

Raising awareness of peripheral artery disease in women

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Practice Points

- Primary care providers, including gynecologists, should identify women with or at high risk for peripheral artery disease (PAD) by targeted use of the ankle brachial index (ABI) test as per current national guidelines.
- Women at risk for PAD should be informed of common PAD risk factors, symptoms and cardiovascular risk by all health professionals.
- Women's cardiovascular health ('heart health') programs should include both PAD awareness campaigns and gender-relevant PAD care pathways designed to lower cardiovascular risk, prevent or decrease limb ischemic symptoms and minimize amputation risk.
- Women with or at risk for PAD should undergo an ABI or alternative diagnostic assessment for PAD.
- African-American women who have one risk factor for atherosclerosis should be evaluated for PAD via use of an ABI.
- Heart attacks, strokes and amputation each represent death of end-organ tissue from severe atherosclerosis, and may all be preventable.
- Medical management of patients with PAD is mandatory to prevent atherosclerosis disease progression, with the same priority as heart disease and stroke. It is defined as evidence based high quality care with use of antiplatelet and statin medications, smoking cessation and achievement of target blood pressure as per current intersocietal national guidelines.

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SUMMARY Peripheral artery disease (PAD) is a common, chronic atherosclerotic disease affecting millions of individuals that causes a major impact on morbidity and cardiovascular mortality. Although the gender- and age-specific prevalence of PAD has been well-defined from published population-based studies, the clinical relevance of these data has not been fully recognized by the public and health professionals. These health facts are now revealing that women suffer the consequences of PAD at rates at least as high as those observed in men. Additionally, PAD is more common in African-Americans over the age of 50 years than in non-Hispanic caucasians, suggesting that African-American women are at particularly high risk for developing PAD. Cardiovascular disease is the leading cause of death in women, making it imperative that the contribution of PAD be included in all future women's 'heart health efforts'.

According to the US Department of Health and Human Services, peripheral artery disease (PAD) occurs in those over the age of 50 years with a history of cigarette smoking, hypertension, diabetes mellitus, abnormal lipid levels and personal or familial history of PAD, coronary artery disease (CAD) or cerebrovascular disease (CVD) [101]. PAD occurs when the leg arteries are hardened and clogged, reducing blood flow to the legs and feet. As a result, PAD has a major impact on leg functionality with the most common symptomatic presentation being exertional leg muscle fatigue, cramping or pain known as claudication [1–5]. Loss of function is caused by a lack of oxygen reaching the 'working' calf muscle. The most severe clinical manifestation of PAD is defined as critical limb ischemia (CLI) and these patients have the most symptomatic and dangerous form of PAD. Patients with CLI present with ulcers, rest pain or gangrene and require urgent revascularization to save their extremity. Patients with CLI represent approximately 1% of the total number of patients with PAD, with overall mortality in these patients approaching 50% at 5 years and 70% at 10 years. Patients with CLI experience significant morbidity, with cardiovascular event rates surpassing those with symptomatic CAD. CLI patients are at a higher risk for amputation and developing cardiovascular events and death than patients with PAD alone [6].

While symptoms may seem to be localized to the lower extremities, PAD is potentially indicative of other cardiovascular ischemic events [5]. It is now known to be associated with equal morbidity and mortality and comparable (or even higher) economic costs as coronary artery disease (CAD) and ischemic stroke (CVD). Over the last several years, clinicians and health organizations have documented this close relationship between

PAD and other widely-known cardiovascular diseases. In spite of these efforts, the cardiovascular impact of PAD is often still overlooked by mainstream society [4,5,7,8]. This oversight may contribute to disease mismanagement, particularly among women, which has furthermore led to preventable morbid and mortal events. To date, the major knowledge gap that exists relative to PAD and women is similar to the knowledge gap that existed some decades ago relative to CHD and women [7,8]. Even though the incidence of CAD was significant among women during that period, women were uninformed of their CAD risk. Like CAD, the disease burden of PAD among women may go under-recognized due to subtle gender-based differences in postmenopausal presentation, women's underrepresentation in clinical research in this area, gender-based measurement differences in PAD leg diagnostic testing and the lack of available large-population clinical research trials evaluating gender-based differences in clinical outcomes and presentations [7].

For decades, clinicians did not recognize the impact of CAD in women and now women in general and those with or at risk for CAD better understand the risk. Through the same measures taken to educate women about CAD, Hirsch *et al.* emphasize the urgency to prevent the same knowledge gap regarding PAD [7].

The proven association and overlap of PAD, CAD and CVD strongly suggests that being diagnosed with either CAD or CVD should mandate that the diagnosis of PAD be ruled out with an ankle brachial index (ABI) test. The ABI is the diagnostic tool for PAD. The ABI is measured with a Doppler device that is used to compare the ratio of the higher ankle systolic pressure to the higher brachial systolic pressure; the diagnosis of PAD is made if the ratio <0.90 [8].

Knowledge gaps in PAD & women

To date, three studies have been published on public awareness of PAD. Two cross-sectional population-based descriptive surveys conducted in the USA and Canada in 2005 and 2006 demonstrate an overwhelming lack of public awareness of PAD when compared with other common chronic diseases such as multiple sclerosis and Lou Gehrig's disease. Most Americans and Canadians are not aware that PAD is a major risk marker for heart attack, stroke, amputation and death. Additionally, the media and not the patient's healthcare giver was the common source of information about PAD [2,8]. In 2009, a cross-sectional study by Bush *et al.* focused on 162 women from a Veteran's Affairs Ambulatory clinic and reported that PAD awareness was poor among women at risk for CVD [3].

The burden of PAD is similar in both men and women but the prevalence is higher in minority women, and in patients with diabetes. Therefore African-American women, with their one nonmodifiable risk of ethnicity, as well as having an increased risk of hypertension, diabetes and obesity, should have an ABI if any of the other risks are present. The prevalence of diabetes is at least two- to four-times higher among African-American, Hispanic/Latino, American Indian and Asian/Pacific Islander women than among white women [102,103]. The risk for diabetes also increases with age. Because of the increasing lifespan of women and the rapid growth of minority populations, the number of women in the USA at high risk for diabetes and its complications is increasing [102].

Diet, physical inactivity and lower socioeconomic status lead to environmental exposures that cause obesity and increase the risk of diabetes [9]. Studies show that more women than men are obese (NHANES 2008 [103]). A recent study published also noted that long term adiposity status is prominently associated with advanced subclinical atherosclerosis and a particularly low ABI [10]. This information may lead to having obesity defined as one of the stated risk factors for PAD, particularly since the recent rise in obesity and subsequent development of diabetes, produced an epidemic in the USA that particularly affects women.

There are significant racial and ethnic disparities in obesity prevalence among US adults that spanned 1988–1994 (NHANES III) and are greater in the most recent survey which spanned 2007–2008 [103].

During 1988–1994, there were no significant differences between racial and ethnic groups in the prevalence of obesity among men. However between 2007–2008, the prevalence of obesity among men increased:

- From 20.3 to 31.9% among non-Hispanic white men.
- From 21.1 to 37.3% among non-Hispanic black men.
- From 23.9 to 35.9% among Mexican-American men.

Among women in 2007–2008, non-Hispanic black women (49.6%) were significantly more likely to be obese than non-Hispanic white women (33.0%). Similarly, Mexican-American women (45.1%) were more likely to be obese than non-Hispanic white women (33.0%). Similar disparities existed in 1988–1994 (22.9% of non-Hispanic white women, 38.3% of non-Hispanic black women, and 35.3% of Mexican-American women were obese). Even without symptoms, the educational process regarding PAD should be started early so that the complications of the disease can be anticipated and avoided.

Recommendations

- The proven association and overlap of PAD, CAD and CVD strongly suggest that being diagnosed with any one of them should mandate that the diagnosis of PAD be evaluated with an ABI;
- Reduction of the PAD knowledge gap can be achieved with improved efforts to provide PAD education of use to the patient, gynecologist, primary care clinicians and general public. Nearly all women have an annual visit to the gynecologist and an annual mammogram. Using recommendations for ABI as noted in the 2011 PAD Guideline focused update [2], a woman 50 years of age or older with a history of smoking or diabetes should have an ABI scheduled with her annual mammogram. This would permit achievement of an earlier PAD diagnosis and initiation of aggressive risk factor modification;
- The 'GO RED' program was used to increase awareness among women regarding CAD and a similar type of program would be helpful to emphasize the comparable importance of PAD;

- Women at risk for PAD should be informed of the common risk factors, symptoms and cardiovascular risk by all health professionals. Minority women who are African-American and Hispanic should be advised that the non-modifiable risk factor 'ethnicity', increases their risk;
- It is recommended that pre-existing cardiovascular programs and campaigns targeting CHD and CVD in women also incorporate PAD education and prophylactic therapies into their program models. Both a heart attack and stroke are caused by a lack of blood flow to the organ. An amputation and the symptoms prior to it are also caused by a lack of blood flow. It makes pathophysiological sense to describe it that way and it may help the clinician minimize the use of clinical jargon and ensure better understanding by the patient;
- Clinical trials assessing the efficacy of pharmacological, exercise and revascularization therapies should aggressively enroll females to reflect their prevalence in the general population;
- Pooled analysis of currently available data from supervised exercise studies could help overcome limitations of small sample size seen in many current clinical trials and

provide sufficient statistical power to conduct gender-specific analyses.

Conclusion & future perspective

Knowledge and awareness of PAD are poor among those individuals at risk for cardiovascular diseases. The aging of the population worldwide will result in increasing numbers of elderly patients with cardiovascular diseases. A focus on public education programs for men and women is necessary to improve awareness. Women live longer than men, and CVD is the main killer of women. It is imperative that women know that PAD is a marker for the leading cause of death and all of the recommendations above should be aggressively utilized.

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