What is the relationship of sexual function to hormone levels in women aged 42-52 years?

Some sexual function domains in the study were linked to testosterone and FSH levels


Summary. Using the Study of Women’s Health Across the Nation (SWAN) population of 3,302 women aged 42 to 52 years (with an intact uterus and at least one ovary and not using exogenous hormones) who self-identified as white, black, Hispanic, Chinese, or Japanese, researchers assessed sexual function with a self-administered questionnaire at baseline and 10 follow-up visits. At these times, blood was drawn to assay serum levels of testosterone, estradiol, follicle-stimulating hormone (FSH), sex hormone-binding globulin, and dehydroepiandrosterone sulfate. The main outcome measures were frequency of masturbation, sexual desire, sexual arousal, orgasm, and pain during intercourse by self-report.

It was found that masturbation, sexual desire, and arousal had a positive association with testosterone, while masturbation, arousal, and orgasm had a negative association with FSH levels. Estradiol was not related to any measured sexual function domain, and pain during intercourse was not associated with any hormone.

Comment. The role of testosterone in female sexual function remains uncertain and has been the topic of much high-quality investigation. When considering research in this area, it is important to distinguish between studies investigating the impact of testosterone in normal female sexual physiology and those examining the potential effectiveness of testosterone in the treatment of women with sexual dysfunction. The current study uses the SWAN database to address whether reproductive hormones are related to sexual function during the menopause transition. SWAN provides a great opportunity to examine this important question, as following a large group of women longitudinally over 10 years provides many observations and high statistical power to identify even small relationships between hormones and behavior. In addition, the study population is a community-based, multi-ethnic cohort, so findings should be generalizable to US women.

Prior research has identified a potential role for endogenous androgens in normal female sexuality. In women of reproductive age, an
increase in midcycle sexual activity, correlating with the midcycle peak in testosterone, is seen in some but not all studies. An association is more likely to be seen in partner-independent activities, such as masturbation, likely because partnered activity is affected by a multitude of factors besides hormones and inherent level of desire, such as relationship quality, partner interest, and habit.

In contrast, a significant association between normal and impaired sexual function and serum androgen levels has not been seen in the majority of population-based studies using validated sexual function questionnaires and high-quality androgen assays. In the Melbourne Women’s Midlife Health Project, relationship factors (rather than changes in hormone levels) were the principal predictors of sexual function across the menopausal transition. In a community-based, cross-sectional study of over 1,000 women aged 18 to 75 years, there was no clinically significant relationship between androgens and level of sexual function. In an earlier study of correlates of circulating androgens in midlife women from SWAN, testosterone levels were associated minimally with increased sexual desire.

In the current SWAN study, masturbation, arousal, and sexual desire were positively associated with testosterone. As the authors clearly state, the relationships between sexual function and androgens are subtle and may be of limited clinical significance. The adjusted odds ratios for a change in sexual function associated with a single standard deviation increase in testosterone levels was 1.052 for desire and 1.073 for masturbation. These very small increases in odds ratios likely are only statistically significant due to the large number of data points available. Although prior research has shown a relationship between estradiol and dyspareunia in midlife women, likely due to the effect of estrogen deficiency on vulvovaginal atrophy, estradiol was not related to any sexual function domain measured in this study, including pain with intercourse.

Limitations of this study are that sexual function was assessed by a questionnaire designed by the SWAN investigators, not validated in other studies, and that hormone levels were drawn between cycle days 2 and 5 (in cycling women), a time when hormone levels are generally low. Interestingly, these findings do not necessarily support the general decline in sexual function observed with aging and across the menopausal transition, as testosterone changed in a U-shaped pattern in this study, with higher median testosterone levels reported at year 10 compared with year 5.

This well-designed study supports a relationship between endogenous androgens and sexual function in midlife women, increasing our understanding of the complex role of reproductive hormones in female sexuality.

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References:
HT use in women veterans higher than in civilian population

Use of HT associated with mental health diagnoses in women veterans


Summary. In this cross-sectional analysis of women veterans over age 45 years (N = 157,195, mean age 59.4 y [standard deviation = 12.2, range = 46-110]) who accessed Veterans Health Administration outpatient care, researchers examined the frequency of hormone therapy (HT) use and whether mental health was predictive of HT use. In the national population, an estimated 4.7% of women over the age of 45 years use HT. Main measures in this study were logistic regression analyses with HT use as the dependent variable.

In this group of veterans, 16,227 (10.3%) used HT. The strongest medical indicators of HT use were hysterectomy (OR, 3.99 [3.53, 4.49]) and osteoporosis (1.35 [1.27, 1.42]). A total of 49,557 (31.5%) in this group of women received at least one primary diagnosis of a mental health disorder and were more likely to use HT than women without a diagnosis. After controlling for demographics and medical comorbidity, women with a mood disorder or an anxiety disorder were more likely to use HT. This study suggests than women veterans aren’t discontinuing HT at the civilian rate.

Comment. The title of this article is misleading as one expects a descriptive study exploring HT use among women veterans. A main hypothesis, however, is that HT use will be increased in this specific population. This assumption was supported through association of decreased estradiol levels and various mental health conditions in the manuscript. I am somewhat concerned that there is a subliminal suggestion that HT could be an adjuvant management strategy for mental health.

Unfortunately, as a clinician and academician the information in this article affords little that I can translate into a practice or educational domain. Certainly more valuable information could have been obtained from this large sample of women about whom we know relatively little.

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Impact of hot flashes on sleep during perimenopause

Though informative, study leaves us with many clinical questions about sleep quality


Summary. In order to quantify the impact of objectively recorded hot flashes on objective sleep in perimenopausal women, this cross-sectional study performed in a sleep laboratory followed 34 perimenopausal women (mean age, 50.4 y) through 1 to 5 polysomnographic recordings for a total of 63 nights. There were 222 hot flashes identified, and data was analyzed with hierarchical mixed-effect models and Spearman’s rank correlations. The main outcome measures included perceived and polysomnographic sleep measures as well as subjective and objective hot flash measures.

There was an average of 3.5 objective hot flashes per night (95% confidence interval [CI], 2.8-4.2, range 1-9). A total of 69.4% of hot flashes were associated with an awakening (average of 16.6 minutes), which accounted for 27.2% of total awake time per night. In women having more perceived and bothersome hot flashes, there was a correlation with more perceived wakefulness and awakenings as well as more objective hot flash-associated time awake and hot flash frequency.

Comments. This paper begins with an excellent review of the complaint of menopausal
insomnia. Rather than only looking at the indirect biomarkers of fatigue or reported health consequences, the researchers applied the science of polysomnography (PSG) to the study of the vasomotor hot flash in laboratory conditions, as well as comparing it to the subjective perception of sleep-associated vasomotor disruption. PSG performs measurement of various physiologic variables, according the American Academy of Sleep Medicine (AASM), and the data obtained is extensive in terms of sleep stage, movements, awakenings, as well as breathing parameters. The study utilized the scoring system for sleep-associated events in the AASM’s 2007 manual and used standard sleep logs for patient-reported data. This technology is well studied and defined in the obstructive sleep apnea group, and less well studied using hypoestrogenemia or vasomotor symptoms as a marker for sleep variables. By using this technology, they can clinically pair skin conductance (as the primary component parameter of the hot flash) with the PSG-documented and patient-perceived wake after sleep onset (WASO) in patients having an average of 3.5 hot flashes per night. The authors tried to achieve robustness in their data by recording patients 1 to 5 times in the laboratory, diminishing the known effect of variability in an individual’s sleep studies. Participants still had a widely variable number of vasomotor episodes, as would be anticipated given these patients were perimenopausal.

In general, this study determined that not all hot flashes wake the patient, and when they do the hot flashes keep patients awake for a variable amount of time. The hot flashes measured by technology only occurred 3% of the time when falling asleep and only 3% of the time during REM, with most occurring during the lightest phases of sleep. The authors do not postulate regarding the stage of sleep affected and whether that would affect the clinical manifestations on mood and memory some patients have. Interestingly, from this study we learned that patients underestimated their time of sleep disruption, so we can assume that patients may be experiencing actually worse effects than they report.

The authors felt the mechanism of hot flashes causing WASO is similar to other sympathetic activation pathways and acknowledged that determining the exact nature of that relationship will help to further the understanding of this physiology. Because skin conductance was the variable they used, they were not able to determine the effects that the presence or absence of sweating or any other physical parameters of the hot flash would have on PSG. Since actual sweating and having wringing wet sheets is a common patient complaint, it would be interesting if we could look into this as well. Other potential confounding factors to poor sleep besides hot flashes, such as stress and anxiety, as well as factors that contribute to overall wakefulness at night, weren’t analyzed with this study yet affect how one would tailor therapy for an individual patient. There has been significant work on sleep disruption in women in other hormonal states, such as pregnancy and on oral contraceptives, relative to testosterone levels, and through life. There is even work that documents changes in estradiol and melatonin with shift work. As informative as this study is, it still seems to be looking at sleep disruption through a very narrow lens that leaves us with many clinical questions about sleep quality. Finally, this is a group of perimenopausal women and it will be interesting, because this is part of an ongoing study, to see whether these data hold for postmenopausal women.

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References:
Small complex ovarian masses in postmenopausal women are rarely malignant

Observing such adnexal masses over time could prevent unnecessary surgery


Summary. Women older than 50 with small (1-6 cm) complex ovarian masses on ultrasound pose diagnostic dilemmas, especially if CA125 levels are normal. Should surgery be performed to rule out malignancy? If not, when should ultrasound be repeated? To address these questions, investigators in California evaluated the clinical outcomes of 1,363 women with small complex masses seen over a 4-year period.

A total of 18 ovarian cancers or borderline tumors occurred, all of which were diagnosed at surgery. Overall, 404 of the 422 women who ultimately underwent surgical removal had benign masses. Six malignancies were identified among the 204 women who underwent surgery immediately after a complex mass was identified. Twelve additional malignancies were identified among the 218 women who underwent surgery after at least one additional ultrasound. Ten of these malignancies had increased in size within 7 months; all were found to be stage 1 tumors at surgery. Among all 994 women who were followed with repeat ultrasound, masses resolved in 160 and regressed in another 155. Among women who did not undergo surgery, no evidence of malignancy was found within 24 months of follow-up.

Comment. The authors suggest that, given the low malignancy rate of small complex adnexal masses, greater consideration should be given to observing them over time to prevent unnecessary surgery. At the time of the follow-up sonogram (in 3-6 months), surgery is appropriate if the mass has increased in dimensions, evolved in its appearance, or both. This “wait and see” strategy is particularly relevant to women in poor health, for whom such surgery might pose inordinate risks. These data should help guide treatment decisions for clinicians and patients alike when faced with a complex adnexal mass and normal CA125 levels.

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Menopause Editor’s picks from December 2014

NAMS spotlights selections from the most recent issue of the Society’s official journal, *Menopause*, chosen by its editor in chief, Isaac Schiff, MD.

Liping Wu, Rong Chen, Di Ma, et al.

Effects of physical exercise on health-related quality of life and blood lipids in perimenopausal women: a randomized placebo-controlled trial.
Jing Zhang, Guiping Chen, Weiwei Lu, et al.

Detection of serum antimullerian hormone in women approaching menopause using sensitive antimullerian hormone enzyme-linked immunosorbent assays.
David M. Robertson, Ajay Kumar, Bhanu Kalra, et al.
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 (e.g., cross-sectional and uncontrolled investigational studies).
- **Level III** Meta-analyses; reports from expert committees; descriptive studies and case reports.

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