

Women and PAD: The Unmet Challenge

Sharon L. Mulvagh, MD: I am Dr. Sharon Mulvagh, Professor of Medicine and Director of Mayo Clinic Women's Heart Clinic. Today during Mayo Clinic Talks we will be discussing peripheral vascular disease in women, the unmet challenge. I am joined today by my colleague, Dr. Amy Pollak, who is an expert in cardiovascular imaging and an expert in women and heart disease. It's great to have you here today, Amy.

Amy W. Pollak, MD: Thanks so much, Sharon.

Dr. Mulvagh: Recently the American Heart Association published a scientific statement titled "A Call to Action: Women and Peripheral Arterial Disease." What was the driving force behind this publication that has brought this entity into the limelight?

Dr. Pollak: Lower-extremity peripheral arterial disease (PAD) has a high prevalence and is associated with high cardiovascular morbidity and mortality. Women are affected by PAD at rates at least as high as men. However, there is much that we haven't known about women and PAD. The authors of the scientific statement aimed to assess the current literature on this topic to give us a sense of where we needed to go in terms of new research and new clinical areas to focus on.

Dr. Mulvagh: Has this changed the way we assess women with heart disease?

Dr. Pollak: There are certainly women who are at risk for PAD who are undiagnosed. Traditionally it has been thought that women suffer from PAD less often than men, and there have been fewer population-based surveys of PAD than of coronary artery disease. As part of this scientific statement, the authors looked at pooled data from about 25,000 individuals to determine the prevalence of PAD in women compared with men. Some findings were already known, and some were novel findings. The incidence of PAD goes up as we age. Starting at age 40-49, the prevalence in women is about 1.7% and in men about 1.3%, which is pretty low, but that figure essentially doubles with each subsequent decade of life up to age 80. Over the age of 80 there is a marked increase in the prevalence of PAD; in men, it is about 29% and in women it is about 25%. That would suggest that there are more men than women with PAD.

The authors also looked at the pooled prevalence to get an estimate of the population burden using the US census data from 2010. This was very interesting, because there were actually more women than men with PAD when considering the 2 separate distributions of age. In younger people (ages 40-49), there are more women than men with PAD, and over the age of 70 there are more women than men with PAD. This is a paradigm shift from the traditional perspective on PAD.

Dr. Mulvagh: It's not just because women live longer that they are more likely to develop PAD; it's actually more prevalent in the younger female population as well.

Dr. Pollak: That is true, and that is a huge area that needs further attention. It was a surprising result from the study.

Dr. Mulvagh: Is this thought to be the usual atherosclerotic type of peripheral vascular disease, or is it more inflammatory, or a disease such as Buerger's? Is it smoking-related? Are we able to identify women who are more at risk, particularly those young women about whom we are now aware?

Dr. Pollak: We don't know. Traditionally, smoking is less associated with women and PAD than it is with men, but this younger group of women is poorly characterized in terms of their risk factors for PAD. We know that diabetes, smoking, and (less so) hypertension and hyperlipidemia are certainly risk factors for PAD, but whether there are other risk factors, such as inflammatory states or potentially prothrombotic states, is not clear at this point.

Dr. Mulvagh: Just as we know that smoking in women is a risk factor for cardiovascular disease, and diabetes carries a greater risk for cardiovascular disease in women than it does in men, it seems that these traditional risk factors may play a stronger role in women as well. Should we wait for symptoms, or should we be doing ankle-brachial index (ABI) tests? What is the approach here? How do you decide how you are going to evaluate this, or do you just wait for symptomatic presentation?

Dr. Pollak: We shouldn't wait for symptoms because we know that most women won't have symptoms. In a small study of women over the age of 65 at risk for PAD, 63% of the women who had an ABI less than 0.9 were asymptomatic. Waiting for symptoms will cause us to miss a huge number of patients who are at increased risk for cardiovascular morbidity and mortality. Screening individuals who are at risk for PAD with a lower-extremity ABI would be appropriate and in concordance with the guidelines. This is not often done, largely because of the bias that women aren't affected as much by PAD or because of a holdover from older thinking that PAD is a benign disease. The same study found that women have higher mortality (both cardiovascular mortality and total mortality) compared with men. Not only is PAD more common in women, but women carry higher total mortality and cardiovascular mortality, which is a sobering statistic.

Dr. Mulvagh: The symptoms of a heart attack can be somewhat different in women, although recent studies suggest that women do have chest pain but they may communicate it differently. Similarly, women might not present with classic claudication symptoms and we say they are asymptomatic, but they might be presenting with other symptoms and we just haven't figured out what those are --

aching, fatigue, or other nonspecific symptomatology.

Dr. Pollak: That part has been clearly documented. Women have more atypical leg symptoms compared with men. Atypical symptoms are common in both groups. The minority of patients present with classic intermittent claudication, such as pain and cramping in the calf with exertion. We need to be attuned to these atypical leg symptoms, which can be a nondescript achiness, fatigue, or cutting back on their exercise capacity. Compared with men, a woman's exercise performance at a given ABI is less. Whether that is because they have more of a microcirculatory effect in the leg compared with men, in a similar way, that women have microcirculatory problems in the heart is not known.

Dr. Mulvagh: That is very thought-provoking. The flipside is that all of our guidelines treat cardiovascular disease risk as if it is already present in a patient with peripheral vascular disease. A patient with documented peripheral vascular disease is at > 20% risk of developing a cardiovascular event in his or her lifetime. This is extremely important. Not only are the symptoms perhaps different, but the implication of the presence of the disease, which may be asymptomatic, is a silent factor that we are missing in much of our female population. Do you think that we should be doing ABIs, and in which women? We can't do them in everybody, or should we? It's a noninvasive, simple thing to do. What would you suggest?

Dr. Pollak: We should be doing a lot more than we are; not in everybody, but we should screen patients for PAD using the ABI in 2 groups. We are trying to identify patients who are at risk for PAD. In patients with clinical evidence of PAD (either leg symptoms or nonhealing wounds), we should be screening with an ABI to diagnose PAD. In a second group, we should be screening those in whom appropriate risk factor modifications could be implemented to change their clinical management, such as individuals with increased risk for PAD (such as age > 65 or age 50-64 with cardiovascular risk factors such as smoking, diabetes, or hyperlipidemia). It's a very cheap test to do. It's noninvasive and fast, and it changes the paradigm for treatment and the estimated risk level in terms of the cardiovascular morbidity and mortality.

Dr. Mulvagh: Let's talk about treatment. Are there gender differences in treatment approaches, or is treatment equally effective in men and women? What is the treatment?

Dr. Pollak: In asymptomatic individuals, it is aimed at preventing cardiovascular morbidity and mortality events for both genders. We are poor at having patients on recommended lipid-lowering and antiplatelet agents. There needs to be additional attention to this, in both men and women. I don't know whether there is a gender disparity in terms of appropriate treatment with lipid-lowering and antiplatelet agents at this time.

For symptomatic disease, we have the option of cilostazol. They have looked to see whether there is a difference in gender response to cilostazol, with a supervised exercise program, and there doesn't seem to be any difference in response. It's a very effective therapy -- somewhat time-consuming, but very critical.

Dr. Mulvagh: Cheap and effective, but it takes time.

Dr. Pollak: Other treatment options are the percutaneous interventions or surgical lower-extremity revascularization. Lower-extremity bypass surgery has worse outcomes in black and Hispanic women, although it is not clear why. Studies haven't been large enough to tease out whether it was reduced access to care following surgery or the contribution of risk factors in terms of diabetes, lipids or ongoing tobacco use. Those factors have not been teased out, but it is certainly important to figure out whether there are not only gender disparities but ethnic and socioeconomic disparities that influence the outcomes with treatment for lower-extremity PAD.

Dr. Mulvagh: That leads us to a very important aspect of this. What do you think is the current public awareness of PAD among women? We have a pretty good effort going right now with the "Go Red," and "Heart Truth" campaigns, which have improved our awareness of "cardiovascular disease" in women, but we often mean coronary heart disease when we say cardiovascular disease. What is the general public awareness about PAD in women and the recognition of it?

Dr. Pollak: We have our work cut out for us. In contrast to women and heart disease, where there has been tremendous education -- and the Go Red campaign over the past 10 years has made huge strides -- PAD has been in the background. There was a 3-year campaign cosponsored by the PAD Coalition and the National Heart, Lung, and Blood Institute to increase awareness of PAD across genders. Despite that, a survey done by Dr. Hirsh showed that 3 of 4 individuals were unaware of PAD and the associated risk factors. That is a very sobering statistic, and it shows that we have a lot of work to do in terms of public education and in focusing on the individuals who have PAD and aren't being treated appropriately, and with the providers to educate them that PAD is not a benign disease. It is very common in women, more so than in men, and it carries a high cardiovascular morbidity and mortality, also more in women than in men at the extremes of age.

Dr. Mulvagh: It is fortunate that at least the modifiable risk factors for both coronary heart disease and PAD (if we lump them together as cardiovascular disease) are overlapping. Are there any plans to try to use the programs that already exist -- the Go Red and Heart Truth public education campaigns -- to improve peripheral vascular disease awareness? People think, "It is not going to kill me," as opposed to a myocardial infarction, which might. How do you think we could reach our patients and enhance that awareness? Is this an avenue that

might be pursued, and is there any thinking in that direction?

Dr. Pollak: That is an avenue that needs to be pursued. I have been working with the Peripheral Vascular Disease Council, part of the American Heart Association, and we have put together a proposal for a comprehensive educational campaign to help bring PAD, particularly in women, to the forefront of our overall cardiovascular risk factor program. We are learning from Go Red and other campaigns how to elevate this to a level of national attention. There is work that we need to do on a national level with patient-specific education, provider education, and expanded research in this area. There is so much that we don't know. I'm hoping that we will be able to make some great strides with our proposal.

Dr. Mulvagh: That is a great summary of a very important issue. The call to action for awareness of women and PAD that has been established by the American Heart Association and the working group will be very important. We look forward to hearing and seeing the results of that soon.