Exercise as an Intervention for Peripheral Arterial Disease

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Peripheral arterial disease (PAD) occurs when plaques build up in arteries that supply blood to areas other than the heart. These plaques are made up of fat, cholesterol, calcium, fibrous tissue and other substances in the blood. Over time what occurs is atherosclerosis, wherein the plaques harden and narrow the arteries, thereby limiting the flow of oxygen-rich blood to areas such as the lower extremities.

The global burden of PAD is extensive and rising, resulting in substantial morbidity and mortality across all walks of life.[1] Patients living with PAD are at risk for myocardial infarction, ischemic stroke, heart failure, renovascular hypertension and vascular death. More localized complications include pain (both at rest and with exercise), decreased function and ulceration of the foot and lower leg, potentially leading to amputation.[1]

Patients may present with a range of symptoms, from none at all to atypical and typical symptoms of claudication. Typical claudication is described as calf pain that is relieved by rest. Approximately one-third of patients have typical claudication,[2] which limits function; however, those who experience atypical symptoms also have associated decreased overall functional exercise capacity.[1]

Why This Matters

Perhaps the most important impacts of PAD for patients are claudication pain, decreased function and decreased exercise capacity. Patients with PAD have approximately 50% reduction in peak exercise performance when compared with those who are age-matched and healthy.[2]

Exercise limitation correlates with marked impairments in daily physical activity.[3] Patients with PAD have also been shown to have an accelerated functional decline over time that is related to the underlying hemodynamic severity of disease in the leg.[4] Impairment in walking ability has been associated with reduced quality of life, a higher prevalence of depression and overall higher mortality.[5]

The Role of Exercise Therapy

Based on the above considerations, the primary goals for

patients with PAD should be to decrease cardiovascular risk, decrease pain, improve exercise performance, enable daily functional activity and enhance quality of life. Exercise therapy has the potential to achieve these goals. Regular and intensive walking programs have been shown to improve walking ability in patients with PAD more than usual care.[6]

A considerable body of evidence[7,8,9] supports the clinical benefits of exercise programming to improve claudication, exercise performance and quality of life in patients living with PAD.

While treadmill walking is the most common therapy studied, other studies have investigated alternative exercise training approaches. Arm ergometry

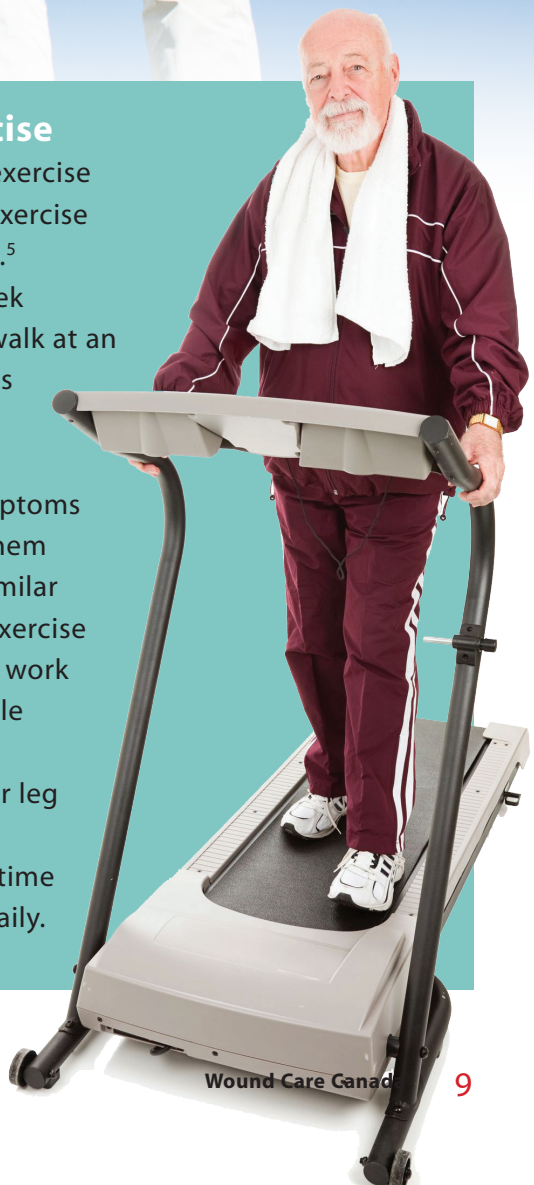
Prescription for Exercise

The following is an optimal exercise prescription for supervised exercise training in patients with PAD.[5]

Frequency: 3–5 days per week

Intensity: Have the patient walk at an incline and rate that creates moderate leg symptoms within 3 to 5 minutes. They should then stop until symptoms resolve completely. Have them resume the exercise at a similar intensity, and repeat rest/exercise bouts. Progress to a higher work rate when the patient is able to walk for 8-minute bouts without needing to stop for leg symptoms.

Duration: The total exercise time should equal 50 minutes daily.



Caution!

People with wounds, particularly those with an active arterial wound or at a critical ischemia stage, people with diabetes and loss of protective sensation, and especially those with a history of ulceration need to be extremely cautious when exercising, and weight-bearing activity may be contraindicated. Activities such as recumbent biking or arm ergometry may be safer and more appropriate. These individuals should not be exercising without proper assessment and supervision.

On the other hand, exercise such as walking is encouraged for people with lower extremity wounds due to venous disease or lymphedema, provided they have intact sensation.

In all cases, the full history of the patient should be investigated before initiating this, or any, program to determine if the program is safe.

Table 1: Physiological Response to Exercise in Patients with PAD*

Healthy Physiology	PAD Pathophysiology	Functional Consequence	Effect of Exercise
Arterial flow	• arterial obstruction	• reduced blood flow • inability to meet metabolic demand of exercise	• minimal increase in collateral flow
Tissue responses to the need for increased blood flow	• endothelial and micro-vascular dysfunction	• decreased vasodilation • increased arterial stiffness • impaired hyperemic response • impaired arterial remodelling • increased inflammatory remodelling	• improved nitric-oxide-dependent vasodilation
Muscle metabolism	• mitochondrial dysfunction • oxidative stress • altered muscle composition	• impaired energy production • impaired oxygen utilization • increased reactive oxygen species • muscle apoptosis and atrophy • fibre type switching • fibre denervation • reduced skeletal muscle content	• increased mitochondrial biogenesis in animal models (increased ATP production) • improved glucose and fatty acid metabolism • improved peripheral nerve function
Inflammation	• inflammatory activation	• adverse skeletal muscle remodelling • increased atherosclerotic progression	• decreased markers of systemic inflammation

Adapted from Hiatt 2015.[1]

(pedaling on a special machine with arms instead of legs) increases walking performance and decreases pain in patients with claudication and may be an appropriate exercise modality for patients who have difficulty performing treadmill walking or for whom walking may be contraindicated, such as those with lower extremity wounds.[10]

Physiological Response to Exercise in Patients with PAD

Multiple mechanisms contribute to reduced exercise capacity in PAD, and exercise contributes to physiological processes to positively affect these mechanisms (Table 1).

Conclusion

As demonstrated by the information contained in Table 1, exercise provides multiple benefits through many physiological mechanisms for patients with PAD, including reduction of limb symptoms, improved functional capacity and reduced cardiovascular risk.

The bottom line? Supervised exercise programs should be considered a frontline treatment for patients with PAD.

***Notes:**

Arterial Flow

Vascular adaptations that enhance distal blood flow could underlie the benefits of exercise therapy in PAD. In animal studies, exercise training augments peripheral artery supply, but this has not translated convincingly to studies of people with PAD.[5] Maximal hyperemic blood flow increased in patients in some[13] studies but not in other exercise training studies.[14] A meta-analysis of seven exercise training studies failed to demonstrate a change in resting ankle-brachial pressure index.[15] An anatomic model of increased blood supply does not account for all of the functional improvements gained with exercise.

Endothelial Function

Healthy blood flow relies on patent arteries to get the blood to where it needs to go as well as a vascular system that can regulate flow. A supervised exercise program increased endothelium-dependent, flow-mediated dilation of the brachial artery by 65% in 19 elderly patients with intermittent claudication.[16] In a randomized controlled trial comparing treadmill walking to lower extremity strengthening and to usual care for PAD, treadmill walking produced the greatest flow-mediated dilation, indicating improved endothelial health in the brachial artery.[17] A study of patients with coronary artery disease showed increased endothelial nitric oxide synthase expression and activation, indicating favourable effects on coronary artery endothelial function with exercise rehabilitation.[18] Exercise-induced improvements in vasodilator function may have the potential to reduce cardiovascular risk.

Muscle Metabolism

Impairments in metabolism at the level of skeletal muscle combined with compromised blood flow have the potential to amplify physical limitation. In experimental models of ischemia, key regulators of mitochondrial biogenesis increase with exercise. These regulators are also important for capillary growth in skeletal muscle.[5]

Inflammation

High levels of inflammation are associated with PAD progression and adverse cardiac and lower extremity outcomes.[5] Inflammation may accelerate functional impairment by favouring plaque growth and inducing skeletal muscle injury. Lower levels of inflammatory markers are found in individuals who participate in regular physical activity. There is an inverse association with C-reactive protein levels and amount of physical activity in patients with PAD. Acute bursts of activity tend to increase inflammatory markers, and chronic exercise training decreases inflammation.[19]

Supervised or Go-it-alone?

Supervised exercise programs have been shown to deliver greater improvement than unsupervised programs.[11] In the case of patients with PAD, supervised programming may enable better adherence and greater intensity of treadmill exercise compared to normal walking. There is limited supporting symptom-based evidence for simply advising patients to walk more independently,[5] though this may have other health benefits. Unsupervised training does have benefits, and it may be an option for patients without access to supervised programs. It may also work as a viable transition for those who have already undergone a supervised program.[12]

References

1. Hiatt W, Armstrong E, Larson C, Brass E. Pathogenesis of the limb manifestations and exercise limitation in peripheral artery disease. Circ Res. 2015;116:1527–1539.
2. McDermott M, Mehta S, Greenland P. Exertional leg symptoms other than intermittent claudication are common in peripheral artery disease. Arch Intern Med. 1999;159:387–392.
3. Gardner A, Killewich L, Katzel L, Womack C, Montgomery P, Otis R, et al. Relationship between free-living daily physical activity and peripheral circulation in patients with intermittent claudication. Angiology. 1999;50:289–297.
4. McDermott M, Lui K, Greenland P, Guralink JM, Criqui M, Chan C, et al. Functional decline in peripheral artery disease: Associations with the ankle brachial index and leg symptoms. JAMA. 2004;292:453–461.
5. Hamburg N, Balady G. Exercise rehabilitation in peripheral artery disease: Functional impact and mechanisms of benefit. Circulation. 2011;123(1):87–97.
6. Lyu X, Li S, Cai H, Lui G, Ran X. Intensive walking exercise for lower extremity peripheral artery disease: A systematic review and meta-analysis. J Diabetes. 2016;8(3):363–77.
7. Tendera M, Aboyans V, Bartelink ML, Baumgartner I, Clément D, Collet JP, et al. ESC guidelines on the diagnosis and treatment of peripheral artery diseases: Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries. The Task Force on the Diagnosis and Treatment of Peripheral Artery Diseases of the European Society of Cardiology (ESC). Eur Heart J. 2011;32(22):2851–2906.
8. Gerhard-Herman MD, Gornik HL, Barrett C, Barshes NR, Corriere MA, Drachman DE, et al. 2016 AHA/ACC guideline on the management of patients with lower extremity peripheral artery disease: Executive summary. A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2016;135(12).
9. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris HA, Fowkes FG. Inter-society consensus for the management of peripheral arterial disease (TASC II). J Vasc Surg. 2007;45(1):S5A–S67A.
10. Treat-Jacobson D, Bronan U, Leon A. Efficacy of arm-ergometry versus treadmill exercise training to improve walking distance in patients with claudication. Vasc Med. 2009;14:203–213.
11. Fokkenrood HJ, Bendermacher B, Lauret GJ, Willingendael EM, Prins MH, Teijink JA. Supervised exercise therapy versus non-supervised exercise therapy for intermittent claudication. Cochrane Database Syst Rev. 2006;2(2).
12. Gardner A, Parker D, Montgomery P, Blevins S. Step-monitored home exercise improves ambulation, vascular function, and inflammation in symptomatic patients with peripheral artery disease: A randomized controlled trial. J Am Heart Assoc. 2014;3(5).
13. Hiatt W, Regensteiner J, Hargarten M, Wolfel E, Brass E. Benefit of exercise conditioning for patients with peripheral arterial disease. Circulation. 1990;81:602–609.
14. Larson O, Lassen N. Effect of daily muscular exercise in patients with intermittent claudication. Lancet. 1966;2:1093–1096.
15. Watson L, Ellis B, Leng G. Exercise for intermittent claudication. Cochrane Database Syst Rev. 2008;2(2).
16. Brendle D, Joseph L, Gardner A, Katzel L. Effects of exercise rehabilitation on endothelial reactivity in older patients with peripheral artery disease. Am J Cardiol. 2001;191:384–390.
17. McDermott MM, Ades P, Guralnik JM, Dyer A, Ferrucci L, Liu K, Nelson M, et al. Treadmill exercise and resistance training in patients with peripheral artery disease with and without intermittent claudication: A randomized control trial. JAMA. 2009;301:165–174.
18. Hambrecht R, Adams V, Erbs S, Linke A, Kränkel N, Shu Y, et al. Regular physical activity improves endothelial function in patients with coronary artery disease by phosphorylation of endothelial nitric oxide synthase. Circulation. 2003;107:3152–3158.
19. Tisi P, Shearman C. Biochemical and inflammatory changes in the exercising claudicant. Vasc Med. 1998;3:189–198.

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