with or without non-severe fractures, the decision to use osteoporosis medications is based on bone mineral density values and, in challenging cases, on probabilities supplied by prediction tools such as FRAX®. All osteoporosis medications are suitable; raloxifene should be reserved for patients at low risk for peripheral fractures. The fracture risk should be reevaluated every 2 to 3 years to decide on the best follow-up treatment. These updated recommendations discuss the selection of first-line osteoporosis medications and treatment sequences.

BMJ Open. 2018 Apr 12;8(4):e018898. doi: 10.1136/bmjopen-2017-018898.

Does bone mineral density improve the predictive accuracy of fracture risk assessment? A prospective cohort study in Northern Denmark.

Dhiman P, Andersen S, Vestergaard P, Masud T, Qureshi N.

OBJECTIVE: To evaluate the added predictive accuracy of bone mineral density (BMD) to fracture risk assessment.
DESIGN: Prospective cohort study using data between 01 January 2010 and 31 December 2012. SETTING: North Denmark Osteoporosis Clinic of referred patients presenting with at least one fracture risk factor to the referring doctor. PARTICIPANTS: Patients aged 40-90 years; had BMD T-score recorded at the hip and not taking osteoporotic preventing drugs for more than 1 year prior to baseline. MAIN OUTCOME MEASURES: Incident diagnoses of osteoporotic fractures (hip, spine, forearm, humerus and pelvis) were identified using the National Patient Registry of Denmark during 01 January 2012-01 January 2014. Cox regression was used to develop a fracture model based on predictors in the Fracture Risk Assessment Tool (FRAX®), with and without, binary and continuous BMD. Change in Harrell's C-Index and Reclassification tables were used to describe the added statistical value of BMD. RESULTS: Adjusting for predictors included in FRAX®, patients with osteoporosis (T-score ≤-2.5) had 75% higher hazard of a fracture compared with patients with higher BMD (HR: 1.75 (95% CI 1.28 to 2.38)). Forty per cent lower hazard was found per unit increase in continuous BMD T-score (HR: 0.60 (95% CI 0.52 to 0.69)). Accuracy improved marginally, and Harrell's C-Index increased by 1.2% when adding continuous BMD (0.76 to 0.77). Reclassification tables showed continuous BMD shifted 529 patients into different risk categories; 292 of these were reclassified correctly (57%; 95% CI 55% to 64%). Adding binary BMD however no improvement: Harrell's C-Index decreased by 0.6%. CONCLUSIONS: Continuous BMD marginally improves fracture risk assessment. Importantly, this was only found when using continuous BMD measurement for osteoporosis. It is suggested that future focus should be on evaluation of this risk factor using routinely collected data and on the development of more clinically relevant methodology to assess the added value of a new risk factor.

Int J Gynaecol Obstet. 1997 Oct;59 Suppl 1:S29-S33. doi: 10.1016/S0020-7292(97)90196-X.

HRT and the risk of deep vein thrombosis.

Barlow DH.

Venous thromboembolism (VTE) has long been recognized as a risk of oral contraceptive use in women, but until recently hormone replacement therapy (HRT) was not thought to be associated with a similar risk; the epidemiological literature having been reassuring. The recent publication of four independent epidemiological studies has changed our perspective on VTE risk on HRT. These studies suggest that the risk of VTE may be increased by up to three-fold during HRT. However, the absolute risk remains low at approximately one occurrence in 5000 woman-years and appears greatest in the early years of HRT use. However, given that mortality from VTE is low, it seems unlikely that these new findings will substantially change the overall balance of benefits and risks associated with long-term HRT.

Int J Gynaecol Obstet. 1997 Oct;59 Suppl 1:S19-S27. doi: 10.1016/S0020-7292(97)90195-8.

Women at cardiac risk: is HRT the route to maintaining cardiovascular health?

Ottesen B, Sørensen MB.

Cardiovascular disease is the leading cause of death in women of postmenopausal age. Data from observational studies suggest that the risk of coronary heart disease in postmenopausal women can be reduced by 30-50% by estrogen replacement therapy. The protective effect of estrogen is multifactorial, affecting lipids, carbohydrate metabolism, hemostasis, body-fat distribution and blood pressure. Although the unopposed use of estrogen is associated with an increased risk of endometrial cancer, this risk can be reduced or even neutralized by the addition of progestogen. The protection against cardiovascular disease provided by combined estrogen/progestogen treatment has been the subject of much debate. However, results from epidemiological studies, intervention trials and animal experiments now suggest that the addition of progestogen does not attenuate the beneficial effects of estrogen. While secondary prevention studies are needed to evaluate the various hormone regimens, the use of combined estrogen/progestogen therapy can be supported.

Int J Gynaecol Obstet. 1997 Oct;59 Suppl 1:S11-S17. doi: 10.1016/S0020-7292(97)90194-6.

Quality of life and patient preference for sequential versus continuous combined HRT: the UK Kliofem® multicenter study experience.

Ulrich LG, Barlow DH, Sturdee DW, Wells M, et al; UK Continuous Combined HRT Study Investigators.

Hormone replacement therapy (HRT) must be taken for many years to attain the long-term benefits on osteoporosis and cardiovascular disease. However, this level of compliance with HRT is rarely achieved. This analysis documents the effect of continuous combined HRT with Kliogest® on the relief of menopausal symptoms, and the patient preference for HRT over a 9-month treatment period. A total of 2151 postmenopausal women, of whom 1435 were currently on sequential therapy and 716 had not been previously treated, were enrolled from 55 centers in the UK. Women received a daily tablet of Kliogest for 9 months. Quality of life was assessed using the Greene Climacteric Scale, and the women completed patient preference questionnaires. Treatment with continuous combined therapy was at least as effective as previous sequential regimens in alleviating menopausal symptoms. By the study conclusion, patient preference was strongly in favor of Kliogest with 91% of completers preferring it to their previous sequential therapy. Improved quality of life and patient preference for continuous combined therapy may encourage long-term compliance with treatment, allowing more women to experience the long-term beneficial effects of HRT on osteoporosis and cardiovascular disease.

Curr Oncol Rep. 2018 Apr 11;20(6):47. doi: 10.1007/s11912-018-0688-8.

The Impact of Obesity on Breast Cancer.

Argolo DF, Hudis CA, Iyengar NM.

The rates of obesity are increasing worldwide and this condition is now recognized as a leading preventable cause of cancer. Several diseases are directly related to obesity, including diabetes, hypertension, atherosclerosis, stroke, musculoskeletal disorders, and a diverse range of malignances-such as breast cancer. Obesity is associated with an increased risk of postmenopausal estrogen receptor-positive breast cancer and worse cancer-related outcomes for all breast tumor subtypes. Several mechanisms have been proposed to contribute to the obesity-cancer link, including high levels of circulating and local estrogens, altered amounts of adipokines (leptin and adiponectin), disrupted insulin/IGF signaling, modifications within the microbiome, and local and systemic effects of inflammation. Here we will review recent advances in our understanding of the complex signaling pathways underlying the obesity-cancer link. An

improved understanding of these processes is anticipated to propel novel and effective intervention strategies to reduce the global obesity-cancer burden.

Hum Reprod. 2018 Apr 9. doi: 10.1093/humrep/dey078. [Epub ahead of print]

The relation of age at menarche with age at natural menopause: a population study of 336 788 women in Norway.

Bjelland EK, Hofvind S, Byberg L, Eskild A.

STUDY QUESTION: Is age at menarche associated with age at menopause or with duration of the reproductive period (interval between menarche and menopause)? SUMMARY ANSWER: The association of age at menarche with age at menopause was weak and non-linear, and the duration of the reproductive period decreased by increasing age at menarche. WHAT IS KNOWN ALREADY: It remains uncertain whether age at menarche is associated with age at menopause. Some studies report that women with early menarche also have early menopause. Other studies report that women with early menarche have late menopause, or they report no association. The duration of the reproductive period may be an indicator of the cumulative endogenous exposure to estrogens and progestogens during life course and is associated with risk of breast cancer and endometrial cancer. STUDY DESIGN, SIZE, DURATION: A retrospective cohort study of 336 788 women, aged 48-71 years, in the BreastScreen Norway during the years 2006-2014 was performed. PARTICIPANTS/MATERIALS, SETTING, METHODS: Information about age at menarche and menopausal status was obtained by self-administered questionnaires. We used time to event approaches to estimate the associations. MAIN RESULTS AND THE ROLE OF CHANCE: Median age at menopause was 51 years in most menarche groups. Women with menarche at age 16 years or age ≥ 17 years had menopause 1 year later [median: 52 years, interquartile range (IQR): 49-54 years] than women with menarche at age 13 years (median: 51 years, IQR: 49-54 years, reference) (crude hazard ratio (HR) = 0.95; 95% CI: 0.93-0.97 and 0.95; 95% CI: 0.92-0.99, Pnon-linearity < 0.001). The reproductive period decreased with increasing age at menarche (Pnon-linearity < 0.001), and women with menarche at age ≤ 9 years had 9 years longer median reproductive period than women with menarche at age ≥ 17 years (median: 43 versus 34 years). Adjustment for year of birth did not change the HR estimates notably. LARGE SCALE DATA: Not applicable. LIMITATIONS, REASONS FOR CAUTION: Information about age at menarche and age at menopause was based on self-reports. Particularly for age at menarche, the long time interval between the event and data collection may have caused imprecise reporting. WIDER IMPLICATIONS OF THE FINDINGS: Our study suggests that age at menarche is a strong indicator for the duration of women's reproductive period. Our findings should encourage studies of the independent role of duration of the reproductive period on the risk of breast cancer and endometrial cancer, since these cancers have been associated with exposure to estrogens and progestogens.

Menopause. 2018 Apr 9. doi: 10.1097/GME.0000000000001103. [Epub ahead of print]

Older women do not have seasonal variations of vitamin D levels: a study from a southern country.

Vallejo MS, Blümel JE, Lavín P, Torres C, Araos A, Sciaraffia C.

OBJECTIVE: The aim was to study whether the seasonal variation of vitamin D [25(OH)-D or calcidiol] is similar or different in younger and older women living in a southern country. METHODS: Measurement of serum 25(OH)-D concentration in 739 Chilean women aged 20 to 87 years, residents of Santiago (latitude: 33.4° South) who, during a routine gynaecological checkup, agreed to be evaluated. RESULTS: The mean serum concentration of 25(OH)-D for the group was 24.1±10.5 ng/mL. In women 20 to 39 years, the mean was significantly different from the mean of the ≥60 years old group (25.8±10.6 ng/mL vs 23.9±11.1 ng/mL; P<0.02). Globally, 38.4% of participants had vitamin D deficiency and 36.1% insufficiency. A deficiency was present in 28.4% of the 20 to 39 years old, and in 43.9% in the ≥60 years old group (P<0.004). In the whole group, a lower proportion (P<0.0001) of vitamin D deficiency cases in the youngest women occurred during the summer (23.7%) in comparison to the winter (47.7%). It was observed that the proportion of participants in the 20 to 39 years old group with vitamin D deficiency fell from 48.9% in winter to 4.9% in summer (P=0.0001). In the older groups, this change (less deficiency) is progressively smaller, 51.2% to 27.6% (P=0.0020) in women 40 to 59 years old, and it does not happen in women ≥60 years (40% with vitamin D deficiency). CONCLUSIONS: Serum vitamin D deficiency [25(OH)-D or calcidiol] is highly prevalent in Santiago, especially in older women (≥60 y) throughout the year. In contrast, in younger women (<40 y), the vitamin D deficiency tends to disappear during summer. More epidemiological studies and targeted prevention actions on vitamin D deficiency are warranted.

Climacteric. 2018 Apr 9:1-9. doi: 10.1080/13697137.2018.1455657. [Epub ahead of print]

Evidence on the use of progesterone in menopausal hormone therapy.

Mirkin S.

A need exists for a regulatory agency-approved hormone therapy (HT) with naturally occurring hormones combining progesterone (P4) and estradiol (E2), since no single product contains both endogenous hormones. Many women choose HT with P4 and millions of women around the world are using unapproved, poorly regulated compounded HT. The use of natural P4 in HT results, for the most part, in favorable outcomes without deleterious effects, as shown in clinical studies of postmenopausal women. Importantly, P4 used in HT prevents endometrial hyperplasia from estrogens while helping relieve vasomotor symptoms and improving quality-of-life measures. Additionally, risk of venous thromboembolism and breast cancer does not appear to increase with use of P4 plus estrogens as shown with synthetic progestins plus estrogens in large observations studies, and no detrimental effects of P4 in HT have been found on outcomes related to cardiovascular disease or cognition. A regulatory agency-approved HT with naturally occurring E2/P4 could be an option for the millions of women who desire a bioidentical product and/or are exposed to potential risks of inadequately studied and under-regulated compounded HT.

J Sex Med. 2018 Apr 5. pii: S1743-6095(18)30178-4. doi: 10.1016/j.jsxm.2018.03.006. [Epub ahead of print]

Effects of Sex Hormones and Age on Brain Volume in Post-Menopausal Women.

Kim GW, Park K, Jeong GW.

BACKGROUND: Investigation of the effect of sex hormones on the brain volume in women provides a unique opportunity to examine menopause-related morphometric alterations. AIM: To evaluate brain morphological alterations in post-menopausal women using voxel-based morphometry and its correlations with sex hormone levels. METHODS: 20 Pre-menopausal women and 20 post-menopausal women underwent structural MRI. OUTCOMES: T1-weighted magnetic resonance data were acquired and serum sex hormones including total estrogen, estriol, estradiol (E2), follicle-stimulating hormone, free testosterone, SHBG, and luteinizing hormone were measured. RESULTS: Post-menopausal women showed decreased gray matter (GM) in the supplementary motor area (SMA), inferior frontal gyrus, olfactory cortex, and superior temporal gyrus as contrasted with pre-menopausal women using analysis of covariance ($P < .05$). The GM volume (GMV) values of the SMA, inferior frontal gyrus, and superior temporal gyrus were positively correlated with the levels of E2 in the pre-menopausal and post-menopausal women, in which the volume of the SMA was negatively correlated with the duration of time after menopause in post-menopausal women. CLINICAL TRANSLATION: This finding is potentially applicable to assess the brain dysfunction with morphological changes in post-menopausal women. CONCLUSIONS: Our study is the first to evaluate a direct relationship between the level of E2 and GMV change. We directly compared pre-menopausal and menopausal women un-matched in age. This study highlights the menopause-related morphological alterations in post-menopausal women, suggesting that the reduced GMV were closely associated with the symptoms of menopause caused by the decreased levels of E2.

Menopause. 2018 May;25(5):483-492. doi: 10.1097/GME.0000000000001043.

Cardiovascular and metabolic morbidity after hysterectomy with ovarian conservation: a cohort study.

Laughlin-Tommaso SK, Khan Z, Weaver AL, Smith CY, Rocca WA, Stewart EA.

The aim of the study was to determine the long-term risk of cardiovascular disease and metabolic conditions in women undergoing hysterectomy with bilateral ovarian conservation compared with age-matched referent women.

METHODS: Using the Rochester Epidemiology Project records-linkage system, we identified 2,094 women who underwent hysterectomy with ovarian conservation for benign indications between 1980 and 2002 in Olmsted County, Minnesota. Each woman was age-matched (±1 y) to a referent woman residing in the same county who had not undergone prior hysterectomy or any oophorectomy. These two cohorts were followed historically to identify de novo cardiovascular or metabolic diagnoses. We estimated hazard ratios (HRs) and 95% CIs using Cox proportional hazards models adjusted for 20 preexisting chronic conditions and other potential confounders. We also calculated absolute risk increases and reductions from Kaplan-Meier estimates. RESULTS: Over a median follow-up of 21.9 years, women who underwent hysterectomy experienced increased risks of de novo hyperlipidemia (HR 1.14; 95% CI, 1.05-1.25), hypertension (HR 1.13; 95% CI, 1.03-1.25), obesity (HR 1.18; 95% CI, 1.04-1.35), cardiac arrhythmias (HR 1.17; 95% CI, 1.05-1.32), and coronary artery disease (HR 1.33; 95% CI, 1.12-1.58). Women who underwent hysterectomy at age ≤35 years had a 4.6-fold increased risk of congestive heart failure and a 2.5-fold increased risk of coronary artery disease. CONCLUSIONS: Even with ovarian conservation, hysterectomy is associated with an increased long-term risk

of cardiovascular and metabolic conditions, especially in women who undergo hysterectomy at age ≤35 years. If these associations are causal, alternatives to hysterectomy should be considered to treat benign gynecologic conditions.