

CARDIOLOGY NEWS

Rising Heart Risks for Young Women Linked to Low Estrogen

Extreme Exercise and Dieting Are Contributing Factors

Bridget M. Kuehn

Investigators studying growing rates of cardiovascular disease in young women have found that an alarmingly high number of women with heart disease—more than two-thirds—have abnormally low estrogen levels.

The WISE [study](#) (Women's Ischemia Syndrome Evaluation) provided many insights into the factors associated with coronary artery disease in women, including that 69% of young women with coronary artery disease have low levels of estrogen compared with just 29% of their heart-healthy counterparts and that low estrogen was associated with worse coronary artery disease.

"These are young women, predominantly, who have stopped having their periods," explained Chrisandra Shufelt, MD, director of the Women's Hormone and Menopause Program and associate director of the Barbra Streisand Women's Heart Center. "It's either due to overexercising, undereating or stress induced, or it can be a combination."

Now, Shufelt and other investigators are beginning to tease out how this endocrine disturbance, which is also called functional hypothalamic amenorrhea (FHA), may harm the heart and young women's health overall. It is already well established that FHA causes stress fractures, osteoporosis, and infertility. Investigators are also testing the best ways to intervene.



For young women, stress, intensive exercise, restrictive diets, or a combination of these factors may interrupt menstrual cycles and have detrimental effects on heart health.

"THE WALKING WELL"

It is easy for women with FHA to escape detection by cardiologists and other physicians, said Sarah Berga, MD, chief of the division of reproductive endocrinology at the University of Utah in Salt Lake City and an expert on FHA. She explained that the women she treats with FHA are typically thin, very fit, and highly ambitious.

"Unless someone asks them about menstrual cycles, a lot of times they escape detection," she said.

The women themselves often do not recognize missing their period for an extended time as a cause for concern and a good reason to visit

a physician, Shufelt said. Some may even be misinformed that it is a good sign for a woman to stop menstruating during intensive training, but it is a really a sign of a [serious energy deficiency](#) that is likely to decrease performance.

"They are surprised to hear that there could be some negative consequences," said Shufelt, who calls these women "the walking well."

Now, emerging data show that all is not well in the heart of young women with FHA. A small pilot [study](#) by Shufelt and her colleagues found that women with FHA had impaired endothelial function compared with women without FHA, as well as signs of inflammation.

"This might represent the first sign of vascular dysfunction in women with low-estrogen states," she said. Now, she and her colleagues are conducting a larger [trial](#) that will add a third group—postmenopausal women—to better understand whether low estrogen may be causing endothelial dysfunction.

Cardiologist Paula Harvey, BMBS PhD, physician-in-chief of the Department of Medicine at Women's College Hospital in Toronto, ON, Canada, and her colleagues have also [found](#) signs of endothelial cell dysfunction in women with FHA, similar to that seen in postmenopausal women. The women with FHA also seemed to have impaired vascular function.

"The whole blood vessel itself seemed to not dilate appropriately when we gave them a good dose of nitroglycerin," Harvey explained. They also discovered that the sympathetic nervous system of the women with FHA was hyperactive and their renin-angiotensin system was nonresponsive in simulated gravity [experiments](#).

"We were concerned that if women are estrogen-deficient and they're young, that we may be switching on these two systems excessively or abnormally, and that this might contribute to potential problems like atherosclerosis, hypertension, and heart failure maybe at an earlier age," Harvey said.

Women with FHA also appear to respond differently to exercise. In a recent [study](#), Berga found that glucose levels dropped and cortisol levels rose in women with FHA during exercise challenge. This may inadvertently activate the sympathetic nervous system, Berga noted. One participant actually passed out during the challenge.

"If they enter the exercise room already with a history of chronic stress, the exercise has a different ef-

fect than if they enter the room and they're not chronically stressed," Berga said.

VITAL SIGN

Shufelt said that it is vital for cardiologists to understand that there are emerging risk factors for heart disease that are unique to women and that FHA may be one of them. She suggests that cardiologists routinely ask women about their menstrual cycles, diet, and exercise. Berga and Harvey agreed.

"The menstrual cycle is a vital sign," she said. "These young women might not be seeing a cardiologist now, but they might see them in their 40s and 50s. We should ask retrospectively not only about menstrual cycle history, but also if they had a prolonged period where they had no menstrual cycles, just like you would ask about pregnancy-related events."

Both the [National Collegiate Athletic Association](#) and [International Olympic Committee](#) have created educational materials for women athletes about "the female athlete triad" of low estrogen, lost periods, and bone loss and how to address it to ensure optimal health and performance.

As part of her current study, Shufelt is testing whether using an estrogen patch to restore estrogen to normal levels will improve the cardiovascular health of women with FHA. But she cautioned against using hormone therapies without first addressing the underlying stress, nutrition, or exercise-related issues that may be causing FHA as recommended in recent [guidelines](#) from the Endocrine Society.

The guidelines recommend first trying to restore energy balance through nutrition or exercise adjustments. It suggests considering short-term use of estrogen therapy

only after a reasonable trial of such interventions has failed to restore normal menses.

"Putting a patch on might just be a Band-Aid, but it could be a Band-Aid to bridge them so they're not getting inflammation and abnormal endothelial function while they are in recovery," she said.

It is also important for physicians to rule out alternative causes of FHA, Berga said. She explained she recently saw a patient whose FHA was caused by celiac disease, which prevented her from getting adequate nutrition.

Small adjustments may be enough to restore energy balance. Harvey noted that research by Penn State University's Mary Jane De Souza, PhD, found that just an extra granola bar or 2 a day may be enough to help some women resume their periods without cutting back on exercise. Harvey noted that women athletes in particular may be influenced by societal pressures for thinness or biases against hearty eating among women and may not get adequate nutrition to keep up with their regimens.

"I just want people to know that you don't need these people to stop exercising," Harvey said. "You need them to eat more."

The guidelines, which Berga co-authored, also recommend cognitive behavioral therapy as a first-line approach to help women cope with chronic stress or other mental health issues.

"Exercise might be a great way to deal with stress if it's not chronic stress that you're dealing with," Berga explained. "If you've got chronic stress, expecting exercise to be that stress buster I think isn't very realistic. You can't really run away from your problems with exercise." ■

<https://www.ahajournals.org/journal/circ>

© 2019 American Heart Association, Inc.