Is physical activity a risk or protective factor for hot flashes?

Hot flash reports without physiologic corroboration more likely after physical activity


Summary. This study of 51 midlife women examined the role of physical activity in menopausal hot flashes by monitoring physiologic hot flashes and activity over two 48-hour periods, along with self-report of hot flashes in an electronic diary. Using hierarchic generalized linear modeling adjusted for potential confounders, researchers found that only hot flash reports without physiologic corroboration were more likely after acute increases in physical activity, especially in women with more depressive symptoms.

Comment. Because the vast majority of women will experience some level of hot flashes during the perimenopause, clinicians are tasked with an ongoing quest for an optimal way to manage this often troublesome experience which spans a spectrum of mild to severe. One frequently mentioned option is the use of physical activity. However, the literature is replete with contradictory evidence of activity’s efficacy in controlling the symptoms of heat dissipation. Some note a protective effect while others describe an exacerbation of hot flashes after an acute bout of exercise. Most studies have relied on self-reporting, which is confounded by retrospective recall as well as the influence of a woman’s affective state on her perception of activity’s effect on her unique hot flash event.

Gibson and colleagues sought to investigate the association between physical activity and hot flashes by more closely examining the relationship between perceived and physiologically demonstrated hot flashes as they relate to physical activity as well as affect. The study group was made up of participants in the Study of Women’s Health across the Nation (SWAN) and the cohort included equal numbers of women of Caucasian and African-American descent. Over two 48-hour periods, hot flashes were monitored by use of a BioLog ambulatory sternal skin conductance monitor in conjunction with a portable electronic diary. Four categories of biological and self-reported responses were analyzed: hot flashes that were physiologic; self-reported; self-reported not corroborated by sternal conductance; and hot flashes that were proven by sternal conductance but not noted on self-report. Accelerometers were used to monitor physical activity before, during, and after a hot flash incident. As well, an average activity level during the waking hours was
derived as a baseline. It is important to note that none of the women performed high or even moderate levels of activity. Their activity was limited to low levels in order to optimize hot flash measurement analysis.

This study does not provide information regarding the relationship between long-term physical activity and its effect on hot flashes. Prior studies have noted a protective relationship between regular cardiovascular fitness and occurrence of hot flashes.1 Fitness per se is not addressed, only habitual and acute bouts of low activity occurring relative to a hot flash incident. Further, the type of (aerobic, resistance) and intensity associated with the activity could not be assessed by an accelerometer, which is limited to noting the presence of activity. The women’s actual normal physical activity is not reflected in the study, as they were complying with study protocol. Finally, the overall study group size was small, resulting in limited ability to generalize to a wider demographic.

Despite these limitations, clinicians will find the study results of interest as this data not only deepens our understanding of the connection between activity and hot flashes, but it also helps us appreciate the significant role a woman’s affect plays in her perception of this relationship. Gibson did not find that acute bouts of physical activity produced enhanced conductance. Of interest, a bout of activity was more likely to result in self-reported but non-physiologic hot flashes, notably among women with higher levels of depression and anxiety.2 For the clinician, this finding is important and supports a more comprehensive assessment of the presence of co-occurring negative mental health states (depression, anxiety) when interpreting a woman’s discernment of the effect of activity on her perception of hot flash occurrence. Integrating the element of affect may then lead to a more individualized and effective treatment plan in the management of hot flashes.

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References


Comparison of current mammography screening and advocated guidelines

This comparison simulated costs of annual, biennial, and USPSTF guideline screening


Summary. Researchers estimated the aggregate cost of US mammography screening in 2010 and, using a model, compared it to the costs of three screening policy recommendations by professional organizations: annual (ages 40-84), biennial (ages 50-69), and US Preventive Services Task Force (USPSTF) guidelines (biennial for those aged 50-74 and personalized based on risk factors). Costs of screening were measured using Medicare reimbursements.

In 2010, the estimated cost of mammography screening in the United States was $7.8 billion (with about 70% of women screened). For annual, biennial, and USPSTF guidelines, the simulated cost of screening 85% of women was $10.1 billion, $2.6 billion, and $3.5 billion, respectively (largest drivers of cost were screening frequency, percentage of women screened, cost of mammography, percentage of
Comment. When NAMS invited me to comment on the paper by O’Donoghue and colleagues about the aggregate cost of mammography screening in the United States, I welcomed the opportunity to do some research, thinking about a clinical decision I face daily. How frequently should I encourage my patients to get mammograms? This article does not directly address that question. Rather, it presents a complicated model that purports to show that we in the United States spent $7.8 billion on mammography in 2010, whereas if we had screened 85% of women following the USPSTF guidelines it would have cost $3.5 billion. And screening 85% of women annually could have cost more than $10 billion. Mammography is big business!

I will not enumerate all of the guidelines out there about mammography, but I will mention the range. The American Congress of Obstetricians and Gynecologists recommends yearly screening starting at age 40 and continuing until a patient and her doctor decide otherwise, whereas in the United Kingdom they screen every 3 years from ages 50 to 70.1 Of some relevance, I received a CRICO Breast Care Management Algorithm in the mail today from Harvard’s Risk Management Foundation, my malpractice carrier, and they recommend that women 40 to 69 years old should be screened annually and women over age 70 years should be screened biennially. And now, through the Affordable Care Act, our government has required payment every 11 months for mammography for women aged older than 39 years.2 What is to be done?

The modeling done in this current article makes the case that frequency of screening is a major driver of cost. Percentage of women screened, film versus digital, and recalls were less significant contributors. However, women for the most part believe they are taking care of themselves when they have a yearly mammogram. Many clinicians share that perspective or sometimes do not have the time, will, or knowledge to discuss the uncertainties surrounding this issue. But healthcare professionals have an obligation to be stewards of healthcare dollars. Our obligation to our individual patients must be considered in the context of ultimately limited healthcare dollars. Do we have $7 billion to spend on yearly mammograms for, at best, a likely marginal gain?

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Cardiovascular risk and oral estradiol versus oral CEEs

CEEs associated with higher risk of incident venous thrombosis


Summary. This population-based, case-control study compared the relative clinical cardiovascular safety of conjugated equine estrogens
(CEEs) and estradiol in 384 postmenopausal women aged 30 to 79 years. It ran from January 1, 2003, to December 31, 2009. The primary outcome was incident venous thrombosis (68 cases), and secondary outcomes were incident myocardial infarction (67 cases) and ischemic stroke (48 cases). There were 201 matched controls. As opposed to estradiol use, CEE use was associated with higher risk of incident venous thromboembolism (VTE) and possibly myocardial infarction (but did not reach statistical significance). Researchers noted the need for replication of their findings and suggested that different oral estrogen drugs may be associated with varying levels of cardiovascular risk.

**Comment.** The current dictum regarding hormone therapy (HT) for postmenopausal women, which says to “use the lowest effective dose for the shortest possible duration,” fails to address key questions regarding HT and continues to generate a substantial amount of confusion for the practitioner. Clarification is needed regarding types of HT, doses, pharmacologic differences, length of treatment, and variations in risks and benefits associated with the indicated options.

Recent data published by Smith and colleagues corroborate previous studies and add important information to the conversation about HT. The findings of their study suggested that oral CEEs contribute to increased VTEs compared with oral estradiol. This is not the first time, however, that Smith and colleagues have suggested that CEE may be associated with higher risks.2,3

A nonhuman estrogen, CEE is the only natural estrogen approved by the Food and Drug Administration (FDA). It is obtained from the urine of pregnant mares. CEEs are a mixture of estrone sulfate, equilin sulfate, 17 alpha-dihydroequilin, 17 alpha-estradiol, and 17 beta-dihydroequilin, along with other estrogenic compounds, including a number that have yet to be described.4,5 It would not be surprising to see different clinical risks between a collection of estrogenic compounds opposed to one estrogenic isolate, although the biologic rationale for this is poorly understood. The results of another study by Smith suggested that the benefit of estradiol over CEE may be particularly strong for the 5% to 10% of postmenopausal women who carry a prothrombotic variant.6

For a decade now, and since the Women’s Health Initiative results were published, there have been many persons touting the benefits of bioidentical HT, with its supposed strength as a combination of estrogenic compounds that mimic what the body would, or should, be producing under ideal conditions. Menopause experts have cited concern, however, that the term “bioidentical” now usually refers to custom-compounded hormones that are not approved by FDA and are produced in varying doses with a lack of safety data. In addition to a lack of scientific evidence, it has also been pointed out that FDA-approved, noncompounded bioidentical products, such as oral estradiol, are available. The current study, therefore, provides some data that FDA-approved bioidentical estradiol may result in a better safety profile than oral CEE.

The mean age of the population in the current study ranged from 63.2 years to 67.6 years. Approximately a third of each group was currently using progestogen therapy, usually medroxyprogesterone acetate (96%). This is certainly an important aspect of the study and patient population. For those taking estrogen therapy at the time of the study, most women (>77.9%) had started estrogen therapy at least 3 years before study initiation. The strength of the study lies in its reflection of the heterogeneity of common clinical practice. Unfortunately, 23.5% of the VTE cases had been recently hospitalized or had inpatient surgery, whereas none of the controls did. Furthermore, duration of exposure to HT or progestogen therapy is not mentioned in this article. It is difficult to assess whether the decreased incidence of VTEs after the formulary
switch in 2005 was because of the changes in HT or was secondary to other healthcare and lifestyle improvements over time that were not captured by this study. Further research, particularly in the form of a randomized, controlled trial, between the two types of estrogen is needed.

Despite the new findings, current recommendations remain unchanged: initiate HT for symptomatic menopausal symptoms and maintain the lowest effective dose for the period of time necessary to alleviate symptoms. Initiating therapy after a thoughtful discussion of risks, benefits, and alternatives continues to be the practical and appropriate clinical approach as further data are accumulating.

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**Reinforcing the value of oophorectomy in women with BRCA mutations**

*Long-term data add confidence that oophorectomy prevents ovarian cancer and saves lives*


**Summary.** Although the current recommendation for care of women with BRCA mutations includes the consideration of risk-reducing salpingo-oophorectomy, the optimal age at surgery and the extent of cancer risk reduction are unknown. In an ongoing prospective observational study of 5783 women with BRCA1 or BRCA2 mutations (mean age at oophorectomy, 47), investigators report extended follow-up (mean, 5.6 years).

Overall, 186 women received diagnoses of ovarian, fallopian, or peritoneal cancer; of these, 68 died. Prior bilateral oophorectomy was associated with 80% lower risk for these malignancies (*P*<0.001). Among cohort members with no known cancer at baseline, the all-cause mortality hazard ratio associated with oophorectomy was 0.23 (*P*<0.001). In 1390
women, 46 occult invasive cancers were identified at oophorectomy; of these, 18 were fallopian tube tumors. Among women with \textit{BRCA1} mutations, prevalence of occult malignancies was substantially higher in those aged 40 or older at surgery.

\textbf{Comment.} The standard of care when performing risk-reducing surgery in \textit{BRCA} mutation carriers is complete removal of the fallopian tubes and ovaries with meticulous abdominal exploration and histopathologic analysis of resected tissue. These investigators previously demonstrated that oophorectomy lowers risk for incident breast cancer by 48\% in \textit{BRCA1} mutation carriers and reduces mortality by 70\% in carriers who already have breast cancer.\textsuperscript{1} Their current findings support the recommendation that such women proceed with risk-reducing surgery by age 35. Moreover, other data suggest that premenopausal mutation carriers without breast cancer can safely use hormone therapy for menopausal symptoms caused by oophorectomy.\textsuperscript{2}

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References


\textbf{Menopause Editor’s picks from March 2014}

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

\textbf{Age at menopause, reproductive history, and venous thromboembolism risk among postmenopausal women: the Women’s Health Initiative hormone therapy clinical trials.}
Marianne Canonico, PhD, Genevieve’ve Plu-Bureau, MD, PhD, Mary Jo O’Sullivan, MD, Marcia L. Stefanick, PhD, Barbara Cochrane, PhD, Pierre-Yves Scarabin, MD, and JoAnn E. Manson, MD, DrPH

\textbf{Employment is associated with a lower prevalence of metabolic syndrome in postmenopausal women based on the 2007-2009 Korean National Health Examination and Nutrition Survey.}
Hee-Taik Kang, MD, Hae-Young Kim, MD, Jong-Koo Kim, MD, MPH, John A. Linton, MD, PhD, and Yong-Jae Lee, MD, MPH, PhD

\textbf{A randomized, double-blind, placebo-controlled study of the lowest effective dose of drospirenone with 17\%estradiol for moderate to severe vasomotor symptoms in postmenopausal women.}
David F. Archer, MD, Thomas Schmelter, PhD, Matthias Schaefers, MD, PhD, Christoph Gerlinger, PhD, and Kerstin Gude, MD, PhD
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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