

## Peripheral Arterial Disease Management in Women



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**L**ower-extremity peripheral arterial disease (PAD) affects approximately 8.5 million people in the United States and more than 200 million people worldwide.<sup>1,2</sup> Peripheral arterial disease is associated with similar morbidity rates, mortality rates, and costs to coronary artery disease and ischemic stroke. Additionally, PAD is associated with a reduced quality of life.<sup>3</sup>

For several years, the prevalence of PAD in women was considered to be less than or equal to that of men. However, recent studies have shown higher total population burden of PAD in women, particularly in age groups younger than 40 years and older than 80 years.<sup>3</sup> Given that PAD is correlated with age and women have a longer life expectancy than men, it is plausible that women will be disproportionately affected by PAD in the future as the population ages. Yet, PAD remains underdiagnosed in women, and women have been underrepresented in several PAD revascularization studies.

The traditional PAD risk factors include diabetes mellitus, cigarette smoking, advanced age, dyslipidemia, and hypertension.<sup>4</sup> Although these conventional risk factors are also involved in PAD development in women, there is growing evidence of additional comorbidities that are prevalent in women with PAD, such as depression and inflammation.<sup>5</sup> Such risk factors are not routinely evaluated in PAD studies, and further research is needed to clarify any existing association with PAD development.

Although intermittent claudication is considered the hallmark symptom of PAD, women with PAD may often be asymptomatic or present with atypical symptoms.<sup>3</sup> Thus, women with PAD are older in age at presentation compared with their male counterparts, more likely to present with critical limb ischemia (CLI), and less likely to undergo surgery.<sup>6</sup>

After lower-extremity bypass surgery, women have higher rates of graft failure, wound complication, and limb loss.<sup>7</sup> Interestingly, elevated baseline levels of C-reactive protein (CRP) and

fibrinogen have been associated with inferior vein-graft patency in women but not in men, suggesting an important interaction between sex and inflammation in the healing response of vein grafts following lower-extremity bypass surgery.<sup>8</sup> Perhaps women with elevated preoperative CRP and fibrinogen levels may benefit from more aggressive postoperative graft surveillance protocols.

In a PAD registry study with 12,379 patients (41% female) who underwent interventions including percutaneous balloon angioplasty, atherectomy, and stent placement, women were older and more likely to present with CLI compared with men, who most commonly presented with claudication.<sup>9</sup> In addition, women were more likely to have multilevel disease and required more femoropopliteal interventions. However, women had similar procedural success compared with men. Periprocedural adverse events including vascular complications, transfusions, and embolism were higher in women. This study is particularly important because the authors showed that women represent a large proportion of patients undergoing lower-extremity peripheral vascular interventions. Despite women having more severe and complex disease, they had similar procedural success when compared with the men in the study who had a less severe disease process.

More recently, randomized controlled trials have demonstrated significantly better outcomes for treatment of femoropopliteal lesions with drug-coated balloon (DCB) angioplasty.<sup>10</sup> However, in a German cohort subgroup analysis, a gender-related difference in primary patency and target-lesion revascularization was detected, suggesting that women may benefit more from treatment with DCB angioplasty.<sup>11</sup> However, other studies have had conflicting results and have shown female gender as a prognostic indicator for restenosis following DCB angioplasty.<sup>12,13</sup> Further investigation is necessary to detect a potential gender-related difference with respect to outcomes following DCB angioplasty.

Through collaboration between the University of California, San Francisco, the University of California, Irvine, and Dr Mahmood Razavi, a meta-analysis was performed to evaluate gender-related differences in the primary patency rate of DCB angioplasty for femoropopliteal lesions. The results of the study will be presented by Crystal Razavi at the upcoming Society for Interventional Radiology meeting in Washington, D.C.

Gender-related differences are present in the development and presentation of PAD. Such differences may also contribute to patient outcomes following interventions. In realizing this, we can design PAD clinical trials with equal sample sizes of men and women to evaluate for such gender-related differences, which may affect patient outcomes. In addition, we must raise awareness for the early diagnosis and management of PAD in women across all specialties in medicine.

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