

41. *Peripheral arterial disease*

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Summary

Peripheral arterial disease (intermittent claudication) is typically age-dependent and is not uncommon after the age of about 65 years. Exercise training in peripheral arterial disease leads to an increased walking distance and reduced pain, and likely also a slowed progression of the disease process itself. For optimal effect, the exercise should be carried out as walk training, preferably intermittently, a minimum of 3 times per week, 30 minutes per session, and over a period of at least 6 months. The biggest effect is achieved through supervised training programmes. Suitable activities include brisk walks and Nordic walking.

Definition

Peripheral arterial disease (intermittent claudication) is typically age-dependent and is not uncommon after the age of about 65 years. Claudication refers to pain in the muscles of the legs upon exertion, such as walking, where symptoms disappear after a short rest, usually a few minutes. The prevalence, that is, the frequency in the population, can be estimated at 1.5 per cent before the age of 50 years, increasing to over 10 per cent in people over 65 years. If the symptoms become worse, that is, the patient experiences pain at rest, persistent sores and/or gangrene, one generally speaks of critical ischaemia (insufficient blood supply to the tissues). Progression to critical ischaemia is not particularly common in intermittent claudication, however, but the risk increases in patients who smoke or have diabetes. The problem is due to narrowing or complete blockage of the arteries that supply the muscles, resulting in impaired perfusion (blood supply).

Various studies have determined the risk factors for intermittent claudication in patients with no prior disease as well as progression to more severe ischaemia of the extremities in

patients with claudication. These risk factors include age, male gender, smoking, diabetes, hypertension, high blood lipid levels and high fibrinogen. A patient with claudication usually seeks medical attention for impaired quality of life due to shorter walking distance, and one problem with treatment is that reduction of the noted risk factors, some of which can be influenced, does not have an immediate effect on the patient's symptoms. An effect may instead be seen in the longer perspective, and then also in the form of improved survival. In that the number of elderly persons in the population is increasing and smoking habits have not changed radically, we can anticipate an increased prevalence of the disease in coming decades. The treatment for claudication is usually conservative, whereas critical ischaemia often requires surgery, which can be performed using different methods.

Effects of physical activity

Physical exercise to improve walking distance is a treatment method where experience suggests a beneficial effect on the symptoms. "Stop smoking and keep walking" is the five-word phrase coined by Scottish internal medicine specialist Housley (1) to describe the treatment of claudication. The aim of this chapter is to discuss in more detail the potential effects of exercise and the scientific bases that suggest that an effect actually does exist.

As early as 1898, Erb (2) from Heidelberg gave a detailed description of intermittent claudication, also pointing out the importance of exercise as a treatment, but it was not until the 1950s that the idea was raised again more systematically (3). The effect of exercise training in connection with peripheral vascular disease is well-documented in meta-analyses and review studies (4–7).

An important factor to consider when evaluating treatment therapies for ischaemia of the extremities is whether there is a correlation between walking distance and the patient's subjective well-being, measured as quality of life. Several studies show that this is the case (8, 9). Walking distance must be measured with objective methods because both the patient's and physician's perception of walking distance can be surprisingly inaccurate (10).

There are several possible explanations as to why exercise may have an effect on intermittent claudication:

- **Increase in blood flow.** The discussion of this possible explanation has been lively, and the general opinion today is that good effects can be achieved from exercise without increased blood flow. The increased flow may be a small part of the explanation, but most studies have not shown any effect (11, 12).
- **Increased collateral development** has been considered but is increasingly questioned due to the absence of effect on blood flow and pressure on the ankle (see above). In any case, there is a poor correlation between possible increase in flow and change in walking distance (13).
- **Effects on muscle metabolism.** Exercise gives rise to various structural and functional changes in the muscles, such as a slower metabolism of glycogen, increased oxidation of fatty acids, high levels of oxidative enzymes, and an increase in the number of

mitochondria per volume unit. The increase in walking distance after exercise training correlates to a reduction in acyl-carnitine plasma levels, which reflect metabolic dysfunction.

- **Improved cardiopulmonary function** is due, among other things, to increased oxygen utilisation after exercise and a reduced heart rate.
- **Psychological effect**. Exercise increases overall well-being. According to Rosfors and colleagues (14), the most important factor in predicting a positive effect from a training programme is the patient's expectation that it will have an effect. An effect via the endorphin system has been suggested, though this has not been proven.
- **Increased muscle strength.**
- **Change in gait pattern.**
- **Change in perception of pain.**

There has been discussion of whether exercise can have an adverse effect due to an inflammatory response during the walking or possibly during the resting phase as a partial phenomenon in a reperfusion syndrome (15, 16). A more general harmful effect of exercise has been suggested to be reflected in the form of microalbuminuria (17). However, it has not been proven that exercise leads to any harmful clinical effects, but rather the inflammatory response is reduced with increased exercise (18). Treadmill training does not increase plasma markers that indicate endothelial injury (19).

Prescription

The recommendation of the Trans-Atlantic Inter-Society for Management of Peripheral Arterial Disease (TASC) for exercise therapy for intermittent claudication states that:

- Supervised exercise should be made available as part of the initial treatment for all patients with peripheral arterial disease.
- The most effective programmes employ intermittent walk therapy that is of sufficient intensity to bring on claudication, followed by rest, for 30–60 minutes, 3 times per week for at least 3 months (20)

A good summary of the effect of exercise training can be found in a meta-analysis by Gardener and Poehlman (4). In a final analysis of 21 studies, which met the required inclusion criteria, six components of the exercise programme were registered for evaluation:

1. Exercise frequency (per week).
2. Duration of exercise (minutes per session).
3. Mode of exercise (walking or combined exercise).
4. Total duration of programme (weeks).
5. Pain used as the endpoint (initial pain or maximal walking distance).
6. Level of supervision (supervised systematic exercise or exercising on one's own in the home).

Overall, the walking range increased significantly from the exercise programmes. The distance to onset of pain increased by 179 per cent or 225 metres, and the maximal walking distance increased by 122 per cent or 397 metres. These can be considered clinically significant improvements. Factors of the exercise programme that were of significant value in the increase of walking distance indicated an exercise frequency of 3 or more times per week, a duration of more than 30 minutes, a total programme length of more than 6 months, and only walking as opposed to combined exercise. The level of supervision seemed to be of less importance, but for many patients exercising in a group motivates them more to continue than exercising alone. Randomised studies suggest the importance of proper supervision in the exercise training (9). The clinical effect of exercise is impacted positively if the patient also quits smoking (19). The optimal exercise programme remains, however, to be defined (5).

Exercise programmes also have a generally beneficial effect on cardiovascular risk factors (20–22) and cardiorespiratory function (11). Exercise also improves the quality of life (23).

In conclusion, exercise training for intermittent claudication leads to an increase in walking distance, with higher quality of life and reduced pain, and probably also slowed progression of the arteriosclerotic disease process. It would appear that the biggest effect is achieved with supervised exercise programmes of 3–6 months. A recently published report from the Swedish Council on Technology Assessment in Health Care (SBU) concludes that, in patients with peripheral arterial disease, supervised exercise therapy leads to increased physical activity, measured as walking distance and/or walking time. The best results are achieved if the exercise is supervised to begin with, is conducted in 30–60-minute sessions 3 or more times per week, at an intensity close to the pain threshold, and lasts for at least 6 months (level of evidence: 3) (7).

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