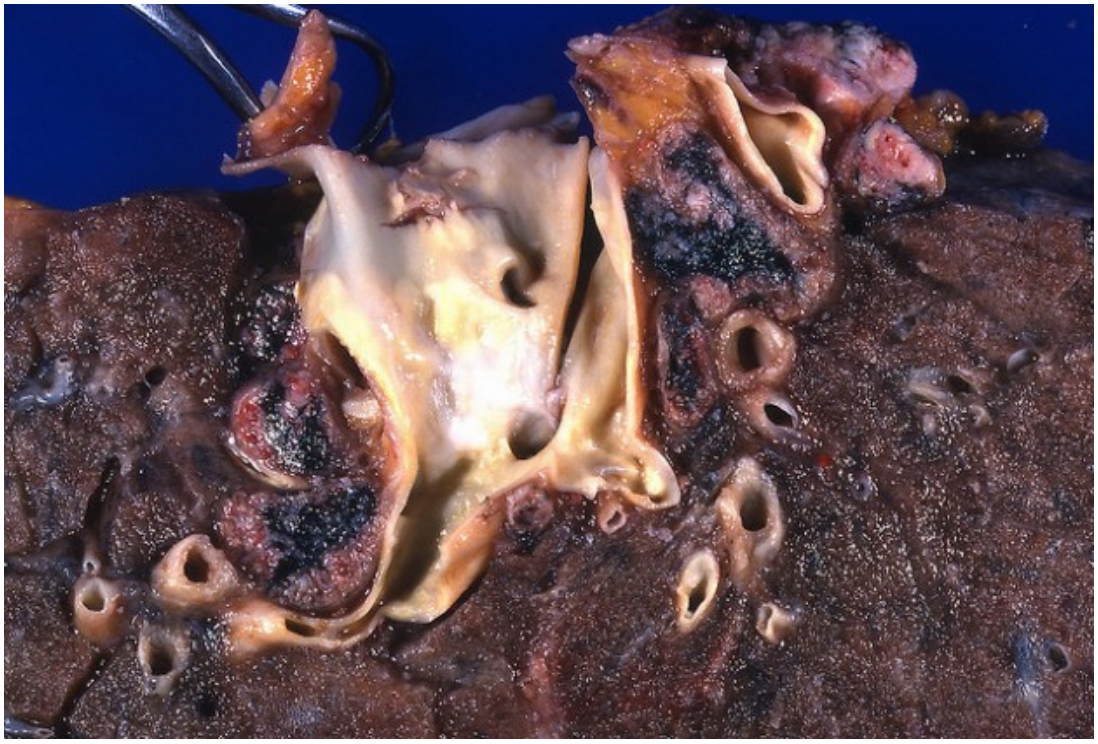
Atherosclerosis (Atherosclerotic Cardiovascular Disease) — Definition and Pathology

See online here

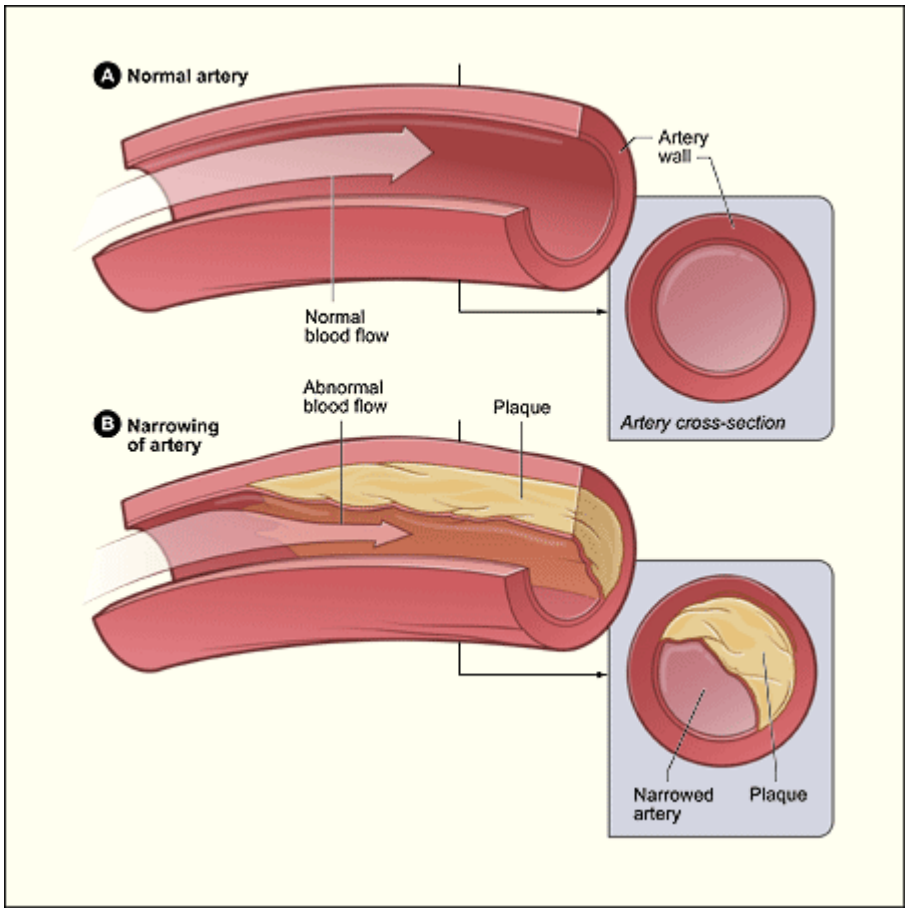
Atherosclerosis is an incurable disease. However, it has clearly defined risk factors that can often be reduced through a change in the lifestyle of the patient. It is the most common primary disease of the arterial vascular system and is responsible for coronary heart disease, the leading cause of death worldwide.



Definition

The term atherosclerosis is derived from the words ‘atheroma’ (focal plaques) and ‘sclerosis’ (multiplication of connective tissue). Atherosclerotic changes take place in the intima and media of blood vessel walls and lead to a stiffening of the vessel walls and narrowing of the **vessel lumen.**

Atherosclerosis includes **atherosclerosis, media sclerosis**, and **arteriolosclerosis.**



Epidemiology

Atherosclerosis is the leading cause of death in industrialized countries. More deaths result from cardiovascular disease than from Alzheimer’s disease, accidents, and cancer combined. Over 152,000 Americans that experience cardiovascular mortality every year are under the age of 65. In 2002, 32% of deaths from cardiovascular disease occurred prematurely (i.e., before age 75, which is close to the average life expectancy).

Etiology

Atherosclerosis is an inflammatory disease of the vessels, which is due to a reaction to oxidized LDL cholesterol. Storage of lipids, calcium, and cellular debris occurs mostly in the intima of large and medium-sized arteries. This leads to a thickening of the vessel walls and the formation of plaques.

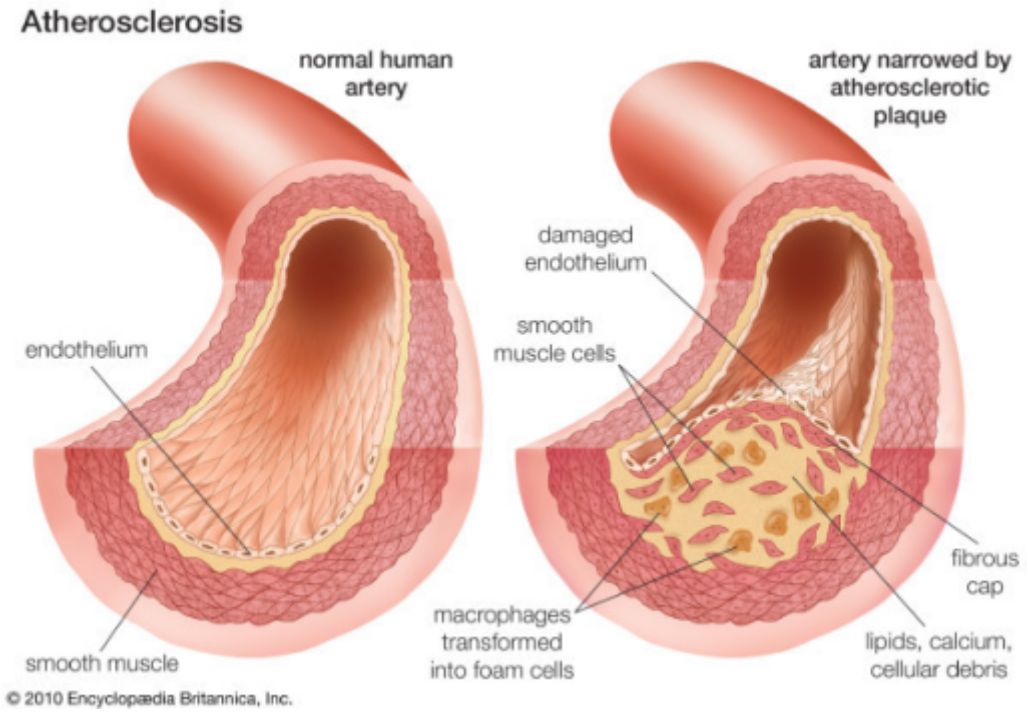


Image: "Coronary atherosclerosis." by Openi. License: CC BY 2.0

Risk factors for atherosclerosis can be modifiable or non-modifiable. Non-modifiable risk factors are male sex, age, and family history. Modifiable risk factors can be divided into first and second-order risk factors.

First-order modifiable **risk factors**

- **Nicotine abuse:** Smoking promotes an early emergence and rapid progression of atherosclerosis
- **Arterial hypertension:** Through increased pressure loads, damage occurs faster in the **endothelium.** Hypertension is a major risk factor for the development of cerebrovascular insufficiency
- **Diabetes mellitus:** Increased phagocytosis and endothelial damage are the results of reactive glycosylation due to increased blood glucose levels
- **Hyperlipoproteinemia:** Excessive LDL cholesterol increases the risk of atherosclerosis, especially when combined with low HDL cholesterol levels

Second-order modifiable risk factors

Second-order risk factors include lack of exercise, stress, obesity, **hyperuricemia, hypertriglyceridemia, fibrinogenemia, homocysteinemia, glucose tolerance disorders, chronic renal failure,** and increased **lipoprotein** (a).

Classification

Atherosclerosis can be classified depending on the affected vessels. We distinguish between microangiopathies affecting large and medium-sized arteries, and microangiopathy that occurs in the arterioles, capillaries, or venules, and is usually found in diabetes mellitus.

Mild	Moderate	Severe

• Endothelium becomes damaged • Factors: high blood pressure, cigarette smoke	• Damage causes an inflammatory response, and white blood cells deposit cholesterol forming an atheroma • Calcium salts and fibrous tissue form plaque • Artery loses elasticity and narrows	• Plaque restricts blood flow • High blood pressure • Increased blood pressure promotes the formation of more plaques

Symptoms and Clinical Diagnosis

Atherosclerosis can be present for years without any symptoms. Common manifestations include **coronary heart disease, cerebrovascular disease, peripheral arterial disease,** and **infrarenal aortic aneurysm**.

Diagnosis

History and physical examination

History should be taken to identify risk factors such as a family history of the disease. Comorbidities and the use of medication and walking distances should also be ascertained.

Physical examination can already provide information about the skin color and temperature or evidence of existing ulcerations or circulatory disorders. The heart should also be auscultated.

ECG or stress ECG can also be helpful.

Laboratory tests

Lipid profile consisting of total cholesterol, LDL and HDL cholesterol, triglycerides, lipoprotein (a) and homocysteine should be done. If myocardial infarction is suspected, cardiac enzymes, such as troponins, CK and CK-MB, GOT, LDH and myoglobin, should be done.

Inflammatory markers such as CRP should also be investigated. Markers of glucose metabolism, such as fasting blood glucose and HbA1c should also be done. Other tests include:

- Complete blood count
- Sodium and potassium
- Coagulation parameters
- TSH
- Creatinine
- Rheumatoid factors

Diagnostic Imaging

Sonography

Ultrasonography can be used to assess superficial vessels and detect morphological changes. The thickness of the vessel walls can also be determined this way. Doppler sonography offers a good, non-invasive way to assess the vessels. It is used for both closure and perfusion measurement and for the determination of the **ankle-brachial**

index, as well as to measure flow velocity pulses.

Duplex (color) sonography combines the B-mode and Doppler ultrasound modalities, and allows the examination of **morphologically conspicuous vessel** sections, yielding a color code depending on the flow direction of the blood. Intravascular ultrasound (IVUS) can be used to assess the **coronary arteries.**

Echocardiography can be conducted to assess cardiac function (cardiac structure, ejection fraction, contractility)

Angiography

CT and MR angiography also offer the advantage of non-invasive diagnosis over conventional angiography. The presentation is detailed and enables 3D reconstruction for precise treatment planning. CT angiography offers a rapid assessment especially in emergency diagnosis, whereas MR angiography has the advantage of low radiation exposure.

Conventional angiography, however, has the advantage of simultaneous intervention options, such as stent angioplasty, and is still the gold standard in terms of accuracy of vascular imaging.

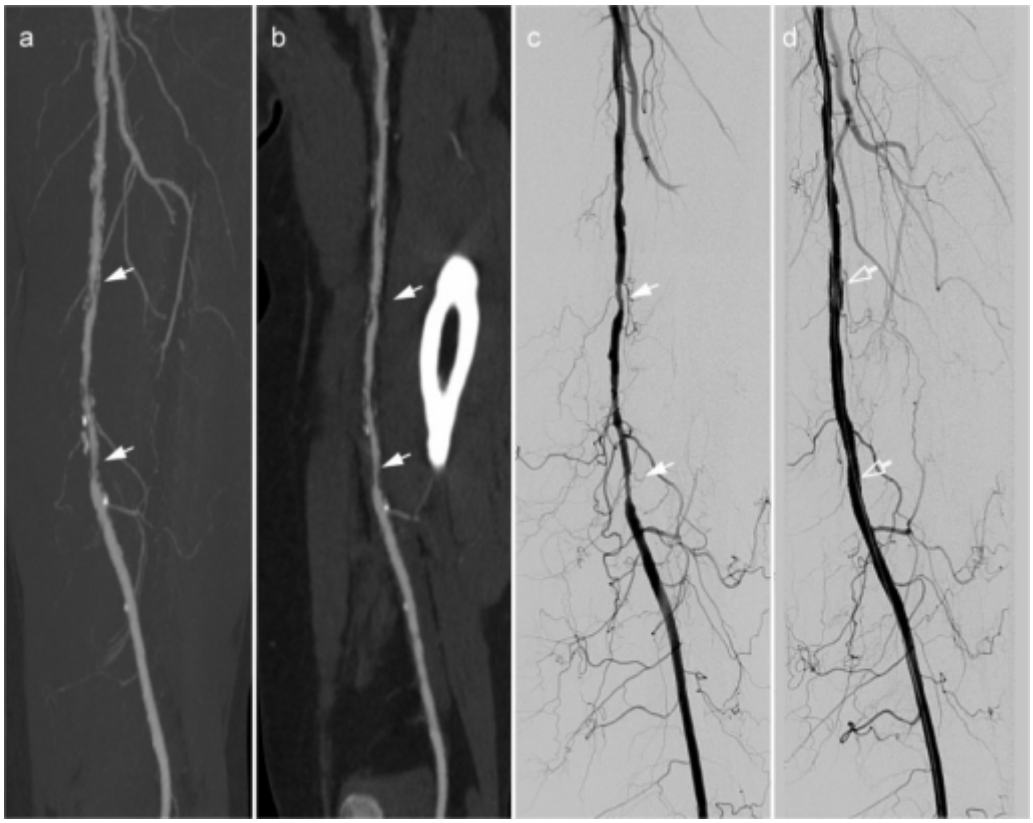


Image: 'Example of a run-off CTA with sufficient diagnostic confidence and diagnostic image quality.69 y old female with intermittent claudication of the left lower leg (Fontaine stage IIB). Run-off CTA showed multiple stenoses (white arrows) of the left superficial femoral artery (TASC B) in the MIP images (a) and curved MPR (b). Stenoses were confirmed by DSA (c) and successfully treated by percutaneous transluminal angioplasty and stenting (d, empty white arrow). ' By Openi. License: CC BY 4.0

Pathology

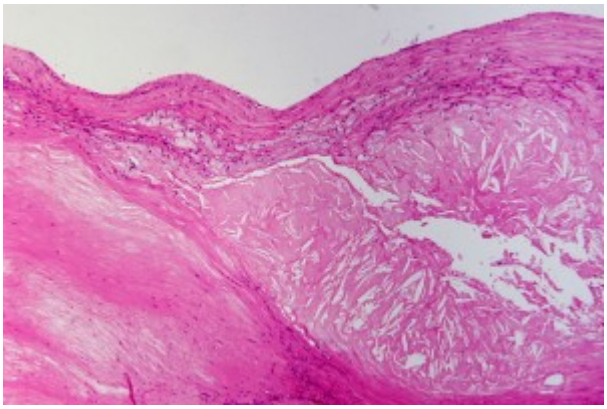


Image: “Atherosclerotic plaque with cholesterol crystal gaps, foam cells and fibrosis. Histology. HE staining.” by Patho. License: CC BY-SA 3.0

Initially, a deposit of LDL cholesterol in the intima of the vessel walls occurs. This is oxidized, and is followed by a local inflammatory response, so monocytes migrate into the tissue. If these monocytes phagocytize the LDL cholesterol, foam cells with embedded lipid droplets are created. These early atherosclerotic lesions are referred to as fatty streaks and especially occur in areas with high mechanical stress (for example at the proximal left anterior descending artery (LAD), or at the carotid bifurcation).

Subsequently, an increased amount of LDL cholesterol is deposited and macrophages appear and release fat. This causes an accumulation of **lipids** and **cellular debris** in the intima. Different cells of the vessel walls release mediators, so that muscle cells from the **tunica media** migrate into the **intima.**

The fatty core is surrounded by connective tissue and is not accessible from the outside so that the stored LDL cholesterol cannot be degraded. These plaques may contain newly formed vessels that originate from the **vasa vasorum** and can cause bleeding into the plaque.

In the growing plaques, calcium is also accumulated. Tears in the endothelium activate the coagulation cascade, causing thrombosis. The plaques initially develop extraluminally. If more than 40% of the lumen is obstructed, stenosis of the vessel occurs. Due to damage of the vascular wall, nitric oxide synthesis is also disrupted, which causes endothelial dysfunction.

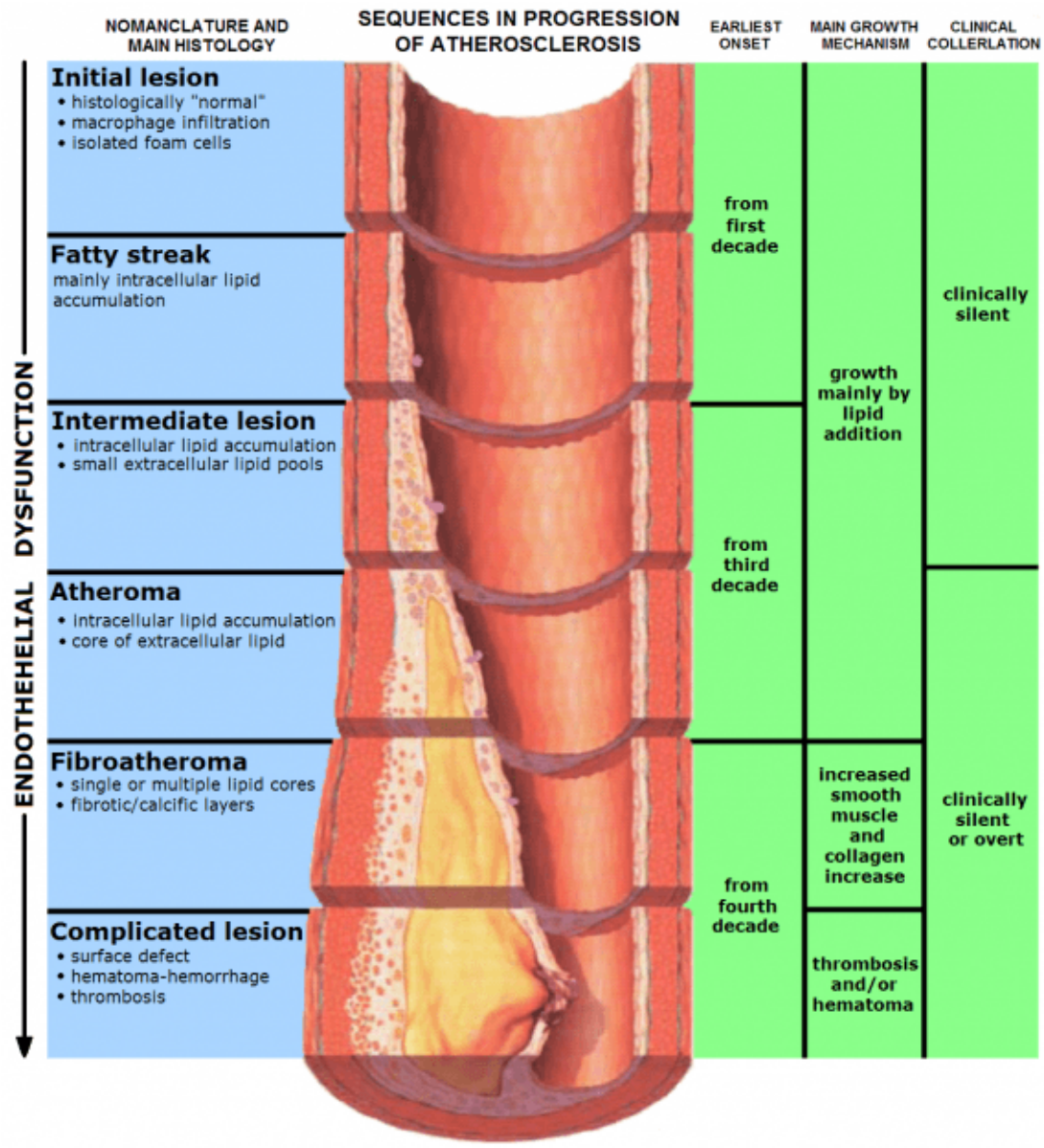


Image: “Stages of endothelial dysfunction in atherosclerosis” by Grahams Child. License: CC BY-SA 3.0

Plaques that have a large fatty core and only a thin fibrous cap are at risk of rupture. The coagulation system is so strongly activated under certain circumstances that it can lead to complete thrombotic occlusion of a vessel. Ninety percent of the closures in myocardial infarction are due to this.

The release of cholesterol due to a plaque rupture can cause cholesterol embolisms that spread to remote vessels such as in the kidney.

Another consequence of atherosclerosis is the formation of aneurysms on the basis of changed **atherosclerotic vascular tissue.** Due to the prolonged restructuring processes, the supply of the **tunica media** may be damaged, so that the tissue atrophies and the stability of the vessel walls decreases.

It is unclear whether endothelial dysfunction (‘response-to-injury hypothesis’) or the oxidation of LDL cholesterol (‘lipoprotein-induced atherosclerosis hypothesis’) is ultimately the starting point of plaque formation.

Differential Diagnoses

Vascular diseases similar to atherosclerosis

Apart from atherosclerosis, there are other vascular diseases that cause structural wall changes and thus, lead to stenosis. Examples include inflammatory diseases, which cause 5% of stenotic vascular diseases. The cause of the inflammatory processes may be autoimmune or infectious; the autoimmune processes are more serious.

If there is inflammation, the vascular wall thickens due to inflammatory infiltrates and secondary vessel wall edema. If the endothelium is damaged, thrombosis may form here. Within the framework of a destroyed **tunica media,** not only stenosis but also dilations or dissections can be consequences of the inflammation.

Autoimmune diseases similar to atherosclerosis

Considering autoimmune diseases, **Buerger's Disease** (**thromboangiitis obliterans**) and **giant cell arteritis** or **Takayasu arteritis** are possible causes of inflammation in the vessel walls. Infectious inflammations can be caused by bacteria such as ***E. coli*** and ***S. aureus***, or **herpes viruses**.

Mechanical damage

Mechanical damage to arterial vessels can also cause stenosis. This can result from trauma or surrounding tissue. Even benign tumors can have vasoconstrictive effects. In malignant tumors, the vascular wall can also be affected by infiltrative growth.

Treatment

Treatment includes lifestyle changes and pharmacological and surgical therapy. All are aimed at the reduction of risk factors.

Non-pharmacological treatment

Weight normalization in combination with sufficient exercise such as jogging, swimming, or cycling, and a healthy, fat-modified diet are helpful. Smoking cessation is also important, as well as stress avoidance.

Walking exercise:

- Walking regularly for at least 30 continuous minutes 3 times per week can improve symptoms by encouraging the formation of new, collateral blood vessels and improving muscle efficiency
- Many patients experience a dramatic increase in the distance they are able to walk without pain
- Patients can also benefit from a vascular rehabilitation program, involving 45 minutes of supervised exercise per week

Drug therapy

This is aimed at treating **hypertension, diabetes mellitus, hypertriglyceridemia**, and **dyslipoproteinemia. Thromboembolism** prophylaxis is also indicated.

Complications

Complications include coronary artery disease and **angina pectoris, cerebrovascular** insufficiency, peripheral arterial disease, and renal artery stenosis. **Subclavian steal syndrome** or **mesenteric stenosis** can also result from chronic stenosis.

Acute vascular occlusions can also cause complications. Mesenteric infarction, renal or splenic infarction, as well as a transient ischemic attack and stroke, are among the acute complications. Aneurysms at various vessel segments, such as an **infrarenal** or **thoracic aortic aneurysm** or **thoracic aortic dissection** as well as **iliac** or **popliteal aneurysms** are consequences of atherosclerosis.

Prevention

Reducing risk factors

The reduction or prevention of modifiable risk factors is important. Prevention primarily involves a healthy diet, adequate physical activity in the form of aerobic exercise, and controlling underlying diseases such as diabetes mellitus and hypertension.

However, the most important lifestyle change is **smoking cessation**!

References

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