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Editorial Open Access

# Treatment of Intermittent Claudication due to Peripheral Arterial Disease

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## Editorial

Peripheral arterial disease may cause intermittent claudication which is pain or weakness with walking that is relieved with rest [1]. Patients with intermittent claudication should be treated with optimal medical therapy to reduce cardiovascular death, nonfatal myocardial infarction, and stroke and also to improve exercise time until intermittent claudication [1]. Optimal medical therapy to reduce cardiovascular events and mortality in patients with peripheral arterial disease include smoking cessation programs [1], treatment of hypertension [1-3], treatment of hypercholesterolemia [1,4], treatment of diabetes mellitus [1,5], antiplatelet drug therapy [1,6-8], treatment with an angiotensin-converting enzyme inhibitor [1,3], treatment with high-dose statins [1,4,9], and treatment with beta blockers if indicated in patients with mild-to moderate peripheral arterial disease [1,10]. Vorapaxar [11] has recently been approved by the United States Food and Drug Administration to treat patients with peripheral arterial disease receiving aspirin or clopidogrel to reduce the need for peripheral artery revascularization. This drug should not be used in patients with a history of stroke or transient ischemic attack or bleeding in the head.

The American College of Cardiology Foundation/American Heart Association guidelines recommend that cilostazol 100 mg orally 2 times daily is indicated to improve symptoms and increase walking distance in patients with intermittent claudication due to lower extremity peripheral arterial disease in the absence of heart failure [1]. In addition to reducing cardiovascular events and mortality, statins also have been demonstrated in randomized, placebo-controlled studies to improve exercise time until intermittent claudication [12-14]. A randomized, placebo-controlled trial showed that in 212 patients with intermittent claudication due to peripheral arterial disease, 24-week treatment with ramipril caused a significant 75 second increase in mean pain-free walking time, a significant 255 second increase in maximum walking time, and a significant improvement in the overall SF-36 median Physical Component Summary score by 8.2 [15].

Exercise rehabilitation programs have been found to increase walking distance in patients with intermittent claudication through improvements in peripheral circulation, walking economy, and cardiopulmonary function [16]. The optimal exercise program for improving claudication pain distance in patients with peripheral arterial disease uses intermittent walking to near-maximal pain during a program of at least 6 months [17]. Strength training is not as effective as a treadmill walking program [18]. A home-based walking exercise program significantly improved walking endurance, physical activity, and speed in patients with peripheral arterial disease and should be used by patients unwilling to participate in a supervised exercise training program [19]. The American College of Cardiology Foundation/American Heart Association guidelines recommend a supervised exercise program for patients with intermittent claudication [1]. Supervised exercise training should be performed for a minimum of 30-45 minutes in sessions performed at least 3 times per week for a minimum of 12 weeks [1], and preferably for 6 months or longer [17].

Endovascular procedures and surgical interventions for intermittent claudication are indicated for patients with intermittent claudication who have a vocational or lifestyle-limiting disability when clnical features suggest a reasonable likelihood of symptomatic improvement with the intervention and there has been an inadequate response to exercise and pharmacological treatment or there is a very favorable risk-benefit ratio as in focal aortoiliac occlusive arterial disease [1]. Patients with intermittent claudication should be considered for revascularization to improve symptoms only in the absence of other disease that would limit exercise improvement such as angina pectoris, heart failure, chronic pulmonary disease, or orthopedic limitations [1]. Endovascular or surgical intervention is not indicated as prophylactic therapy in an asymptomatic patient with lower extremity peripheral arterial disease or to prevent progression to limb-threatening ischemia in patients with intermittent claudication [1].

The Claudication Exercise Versus Endoluminal Revascularization (CLEVER) study randomized 111 patients with intermittent claudication due to aortoiliac peripheral arterial disease to optimal medical therapy, optimal medical therapy plus supervised exercise, or optimal medical therapy plus stent revascularization [20]. This study showed at 6-month follow-up that the greatest increase in treadmill walking performance occurred in the patients randomized to optimal medical therapy plus supervised exercise [20]. Seventy-nine of the 111 patients (71%) in the CLEVER study completed the 18-month clinical and treadmill follow-up assessment [21]. Supervised exercise consisted of 6 months of supervised exercise and an additional year of exercise counseling by telephone. Peak walking time increased from baseline to 18 months 5.0 minutes more with supervised exercise than with optimal medical therapy (0.2 minutes) ($p<0.001$) [21]. Peak walking time increased from baseline to 18 months 3.2 minutes more with supervised exercise than with optimal medical therapy (0.2 minutes) ($p=0.04$) [21]. These data support a supervised exercise program as a durable primary treatment of intermittent claudication due to peripheral arterial disease [21].

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