The effect of supervised exercise therapy for intermittent claudication on lower limb lean mass

Simon Vui Vun, BMedSc, MBBS (Hons),[a] Michelle D. Miller, MNutDiet, PhD,[b] Christopher L. Delaney, BM, BS, PhD,[a] Richard B. Allan, BHlthSc (Hons), DMU,[a] *and* J. Ian Spark, MBChB, MD,[a] *Bedford Park, South Australia, Australia*

ABSTRACT

Objective: Supervised exercise is currently recommended for the first-line treatment of intermittent claudication based on improvement in walking capacity. However, the promotion of skeletal muscle atrophy by repetitive ischemia-reperfusion caused by treadmill-based programs remains a concern. Because preservation of skeletal muscle mass (SMM) and lean mass (LM) is integral to functional capacity and longevity, this study measured the effect of standard treadmill-based supervised exercise on SMM and regional lower limb LM in patients with intermittent claudication.

Methods: Patients with calf claudication caused by infrainguinal peripheral artery disease underwent whole-body dual-energy X-ray absorptiometry scanning before and after completion of a 12-week supervised treadmill exercise program. Total body SMM and lower limb LM were measured according to anatomical regions of the lower limb (thigh vs calf) and side of symptoms. Walking performance was assessed using pain-free walking distance and 6-minute walking distance tests.

Results: Thirty-six patients with calf claudication completed exercise training and dual-energy X-ray absorptiometry scanning, allowing analysis of 55 symptomatic and 17 asymptomatic lower limbs. No difference in total body SMM ($P = .41$) or LM of symptomatic ($P = .53$) or asymptomatic calves ($P = .59$) was detected after the program. In contrast, a significant decrease in LM was observed in symptomatic ($P = .04$) and asymptomatic thighs ($P = .005$). Pain-free walking distance ($P = .001$) and the 6-minute walking distance both improved significantly ($P = .004$) but were not associated with changes in LM.

Conclusions: Twelve weeks of standard treadmill-training for intermittent calf claudication did not result in loss of calf LM; however, a significant decrease in bilateral thigh LM was observed, even in patients with unilateral symptoms. Further research on optimum exercise modalities and end points are required to determine the pathophysiology and effects of these changes on function and survival. (J Vasc Surg 2016;■:1-7.)

Peripheral artery disease (PAD) is an atherosclerotic disease estimated to affect >200 million people globally.[1] Ischemic muscle pain affecting the legs is the most common manifestation of PAD, and many guidelines prescribe supervised walking exercise as the first line of treatment based on growing evidence of short-term improvements in walking performance.[2-5] In contrast to interventions for other cardiovascular diseases, evidence is sparse regarding the mechanisms that improve walking performance or whether they translate into survival benefit.[6] Alterations to muscle function are thought to explain some of the improvement in walking performance as a result of supervised exercise programs (SEPs), with a number of studies demonstrating changes in muscle architecture, mitochondrial content, and fiber type.[7,8] These adaptations are currently thought to be beneficial; however, repetitive exercise of an ischemic muscle group is accompanied by an ischemia-reperfusion phenomenon that may be deleterious to muscle function and, perhaps, the whole patient longer-term.

Previous work has demonstrated that patients with increasing severity of lower limb PAD have reduced calf muscle cross-sectional area suggesting a negative relationship between ischemia and muscle mass.[9] In addition, lower limb muscle strength is adversely affected by chronic ischemia, with lower ankle-brachial pressure index (ABI) values associated with weaker lower limb strength.[10,11] However, treadmill-based exercise programs have not been found to improve lower limb strength.[12,13] In fact, a loss of bilateral leg strength has been reported when patients change from a resistance-training program to a treadmill-training program.[13]

Given the known association between lower limb strength and death in patients with PAD, preservation of strength and muscle mass is undoubtedly vital.[14]

From the Department of Vascular Surgery,[a] and Nutrition and Dietetics,[b] Flinders University.

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Correspondence: J. Ian Spark, MBChB, MD, Department of Vascular Surgery, Flinders University, Flinders Dr, Bedford Park, SA 5007, Australia (e-mail: ian.spark@sa.gov.au).

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Moreover, a recent randomized controlled trial in which standard treadmill walking was compared with combination walking and resistance exercise demonstrated that a treadmill-only exercise program elevated activity of muscle calpain, a protease implicated in myocyte damage and apoptosis, whereas combination training did not.[15] In addition, change in lean mass (LM) after 12 weeks of treadmill-only training showed a decline, whereas symptomatic lower limb LM increased when combined with resistance-training.[15] Together this suggests that prolonged exercise of muscle groups under ischemic conditions may accelerate muscle atrophy.

What is not known is whether the changes in muscle mass are regional, affecting proximal or distal muscle groups related to blood supply. This study therefore tested the hypothesis that standard treadmill training for calf claudication adversely affects regional lower limb skeletal muscle mass (SMM), despite improvements walking performance, in patients with calf claudication secondary to infrainguinal PAD.[16]

METHODS

The Southern Adelaide Local Health Network Human Research Ethics Committee approved this study, and participants provided written informed consent.

Sample. Patients presenting to the Southern Adelaide Local Health Network Vascular Surgery outpatients clinics between January 2013 and December 2014 were screened for eligibility. Inclusion criteria consisted of a clinical history of calf claudication along with low ABI (<0.9) and duplex ultrasound scanning or computed tomography angiographic evidence of infrainguinal disease in the absence of significant aortoiliac disease. Patients were excluded if they (1) had evidence of rest pain or tissue loss; (2) had recently (<12 months) undergone peripheral vascular revascularization; (3) had recent exercise training; (4) suffered blood dyscrasias or were anticoagulated; or (5) had cardiorespiratory morbidities limiting exercise capacity. Those who met the inclusion criteria were offered a 12-week program of twice-weekly supervised treadmill walking.

Additional data on 11 patients who were part of a treadmill-only training arm of a randomized controlled trial were also included in the data analysis.[17] Inclusion and exclusion criteria were identical between studies, as were the exercise regimen, as described below, and the measurements of physical variables and collection of blood and tissue samples.

Exercise regimen. The SEP lasted 12 weeks and consisted of two 60-minute supervised exercise sessions per week. The program took place in the Repatriation General Hospital Rehabilitation Gymnasium and was supervised by a senior clinical physiotherapist or exercise physiologist with experience in administering exercise interventions for patients with cardiorespiratory disease. In accordance with international guidelines, participants were instructed to begin walking at a speed and incline to induce claudication pain within 3 to 5 minutes, stop and rest until pain abated, then repeat for the duration of the 1-hour session.[3] Initial treadmill speed was commenced at the average speed calculated from the result of the individual's initial 6-minute walk distance (6MWD) test. During each training session, the physiotherapist monitored the patient's progress to ensure onset of symptoms ≤5 minutes of walking. If patients were able to walk >5 minutes without symptoms, the workload of the treadmill was first adjusted by increasing the speed up to the patient's maximum safe walking speed and then by increasing the incline.

Exercise testing. All participants were assessed by a physiotherapist within the week before commencing the exercise program and within 1 week after completing the program using a standardized over ground 6MWD test.[17] The pain-free walking distance (PFWD), defined as the distance at the first sign of claudication, and the total 6MWD were recorded.

Testing. Between 1 and 2 weeks before and after the 12-week exercise program, participants attended a research clinic where comorbidities and current medications were recorded and routine blood investigations, body measurements, and dual-energy X-ray absorptiometry scans (DEXAs) were obtained, as described below.

Regional muscle mass quantification. Whole-body composition scanning was performed using a DEXA system (Lunar Prodigy, GE Healthcare, Hertfordshire, United Kingdom) with EnCORE 10.51.006 software (GE Healthcare). Participants were positioned supine on the DEXA table top with their feet in a neutral position and hands flat by their sides. After acquisition, whole-body composition was estimated using default automated segmentation. Appendicular soft tissue LM was then used to determine total body SMM according to previously validated methods.[18]

For regional body composition, custom regions of interest (ROI) were traced manually over the DEXA planogram to segment the lower limb into thigh and leg regions. This study defined the thigh as the part of the lower limb between the hip and knee joint and the calf as the part of the lower limb below the knee joint. ROI borders were adapted from previously validated methods.[19]

The proximal extent of the thigh ROI was modified because it was defined by an angled line connecting the lateral aspect of the anterior superior iliac spine and the inferior ramus of the pubis. This line is influenced by sex, with men having a more vertical line than women, given their taller and narrower pelvic structure. The potential effect of this is exclusion of proximal medial thigh musculature and contamination by lower