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. 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.

A considerable body of evidence 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.

**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*

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

Adapted from Hiatt 2015.
(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..END

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*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.¹¹ Maximal hyperemic blood flow increased in patients in some 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. 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, 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.

References

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