



## Selección de Resúmenes de Menopausia

Semana del 26 de Octubre al 2 de Noviembre, 2016  
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**Menopause. 2016 Oct 31. [Epub ahead of print]**

### **Age of menopause and fracture risk in postmenopausal women randomized to calcium + vitamin D, hormone therapy, or the combination: results from the Women's Health Initiative Clinical Trials.**

Sullivan SD, Lehman A, Nathan NK, Thomson CA, Howard BV.

**OBJECTIVE:** We previously reported that in the absence of hormone therapy (HT) or calcium/vitamin D (Ca/D) supplementation, earlier menopause age was associated with decreased bone mineral density and increased fracture risk in healthy postmenopausal women. Treatment with HT and Ca/D is protective against fractures after menopause. In this analysis, we asked if the age of menopause onset alters fracture risk in healthy postmenopausal women receiving HT, Ca/D, or a combination. **METHODS:** Hazard ratios (HRs) for any fracture among 21,711 healthy postmenopausal women enrolled in the Women's Health Initiative Clinical Trial, who were treated with HT, Ca/D, or HT + Ca/D, and who reported age of nonsurgical menopause of <40, 40 to 49, and  $\geq 50$  years, were compared. **RESULTS:** Women with menopause <40 years had significantly higher HR for fracture than women with menopause 40 to 49 or  $\geq 50$  years, regardless of treatment intervention (HR [95% CI]: menopause <40 y vs  $\geq 50$  y, 1.36 [1.11-1.67]; menopause <40 y vs 40-49 y, 1.30 [1.06-1.60]). **CONCLUSIONS:** In the overall Women's Health Initiative Clinical Trial cohort and within each treatment group, women with younger menopause age (<40 y) had a higher risk of any fracture than women reporting older menopause ages. The effect of menopause age on fracture risk was not altered by any of the treatment interventions (HT, Ca/D, HT + Ca/D), suggesting that early age of menopause is an independent contributor to postmenopausal fracture risk.

**Menopause. 2016 Oct 31. [Epub ahead of print]**

### **Change in sexual functioning over the menopausal transition: results from the Study of Women's Health Across the Nation.**

Avis NE, Colvin A, Karlamangla AS, Crawford S, Hess R, Waetjen LE, Brooks M, Tepper PG, Greendale GA.

**OBJECTIVE:** The aim of the study was to identify whether there is a decline in sexual functioning related to the menopausal transition or to hysterectomy. **METHODS:** In a cohort of 1,390 women aged 42 to 52, with intact uterus and at least one ovary, not using hormone therapy, and pre- or early perimenopausal at baseline, we fit piecewise linear growth curves to 5,798 repeated measurements (seven visits spanning 14.5 y) of a sexual functioning score (range, 5-25) as a function of time relative to date of final menstrual period (FMP) or hysterectomy. **RESULTS:** Mean sexual functioning at baseline in women with a dateable FMP was 18.0 (SD, 3.4). There was no change in sexual function until 20 months before the FMP. From 20 months before until 1 year after the FMP, sexual function decreased by 0.35 annually (95% CI, -0.44 to -0.26) and continued to decline more than 1 year after the FMP, but at a slower rate (-0.13 annually, 95% CI, -0.17 to -0.10). The decline was smaller in African Americans and larger in Japanese than whites. Vaginal dryness, lubricant use, depressive symptoms, or anxiety did not explain decline in sexual function. Women who had a hysterectomy before the FMP did not show a decline in sexual function before hysterectomy, but scores declined afterward (0.21 annually, 95% CI, -0.28 to -0.14). **CONCLUSIONS:** Decline in sexual function became apparent 20 months before FMP and slowed 1 year after FMP through 5 years afterward. A decline in sexual function was observed immediately after hysterectomy and persisted for the 5 years of observation.

**Cochrane Database Syst Rev. 2016 Oct 12;10:CD008536.**

### **Short-term and long-term effects of tibolone in postmenopausal women.**

Formoso G, Perrone E, Maltoni S, Balduzzi S, Wilkinson J, Basevi V, Marata AM, Magrini N, D'Amico R, et al.

**BACKGROUND:** Tibolone is a synthetic steroid used for the treatment of menopausal symptoms, on the basis of short-term data suggesting its efficacy. We considered the balance between the benefits and risks of tibolone. **OBJECTIVES:** To evaluate the effectiveness and safety of tibolone for treatment of postmenopausal and perimenopausal women. **SEARCH METHODS:** In October 2015, we searched the Gynaecology and Fertility Group

(CGF) Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase and PsycINFO (from inception), the Cumulative Index to Nursing and Allied Health Literature (CINAHL) and clinicaltrials.gov. We checked the reference lists in articles retrieved. **SELECTION CRITERIA:** We included randomised controlled trials (RCTs) comparing tibolone versus placebo, oestrogens and/or combined hormone therapy (HT) in postmenopausal and perimenopausal women. **DATA COLLECTION AND ANALYSIS:** We used standard methodological procedures of The Cochrane Collaboration. Primary outcomes were vasomotor symptoms, unscheduled vaginal bleeding and long-term adverse events. We evaluated safety outcomes and bleeding in studies including women either with or without menopausal symptoms. **AUTHORS' CONCLUSIONS:** Moderate-quality evidence suggests that tibolone is more effective than placebo but less effective than HT in reducing menopausal vasomotor symptoms, and that tibolone is associated with a higher rate of unscheduled bleeding than placebo but with a lower rate than HT. Compared with placebo, tibolone increases recurrent breast cancer rates in women with a history of breast cancer, and may increase stroke rates in women over 60 years of age. No evidence indicates that tibolone increases the risk of other long-term adverse events, or that it differs from HT with respect to long-term safety. Much of the evidence was of low or very low quality. Limitations included high risk of bias and imprecision. Most studies were financed by drug manufacturers or failed to disclose their funding source.

**Fertil Steril. 2016 Oct 25. 10.1016/j.fertnstert.2016.09.018. [Epub ahead of print]**

### **Hormone replacement therapy in young women with surgical primary ovarian insufficiency.**

Sarrel PM, Sullivan SD, Nelson LM.

Bilateral oophorectomy performed in women before they are menopausal induces surgical primary ovarian insufficiency, an acute and chronic deficiency of the hormones normally produced by the ovaries. Without hormone replacement therapy (HRT) most of these women develop severe symptoms of estrogen (E) deficiency and are at increased risk for osteoporosis, cardiovascular disease, cognitive decline, dementia, and the associated increases in morbidity and mortality. In cases in which a hysterectomy has been performed at the time of bilateral oophorectomy transdermal or transvaginal E2 replacement therapy without cyclic progestin replacement is the optimum hormonal management for these women. There is substantial evidence this approach even reduces the risk for breast cancer. Unfortunately, unwarranted fear of all menopausal HRTs has become widespread following the reports of the Women's Health Initiative studies. This fear has led to a steep decline in use of E therapy, even in women in whom HRT is clearly indicated. Discussion of possible ovarian conservation in women who are premenopausal is an integral part of the preoperative planning for any women undergoing hysterectomy. Timely and effective HRT for women who will experience surgical primary ovarian insufficiency is clearly indicated.

**PM R. 2016 Oct 8. pii: S1934-1482(16)30988-1. doi: 10.1016/j.pmrj.2016.10.001. [Epub ahead of print]**

### **Predicting Functional Capacity From Measures of Muscle Mass in Postmenopausal Women.**

Orsatti FL, Nunes PR, de Paula Souza A, Martins FM, Alves de Oliveira A, Nomelini RS, Michelin MA et al.

**BACKGROUND:** Menopause increases body fat and decreases muscle mass and strength, which contribute to sarcopenia. The amount of appendicular muscle mass has been frequently used to diagnose sarcopenia. Different measures of appendicular muscle mass have been proposed. However, no studies have compared the most salient measure (appendicular muscle mass corrected by body fat) of the appendicular muscle mass to physical function in postmenopausal women. **OBJECTIVE:** To examine the association of 3 different measurements of appendicular muscle mass (absolute, corrected by stature, and corrected by body fat) with physical function in postmenopausal women. **DESIGN:** Cross-sectional descriptive study. **SETTING:** Outpatient geriatric and gynecological clinic. **PARTICIPANTS:** Forty-eight postmenopausal women with a mean age (standard deviation [SD]) of  $62.1 \pm 8.2$  years, with mean (SD) length of menopause of  $15.7 \pm 9.8$  years and mean (SD) body fat of  $43.6\% \pm 9.8\%$ . **INTERVENTIONS:** Not applicable. **MAIN OUTCOME MEASURES:** Appendicular muscle mass measure was measured with dual-energy x-ray absorptiometry. Physical function was measured by a functional capacity questionnaire, a short physical performance battery, and a 6 minute-walk test. Muscle quality (leg extensor strength to lower-body mineral-free lean mass ratio) and sum of z scores (sum of each physical function tests z score) were performed to provide a global index of physical function. **RESULTS:** The regression analysis showed that appendicular muscle mass corrected by body fat was the strongest predictor of physical function. Each increase in

the standard deviation of appendicular muscle mass corrected by body fat was associated with a mean sum of z score increase of 59% (standard deviation), whereas each increase in absolute appendicular muscle mass and appendicular muscle mass corrected by stature were associated with a mean sum of z scores decrease of 23% and 36%, respectively. Muscle quality was associated with appendicular muscle mass corrected by body fat. **CONCLUSION:** These findings indicate that appendicular muscle mass corrected by body fat is a better predictor of physical function than the other measures of appendicular muscle mass in postmenopausal women.

**Int J Womens Health. 2016 Oct 13;8:599-607. eCollection 2016.**

### **Has testosterone passed the test in premenopausal women with low libido? A systematic review.**

Reed BG, Bou Nemer <sup>1</sup>, Carr BR.

**BACKGROUND:** There are limited evaluation and treatment options for low libido in premenopausal women. This review sought to evaluate the available evidence supporting the evaluation of testosterone serum levels and testosterone treatment of premenopausal women with low libido. **METHODS:** MEDLINE, PubMed, and ClinicalTrials.gov were searched for articles that referenced the evaluation of testosterone serum level and/or testosterone treatment on premenopausal women with low libido from 1995 to 2015. Additional references were obtained from the reference sections of other papers and from peer review. Studies that included only postmenopausal women were excluded. A total of 13 studies were reviewed in detail. Nine studies examined the relationship between testosterone serum levels and sexuality, an additional three studies examined the effect of testosterone treatment on premenopausal women with low libido, and one study examined both the topics. **RESULTS:** Six of the ten testosterone serum evaluation studies failed to show a significant association between testosterone serum level and libido. Only one out of four studies examining testosterone treatment in premenopausal women was able to show any clear improvement in libido; however, the effect was limited to only the intermediate dose of testosterone, with the low and high doses of testosterone not producing any effect. **CONCLUSION:** The currently available evidence does not support testosterone serum evaluation or treatment in premenopausal women with low libido. Hence, further studies are warranted.

**Sex Med Rev. 2015 Oct;3(4):298-315. doi: 10.1002/smrj.63. Epub 2015 Nov 10.**

### **Osteoporosis and Low Bone Mineral Density in Men with Testosterone Deficiency Syndrome.**

Gaffney CD, Pagano MJ, Kuker AP, Stember DS, Stahl PJ.

**INTRODUCTION:** Testosterone deficiency syndrome (TDS) is a risk factor for low bone mineral density (BMD) and osteoporosis. Knowledge of the relationship between TDS and bone health, as well as the practical aspects of how to diagnose and treat low BMD, is therefore of practical importance to sexual medicine practitioners. **AIM:** The aim of this study was to review the physiologic basis and clinical evidence of the relationship between TDS and bone health; and to provide a practical, evidence-based algorithm for the diagnosis and management of low BMD in men with TDS.

**METHODS:** Method used was a review of relevant publications in PubMed. **MAIN OUTCOME MEASURES:** Pathophysiology of low BMD in TDS, morbidity, and mortality of osteoporosis in men, association between TDS and osteoporosis, indications for dual X-ray absorptiometry (DXA) scanning in TDS, evidence for testosterone replacement therapy (TRT) in men with osteoporosis, treatment for osteoporosis in the setting of TDS. **RESULTS:** Sex hormones play a pleomorphic role in maintenance of BMD. TDS is associated with increased risk of osteoporosis and osteopenia, both of which contribute to morbidity and mortality in men. DXA scanning is indicated in men older than 50 years with TDS, and in younger men with longstanding TDS. Men with TDS and osteoporosis should be treated with anti-osteoporotic agents and TRT should be highly considered. Men with osteopenia should be stratified by fracture risk. Those at high risk should be treated with anti-osteoporotic agents with strong consideration of TRT; while those at low risk should be strongly considered for TRT, which has a beneficial effect on BMD. **CONCLUSION:**

Low BMD is a prevalent and treatable cause of morbidity and mortality in men with TDS. Utilization of a practical, evidence-based approach to diagnosis and treatment of low BMD in men with TDS enables sexual medicine practitioners to make a meaningful impact on patient quality of life and longevity. Gaffney CD, Pagano MJ, Kuker

AP, Stember DS, and Stahl PJ. Osteoporosis and low bone mineral density in men with testosterone deficiency syndrome.

**Menopause. 2016 Oct 24. [Epub ahead of print]**

### **Longitudinal changes in menopausal symptoms comparing women randomized to low-dose oral conjugated estrogens or transdermal estradiol plus micronized progesterone versus placebo: the Kronos Early Estrogen Prevention Study.**

Santoro N, Allshouse A, Neal-Perry G, Pal L, Lobo RA, Naftolin F, Black DM, Brinton EA, Budoff MJ, et al.

**OBJECTIVE:** The objective of the present study was to compare the efficacy of two forms of menopausal hormone therapy in alleviating vasomotor symptoms, insomnia, and irritability in early postmenopausal women during 4 years.

**METHODS:** A total of 727 women, aged 42 to 58, within 3 years of their final menstrual period, were randomized to receive oral conjugated estrogens (o-CEE) 0.45mg (n=230) or transdermal estradiol (t-E2) 50µg (n=225; both with micronized progesterone 200mg for 12 d each mo), or placebos (PBOs; n=275). Menopausal symptoms were recorded at screening and at 6, 12, 24, 36, and 48 months postrandomization. Differences in proportions of women with symptoms at baseline and at each follow-up time point were compared by treatment arm using exact  $\chi$  tests in an intent-to-treat analysis. Differences in treatment effect by race/ethnicity and body mass index were tested using generalized linear mixed effects modeling. **RESULTS:** Moderate to severe hot flashes (from 44% at baseline to 28.3% for PBO, 7.4% for t-E2, and 4.2% for o-CEE) and night sweats (from 35% at baseline to 19% for PBO, 5.3% for t-E2, and 4.7% for o-CEE) were reduced significantly by 6 months in women randomized to either active hormone compared with PBO ( $P<0.001$  for both symptoms), with no significant differences between the active treatment arms. Insomnia and irritability decreased from baseline to 6 months postrandomization in all groups. There was an intermittent reduction in insomnia in both active treatment arms versus PBO, with o-CEE being more effective than PBO at 36 and 48 months ( $P=0.002$  and  $0.05$ ) and t-E2 being more effective than PBO at 48 months ( $P=0.004$ ). Neither hormone treatment significantly affected irritability compared with PBO. Symptom relief for active treatment versus PBO was not significantly modified by body mass index or race/ethnicity. **CONCLUSIONS:** Recently postmenopausal women had similar and substantial reductions in hot flashes and night sweats with lower-than-conventional doses of oral or transdermal estrogen. These reductions were sustained during 4 years. Insomnia was intermittently reduced compared with PBO for both hormone regimens.

**Curr Opin Endocrinol Diabetes Obes. 2016 Dec;23(6):440-444.**

### **An update on vitamin D for clinicians.**

Hansen KE, Johnson MG.

**PURPOSE OF REVIEW:** The clinical benefits of vitamin D therapy have received substantial attention over the past decade. Recently, several trials looked to clarify the optimal vitamin D dose or serum level needed to promote human health. The purpose of this review is to highlight selected studies published since January 2015. **RECENT FINDINGS:**

Several recent trials challenge whether serum vitamin D levels at least 30ng/ml promote human health. In postmenopausal women with 25-hydroxyvitamin D [25(OH)D] levels  $21\pm 3$ ng/ml, high-dose vitamin D for 1 year increased calcium absorption by 1%, without changes in bone mineral density, physical function, or falls when compared with low-dose vitamin D and placebo. High-dose vitamin D increased risk of falling in 200 adults  $78\pm 5$  years old with baseline 25(OH)D levels of  $\sim 19\pm 9$ ng/ml. High-dose vitamin D in adults increased the number and duration of upper respiratory tract infections compared with placebo. Asthma patients achieving 25(OH)D levels more than 30ng/ml during a trial experienced more respiratory infections than those not achieving such levels. **SUMMARY:** Recent studies are congruent with the Institute of Medicine's conclusion that humans are vitamin D replete when their serum 25(OH)D levels are at least 20ng/ml. Higher levels seem to promote falls and respiratory infections.