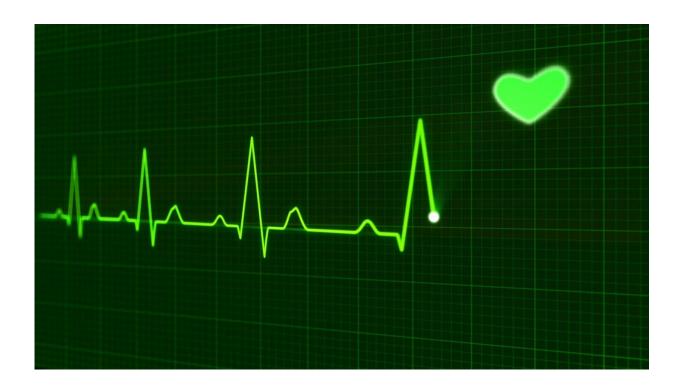


Heart disease in women: How pregnancy, menopause, and more affect risk

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It's a common scenario. A woman in her 50s wakes up feeling nauseous. Dismissing it, she moves through her day, feeling a bit fatigued during her morning walk, even short of breath. Her friends urge her to go to the doctor after she experiences shooting pain in one arm. Despite thinking it's nothing, she goes to the emergency room where she is put through a battery of tests. She is told there isn't a blockage in one of the three main



arteries, and that instead she may have a stomach issue or anxiety, and is sent home.

There is no major blockage, no chest pain. It couldn't be a heart attack, right?

For years, the above scenario wouldn't have merited a second thought. That's because our understanding of <u>heart</u> attacks was, until recently, primarily based on men. And when men have heart attacks, they have chest pain due to blockages in heart arteries. Doctors are now learning how different heart attacks and heart disease can be in men and <u>women</u>.

We spoke with Yale Medicine cardiologist Erica Spatz, MD, MHS, a clinical investigator for the Yale Center for Outcomes Research and Evaluation (CORE), which focuses on health care quality, about how the knowledge of women and heart disease is changing.

How are the risk factors for heart disease different for a woman? Do hormones play a role?

Yes. Hormonal cycles can affect women's cardiovascular health. In the pre-menopausal years, estrogen is protective of the heart—estrogen relaxes the arteries and promotes good cholesterol. In the peri-menopausal years, however, as estrogen declines, there is an emergence of cardiovascular <u>risk factors</u> such as high cholesterol and hypertension, including in women who previously had normal or even low cholesterol and blood pressure numbers. The incidence of heart disease in women starts going up around age 65—about 10 years later than in men, likely due to the protective effects of estrogen.

Whether hormone replacement therapy (estrogen plus or minus progesterone) increases or decreases the risk of heart disease is nuanced,



and the story is still unfolding. In the 1980s and 1990s, estrogen was thought to protect women against developing heart disease—and it was used liberally for this purpose. However, when the Women's Health Initiative tested the effects of estrogen in a randomized clinical trial, they found a higher risk of heart attack and stroke. More recently, the pendulum is swinging back—but not fully. Estrogen is mostly safe and there may be some lowering of cardiovascular risk, but only in women under the age of 60 or who are less than 10 years into menopause. If a woman is considering using estrogen to treat menopausal symptoms, this is a great time to discuss cardiovascular risk and have a shared decisionmaking discussion about whether hormone replacement therapy is right for them.

What about women's different heart attack symptoms?

Chest pain is the most common symptom in both sexes, but women may not experience intense pain like an elephant sitting on their chest. They may have chest tightness or a dull ache; they also may have shortness of breath, jaw pain, or nausea. Sometimes the symptoms are more diffuse, like dizziness, clammy skin, or unusual fatigue when they are going for a walk or doing something that is usually easy for them. It's often the case that women have a multitude of symptoms—maybe chest pain, but also a bunch of other symptoms that dilute the chest pain. All this may lead to under-recognition of symptoms by the women themselves and by their doctors.

Is it true that women's actual heart attacks are different, too?

Sometimes. Not only can the symptoms be different, but findings on tests may not follow the typical pattern. Women don't always present



with the classic pathological mechanisms that lead to heart attacks (and that most of our tests are designed to detect). Specifically, our tests are designed to look for blockages in one of the three main arteries that supply blood to the heart, and many women we see in the emergency room don't have blockages in those arteries. Yet, they have everything else that looks like a heart attack: They have the symptoms, the electrocardiogram findings, and the blood test results, but we don't find a major blockage.

Then, how do you know they've had a heart attack?

There is greater recognition now that women have non-traditional forms of heart attack. Some of our newer imaging tests and catheter-based assessments can reveal disease in the small arteries of the heart [known as microvascular dysfunction], which can lead to heart attacks. In other cases, a cardiac event may be due to spasm of the artery, which is dynamic. So the spasm may have occurred at the time of the <u>chest pain</u>, but by the time women are in the catheterization lab, the spasm has resolved and the artery looks normal.

Both microvascular dysfunction and coronary vasospasm may go undetected, and the event may be dismissed as 'not cardiac'—instead, doctors may attribute the symptoms to anxiety or a stomach-related problem. Sometimes, women leave the hospital with a mixed message: "Well, you had a heart attack, but the heart arteries were clean, so good luck."

The lack of a firm diagnosis can lead to uncertainty about treatment and prognosis. Women often feel unsure about whether to seek care the next time they have that kind of pain, because doctors didn't find anything the first time.



The VIRGO study was a step that brought more awareness to these different heart attacks, correct?

That's right. Harlan Krumholz, MD, the director of CORE, led a large study that aimed to understand the experiences and outcomes of patients after a heart attack, and also to compare men and women. In reviewing nearly 3,000 case reports, we found that one in eight women in the study did not have evidence of a classic heart attack, and, in fact, did not fit into our traditional classification system known as the Universal Definition [a tool developed by the American Heart Association and other organizations to define different types of heart attacks]. So, we developed an alternative taxonomy called VIRGO (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients) to capture different types of heart attacks, and the biological and pathological mechanisms that underlie them. The taxonomy also acknowledges that often we don't know what caused the heart attack. This is just as important, as it can open the door to further research and discoveries. This taxonomy isn't in practice at this time, but the concept is out there, and more and more clinicians are attuned to women's heart disease and employing newer approaches of detection. Additionally, more studies are being done to evaluate prognosis and optimal treatment strategies for different types of heart attacks. This is an exciting time—and I am very optimistic that we are entering into a new era of women's cardiovascular health.

There has been debate around statin therapy. What do women need to know about that?

Statins are medications that lower LDL, or bad cholesterol; they are a mainstay for preventing heart attack and stroke—resulting in about a 30% to 40% reduction in risk. One reason there is backlash is that statins are recommended to so many people, especially as they get older. Our



job as cardiologists is to figure out who is likely to benefit from statins, and who are the people who don't need to take them, because they were never going to have a heart attack in the first place.

Historically, women have often been under-prescribed preventive medications, because doctors saw them as being less at risk for heart disease than men. On the other hand, some women have been told they need to take a statin, and they feel like, "Maybe that's not right for me." It is imperative that we promote personalized approaches to the decision to take a statin.

For women with established heart disease, there is a strong recommendation to take a statin since there is a big reduction in risk of future heart attacks. For women without heart disease, we need to engage them in shared decision-making, which involves discussions about their personal risk for developing heart disease and the potential for statins to lower that risk. Then, taking into account their preferences, values, and goals, determine what is best for them. Some of the research I'm doing is to encourage these conversations with women around what contributes to cardiovascular risk and how much statins can impact that risk.

Hypertension is another big topic, correct?

Hypertension is the most important risk factor that we can control. Yale New Haven Health Heart & Vascular Center and Yale Medicine are working to improve blood pressure control with a strategic focus on the New Haven community. We are collaborating with pharmacists and implementing more person-centered ways of monitoring blood pressure, including remote monitoring [measuring blood pressure at home] and telemedicine visits.

We are also working to identify and address barriers to poor blood



pressure control—such as poor diet, financial stress, and transportation. We're in the infancy of this program, but we hope to expand it to some key populations—including postpartum women who've had hypertension or preeclampsia (characterized by high blood pressure and signs of damage to another organ system during pregnancy) and who are at risk for having high blood pressure after they deliver.

Can you talk about your efforts to inform women in the community about all these things?

We are conducting peer sessions with women around their cardiovascular health. We have a grant from the Alpha Phi Foundation, and together with cardiologist Lisa Freed, MD, and interventional cardiologist Sasanka Jayasuriya, MD, and an organization called the Patient Revolution, we are facilitating conversations to help women better understand and engage with the personal factors contributing to their risk for heart disease, and empowering them with the knowledge and skills to have better discussions with their clinicians about their cardiovascular health.

We will typically ask a woman, sometimes a patient of mine, to host a session by inviting 10 to 12 women she thinks may be interested—colleagues, friends, family members, maybe members of her book club. I'm there with a co-facilitator from the Patient Revolution. We discuss a lot of women-specific issues, and they share stories about their experiences in life and with the health care system, and their thoughts on statins and other interventions that could lower their risk. Truly, they learn from each other. We hope women will feel comfortable enough to bring up these deeply personal topics the next time they discuss cardiovascular health with their physician.

With all of this information, what should women



expect when they talk to their doctor?

Women should expect a personalized approach and accept nothing less. Personalized medicine means taking the time to understand the person in front of me—and how their biology and biography may be contributing to their cardiovascular health. We have calculators to estimate people's risk of developing a heart attack in the next 10 years, and this is a good starting place.

But typically, more information is needed—what is their diet, activity level, daily stressors, experience with depression and trauma, and their general well-being? Specific to women, it's important to know about their pregnancy experiences, including issues such as diabetes, preeclampsia, high blood pressure, or pre-term delivery, which are all risk factors for heart disease. What is their family history? Is there a role for more advanced lipid testing, a calcium score, or genetic testing? Finally, we need to work with our patients to put it all together to estimate—as best as possible—their personalized risk and the potential to reduce that risk, and to consider their preferences, values, and goals to help reach the best strategies for promoting cardiovascular health.

And what if they don't get a clear diagnosis from their doctor?

I urge women to take concerning symptoms to heart, literally, and to speak up if they don't get a clear diagnosis following a cardiac event. We know now that when something is not right in a woman, the first line of testing may not reveal the answer. In my work, I am encouraging women to go for a second line of testing or a second opinion.

What should women be doing to prevent heart disease?



A good starting place is for women to talk more among themselves and to their doctors about <u>heart disease</u>. Family history is one of the most important things they can share—that's especially true for young and middle-aged women, as there are many opportunities to identify whether they, too, are at risk, and to lower that risk. Also, it's important to discuss pregnancy and menopause experiences, diet, activity, and stress.

I want women to feel comfortable asking, "Knowing what you know about me, what is my risk, and what can I do to modify my risk?" Then, we can work work together to find a personalized plan.

Provided by Yale University

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