Selección de Resúmenes de Menopausia

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Calcif Tissue Int. 2016 Apr 1. [Epub ahead of print]

How Good is Our Best Guess? Clinical Application of the WHO FRAX Tool in Osteoporotic Fracture Risk Determination and Treatment Decisions.

Hinz L, Freiheit E, Kline G.

Historically, treatment decisions for osteoporosis were based on bone mineral density. However, many fractures occur in patients with T-scores outside the osteoporotic range, emphasizing the importance of multi-factorial risk assessments. The World Health Organization Fracture Risk Assessment Tool (FRAX) predicts 10-year risk of osteoporotic fracture. We hypothesized that physicians' clinical estimates of osteoporotic fracture risk would differ significantly from that calculated by FRAX. Thus, treatment decisions would differ depending whether or not physicians used FRAX. A survey consisting of five clinical scenarios was administered to 76 endocrinologists, family physicians, internists, and internal medicine residents. They were asked to estimate the osteoporotic fracture risk and decide whether they would offer preventative treatment. Their estimates were compared to the risk predicted by FRAX and national treatment threshold guidelines. The primary outcome was the difference between the participant's estimate and the FRAX-based estimate of the 10-year risk of osteoporotic fracture for each scenario. In each scenario, physicians statistically significantly over-estimated fracture risk compared to that predicted by FRAX. Estimates for hip fracture risk were 2-4 times higher than FRAX estimates. The major osteoporotic fracture risk at which participants would offer treatment varied with physician group, with endocrinologists, family physicians, and residents requiring a 10-20 % 10-year risk, while internal medicine physician thresholds ranged from 2 to 20 %. Physicians greatly over-estimated the risk of hip fracture based on clinical information. FRAX is necessary to accurately quantify risk, but because physicians varied in the level of risk required before they would offer treatment, uniform approaches to risk estimation may still not result in uniform clinical treatment decisions.

Ther Adv Urol. 2016 Apr;8(2):147-60. doi: 10.1177/1756287215617648. Epub 2015 Dec 9.

An update on the role of testosterone replacement therapy in the management of hypogonadism.

Hackett G.

While US testosterone prescriptions have tripled in the last decade with lower trends in Europe, debate continues over the risks, benefits and appropriate use of testosterone replacement therapy (TRT). Some authors blame advertising and the availability of more convenient formulations whilst other have pointed out that the routine testing of men with erectile dysfunction (a significant marker of cardiovascular risk) and those with diabetes would inevitably increase the diagnosis of hypogonadism and lead to an increase in totally appropriate prescribing. They commented that this was merely an appropriate correction of previous underdiagnosis and undertreatment by adherence to evidence-based guidelines. Urologists and primary care physicians are the most frequent initiators of TRT, usually for erectile dysfunction. Benefits are clearly established for sexual function, increase in lean muscle mass and strength, mood and cognitive function, with possible reduction in frailty and osteoporosis. There remains no evidence that TRT is associated with increased risk of prostate cancer or symptomatic benign prostatic hyperplasia, yet the decision to initiate and continue therapy is often decided by urologists. The cardiovascular issues associated with TRT have been clarified by recent studies showing clearly that therapy associated with clear rise in testosterone levels are associated with reduced mortality. Studies reporting to show increased risk have been subject to flawed designs with inadequate baseline diagnosis and follow-up testing. Effectively they have compared nontreated patients with undertreated or on-compliant subjects involving a range of different therapy regimens. Recent evidence suggests long acting injections may be associated with decreased cardiovascular risk but the transdermal route may be associated with potentially relatively greater risk because of conversion to dihydrotestosterone by the effect of 5α reductase in skin. The multiple effects of TRT may add up to a considerable benefit to the patient that might be underestimated by the physician primarily concerned with his own specialty. This paper will attempt to identify who should be treated, and how they should be treated safely to achieve best outcomes, based on a comprehensive MEDLINE and EMBASE and Cochrane searches on hypogonadism, TRT and

cardiovascular safety from May 2005 to May 2015. This revealed 1714 papers with 52 clinical trials and 32 placebo-controlled randomized, controlled trials.

Int Orthop. 2016 Mar 31. [Epub ahead of print]

Increased risk of vertebral fracture in patients with diabetes: a meta-analysis of cohort studies.

Wang J, You W, Jing Z, Wang R, Fu Z, Wang Y.

PURPOSE: The relationship between diabetes and risk of fracture has been reported differently in study design and risk estimates, and the relationship between diabetes and risk of vertebral fracture remained unclear. Therefore, we performed a meta-analysis of prospective or retrospective cohort studies to assess the potential relationship between diabetes and vertebral fracture. METHODS: We searched medical databases for prospective or retrospective cohort studies on the association between diabetes and vertebral fracture risk. Pooled relative risks (RR) and corresponding 95 % confidence intervals (95 % CI) were calculated with a random-effects model of meta-analysis. RESULTS: Meta-analysis of eight studies showed that the pooled RR of vertebral fracture for diabetic individuals was 2.03 (95 % CI 1.60-2.59; $p < 0.0001$). Subgroup analysis by gender showed that the corresponding RRs for male and female were 2.70 (95 % CI 1.34-5.43; $p = 0.005$) and 1.93 (95 % CI 1.18-3.13; $p = 0.008$), respectively. Subgroup analysis by study design showed that the corresponding RRs for prospective design and retrospective design were 1.81 (95 % CI 1.19-2.75; $p = 0.006$) and 2.23 (95 % CI 1.60-3.10; $p < 0.0001$), respectively. Subgroup analysis by time of follow-up showed that the RR of vertebral fracture for patients with >20 and <20 years of follow-up were 2.23 (95 % CI 1.98-3.62; $p < 0.0001$) and 1.67 (95 % CI 1.29-2.16; $p < 0.0001$), respectively. CONCLUSIONS: Diabetes is an independent risk factor for vertebral fracture, primarily being due to diabetic osteoporosis.

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Vascular Effects of Early versus Late Postmenopausal Treatment with Estradiol.

Hodis HN, Mack WJ, Henderson VW, Shoupe D, Budoff MJ, et al; ELITE Research Group.

BACKGROUND: Data suggest that estrogen-containing hormone therapy is associated with beneficial effects with regard to cardiovascular disease when the therapy is initiated temporally close to menopause but not when it is initiated later. However, the hypothesis that the cardiovascular effects of postmenopausal hormone therapy vary with the timing of therapy initiation (the hormone-timing hypothesis) has not been tested. METHODS: A total of 643 healthy postmenopausal women were stratified according to time since menopause (<6 years [early postmenopause] or ≥10 years [late postmenopause]) and were randomly assigned to receive either oral 17β-estradiol (1 mg per day, plus progesterone [45 mg] vaginal gel administered sequentially [i.e., once daily for 10 days of each 30-day cycle] for women with a uterus) or placebo (plus sequential placebo vaginal gel for women with a uterus). The primary outcome was the rate of change in carotid-artery intima-media thickness (CIMT), which was measured every 6 months. Secondary outcomes included an assessment of coronary atherosclerosis by cardiac computed tomography (CT), which was performed when participants completed the randomly assigned regimen. RESULTS: After a median of 5 years, the effect of estradiol, with or without progesterone, on CIMT progression differed between the early and late postmenopause strata (P=0.007 for the interaction). Among women who were less than 6 years past menopause at the time of randomization, the mean CIMT increased by 0.0078 mm per year in the placebo group versus 0.0044 mm per year in the estradiol group (P=0.008). Among women who were 10 or more years past menopause at the time of randomization, the rates of CIMT progression in the placebo and estradiol groups were similar (0.0088 and 0.0100 mm per year, respectively; P=0.29). CT measures of coronary-artery calcium, total stenosis, and plaque did not differ significantly between the placebo group and the estradiol group in either postmenopause stratum. CONCLUSIONS: Oral estradiol therapy was associated with less progression of subclinical atherosclerosis (measured as CIMT) than was placebo when therapy was initiated within 6 years after menopause but not when it was initiated 10 or more years after menopause. Estradiol had no significant effect on cardiac CT measures of atherosclerosis in either postmenopause stratum.

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Association of Leptin with Body Pain in Women.

Younger J, Kapphahn K, Brennan K, Sullivan SD, Stefanick ML.
Leptin, an appetite-regulatory hormone, is also known to act as a proinflammatory adipokine. One of the effects of increased systemic leptin concentrations may be greater sensitivity to pain. We report the results of two studies examining the association between leptin and pain: a small pilot longitudinal study, followed by a large cross-sectional study. In Study 1, three women with physician-diagnosed fibromyalgia provided blood draws daily for 25 consecutive days, as well as daily self-reported musculoskeletal pain. Daily fluctuations in serum leptin were positively associated with pain across all three participants ($F(1,63) = 12.8$, $p < 0.001$), with leptin predicting ~49% of the pain variance. In Study 2, the relationship between leptin and body pain was examined in a retrospective cross-sectional analysis of 5676 generally healthy postmenopausal women from the Women's Health Initiative. Leptin levels obtained from single blood draws were tested for a relationship with self-reported body pain. Body mass index (BMI) was also included as a predictor of pain. Both leptin and BMI were found to be independently associated with self-reported pain ($p = 0.001$ and $p < 0.001$, respectively), with higher leptin levels and greater BMI each being associated with greater pain. Leptin appears to be a predictor of body pain both within- and between-individuals and may be a driver of generalized pain states such as fibromyalgia.

Menopause. 2016 Mar 18. [Epub ahead of print]

Risk of venous thromboembolism associated with local and systemic use of hormone therapy in peri- and postmenopausal women and in relation to type and route of administration.

Bergendal A, Kieler H, Sundström A, Hirschberg AL, Kocoska-Maras L.
OBJECTIVE: The aim of the study was to assess the risk of venous thromboembolism (VTE) associated with systemic hormone therapy according to type and to route of administration and the risk of VTE associated with locally administered estrogen. METHODS: In this case-control study, conducted in Sweden between 2003 and 2009, we included 838 cases of VTE and 891 controls with a mean age of 55 years. Controls were matched by age to the cases and randomly selected from the population. We used logistic regression to calculate odds ratios (ORs) with 95% CIs and adjusted for smoking, body mass index, and immobilization. RESULTS: Current use of any hormone therapy was associated with an increased risk of VTE (OR 1.72, 95% CI 1.34-2.20). For estrogen in combination with progestogen the OR was 2.85 (95% CI 2.08-3.90), and for estrogen only the OR was 1.31 (95% CI 0.78-2.21). In orally administered estrogen combined with progestogen, the OR was slightly, but not significantly, higher among users of medroxyprogesterone acetate (OR 2.94, 95% CI 1.67-5.36) than among norethisterone acetate users (OR 2.55, 95% CI 1.50-3.40). Transdermal estrogen combined with progestogen was not associated with VTE risk (crude and imprecise ORs ranging from 0.87 to 1.16). For local effect of estrogen, there was no association with VTE risk (OR 0.69, 95% CI 0.43-1.10). CONCLUSIONS: The risk of VTE risk is higher in users of systemic combined estrogen-progestogen treatment than in users of estrogen only. Furthermore, the risk of VTE was lower for women who used local estrogen than among those using oral estrogen only. Transdermal estrogen only treatment and estrogen for local effect seem not to be related to an increased risk of VTE.

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Thyroid function and autoimmunity are associated with the risk of vertebral fractures in postmenopausal women.

Lambrinoudaki I, Armeni E, Pliatsika P, Rizos D, Kaparos G, Augoulea A, Alexandrou A, Flokatoula M, et al.
Overt or subclinical thyroid dysfunction may affect the risk of fragility fractures. The aim of the present study was to assess the association of thyroid function and autoimmunity with vertebral fractures (VF) in a large sample of Greek postmenopausal women. This cross-sectional study recruited 335 euthyroid postmenopausal women, aged 35-79 years. Euthyroidism was verified by serum thyroid-stimulating hormone (TSH) within the laboratory reference range (0.4-4.5 μIU/mL). VFs were diagnosed by lumbar spine lateral radiographs, according to quantitative procedures. Serum free triiodothyronine (FT3), free thyroxine (FT4), TSH, as well as levels of anti-thyroglobulin (anti-TG) and thyroid peroxidase antibodies (anti-TPO) were compared according to the presence of VFs. Multivariate logistic regression showed that the presence of VFs was predicted independently by ln-TSH levels (OR = 0.290, p = 0.037) and positive anti-TG antibodies (OR = 3.308, p = 0.026) in models adjusted for age, menopausal age, and ln-HOMA-IR. Stepwise logistic regression analysis showed that the presence of VFs was predicted by menopausal age (OR = 1.120, p = 0.001), ln-TSH (OR = 0.312, p = 0.052), and thyroid autoimmunity (anti-TG and anti-TPO positive: OR =

6.637, p = 0.007) in a model that also included age and ln-HOMA-IR. Women with lower circulating TSH had higher risk of having a VF, independently of age, menopausal age, and insulin resistance. The presence of positive anti-TG/anti-TPO antibodies also indicated an elevated risk of fracture. Levels of thyroid hormones had no apparent effect on the risk of fracture. Further studies are necessary to establish the significance of our findings.

World J Diabetes. 2016 Mar 25;7(6):122-33. doi: 10.4239/wjd.v7.i6.122.

Metformin revisited: Does this regulator of AMP-activated protein kinase secondarily affect bone metabolism and prevent diabetic osteopathy.

McCarthy AD, Cortizo AM, Sedlinsky C.

Patients with long-term type 1 and type 2 diabetes mellitus (DM) can develop skeletal complications or "diabetic osteopathy". These include osteopenia, osteoporosis and an increased incidence of low-stress fractures. In this context, it is important to evaluate whether current anti-diabetic treatments can secondarily affect bone metabolism. Adenosine monophosphate-activated protein kinase (AMPK) modulates multiple metabolic pathways and acts as a sensor of the cellular energy status; recent evidence suggests a critical role for AMPK in bone homeostasis. In addition, AMPK activation is believed to mediate most clinical effects of the insulin-sensitizer metformin. Over the past decade, several research groups have investigated the effects of metformin on bone, providing a considerable body of pre-clinical (in vitro, ex vivo and in vivo) as well as clinical evidence for an anabolic action of metformin on bone. However, two caveats should be kept in mind when considering metformin treatment for a patient with type 2 DM at risk for diabetic osteopathy. In the first place, metformin should probably not be considered an anti-osteoporotic drug; it is an insulin sensitizer with proven macrovascular benefits that can secondarily improve bone metabolism in the context of DM. Secondly, we are still awaiting the results of randomized placebo-controlled studies in humans that evaluate the effects of metformin on bone metabolism as a primary endpoint.