

BroadcastMed | Early Menopause: Precursor to Coronary Heart Disease?

SCOTT WRIGHT: Hello, and welcome to another Mayo Clinic broadcast on theheart.org at Medscape. I'm Dr. Scott Wright, professor of medicine and cardiology at the Mayo Clinic. Today, I'm joined by a colleague, Dr. Sharon Mulvagh, a good friend and a well-respected colleague at Mayo.

Sharon has had an incredible career at Mayo. Prior to coming to Mayo, she worked in Houston and did some consulting work at NASA. And she's a very accomplished physician and researcher.

Today, Sharon holds the title as director of the Women's Heart Clinic and is a well-known and respected imaging cardiologist as well as a preventive cardiologist. She's here to join me in a discussion today on early menopause, precursor to coronary artery disease and stroke. So, Sharon, welcome to the broadcast.

SHARON MULVAGH: Thanks so much, Scott. Great to be here.

SCOTT WRIGHT: It's great to have you. Thanks for tackling what is a very important and tough topic. Sharon, help us understand. What is early menopause? Can you define that for the people watching today?

SHARON MULVAGH: Sure, first of all, what's the average age of menopause in women in North America?

SCOTT WRIGHT: I would say around 50, I would imagine.

SHARON MULVAGH: Yeah, it's 51. And the range is about 50 to 54. So early menopause is considered to be if you have a menopause between the ages of 40 and 45, so less than 46. And actually, the term premature menopause is used if menopause onsets before age 40.

SCOTT WRIGHT: OK, so premature is before age 40. Does the onset of menstruation at all predict when menopause might happen?

SHARON MULVAGH: It's more predicted by the family history, actually.

SCOTT WRIGHT: OK, so what your mom and grandma have gone through, you may go through, OK.

SHARON MULVAGH: Right.

SCOTT WRIGHT: Well, is there a difference in terms of cardiovascular risk for surgical menopause, which happens in some women, versus natural menopause, if we may call it that?

SHARON MULVAGH: Sure, well, I think you're bringing in an important point. There is an increased cardiovascular risk with early menopause and obviously early and premature menopause. And there have been several studies, smaller studies. We're going to talk more about that as we go on.

But there have been several studies looking at whether there's a difference between natural versus surgical menopause. And, indeed, it doesn't really seem that there is a difference. It's just the fact of the matter that if you have an early or premature menopause, that cardiovascular risk increases. And it increases on the order of at least two times.

SCOTT WRIGHT: Wow, so a twofold risk, that's comparable to diabetes and heterozygous FH maybe. It's a very significant risk factor. Do you think it's appreciated by the medical community as much as the risk that it is?

SHARON MULVAGH: No, not at all, and part of that is actually because of the hysteria that almost developed about hormone replacement therapy after the earlier trials. And we can talk a little bit more about that as well.

SCOTT WRIGHT: Why don't you summarize for our audience your take on the estrogen replacement therapy studies? Do they raise cardiovascular risks? Do they alter them at all? Do they improve risks? What's your take on that?

SHARON MULVAGH: Right, so we're going to talk about early menopause and premature menopause. And certainly, repleting hormones in those situations have nothing but benefit as far as the cardiovascular system goes, unless there's a separate contraindication to having hormone therapy such as a breast cancer history or history of a prior stroke or a thromboembolic event.

SCOTT WRIGHT: So like a pulmonary embolism would be a contraindication.

SHARON MULVAGH: Right, it would be a relative contraindication in that case.

SCOTT WRIGHT: Relative, OK.

SHARON MULVAGH: Yes, exactly, but in general, the large studies-- and I think we're talking mostly about the Women's Health Initiative study. Unfortunately, it was not really a study of what happens physiologically for women. The average age of women enrolled in the Women's Health Initiative was 62. That's a decade well passed the onset of natural menopause in the United States.

SCOTT WRIGHT: And the average North American woman.

SHARON MULVAGH: Exactly.

SCOTT WRIGHT: And so if there is a risk you're mitigating, you started late in the process.

SHARON MULVAGH: Exactly, and I think what we learned from the WHI was that you don't give hormone therapy to women that are a decade after their natural menopause, like that makes good sense. But, indeed, only less than a quarter of the patients that were in the WHI were in the age group of 50 to 60. There were no women less than 50. And it's not really readily known, but it certainly has been published, that that particular cohort of women, that tertile of women, had a lower cardiovascular risk, had lower events with respect to heart attacks and strokes than did the women not on hormone therapy. So it's very, you know, thought-provoking.

So, actually, there have been subsequent studies, too, at WHI, one that we participated here at Mayo in, and that was the KEEPS, or Kronos Early Estrogen Prevention Study. And the objective of that study was to look at women at the time of their menopause. And everyone had a natural menopause. No hysterectomies were in this particular group. And all women were administered hormone therapy, which was an estrogen, either oral or transdermal, and a progestogen. And they were tracked with respect to the surrogate endpoints of coronary artery calcification and carotid intermediate thickness.

SCOTT WRIGHT: OK, which are good predictors of subsequent cardiovascular and neurologic risks.

SHARON MULVAGH: Right, right, and so there was very reassuring data. They were followed for five years. And the data showed that, indeed, there was no increased risk of increased carotid intermediate thickness nor increased coronary calcification. And there was a trend to less coronary artery calcification in those women who were treated with hormones. And it probably was, you know, a time factor and a number of factors to why we couldn't detect significance.

But I think it's reassuring, that data, that there are no untoward cardiovascular effects when taken in a physiologic manner. So actually all women were within three years of their menopause in that particular study. But I think that most of us that see patients every day that are going through menopause that have significant vasomotor systems that are feeling very uncomfortable, we can feel very confident in saying, it's OK to use hormone therapy, as long as you don't have any specific contraindications.

SCOTT WRIGHT: Do you feel Kronos was powered adequately? Or if you were given a budget that was sufficient by the NHLBI, would you redo it with higher numbers?

SHARON MULVAGH: Yeah, well, you know, we're never going to be able to repeat the WHI. I was, like, a \$650 million study. There were 16,000 women in each arm, and it's just not going to be able to do that. So, unfortunately, you know, the KEEPS study was just about 700 to 800 patients at a much lower budget. And so the findings are not going to be as powerful because of that.

SCOTT WRIGHT: But the trend was suggestive.

SHARON MULVAGH: The trend was suggestive. And I think that as I said, it gives us confidence to say in our women who are very confused about using hormones because of their vasomotor symptoms, that they might be hurting their heart, that we can say, no. Indeed, you may be actually benefiting it. But the data is not strong enough to make that statement, so, of course, it's not recommended for the prevention of cardiovascular disease.

SCOTT WRIGHT: OK, so in a guideline document, it might be a 2b indication, certainly not a 3, and not a 1 or a 2a.

SHARON MULVAGH: Well, it's better than moving from a 3, which was hormones are completely contraindicated, which was actually what was in the document for the prevention of cardiovascular disease in women. So I think that we have to, you know, temper with our judgment and our common sense, but recognizing that, again, the WHI was really a study of older women a decade passed their menopause and that we really need to individualize for the patient that's sitting in front of us.

SCOTT
WRIGHT: I think that's well said. That's true for all clinical trials. And I think generally, trials, while they answer a great question, sometimes create even more issues and questions we had not contemplated until we do them because we learned with each study where we have perhaps designed it less than fully adequately, or other issues pop up. So this is a great area to, as you say, personalize the care.

What preventive advice do you give the patients, the female patients who come through our Women's Heart Clinic? What can one do to lower one's cardiovascular risk when they're either in menopause naturally, or early menopause, or they feel they're approaching it, and they want to do what they can do to prevent heart disease? What can we give our audience today to teach their patients?

SHARON
MULVAGH: Well, I think that the onset of menopause is an extraordinarily good time to take stock. You know, most women, it's mid-lifetime. We have been perhaps very busy and neglecting some of our optimization of our cardiovascular risk factors.

So it is a very good opportunity for the physician to discuss with their patient getting things in line, knowing, of course, your numbers, knowing what your lipid profile is. Knowing what your weight is is very important because natural hormones, estrogen in particular, have very positive effects on our physiologic cardiovascular benefits. For example, the lipid profile is benefited. HDL is augmented with estrogen, and LDL is decreased.

So when we transition into the menopause, those things, we lose that protection, so to speak. So it's also true that women have a tendency to gain a little weight. And the distribution of that weight may be different, more in the central adiposity aspect, which is, of course, as we know, another unfavorable spot to have it for cardiovascular risk.

So it's extremely important to take those things into consideration. Know what your numbers are, and particularly, go into menopause. The more you can be close to an ideal body weight, the better it is.

And then, of course, how do we achieve that? You know, adequate physical activity and excellent nutritional choices, avoiding portion overdose, so to speak.

SCOTT
WRIGHT: And restricting calories to reasonable numbers, right?

SHARON
MULVAGH: Yes, yes, portion control and restricting calories, making good choices, and, of course, another good choice is not smoking. It's interesting. In some of the studies that have been looked at more recently about-- the MESA study looked very in detail about women and their age at menopause and their risk for developing atherosclerosis.

And they found that women who were smokers had an even higher risk if they had an early menopause of developing early atherosclerosis. So that's true. And another very recent Swedish study looked at the onset of heart failure in women that had an early or premature menopause. And if those women, the risk was actually increased 40% if they'd had an early menopause and not been treated with hormone therapy. And if they were smokers, it was even higher.

SCOTT
WRIGHT: So observational data, but still the best we have to apply to the patients we see, supporting a use of hormone replacement therapy at physiologic doses, is that fair to say?

SHARON I would say so, exactly, particularly in women with early and absolutely in women with premature menopause.

MULVAGH:

SCOTT With early menopause, so between 40 and 47 or 46.

WRIGHT:

SHARON Right, right, right, that's a very good point. Another important thing is that in women that are undergoing
MULVAGH: hysterectomy now, the Mayo data actually showed that 40% of women that had a hysterectomy, and it was about 10% of women in the ages of 35 to 45. Fully 40% of those women were getting prophylactic oophorectomies. I mean, maybe the thought was to prevent ovarian cancer or something.

So in 2008, ACOG, which is the association of the gynecology group, they determined that it's not appropriate to do prophylactic oophorectomy or to perform oophorectomy at the time of hysterectomy. That's very important, indeed. So women should be aware that if they are less than 40, less than 45, undergoing hysterectomy, if it's recommended to have the ovaries removed, they need to question that and to know, is this really--

SCOTT Have a discussion with their provider.

WRIGHT:

SHARON Right, have a discussion with their provider, because that will put them at increased risk for cardiovascular
MULVAGH: disease subsequently, unless they are replenished with hormones.

SCOTT Wow, wow, well, that's an important change in practice recommendation which will hopefully benefit the long-
WRIGHT: term cardiovascular health of women. And correct me if my impressions are incorrect. But the risk of ovarian cancer is substantially lower than the lifetime risk of cardiovascular disease.

SHARON Well, Scott, you know one in three women die of heart disease, the same as men, and absolutely.

MULVAGH:

SCOTT That's right. Heart disease spares no gender issues, financial issues, ethnic issues. We all have the same risks.

WRIGHT:

SHARON It's an equal opportunity killer.

MULVAGH:

SCOTT It is, yes.

WRIGHT:

SHARON It is, yeah, that's very true.

MULVAGH:

SCOTT Well, Sharon, this has been very enlightening. And I know the audience appreciates your expertise today. And
WRIGHT: finally, I have to say that you live what you preach. I live not too far from Sharon, and I see her running nearly every day, during the temperate season. I don't know if you run in the winter.

SHARON You're not out in the winter, but I'm there.

MULVAGH:

SCOTT
WRIGHT:

I'm not out in the winter any more than I have to be. But you certainly practice this. And I think if our viewers have questions, they can contact you at Mayo Clinic. And you're certainly happy in the Women's Heart Center to see any patients they would like to see where they feel there are particular challenges at providing cardiovascular counseling.

So, well, thank you for joining us today on this discussion about menopause, early menopause, and premature menopause. And I want to thank Dr. Sharon Mulvagh for her great insights for all of us who have joined this conversation, for me as the moderator, for you as viewers. We hope that you will continue to check out future content on the Mayo Clinic page at theheart.org at Medscape. Thank you for joining us, and have a good day.