Incidence of peripheral vascular disease in women: Is it different from that in men?

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Editorial Note: The gender initiative continues with editorials addressing noncardiac vascular surgery: (1) Experts discuss sex-based differences in the prevalence of vascular disease; (2) the pathophysiology, risks, and benefits of surgical treatment of carotid disease in women; (3) the need for clarifying optimal timing for surgical repair of abdominal aortic aneurysms in women and for refining endovascular repair technology for small patients; and (4) current outcomes (limb salvage, graft patency, and mortality) and future research in women with peripheral arterial occlusive disease. The series continues next month with editorials on end-stage heart failure.

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See related editorials on pages 318, 322, and 325.

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Knowledge of the clinical consequences of atherosclerosis and cardiovascular disease has grown tremendously over the years. Most persons, patients and physicians alike, understand and accept the critical importance of heart disease, yet the significance of noncardiac vascular disease remains largely underappreciated. The 3 major areas of noncardiac vascular disease include carotid artery occlusive disease, aortic aneurysmal disease, and peripheral arterial occlusive disease (PAD). These diseases, with their associated risks of stroke, limb loss, and death, are often undiagnosed and untreated despite being common causes of death and loss of function in the United States. Although previous studies have reported that the prevalence of vascular disease is greater in men than in women, that gap closes quickly with increasing age. As the American population ages, the prevalence of noncardiac vascular disease in women will increase, making it a leading cause of mortality and morbidity for women. The importance of disease prevention and detection of noncardiac vascular disease in women cannot be overlooked. To date, few studies have focused on the prevalence and importance of vascular disease in women.

Carotid Artery Occlusive Disease

Stroke is the third leading cause of death in the United States and a leading cause of permanent disability among older Americans. Nearly \$70 billion is estimated to be spent each year on the care of stroke survivors.¹ Most strokes are ischemic, and most ischemic strokes are caused by cerebrovascular disease. According to the Atherosclerosis Risk in Communities Study from the American Heart Association, approximately 83% of strokes are ischemic (thromboembolic), whereas 17% are hemorrhagic. The risk of stroke is reported to be 1.5 times greater in men than in women of the same age. The natural history of the patients experiencing a stroke suggests that only 50% will be alive at 5 years, with 38% dying from the initial stroke. Of those who survive the initial event, only 30% will function normally, and up to 5% will require custodial care. Any patient with symptoms of cerebrovascular disease should be managed aggressively because the sequelae of a stroke can be devastating. However, only 30% to 50% of patients have any symptoms before a stroke, and therefore the importance of detecting cerebral vascular disease cannot be overemphasized.

The benefit of carotid endarterectomy for both symptomatic and asymptomatic carotid artery stenosis has been well studied. However, those studies that examined the role of carotid endarterectomy for occlusive disease included a low percentage of women.^{2,3} Men comprise the majority of patients recruited for the major clinical trials on asymptomatic and symptomatic carotid disease. (Asymptomatic Carotid Atherosclerosis Study: 67% were men, and 33% were women; North American Symptomatic Carotid Endarterectomy Trial: 71% were men, and 30% were women; the Veterans Affairs cooperative study enrolled no women).⁴⁻⁷ A study that specifically reviewed the sex differences in carotid endarterectomy outcomes from Ontario, Canada, reported that only 35% of the 6038 patients in their registry were women.⁸ Consequently, conclusions have been drawn on the potential benefits of carotid surgery for women. These studies, however, might not necessarily reflect the

true incidence of the disease in women, and a clear understanding of cerebrovascular disease in women is clouded by a scarcity of studies with an adequate number of women.

Aortic Aneurysmal Disease

Abdominal aortic aneurysms (AAAs) account for at least 15,000 deaths per year in the United States. This figure might even be a gross underestimate because many patients with ruptured aneurysms are not given a diagnosis before their rupture, and furthermore, a number of these patients might not even make it to the hospital.^{9,10} Most surgical series suggest that AAAs are primarily a disease of elderly men, with the number of affected men outnumbering women.¹¹⁻¹³ Age-adjusted incidence for both asymptomatic and ruptured AAAs is 4 to 6 times higher in men compared with that in women.^{14,15} This risk of AAA increases with age, and the difference in prevalence between men and women closes in the eighth decade of life.

Although most patients with AAAs are asymptomatic and often are given a diagnosis during routine physical examination or evaluation for other disease processes, the mortality rate for those symptomatic can be as high as 90%. Rupture from AAA constitutes the 10th leading cause of death among men older than 55 years of age. When aneurysms are diagnosed early, they can be treated safely, with a mortality rate of 5% or less.¹⁶⁻¹⁹ Currently, many AAAs can be treated by using less-invasive techniques that avoid the need for major surgical procedures. However, when AAAs progress to rupture, they are fatal in more than half the cases. AAAs can be diagnosed easily in minutes without risk or discomfort by using duplex ultrasound scanning.²⁰⁻²² AAA and its pathogenesis remain a central concern in the study of vascular disease because of the incidence and catastrophic consequences of rupture.

As the population ages and the gap in prevalence of AAAs between men and women narrows, it will become increasingly important to determine specific risks that might affect women. Women are often given a diagnosis at a later age and are offered elective repair at a significantly lower rate than men.^{23,24} In addition, AAAs diagnosed in women are more likely to be ruptured at the time of diagnosis than is the case among men.²⁵ Women also are less likely candidates for current less-invasive techniques of repair, often because of anatomic limitations. Perhaps sex differences in outcomes of diagnostic and therapeutic procedures influence physicians' patterns in referring women for treatment.

Peripheral Arterial Occlusive Disease

PAD affects 8 to 12 million Americans. The estimate is that nearly 20% of persons older than 70 years of age have PAD. PAD is associated with a 5-fold to 6-fold increased risk of cardiovascular morbidity and death.^{26,27} Intermittent clau-

dication is the classic manifestation and is associated with impaired lifestyle and lower extremity functioning. Patients also might have limb-threatening ischemia. The ankle-brachial index (ratio of the systolic blood pressure in the ankle to that in the arm) is a reliable, simple, and objective measurement used to assess PAD.²⁸⁻³⁰ Many patients are not given a diagnosis of PAD until they have symptoms of intermittent claudication.³¹ It has been well documented that development of mild-to-moderate intermittent claudication poses a low threat of limb loss, with up to 75% of patients stabilizing or improving, whereas only 5% to 7% eventually require amputation. The effect of amputation can be devastating, with an overall survival rate of 50% or less at 10 years compared with 90% at 5 years in age-adjusted control subjects. Many patients with claudication, however, do not complain of symptoms and often accept difficulty in walking as part of the normal aging process.

Previous studies have shown that women are less likely to be given a diagnosis on the basis of symptoms but do have clinically significant PAD when tested.^{32,33} The traditional belief that the prevalence of PAD is greater in men than in women does not take into account that women might have more asymptomatic disease. Symptomatic PAD so predominates in men that many reports of surgical therapy do not investigate sex-specific outcomes.³⁴ Moreover, studies have shown that infrainguinal arterial reconstructions performed on women tend to be for more advanced disease compared with those in their male counterparts, and the women tend to be older.^{35,36} In addition, experience at the University of Maryland over the past 5 years disclosed that more than 50% of women who have PAD are seen initially with such advanced limb-threatening ischemia that they undergo primary amputation without the opportunity for revascularization (unpublished data). We speculate that some of the reasons women might be given diagnoses at a more advanced stage of ischemia are (1) that women might focus more on seeking medical care for their families than for themselves, (2) that women are more likely to ignore mild-to-moderate symptoms (attributing symptoms to "old age") and therefore present with more advanced occlusive disease, and (3) economic considerations. Without correcting for the more advanced presentation, women might appear to have worse outcomes as a group.

The American Vascular Association National Screening Program

Accurate incidence estimates for carotid artery disease, peripheral arterial disease, and aneurysmal disease have not been available because nationwide screening surveys of the population were not conducted until 2002. The American Vascular Association (AVA) then performed its first National Screening Program for carotid disease, AAA, and PAD in older Americans at high risk for atherosclerosis. In its first year, more than 850 persons were tested at 17

centers across the nation. The mean patient age was 65 years. More than 60% of those who presented for screening were women, and more than 13% of those tested had abnormal examinations. This screening was expanded to 48 centers in 2003, during which a total of 1587 persons were screened. Again more than 60% of those screened were women. The mean patient age was 68 years. These 2 screenings combined totaled 2446 persons (1479 women and 967 men).

Through the AVA screening, carotid artery stenosis (internal carotid artery stenosis >50%) was observed in approximately 8% of the population screened. An additional 2% were found to have severe carotid artery disease (80%-99%). Thus clinically relevant carotid artery disease was found in approximately 9% of the persons screened. Overall, carotid artery stenosis was significantly more likely in men (8%) than in women (6%, $P = .03$). Less than half (47%) of the persons determined to have more than 50% internal carotid artery stenosis were receiving antiplatelet medications (aspirin, clopidogrel, or ticlopidine) that might reduce their risk of stroke. Among those with 80% to 99% internal carotid artery stenosis, nearly one third (29%) were not receiving antiplatelet treatment. Interestingly, of those patients with carotid artery stenosis, men were more likely than women to be taking antiplatelet medications (58% vs 32%, $P = .0006$).

AAAs (aortic diameter >3.0 cm) were observed in 2% of the population screened; approximately 11% were more than 5.0 cm in diameter, and none of these had been diagnosed previously. Of the total persons in both screenings combined with an aorta of greater than 3.0 cm, 2% were women, and 4% were men. Although more AAAs were detected in men than in women during this screening, the ratio of men to women was not as disparate as traditionally reported.

PAD (ankle-brachial index <0.85) was observed in 9% of the population screened, 11% of men and 8% of women ($P = .001$). Among those observed to have PAD at the time of screening, less than half (47%) were not receiving medical treatments (eg, antiplatelet or lipid-lowering agents) that might reduce the risk of myocardial infarction and stroke (known incidence to be 2-3 times more common in those with PAD). As with carotid disease, men were more likely to be taking antiplatelet medications than women (58% vs 40%, $P = .0067$). Moreover, men were more likely (87%) than women (63%) to be receiving lipid-lowering medications ($P = .0062$).

Overall, this national screening program confirms that vascular disease is underdiagnosed and undertreated in a broad segment of the US population. Similarly, a regional screening program of 8476 persons in New England reported a high prevalence (37%) of previously undiagnosed peripheral vascular disease. Peripheral vascular disease was identified on the basis of either an ankle-brachial index of

less than 0.90, carotid artery stenosis of more than 15%, or AAA of greater than 3 cm in the population tested. As in the AVA national screening program, 67% of the population screened were women with a mean age of 65 years.³⁷ These screenings showed that although men were more likely to have carotid artery stenosis, PAD, and aneurysmal disease, the ratios are not as disparate as touted previously. Over the next 5 years, this annual AVA screening program will continue to expand, with a goal of greater than 5000 patients screened. The data collected will become the most comprehensive collection of information regarding the prevalence of vascular disease assembled.

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