Association of Peripheral Arterial Disease with All-cause Mortality, Cardiovascular Mortality and Cardiovascular Events

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Persons with Peripheral Arterial Disease (PAD) are at increased risk for all-cause mortality, cardiovascular mortality and cardiovascular events [1-20]. At 10-year follow-up of 565 persons, mean age 66 years, PAD significantly increased the risk of all-cause mortality (relative risk=3.1), of mortality from cardiovascular disease (relative risk=5.9), and of mortality from Coronary Artery Disease (CAD) (relative risk=6.6) [1]. At 4-year follow-up of 1,492 women, mean age 71 years, an Ankle-Brachial Index (ABI) of 0.9 or less was associated with a relative risk of 3.1 for all-cause mortality after adjustment for age, smoking and other risk factors [2].

In a prospective study of 291 women and men, mean age 82 years, with PAD, Coronary Artery Disease (CAD) was present in 160 persons (55%) [3]. Silent myocardial ischemia diagnosed by 24-hour ambulatory electrocardiography was present in 60 of 160 persons (38%) with PAD and CAD, and in 26 of 131 persons (20%) with PAD and no clinically manifest CAD [3]. At 43-month follow-up, new coronary events developed in 54 of 60 persons (90%) with PAD, CAD and silent myocardial ischemia, and in 39 of 100 persons (39%) with PAD, CAD and no silent myocardial ischemia [3]. New coronary events developed in 18 of 26 persons (69%) with PAD, no CAD and silent myocardial ischemia, and in 34 of 105 persons (32%) with PAD, no CAD and no silent myocardial ischemia [3].

A pooled analysis of mortality in 8 large randomized Percutaneous Coronary Intervention (PCI) trials of 19,867 persons showed that the presence of PAD was associated with higher rates of post-PCI death and myocardial infarction [4]. PAD was also an independent predictor of short-term and of long-term mortality [4]. At 7.5-year follow-up in the Cardiovascular Health study in a propensity-matched study of community dwelling older adults, matched hazard ratios for PAD for all-cause mortality, incident heart failure and symptomatic PAD were 1.57, 1.32, and 3.92, respectively [5]. In a well-balanced propensity-matched population of 2,689 persons with advanced chronic systolic heart failure, during 4.1 years of follow-up, PAD was significantly associated with increased mortality and hospitalization [6].

At 33-month follow-up of 414 persons with PAD and at 48-month follow-up of 89 persons without PAD followed in a vascular surgery clinic, the incidence of death, new stroke/transient ischemic attack, new myocardial infarction, new coronary revascularization, new carotid endarterectomy or new PAD revascularization was significantly higher in patients with PAD (63%) than in persons without PAD (24%) [7]. PAD was a significant independent risk factor for all-cause mortality with a hazard ratio of 2.2 [7]. At 5.3-year follow-up of 6,647 men and women between ages 45 to 84 years, an ABI of less than 1.0 was associated with a 77% significant increase in cardiovascular events, and an ABI of 1.40 or higher was associated with a 85% significant increase in cardiovascular events independent of other measures of subclinical cardiovascular disease [8]. At 5-year follow-up of 6,880 patients aged 65 years and older (593 with symptomatic PAD, 836 with asymptomatic PAD, and 5,392 with no PAD), all-cause mortality was significantly increased 89% in patients with symptomatic PAD and 66% in patients with asymptomatic PAD [9]. All-cause mortality or severe vascular event was significantly increased (hazard ratio=2.66) in patients with symptomatic PAD, and in patients with asymptomatic PAD (hazard ratio=1.81) [9]. Progression of PAD with a decrease in ABI of greater than 0.15 was significantly associated with an increase in all-cause mortality (relative risk=2.4) and cardiovascular mortality (relative risk=2.8) at 3 years, and with an increase in cardiovascular morbidity/mortality (relative risk=1.9) at 6 years independent of other risk factors [10].

Intermittent claudication was a significant independent predictor of all-cause mortality and of cardiovascular events in persons aged 40-64 years [11], aged 40-59 years [12] and aged 65 years and older [13]. At 5-year follow-up of 5,738 men aged 40-59 years, intermittent claudication was associated with a 2.2 times increased risk of all-cause mortality, a 2.6 times increased risk of cardiovascular mortality and a 2.9 times increased risk of coronary mortality [12].

At greater than 10-year follow-up in the Coronary Artery Surgery Study Registry of 2,296 patients with PAD and 13,953 patients without PAD with stable CAD, patients with PAD had a significant 25% increase in mortality [14]. Coronary events are the most important cause of long-term mortality and morbidity after peripheral vascular surgery [15]. Patients with PAD who undergo PCI have an increased rate of death and myocardial infarction [16]. At 2-year follow-up, 243 patients with PAD who underwent coronary artery bypass graft surgery had a significant increased 3.2 times risk of all-cause mortality than 346 patients without PAD [17]. Preoperative coronary revascularization in high-risk patients undergoing major vascular surgery was not associated with improved postoperative or long-term outcome compared with optimal medical management [18].

At 4-year follow-up of 1,537 patients in the Systolic Hypertension in the Elderly Program, patients with a decreased ABI had a significant increase in all-cause mortality (relative risk=3.00 for men and 2.67 for women) [19]. The post exercise ABI is also a significant predictor of all-cause mortality and adds additional risk stratification beyond the resting ABI [20]. These studies [1-20] and other studies have demonstrated a significant association between PAD and all-cause mortality, cardiovascular mortality and cardiovascular events.
References


