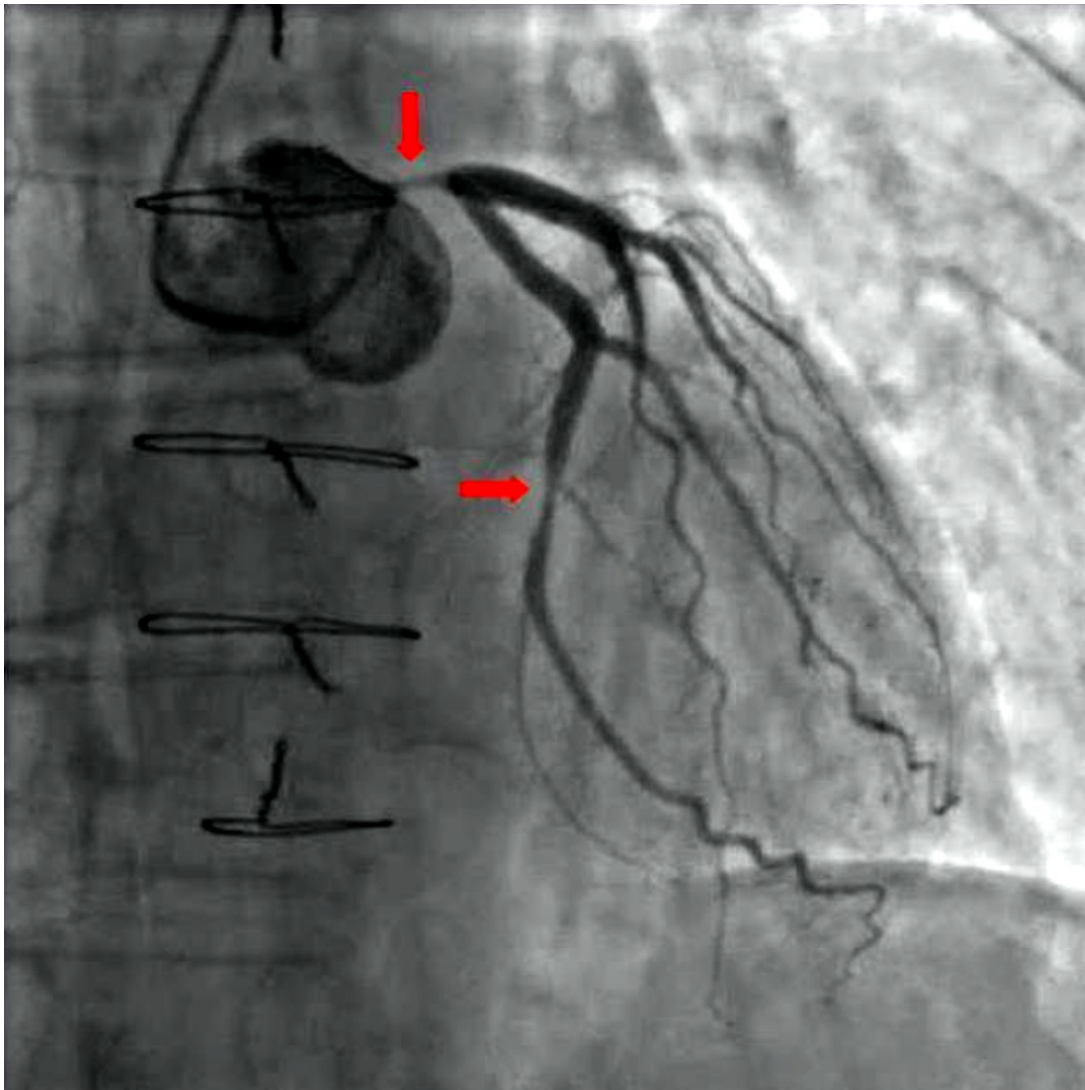


Coronary Artery Disease (CAD, Atherosclerotic Heart Disease) — Risk Factors and Prevention

[See online here](#)

Coronary heart disease (CHD) is the leading cause of death in industrialized countries. Numerous risk factors, which can be reduced through both behavioral and lifestyle changes as well as drug therapy, are known for its origin.



Definition of Coronary Artery Disease

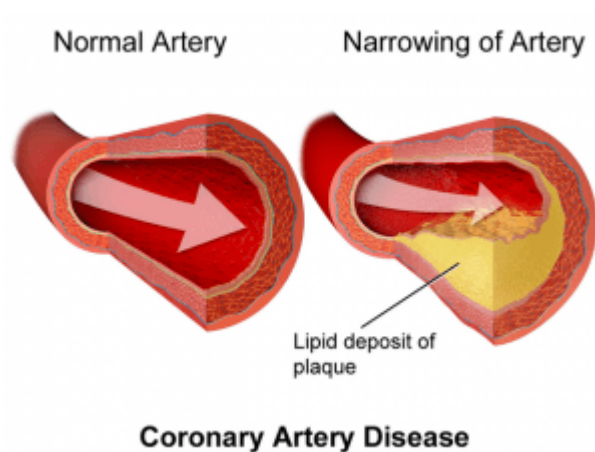
Coronary artery disease is a term used to describe a wide range of clinical conditions

in which there is an **imbalance between oxygen supply and the myocardial demands** resulting in ischemia to a portion of the myocardium.

Coronary heart disease is the **manifestation of atherosclerosis in the coronary arteries** so that the oxygen demand of the [heart muscle](#) cannot be sufficiently covered by the oxygen supply, because of stenotic coronary vessels. Thus, the myocardium becomes ischemic.

The most common cause of coronary heart disease is **atherosclerosis** of epicardial coronary arteries, resulting in partial or complete obstruction with subsequent inadequate perfusion of the myocardium supplied by the involved coronary artery.

Many risk factors have been involved in the pathophysiology of coronary heart disease. The most common are **obesity, high-fat diet, insulin resistance, diabetes, and smoking**. Risk factor modifications delay the onset of the disease and its progression to later life.



[Image](#): "Coronary Artery Disease," by BruceBlaus. License: [CC BY 3.0](#)

Epidemiology of Coronary Artery Disease

Coronary artery disease is one of the leading causes of death worldwide. It is considered the **most common, serious chronic illness** in the United States, as more than 13 million patients are suffering from coronary artery disease. More than 6 million have angina pectoris, and more than 7 million have myocardial infarction. Because of the large increase in the prevalence of IHD worldwide, it's likely to become the leading cause of death by 2020.

Coronary heart disease has an incidence rate of 0.6 % per year with an **increase in the elderly. Men are affected more often** than women. Together with its manifestations, it is the leading cause of death in industrialized countries, making up almost 20 % of all deaths.

The international **MONICA study (Monitoring of trends and determinants of cardiovascular diseases)** records the causes and trends of coronary heart disease.

Etiology of Coronary Artery Disease

Causes and risk factors of coronary artery disease

Significant risk factors can be recognized for the occurrence of coronary heart disease. Among the main risk factors, in addition to an **increase of LDL cholesterol** or a **decrease of HDL cholesterol**, including arterial hypertension, **diabetes mellitus**, **smoking** as well as **family history** and **male gender**.

Other risk factors include **unhealthy, atherosclerosis favoring nutrition, severe obesity**, and **too little physical activity**. **Metabolic disorders**, such as impaired glucose tolerance or lipid metabolism disorder, also favor the emergence of coronary heart disease.

In patients who suffer a heart attack at a younger age (< 30 years), other causes may play a role. These include **familial lipid metabolism disorders** as well as **hypothyroidism** and vasculitis. Coronary anomalies, antiphospholipid syndrome, and hyperviscosity syndrome should also be excluded. During history taking, possible **drug abuse should be inquired about**.

Since myocardial ischemia develops most commonly as a result of obstruction of one or more coronary arteries in the form of **coronary atherosclerosis**, a number of risk factors predispose to this condition.

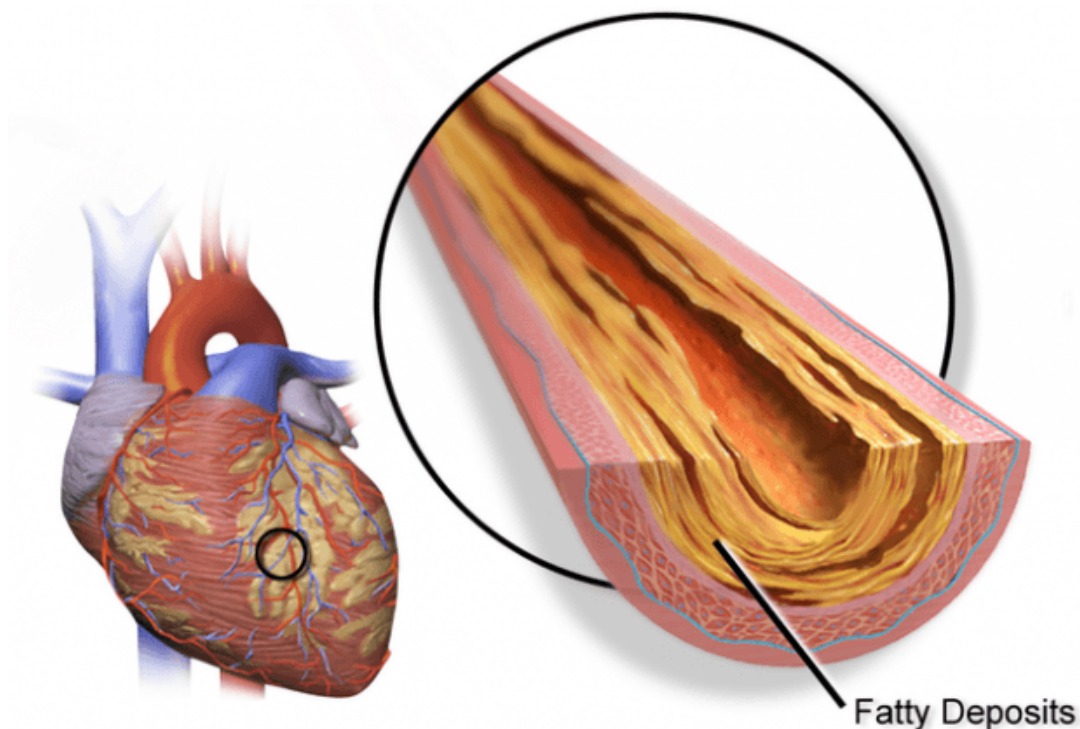


Image: "Coronary Artery Disease." By BruceBlaus. License: [CC BY 3.0](https://creativecommons.org/licenses/by/3.0/)

Fixed Risk Factors	
Age	Risk increases with age and is rare during childhood, except in cases where the patient has familial hyperlipidemia.

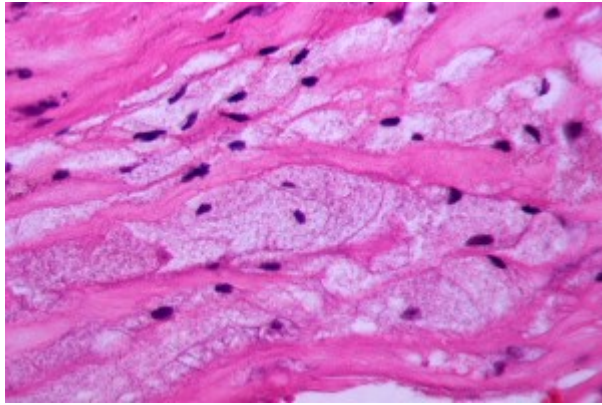
Male Sex	Men have a higher incidence of coronary artery disease than premenopausal women. The incidence of atherosclerosis in women increases after menopause due to the deficiency of estrogen hormone.
Family history	Positive family history is defined as development of coronary heart disease in a first-degree relative before the age of 50 years.
Modifiable Risk Factors	
Hyperlipidemia	High level of cholesterol, especially increased low-density lipoprotein (LDL) and decreased high-density lipoprotein (HDL), is associated with an increased risk of atherosclerosis.
Hypertension	Systolic and diastolic hypertension are associated with an increased risk of coronary heart disease.
Cigarette smoking	The number of cigarettes smoked is directly related to the risk of coronary heart disease. Cessation of smoking reduces the risk by 25 %.
Diabetes mellitus	Abnormal glucose tolerance, or diabetes mellitus, increases the risk of coronary artery disease and progresses the other risk factors, such as dyslipidemia, obesity, and hypertension.
Lack of exercise	It's recommended to exercise regularly for 30 minutes with moderate intensity for 5 days/week.
Obesity	Reduction of body weight by exercise and healthy diet decreases the risk of coronary heart disease and controls diabetes and insulin resistance.
Alcohol	Moderate intake of alcohol (1 or 2 drinks/day) is associated with a reduced risk of coronary artery disease. At higher levels, the risk is increased.

Classification of Coronary Artery Disease

We differentiate between **asymptomatic** and **symptomatic coronary heart disease**. While the asymptomatic form is silent ischemia, symptomatic coronary heart disease manifests in different ways. This can range from unstable angina pectoris to acute coronary syndrome and from coronary heart muscle damage to cardiac arrhythmia and sudden cardiac death.

Pathophysiology of Coronary Artery Disease

If **damage to the coronary arteries** already exists, for example, due to [arterial hypertension](#), **endothelium platelets** attach themselves to the damaged site. They **attract macrophages, among others, with the help of mediators**. If macrophages take up LDL cholesterol, they are incorporated as so-called **foam cells** into the vessel wall.



[Image](#): "Foam cells in atherosclerotic plaque. Histology." by Patho. License: [CC BY-SA 3.0](#)

These remodeling processes, in which fibrotic altered tissue is created, make it impossible to reduce the resulting plaque again. Thus, the calcification process of the coronary vessels has begun.

Stenosis of the coronary arteries can lead to an **insufficient supply of oxygen to the heart muscle tissue, starting with a narrowing of 50 %** on exertion, because the oxygen demand increases by approximately fourfold on exertion.

The so-called coronary reserve, i.e., the difference between the minimum blood flow and the fourfold, increased, maximum blood flow during exercise, is so severely limited in patients with coronary heart disease, that often not even an increase of blood flow to two times the resting blood flow is possible. The result is coronary pain.

Angina occurs when there is an imbalance between the oxygen supply and the myocardial demand, resulting in myocardial ischemia.

Myocardial oxygen demand

Four major **factors determine the oxygen demand** of the myocardium:

1. Heart rate
2. Systolic blood pressure (afterload)
3. Tension on the myocardial wall (preload)
4. Myocardial contractility.

Any clinical condition increasing one or more of these factors will also increase the myocardial oxygen demand and can result in ischemia, such as extreme tachycardia, hypertension, ventricular hypertrophy.

Myocardial oxygen supply

The **capacity of the blood to carry oxygen** to the myocardium is affected by different factors:

Hemoglobin and oxygen tension and the **amount of extracted oxygen from hemoglobin to the tissue**, and it is related to 2,3 diphosphoglycerate levels. Another factor is **Coronary artery blood flow**, which is affected by the following factors:

- Coronary artery diameter: Coronary atherosclerosis is the most frequent cause of narrowing and obstructing the coronary artery, and the clinical presentation differs according to the extent of obstruction.
- Coronary artery tone: Coronary vasospasm as in variant or Prinzmetal's

angina, reduces the oxygen supply without significant underlying atherosclerotic changes.

- Perfusion pressure: It's determined by the pressure gradient from the aorta to the coronary artery.
- Heart rate: Coronary artery flow occurs mainly during diastole, therefore extreme tachycardia will decrease the duration of diastole, and thus will decrease the blood flow into the coronary arteries.

Any clinical condition affecting one or more of the above-mentioned factors will reduce the myocardial oxygen supply and can result in ischemia.

Symptoms and Clinical Diagnosis of Coronary Artery Disease

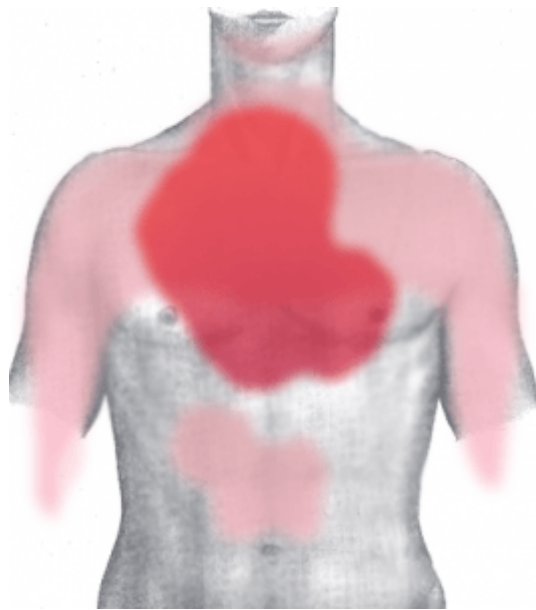


Image: "Pain in acute myocardial infarction (front)," by J. Heuser. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

The main symptom of coronary heart disease is **angina pectoris**, which can be divided into a stable and an unstable form.

The symptoms are often indicated as **retrosternal pain** or **pressure**. Tightness in the chest is also typical. A **radiating pain** in the left (or right) arm, reaching up to the lower jaw and neck, is a common symptom.

Patients with coronary heart disease (IHD) can present with either:

Chronic artery disease (CAD), which most commonly presents as **stable angina**, or

Acute coronary syndromes (ACSs), which is a term that encompasses:

- Unstable Angina (UA)
- Myocardial infarction
- ST-segment Elevation Myocardial Infarction (STEMI)
- Non-ST-segment Elevation Myocardial Infarction (NSTEMI)

Note: When occurring for the first time angina pectoris is considered unstable!

Acute Coronary Syndrome

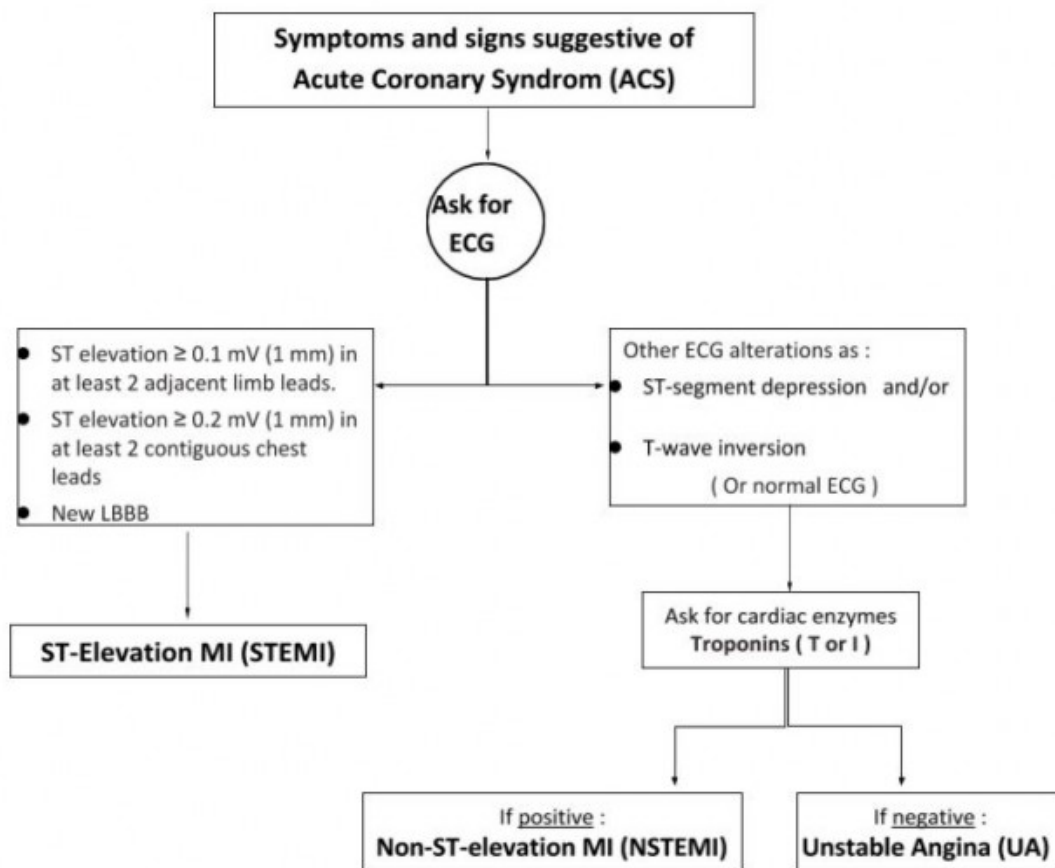


Image: Symptoms and signs of Acute Coronary Syndrome. Copyright by MedicoNotes.

ST-segment Elevation Myocardial Infarction (STEMI)

Diagnosis

Diagnosis of STEMI also depends on history, abnormalities on ECG and the cardiac biomarkers.

History

Chest pain is similar in character to stable angina pectoris, but more severe lasts longer (usually > 20 minutes) and not fully relieved by rest or nitroglycerin.

Abnormalities on ECG

ST-elevation, followed by T-wave inversion if no reperfusion was achieved, followed by Q-wave development over several hours. The **ECG criteria for ST-elevation MI (a, b or c) are:**

- a. ST-elevation ≥ 0.1 mV (1 mm) in at least 2 leads of either:
 1. Inferior group: II, III, aVF
 2. Lateral group: I, aVL, V5, V6
- b. ST-elevation ≥ 0.2 mV (1 mm) in at least 2 contiguous anterior leads (V1-V4)

c. New LBBB

Cardiac biomarkers

Troponin I and T are more specific than **CK-MB** cardiac enzymes. Normally, Troponin enzymes are not detectable in the blood of healthy individuals, but they are increased to levels more than 20 times higher than the upper reference limit in myocardial infarction (MI).

Troponins	Rises within 4-8 hours.	Remain elevated for 7-10 days.
CK-MB	Rises within 4-8 hours.	Returns to normal by 48-72 hours.

Note: Troponins can't detect reinfarction occurring a few days after the first one because they remain elevated for 7-10 days. In contrast, CK-MB returns to normal levels within 2-3 days and therefore can be used to identify a new coronary event in a patient with a new episode of pain.

Treatment

Management of patients with suspected ST-Elevation MI in the emergency department should focus on relieving the coronary pain, identification of candidates, urgent reperfusion therapy and avoiding the discharge of a patient with suspected STEMI.

- Patients should be immediately admitted to a hospital with **ECG rhythm monitoring** due to the risk of sudden death.
- Take a targeted **history and examination**
- Intravenous access and blood sample for **cardiac markers**

Immediate treatment:

- **Aspirin:** should be administered immediately.
- **Sublingual glyceryl trinitrate**, repeat if no effect in 5 min
- **Begin oxygen** by nasal cannula or mask if hypoxia is present
- **Intravenous opiates** (such as Morphine)
- **Beta-Blocker** (if no contraindication) for ongoing chest pain, hypertension, tachycardia

Reperfusion therapy:

Primary percutaneous coronary intervention (primary PCI):

Primary PCI refers to angioplasty and/or stenting without preceding fibrinolysis. It is more effective and preferred than IV fibrinolysis, especially when:

1. The diagnosis is in doubt.
2. Cardiogenic shock is present.
3. There is an increased risk of bleeding.
4. Symptoms have been present for > 3 hours.

Fibrinolysis:

IV fibrinolysis is indicated if:

1. Primary PCI is not available.
2. Delay to PCI would be > 1 hour longer than the initiation of fibrinolysis.

Before starting fibrinolytic drugs, assess for contraindications:

- Prior intracranial bleeding
- Intracranial malignancy or vascular malformation
- coronary stroke or head trauma in the previous 3 months
- Aortic dissection
- Active bleeding (with exception of menses)
- Internal bleeding in the previous 4 weeks
- Severe hypertension (systolic > 180 or diastolic > 110)
- Prolonged (> 10 min) CPR chest compressions
- INR \geq 2.0 on warfarin or known bleeding diathesis
- Pregnancy

Coronary angiography after fibrinolysis (rescue PCI) is indicated in case of:

- Failure of reperfusion (as evidenced by < 50 % resolution of ST-segment elevation > 90 min after completion of fibrinolytic treatment)
- Spontaneous recurrent ischemia while in a hospital
- High-risk features, e.g., extensive ST-segment elevation, signs of heart failure and hypotension (systolic blood pressure < 100 mmHg)

Progression and Special Forms of Coronary Artery Disease

Progressive forms of coronary artery disease

In addition to typical angina pectoris, with the retrosternal discomfort that is triggered by stress and gets better at rest, we have **atypical angina pectoris**, which involves only two of the three typical criteria. **Angina at rest** describes a form, in which the symptoms occur at rest. There is also **nocturnal angina**, where complaints manifest only at night.

Special forms of coronary artery disease



Image: "ECG of a patient with Prinzmetal's Angina," by Gogradgme. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

Special forms are the so-called **variant angina**, which is caused by vasospasm occurring at rest. The **"walking-through-angina"** describes problems that occur at the beginning of exertion, but improve during the course.

Silent myocardial ischemia can also be a form. Here, the typical symptoms are missing. It occurs frequently in **diabetics** (due to neuropathy), **patients with renal insufficiency, women, and elderly patients**. The symptoms can be very nonspecific here. Dizziness and nausea, as well as shortness of breath and symptoms that radiate

into the epigastrium, are often at the foreground.

Another special form is **postinfarction angina** which may occur within two weeks after myocardial infarction.

Diagnostics of Coronary Artery Disease

History and laboratory diagnosis of coronary artery disease

For the diagnosis, a **history** that covers the symptoms and their time of onset, triggering factors and the presence of risk factors has to be explored first. In the **physical examination**, factors such as hypertension and obesity stand out, but auscultation can also detect an indication of heart disease.

In the laboratory, markers such as **CK**, **CK-MB**, and **troponins** indicate myocardial damage, which, however, is not present in stable angina pectoris. Furthermore, an **ECG can be taken at rest**, which often remains unchanged, even with severe coronary heart disease. A **stress test** typically shows a **descending or horizontal ST depression of 0.1-0.2 mV**.

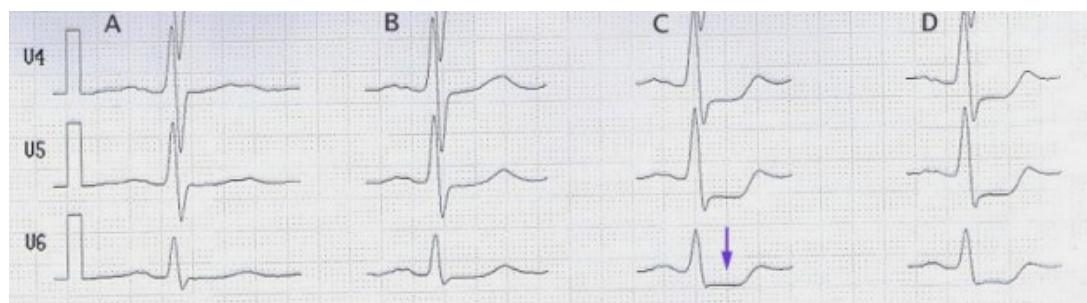


Image: "Stress-ECG with ST-segment-depression (arrow) beginning at 100 W (column C)," by J. Heuser. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

A **holter monitor** can be useful as well if, for example, the symptoms occur in everyday situations. **Transthoracic echocardiography** can exclude other causes of angina, such as aortic stenosis, and wall motion abnormalities can give an indication of myocardial infarction.

Gold standard of diagnostics

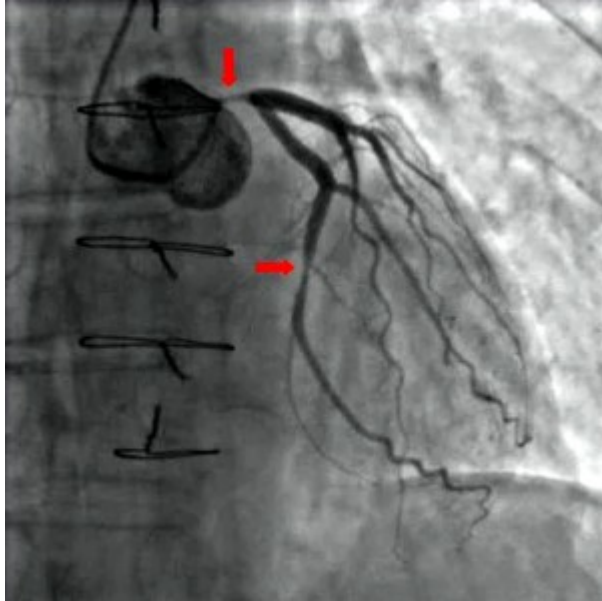


Image: "Coronary angiography of a critical sub-occlusion of the common trunk of the left coronary artery and the circumflex artery (see arrows)." by Kuebi. License: [CC BY-SA 2.0](https://creativecommons.org/licenses/by-sa/2.0/)

The gold standard of diagnostics is **coronary angiography** with access via the femoral artery, the brachial artery, or the radial artery, to determine the degree of stenosis of the coronary artery. Representations via a **multislice spiral CT** or **dual-source CT** or **MR angiography** are also possible.

To investigate stress-related ischemia, a stress echocardiography or stress MRI with dobutamine can be performed.

Pathology of Coronary Artery Disease

The pathology of coronary heart disease is primarily based on an **increased resistance in the coronary arteries**. These also include **intracoronary additional factors** such as cardiac disease or other increased O_2 demands, for example during a fever, as well as a reduced amount of O_2 , among other things, in lung diseases.

The increased resistance of the coronary **vessels** can be explained by coronary artery stenosis due to **atherosclerosis** in 90 % of all cases.



Image: "Gross pathology of atherosclerosis, aorta," by Patho. License: [Public domain](#)

These so-called **microangiopathies** initially only narrow the vessels. But if one of these plaques ruptures, it can lead to the formation of clots that close the vessel completely, which in turn leads to a heart attack.

In a few cases, microangiopathies, where small coronary vessels are located intramural, are responsible for coronary artery disease. Consumption of cocaine, for example, can cause coronary spasms, which can lead to angina pectoris, just like **coronary anomalies**, **coronary fistulas**, or **congenital myocardial bridges**.

The resistance of the coronary vessel may also be increased in **cardiac hypertrophy**, **hypertension**, **tachycardia** or **increased end-diastolic valve flow**. Thus, these factors may be responsible for angina pectoris as well.

Differential Diagnosis of Coronary Artery Disease

Similar clinical pictures to coronary artery disease

Since the symptom of coronary artery disease is angina pectoris, the differential diagnoses are numerous. **The five most important differential diagnoses to be excluded quickly—as they are immediately life-threatening are an acute coronary syndrome, pulmonary embolism, aortic dissection, tension pneumothorax, and spontaneous rupture of the esophagus ([Boerhaave's syndrome](#)).**

In general, the differential diagnosis of chest pain can be divided into cardiac and non-cardiac chest pain:

Differential diagnoses of cardiac chest pain, in addition to **acute coronary syndrome**, include, for example, **hypertensive crisis**, **valvular heart disease**, **perimyocarditis**, or **hypertrophic cardiomyopathy**, but also **Dressler's syndrome** following a **myocardial infarction** or **coronary anomalies**.

Non-cardiac causes of chest pain include diseases of the lungs or the pleura, such as pulmonary **embolism** and **lung carcinoma** or **pleurisy**. An **aortic dissection** may also

be present. Furthermore, there may be diseases of the **esophagus** or the **mediastinum**, and **diseases of the spine** and the **ribs** or **abdominal discomfort**.

Therapy of Coronary Artery Disease

Acute therapy

Therapy can initially be divided into **acute therapy** and **long-term therapy**. In acute cases, nitro compounds that are acting as a vasodilator and thus improve the coronary circulation are suitable. They are contraindicated for patients who are taking PDE-5 inhibitors (e.g., sildenafil, Viagra) or who have HOCM, hypotension or present aortic stenosis.

Long-term therapy



Image: "Drug-based therapy,"
by e-Magine Art. License: [CC BY-SA 2.0](#)

Long-term therapy can be divided into **causal** and **symptomatic therapy**. The causal approach is directed towards the main risk factors that support the emergence of coronary heart disease. **Lifestyle changes** such as **weight reduction**, **smoking cessation**, **dietary changes** to a Mediterranean diet, controlled **physical activity** and **courses on stress management** and relaxation are crucial.

This approach aims to control blood pressure and cholesterol as well as triglyceride levels via a non-drug therapy. Symptomatic treatment, on the other hand, includes medication and invasive approaches. Drug-based therapy aims to prevent myocardial infarction and reduce mortality. It includes aspirin, beta-blockers, statins, and ACE inhibitors.

Antianginal therapy

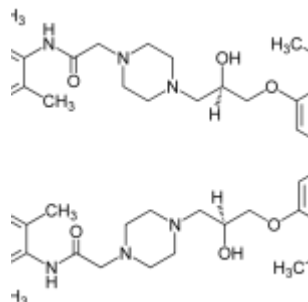


Image: "(±)-Ranolazine
Structural Formula," by JÜ.
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Antianginal therapy offers several options: **beta-blockers** to reduce myocardial oxygen demand, **nitrates**, which hardly find application during long-term treatment, **Molsidomine** and **calcium antagonists**, as well as **ivabradine** and **ranolazine**.

Revascularization as invasive therapy

Revascularization offers an invasive treatment option. This may also be achieved by means of **PTCA** (percutaneous transluminal coronary angioplasty) during which dilation via a balloon catheter, followed by stenting, is performed. Impending closures can then be eliminated and the permeability of the vessel can be improved.

A second possibility of revascularization is offered via **coronary artery bypass surgery** (CABG = coronary artery bypass graft). This can be done via the traditional method with sternotomy access and the use of a heart-lung apparatus. An alternative is a minimally invasive way. The last possibility of therapy that is indicated for coronary heart disease in combination with terminal heart failure is the heart transplant.

Prevention of Coronary Artery Disease

Prevention of coronary heart disease includes the **elimination of risk factors**, especially the main risk factors of cholesterol, arterial hypertension, diabetes mellitus, and nicotine abuse. The approaches should initially manifest in the patients' behavior, for example, diet and sporting behavior. Pharmacological support of these approaches is possible, and it may include statins for the regulation of lipid metabolism.

Prognosis of Coronary Artery Disease

Several prognostic indicators determine the outcome of coronary heart disease (IHD):

1. **Function of the left ventricle:** increased left ventricular end-diastolic pressure, increased ventricular volume and reduced ejection fraction are associated with poor prognosis.
2. **Location and severity of coronary artery stenosis:** stenosis of the main left anterior descending coronary artery is associated with greater risk and poor prognosis.
3. **Number and severity of risk factors:** a large number of risk factors for atherosclerosis are associated with increased risk of myocardial infarction with worse prognosis.

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