Sex hormones & body weight


Summary. This study examined the associations between sex hormone-binding globulin (SHBG), testosterone, follicle-stimulating hormone (FSH), and estradiol versus waist circumference in midlife women. In 1,528 women (mean age, 46) from the Study of Women’s Health Across the Nation (SWAN) over 9 years of follow-up, current waist circumference predicted future SHBG, testosterone, and FSH but not vice versa. With each additional standard deviation (SD) of current waist circumference, SHBG was lower by 0.04 to 0.15 SD; testosterone was higher by 0.08 to 0.13 SD; and log² FSH was lower by 0.15 to 0.26 SD at the following visit.

There was a negative association between estradiol and waist circumference in early menopausal transition stages and a positive association in later stages. SWAN data suggest that weight gain leads to sex steroid changes rather than sex steroids leading to weight gain.

Comment. Weight gain is a common concern for midlife women, who often associate increasing weight and abdominal girth with the hormonal changes of menopause. Indeed, when one types “weight gain and menopause” into any web browser, most popular web pages will describe weight gain as a menopausal symptom. The development of obesity is certainly associated with behavior and aging, however the relationship between weight gain in midlife and ovarian aging is not fully understood. Both surgical menopause and early use of hormone therapy (HT) have been associated with development of obesity in observational studies, while HT does not appear to prevent or cause weight gain in randomized trials.

This new longitudinal analysis from SWAN adds information to this epidemiological problem. Of importance, and consistent with the previous literature, the authors found that weight changes preceded testosterone, FSH, and SHBG changes; such a temporal sequence implies that endogenous levels of reproductive hormones in natural menopause do not cause weight gain. The relationship between estradiol and waist circumference (central adiposity) was more complex, suggesting that declining estradiol levels may have a small effect on weight distribution as women age.
Longitudinal studies like this are beginning to dissect the complex relationship between chronological aging and ovarian aging. Overall, this study contributes to an accumulating body of evidence that weight gain is not significantly influenced by physiological changes in reproductive hormone levels across the menopause transition. Midlife women seeking explanations for their weight gain should be counseled that weight gain is not a menopausal symptom, but rather that weight gain is more likely to affect their hormone levels as they transition through menopause.

L. Elaine Waetjen, MD
Associate Professor
Department of Obstetrics and Gynecology
Division of Gynecology/Urogynecology
University of California, Davis
Sacramento, CA

References:

**Effect of personality type on HT use**


**Summary.** What is the association of personality with hormone therapy (HT) use before and after the Women’s Health Initiative (WHI)? Researchers mailed questionnaires to measure type A personality and hostility in 1,803 women who reached natural menopause during the French GAZEL Cohort Study. Additional questionnaires were mailed every 3 years to determine date of menopause and use of HT. Association was measured by the relative index of inequality determined through binary logistic regression and main outcome measure was HT use within 1 year after menopause.

HT use (916 users vs 887 nonusers) was associated with type A personality, even after adjustment for vascular and breast cancer risk factors. There was no significant interaction between type A personality and date of menopause in relation to the WHI publication.

**Comment.** This prospective study correlates type A personality with greater likelihood to initiate and continue HT. Personality, defined as a person’s characteristic pattern of behavior, thoughts, and feelings, is seldom formally evaluated when determining choice of medical therapies. However, such understanding can help achieve a satisfactory therapeutic alliance, impacting medical adherence. Lemogne et al determined type A personality using the Bortner scale of several typical traits: a sense of time urgency, high job involvement, hard driving, need for achievement, ambition, and competitiveness. Data from this study also revealed that cognitive hostility (hostile thoughts rather than hostile behavior), but not type A behavior, increased all-cause and cardiovascular mortality. Since 2002, our understanding of cardiovascular disease (CVD) in postmenopausal women has been refined, with additional reassuring information from this study: type A personality does not increase CVD risk.

An additional finding of the study reveals impact of the WHI upon HT decision-making irrespective of personality. GAZEL started in 1993, 9 years prior to the initial publication of the WHI. Among this cohort, women who entered menopause prior to the initial *JAMA* publication of WHI results were significantly more likely to begin HT within the first year of menopause than those after publication.

In everyday practice we discuss the risks and benefits of all health management decisions with our patients. In addition to HT, we address the numerous health-promoting and risk-
reducing lifestyle factors over which women have direct daily control. Clinicians try to inspire optimal nutrition, weight, and exercise patterns to enhance quality of life and lower long-term disease risks. Time pressures render such in-depth discussions increasingly difficult. Paying attention to personality type may assist us in providing information in a manner that is more likely to resonate with the patient’s belief system and improve the efficiency of the process.

Ricki Pollycove MD, MS, NCMP, FACOG
Private Practice
San Francisco, CA

Hormonal influence on cognitive decline


Summary. Researchers examined differences in cognitive function and their association with reproductive and chronological age. This was a cross-sectional study at a university hospital combining neuropsychological measures with functional magnetic resonance imaging (fMRI) to assess cognitive function. A total of 67 menopausal women (ages 42-61) were recruited from a population-based menopause study and grouped into premenopause, perimenopause, and postmenopause sections.

Main outcome measures were neuropsychological and fMRI imaging of verbal, visual, and executive cognitive function. Researchers found age-independent menopause effects on verbal function: groups differed in phonemic verbal fluency and regional brain activation. Verbal measures correlated with estradiol and FSH. Results suggested that verbal fluency mechanisms are vulnerable during the menopause transition.

Comment. Despite a cross-sectional design and small sample size, this new study is important because it is the first to examine the relationship between menopausal stage and fMRI measures of brain function during tasks that may have clinical significance to women as they transition through menopause. Neuroimaging studies help to identify the neural changes that might contribute to women’s subjective cognitive complaints and that might account for changes in objective cognitive performance.

Fortunately, the new study also included behavioral measures of cognitive performance from a carefully selected battery of neuropsychological tests. The inclusion of those cognitive outcomes helps to gauge the clinical significance of the neuroimaging findings. For example, if participants in the new study show cognitive results that are similar to those observed in larger longitudinal studies, then their brain function is likely to be representative of that of the broader population. Alternatively, if their cognitive results are dissimilar to those observed in larger studies, then the clinical significance and external validity of the neuroimaging findings is unclear.

The largest and best designed study of the effects of menopausal stage on cognitive function came from SWAN.¹,² That study involved 2,362 participants who were followed for 4 years and provided evidence that psychomotor speed and, to a lesser extent, verbal memory decrease in late perimenopause but resolve during the postmenopausal period.³ Like SWAN, Berent-Spillson also reported group differences in psychomotor speed but, in contrast to SWAN, the worst performance was observed among postmenopausal women rather than perimenopausal women. Berent-Spillson et al also found group differences in verbal fluency, with the worst performance among the postmenopausal women.

The Kinmen study of 495 Taiwanese women followed for 18 months found decreases in verbal fluency in perimenopausal women compared to premenopausal women (no postmenopausal women were included).³
Together, the two large longitudinal studies—SWAN and Kinmen—suggest that reproductive aging has small but measurable effects on cognition that are most evident in perimenopause, whereas this current smaller, cross-sectional study suggests that effects are most pronounced postmenopause.

Broadly, the clinical significance of the neuroimaging findings are unclear given differences in behavioral performance between the new smaller, cross-sectional study and the larger longitudinal studies. On the other hand, the final word on how reproductive aging influences verbal memory is not yet out, because the neuropsychological test used to measure verbal memory in SWAN is quite easy compared to the neuropsychological test used by Berent-Spillson. The verbal task used in the neuroimaging test focused on the encoding and consolidation of words into memory. The neuroimaging findings therefore provide a first glimpse into why women might have subjective memory complaints and show objective memory deficits as they transition through menopause. To that end, the most interesting finding from this new study suggests that reproductive aging may affect the function of the frontal cortex when women are trying to encode and remember complex verbal information.

Pauline M. Maki, PhD
Professor of Psychiatry and Psychology
Director, Women’s Mental Health Research
University of Illinois at Chicago
Chicago, IL

References:

**Embolizing uterine leiomyoma is effective long-term treatment**


**Summary.** Embolization of uterine fibroids is now an accepted alternative to hysterectomy, but how effective is it in the long term? Italian investigators prospectively followed 176 consecutive women (median age, 43.5; median follow-up, 48 months [range, 12–84 months]) undergoing embolization of leiomyomas; the analysis was designed to identify correlations between clinical failure (defined as persistence or recurrence of symptoms) and various baseline patient characteristics.

Treatment failures occurred in 18 women at a median of 36 months, and cumulative failure rate after 7 years was 18%. During the same period, a second intervention was required in a cumulative total of 15% of patients. After controlling for confounding factors, only age ≤40 at embolization (HR, 5.9) and history of previous myomectomy (HR, 3.8) were significant predictors of embolization failure.

**Comment.** These findings add to the body of evidence supporting embolization of leiomyoma as an alternative to hysterectomy in carefully selected symptomatic women. As the data accumulate and even longer-term results become available, we will be better able to counsel our patients with leiomyomas as to the therapeutic approach with the greatest likelihood of success.

Robert W. Rebar, MD
Executive Director
American Society for Reproductive Medicine
Volunteer Clinical Professor
Department of Obstetrics and Gynecology
University of Alabama, Birmingham
Birmingham, AL

Menopause Editor’s picks from August 2012

In this 8-week randomized controlled trial in healthy postmenopausal women with hot flashes, treatment with escitalopram, compared with placebo, reduced insomnia symptoms and improved subjective sleep quality.

In this study, treatment with formononetin in adult ovariectomized rats reverses established osteopenia, raising the possibility of its use in the treatment of postmenopausal osteoporosis.

This study examines for the first time latent classes or clusters of symptoms during a prolonged period from late reproductive stage through early post-menopause. The data contribute to our understanding of symptom experiences beyond early efforts to characterize the late menopausal transition stage.

In this study, similar changes in body composition and metabolic profile were observed in postmenopausal women on an intermittent diet and postmenopausal women on a continuous diet. Most metabolic improvements occurred during the first 5 weeks of treatment on both diets.

The level of evidence indicated for each study is based on a grading system that evaluates the scientific rigor of the study design, as developed by the US Preventive Services Task Force. A synopsis of the levels is presented below.

Level I Properly randomized, controlled trial.
Level II-1 Well-designed controlled trial but without randomization.
Level II-2 Well-designed cohort or case-control analytic study.
Level II-3 Multiple time series with or without the intervention (eg, cross-sectional and uncontrolled investigational studies).
Level III Meta-analyses; reports from expert committees; descriptive studies and case reports.
NAMS 23rd Annual Meeting
Midlife & Beyond: The Power of Prevention
Orlando, FL
October 3-6, 2012

Register now (at http://www.menopause.org/meetings/regagm.aspx) for a unique opportunity to tap into world-class expertise geared to today’s tipping point in healthcare policy and practice. Here is a sampling:

• Pre-meeting Symposium on “Midlife Screening: What, When, How?”
• The highly anticipated findings from the KEEPS and MsFLASH trials
• Keynote lectures on risk assessment and implications of policy change for women’s health
• Preventive strategies for breast, heart, bone, and mental health
• Tips on how to make lifestyle modifications really work
• Case discussions on women with complex medical conditions
• A clarification of the paradox of estrogen effects on the breast
• Bone advice for vitamin D and calcium, drug holidays, and sequential therapy
• An “it takes two to tango” symposium on reviving a languishing libido

And much more—100+ scientific posters specific to midlife women’s health, 50 “Meet the Experts” CME breakfast sessions, a Research Video Challenge, all-day networking, the chance to earn up to 26.5 AMA PRA Category 1 Credits™, and the perfect time to take the NCMP exam.