

Stable forms of ischemic heart disease

LECTURE IN INTERNAL MEDICINE FOR V COURSE STUDENTS

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William Heberden on Angina Pectoris, 1

But there is a disorder of the breast marked with strong and peculiar symptoms, considerable for the kind of danger belonging to it, and not extremely rare, which deserves to be mentioned more at length. The seat of it and the sense of strangling and anxiety with which it is attended, may make it not improperly be called angina pectoris. Those who are afflicted with it, are seized while they are walking (more especially if it be uphill, and soon after eating) with a painful and most disagreeable sensation in the breast, which seems as if it would extinguish life if it were to increase or to continue; but the moment they stand still, all this uneasiness vanishes.



William Heberden on Angina Pectoris, 2

In all other respects, the patients are, at the beginning of this disorder, perfectly well, and in particular have no shortness of breath, from which it is totally different.

The pain is sometimes situated in the upper part, sometimes in the middle, sometimes in the bottom of the os. sterni, and often more inclined to the left than to the right side. It likewise very frequently extends from the breast to the middle of the left arm. The pulse is, at least sometimes, not disturbed by this pain, as I have had opportunities of observing by feeling the pulse during the paroxysm. Males are more liable to this disorder, especially such as have past their fiftieth year. After it has continued a year or more, it will not cease so instantaneously upon standing still; and it will come on not only when the persons are walking, but when they are lying down, especially if they lie on the left side and oblige them to rise out of their beds.

William Heberden on Angina Pectoris, 3

In some inveterate cases it has been brought on by the motion of a horse, or a carriage, and even by swallowing, coughing, going to stool or speaking, or any disturbance of mind.

Such is the most usual appearance of this disease; but some varieties may be met with. Some have been seized while they were standing still, or sitting, also upon first waking out of sleep; and the pain sometimes reaches to the right arm, as well as to the left and even down to the hands, but this is uncommon; in a very few instances the arm has at the same time been numbed and swelled. In one or two persons the pain has lasted some hours or even days; but this happened when the complaint has been of long standing, and thoroughly rooted in the constitution; once only the very first attack continued the whole night.

William Heberden on Angina Pectoris, 4

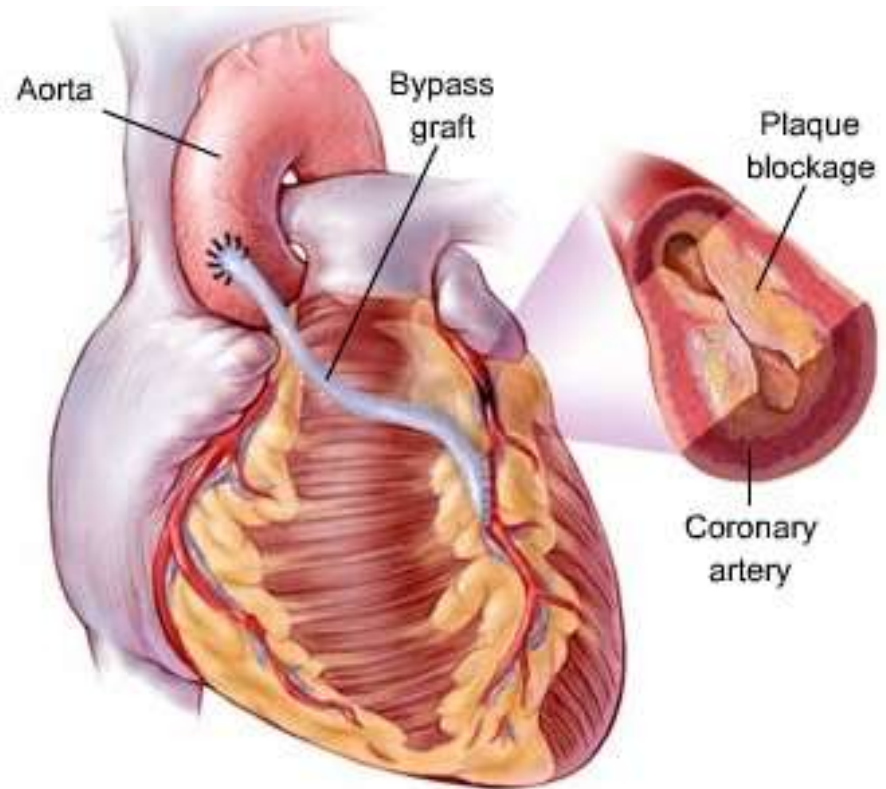
I have seen nearly a hundred people under this disorder, of which number there have been three women and one boy twelve years old. All the rest were men near or past the fiftieth year of their age...

The termination of the angina pectoris is remarkable. For if no accident interferes, but the disease goes on to its height, the patients all suddenly fall down, and perish almost immediately. Of which indeed their frequent faintness and sensations as if all the powers of life were failing, afford no obscure intimation.

Heberden, W. 1772. Some account of a disorder of the breast.

Plan of the Lecture

- Definition
- Epidemiology
- Risk factors
- Etiology
- Mechanisms
- Classification
- Clinical investigation
- Diagnosis
- Treatment
- Prognosis
- Prophylaxis
- Abbreviations
- Guidelines



Definition

Ischemic heart disease (IHD) or Coronary artery disease (CAD) is a group of diseases that characterized by impaired myocardial function due to decrease blood flow through the affected coronary arteries and includes silent ischemia, stable angina, unstable angina, myocardial infarction, and sudden cardiac death.

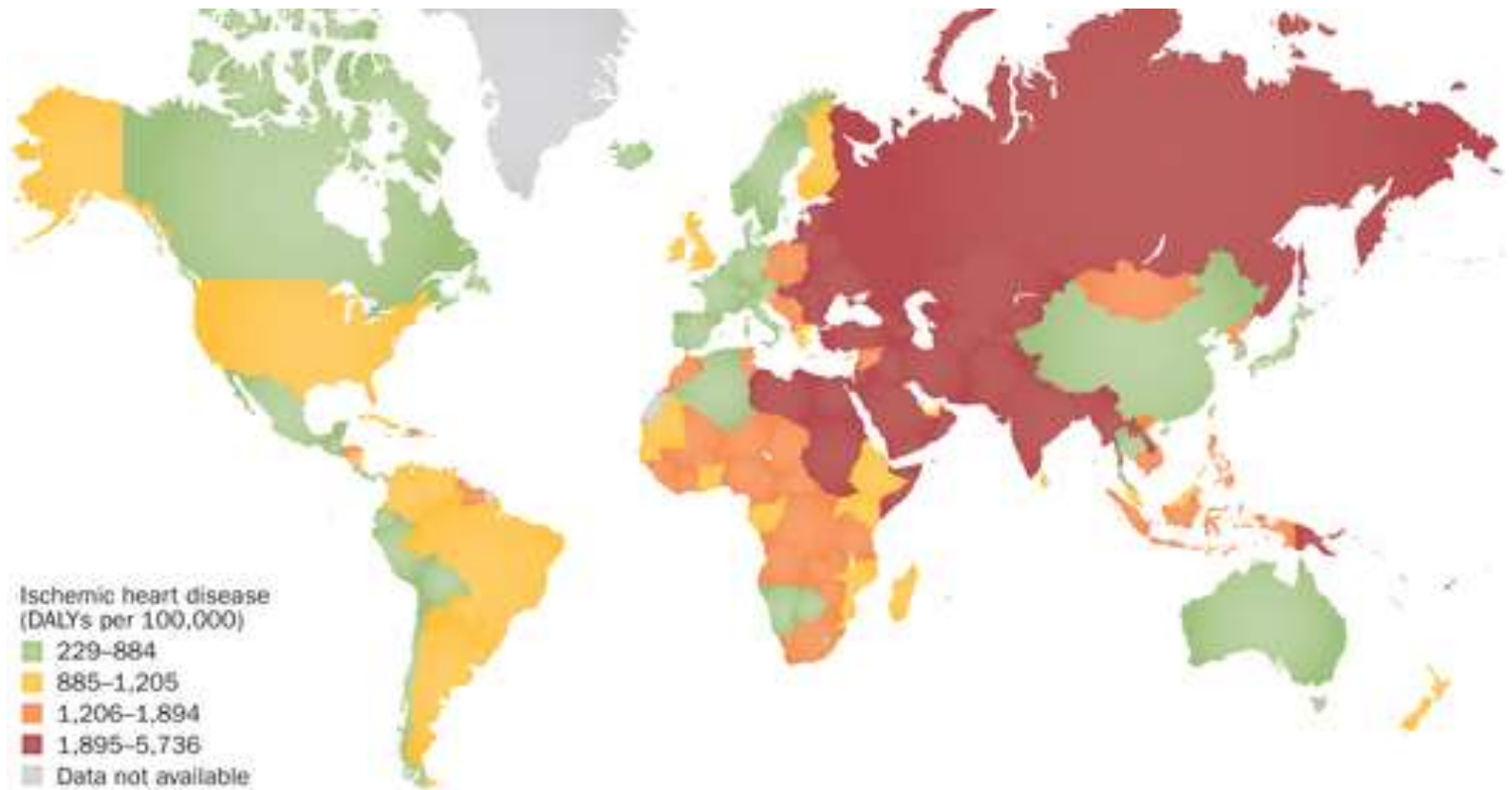
Most IHD is caused by atherosclerotic vascular disease (ASVD), usually present even when the artery lumens appear normal by angiography.

Stable forms of IHD (SIHD) include first two from the list

SIHD cause narrowing of coronary arteries with chronic inadequate blood supply to the myocardium that can ultimately lead from silent ischemia to heart attacks with chest pain or discomfort known as stable angina pectoris most commonly experienced during physical and/or emotional distress.

Epidemiology

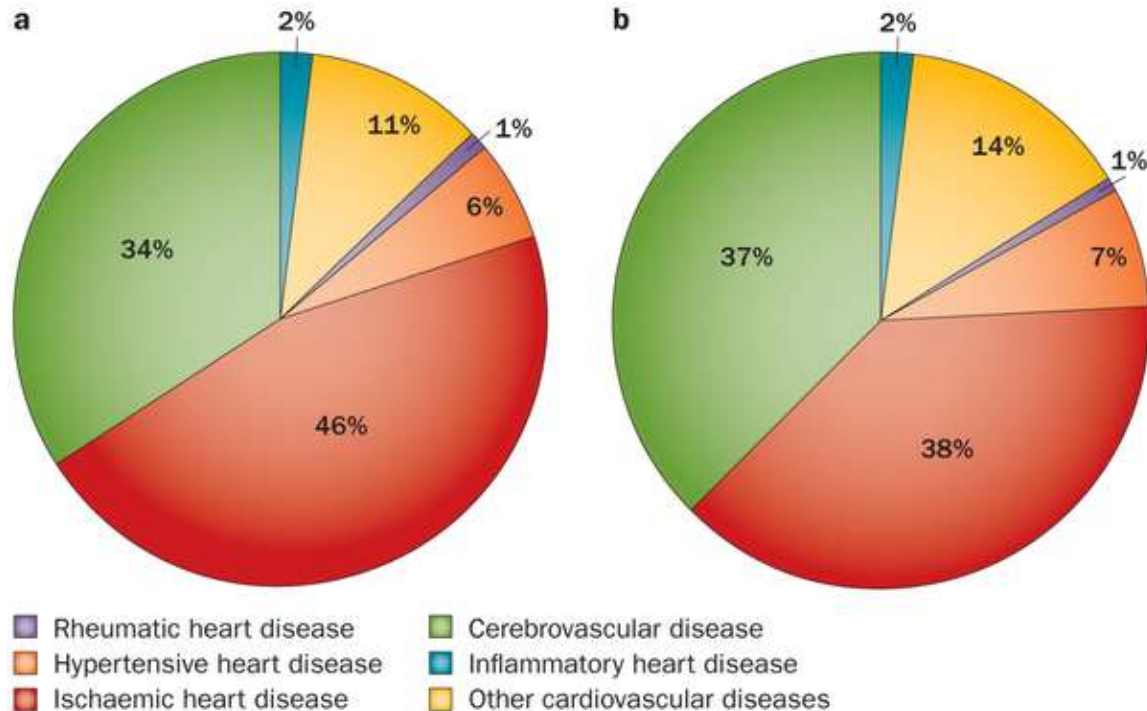
(Coronary Artery Disease around the World)



The global distribution of ischaemic heart disease burden, in disability-adjusted life years (DALYs), in 2011.

Epidemiology

(Focus on Key Heart Diseases)



The proportions of cardiovascular deaths (a) Men, (b) Women) caused by IHD, cerebrovascular disease, inflammatory heart disease, rheumatic heart disease, hypertensive heart disease, and other cardiovascular diseases in 2011.

Risk Factors

(Modifiable)

- Diabetes or impaired glucose tolerance (IGT)
- Dyslipoproteinemia: high serum concentration of low-density lipoprotein (LDL), and / or very low density lipoprotein (VLDL) particles; low serum concentration of functioning high density lipoprotein (HDL); an LDL:HDL ratio greater than 3:1
- Tobacco smoking
- Overweight and Obesity
- Physical inactivity
- Elevated serum C-reactive protein concentrations
- Hypertension
- Vitamin B₆ deficiency
- Dietary iodine deficiency and hypothyroidism

Risk Factors

(Nonmodifiable)

- Advanced age
- Male sex
- Having close relatives who have had some complication of atherosclerosis (e.g. coronary heart disease or stroke)
- Genetic abnormalities, e.g. familial hypercholesterolemia

Risk Factors

(Lesser or Uncertain)

- Being of South Asian ethnicity
- Hypercoagulability
- Postmenopausal estrogen deficiency
- High intake of saturated fat
- Trans fat intake
- High carbohydrate intake
- Elevated serum levels of triglycerides
- Elevated serum levels of homocysteine
- Elevated serum levels of uric acid
- Elevated serum fibrinogen concentrations
- Elevated serum lipoprotein concentrations
- Chronic systemic inflammation
- Elevated serum insulin levels
- Short sleep duration
- *Chlamydia pneumoniae* infection
- Air pollution

Risk Factors

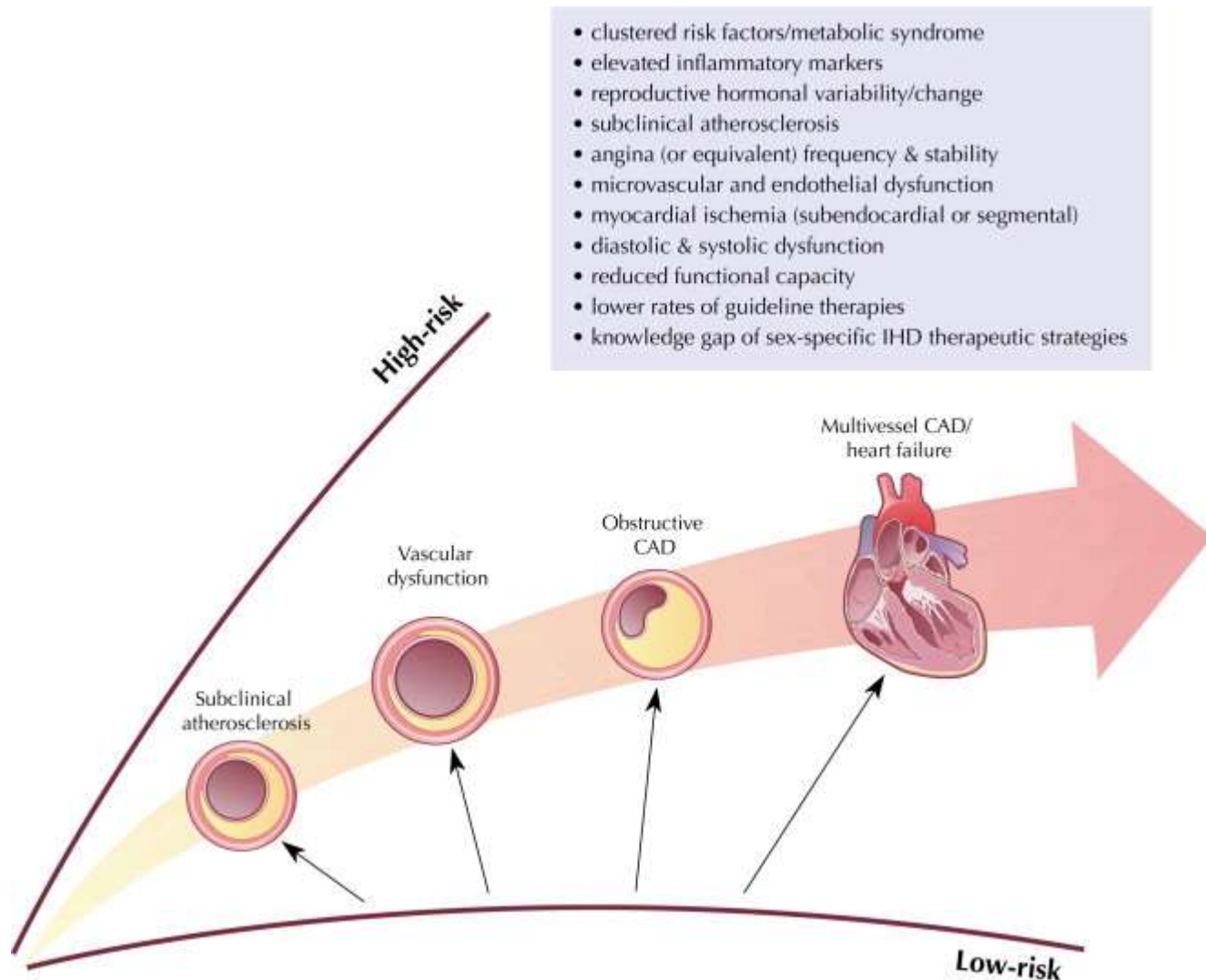
(Traditional versus Nontraditional Risk Factors)



The expanding list of nontraditional biomarkers is outweighed by the standard risk factors for predicting future cardiovascular events and adds only moderately to standard risk factors. BNP = B-type natriuretic peptide; BP = blood pressure; CRP = C-reactive protein; HDL = high-density lipoprotein cholesterol; HIV = human immunodeficiency virus infection.

Risk Factors

(Factors That Have an Impact on the IHD Events' Risk)



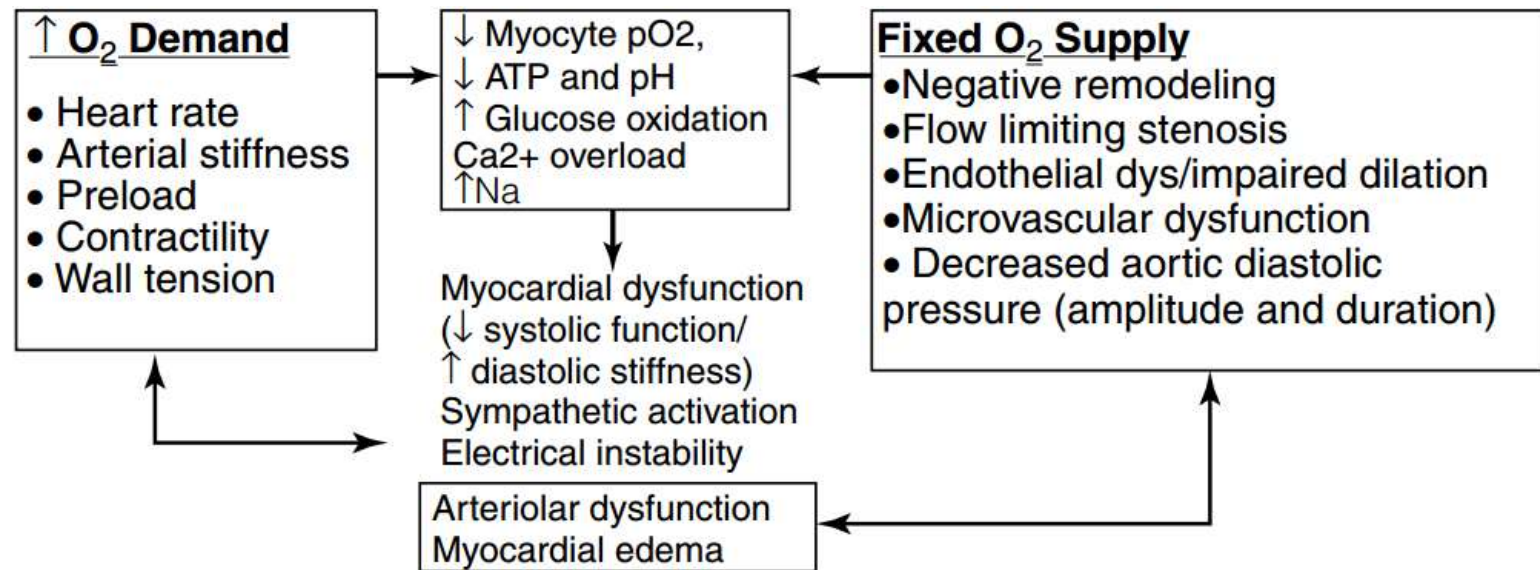
Mechanisms

(Key Moments)

- Chronic myocardial ischemia is a consequence of reduced blood flow in coronary arteries, due to a combination of fixed vessel narrowing and abnormal vascular tone as a result of ASVD and endothelial dysfunction with an imbalance between myocardial oxygen supply and demand:
 - The degree and the length of vessel narrowing affect the hemodynamic significance of a stenotic lesion
 - Endothelial dysfunction contributes to myocardial ischemia in inappropriate vasoconstriction of coronary arteries
- Non-ASVD causes of myocardial ischemia include decreased coronary perfusion pressure due to hypotension; decreased blood oxygen content due to marked anemia and pulmonary disease, unusual (e.g. congenital) coronary abnormalities, etc.

Mechanisms

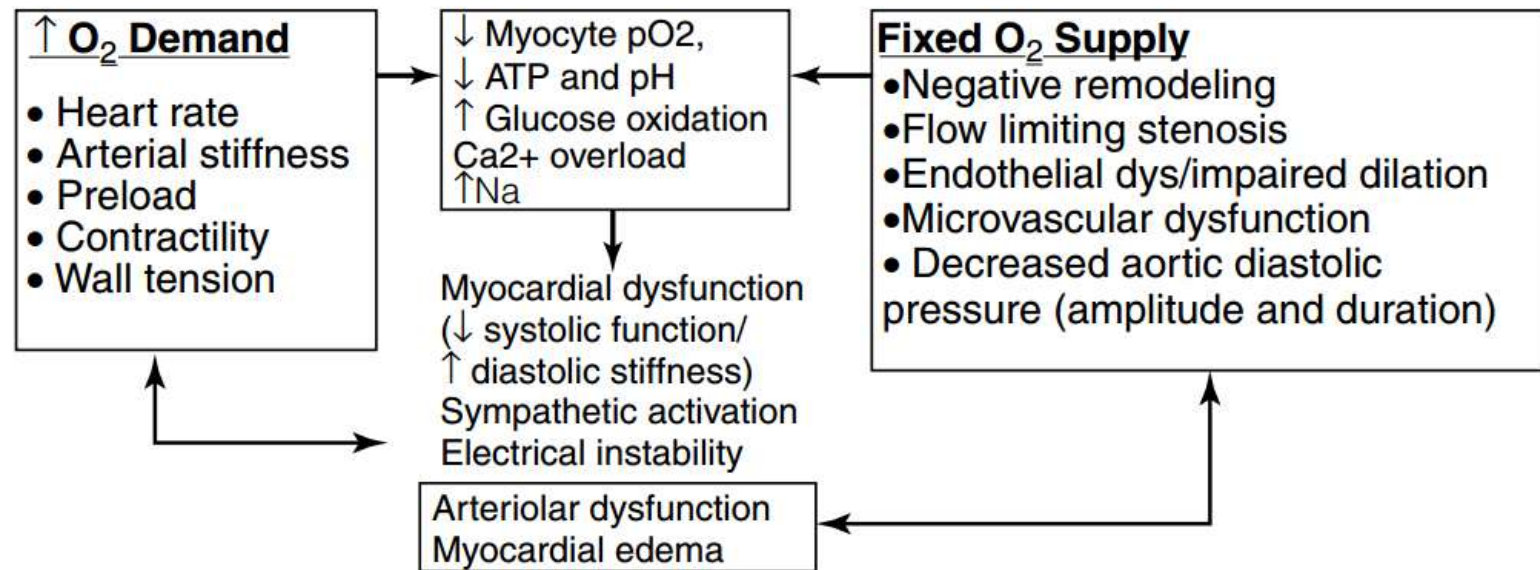
(Myocardial Ischemia begets more Ischemia)



Factors Important in SIHD

Mechanisms

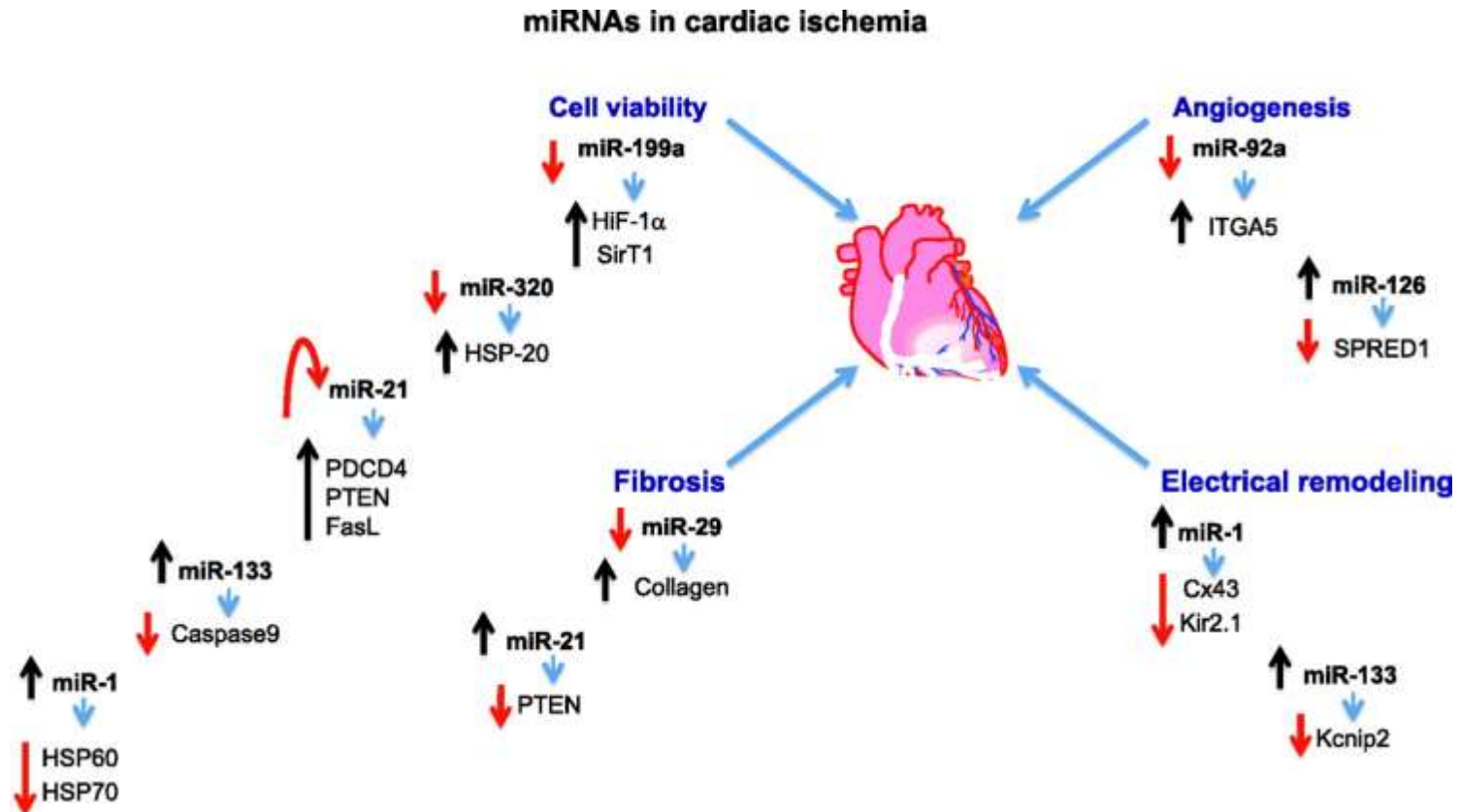
(Myocardial Ischemia begets more Ischemia)



Factors Important in SIHD

Mechanisms

(miRNAs and their targets in Cardiac Ischemia)



The different miRNAs (posttranscriptional regulators) and their targets that are involved in cell viability, angiogenesis, fibrosis, and electrical remodeling during cardiac ischemia.

Classification

(International Classification of Diseases (ICD))

Chapter IX

Diseases of the circulatory system

(I00-I99)

I20-I25 Ischaemic heart diseases

I20.1 Angina pectoris with documented spasm

Angina (angiospastic, Prinzmetal, spasm-induced, variant)

I20.8 Other forms of angina pectoris

Angina of effort

Coronary slow flow syndrome

Stable angina

Stenocardia

I20.9 Angina pectoris, unspecified

Angina (NOS (not otherwise specified), cardiac)

Anginal syndrome

Ischaemic chest pain

Classification

(Canadian Cardiac Society Angina Class Scale (C CSA))

Class Definition		Specific Activity Scale
I	Ordinary physical activity (eg, walking and climbing stairs) does not cause angina; angina occurs with strenuous, rapid, or prolonged exertion at work or recreation.	Ability to ski, play basketball, jog at 5 mph, or shovel snow without angina
II	Slight limitation of ordinary activity. Angina occurs on walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, in cold, in wind, or under emotional stress, or only during the few hours after awakening, when walking more than 2 blocks on level ground, or when climbing more than 1 flight of stairs at a normal pace and in normal conditions.	Ability to garden, rake, roller skate, walk at 4 mph on level ground, have sexual intercourse without stopping
III	Marked limitation of ordinary physical activity. Angina occurs on walking 1 to 2 blocks on level ground or climbing 1 flight of stairs at a normal pace in normal conditions.	Ability to shower or dress without stopping, walk 2.5 mph, bowl, make a bed, play golf
IV	Inability to perform any physical activity without discomfort.	Anginal symptoms may be present at rest. Inability to perform activities requiring 2 or fewer metabolic equivalents without angina

Classification

(from Stable Angina until Accelerating Angina)

- Angina is stable when its pattern of frequency, intensity, ease of provocation, or duration does not change over a period of several weeks. Identification of activities that provoke angina and the amount of sublingual nitroglycerin required to relieve symptoms are helpful indicators of stability versus progression.
- Angina is accelerating when there is a change in the pattern of stable angina. This may include a greater ease of provocation, more prolonged episodes, and episodes of greater severity, requiring a longer recovery period or more frequent use of sublingual nitroglycerin. This suggests a transition and most likely reflects a change in coronary artery blood flow and perfusion of the myocardium.

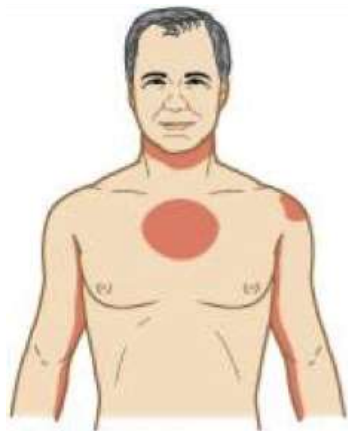
Clinical Investigation

(Passions around Symptoms)

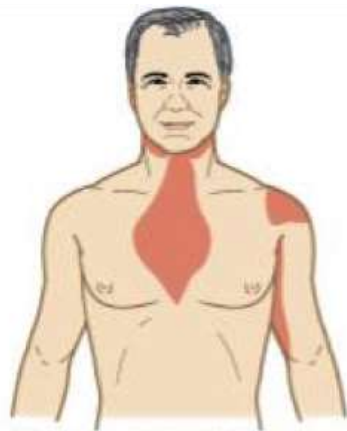
- Chest pain (angina) can be described as a heaviness, pressure, aching, burning, numbness, fullness, squeezing, discomfort or painful feeling in the chest, but may also be felt in the left shoulder, arms, neck, back, or jaw.
- Shortness of breath.
- Palpitations.
- Weakness or dizziness.
- Nausea.
- Sweating.
- Some patients have no signs or symptoms (silent ischemia) until there will be developed symptoms of a heart_attack, heart failure, or an arrhythmia.

Clinical Investigation

(Common Locations and Patterns of Angina Pain)



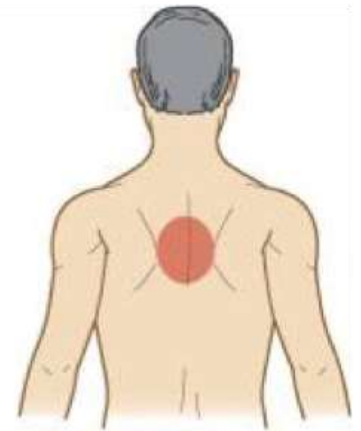
- Mid sternum
- Left shoulder and down both arms
- Neck and arms



- Substernal radiating to neck and jaw
- Substernal radiating down left arm



- Epigastric
- Epigastric radiating to neck, jaw, and arms



- Intrascapular

The characteristics of discomfort-related to angina may be divided into four categories: location, character, duration and relationship to exertion and other exacerbating or relieving factors. The discomfort caused by myocardial ischaemia is usually located in the chest, near the sternum, but may be felt anywhere from the epigastrium to the lower jaw or teeth, between the shoulder blades or in either arm to the wrist and fingers.

Clinical Investigation

(Traditional Clinical Classification of Chest Pain)

Typical angina (definite)	Meets all three of the following characteristics: <ul style="list-style-type: none">• substernal chest discomfort of characteristic quality and duration;• provoked by exertion or emotional stress;• relieved by rest and/or nitrates within minutes.
Atypical angina (probable)	Meets two of these characteristics.
Non-anginal chest pain	Lacks or meets only one or none of the characteristics.

Clinical Investigation

(Hallmark of Prinzmetal Angina)

- In contrast to patient with stable angina secondary to coronary atherosclerosis, patients with Prinzmetal (variant) angina (until 10% of angina patients) are younger and have fewer coronary risk factors (except smoking).
- Episode of chest pain usually does not progress from a period of chronic stable angina.
- Cardiac examination is normal in the absence of ischemia.
- Symptoms occur at rest (usually at night), rather than on exertion.
- 2/3 of patients have concurrent atherosclerosis of a major coronary artery, but this is often mild or not in proportion to the degree of symptoms.

Clinical Investigation

(Passions around Cardiac Syndrome X)

- Cardiac syndrome X is angina associated with decreased blood flow to the heart tissue with normal coronary arteries and referred to microvascular dysfunction.
- Angina is most of the time unpredictable and it can occur when at rest and/or during exercise.
- Pain is normally more intense and it lasts for longer periods of time compared to pain caused by other conditions.
- Some studies have found increased risk of other vasospastic disorders, such as migraine and Raynaud's phenomenon.
- It is treated with beta-blockers and usually carries a favorable prognosis.
- This is a distinct diagnosis from Prinzmetal angina.

Clinical Investigation

(Stable Angina versus Myocardial Infarction Comparison Chart)

Symptoms	Myocardial Infarction	Stable Angina
Occurrence of pain	Occurs at any time	Occurs due to physical or emotional stress
Modality of pain	With damage to the heart and usually described as severe, steady, and crushing	With no damage to the heart
Outcome	May be fatal	Usually not fatal
Relieving factors of pain	Symptoms persists after 15 min. and not relieved by rest or nitro	Symptoms relieved by rest or nitro within 10-15 min.
Duration of pain	Usually lasts for more than 15 min.	Usually for less than 15 min.; discomfort is transient, lasting 3-5 min.
Serum cardiac marker	Present	Not present

Clinical Investigation (History)

- The history should include any current symptoms and a complete inventory of comorbid conditions.
- An inventory of cardiac risk factors, and a complete family history are essential components.
- The history should also include information about the character and location of discomfort, radiation of discomfort, associated symptoms, and precipitating, exacerbating, or alleviating factors.
- The importance of the family history should not be underestimated.
- A detailed assessment, particularly of first-degree relatives for the presence of IHD and age of diagnosis is imperative when evaluating a patient's risk factor profile.

Clinical Investigation

(Physical Examination 1)

- The results of the physical examination of a patient may be entirely normal.
- The presence of multiple risk factors or atherosclerosis in the carotid or peripheral arteries increases the likelihood that a chest pain syndrome is related to myocardial ischemia.
- Evaluation should include measurements of blood pressure and the ankle-brachial index.
- Examination of the carotid arteries should include auscultation for bruits.
- Examination of the chest wall, neck, and shoulders for deformities and tenderness may be helpful in diagnosing musculoskeletal chest discomfort.

Clinical Investigation

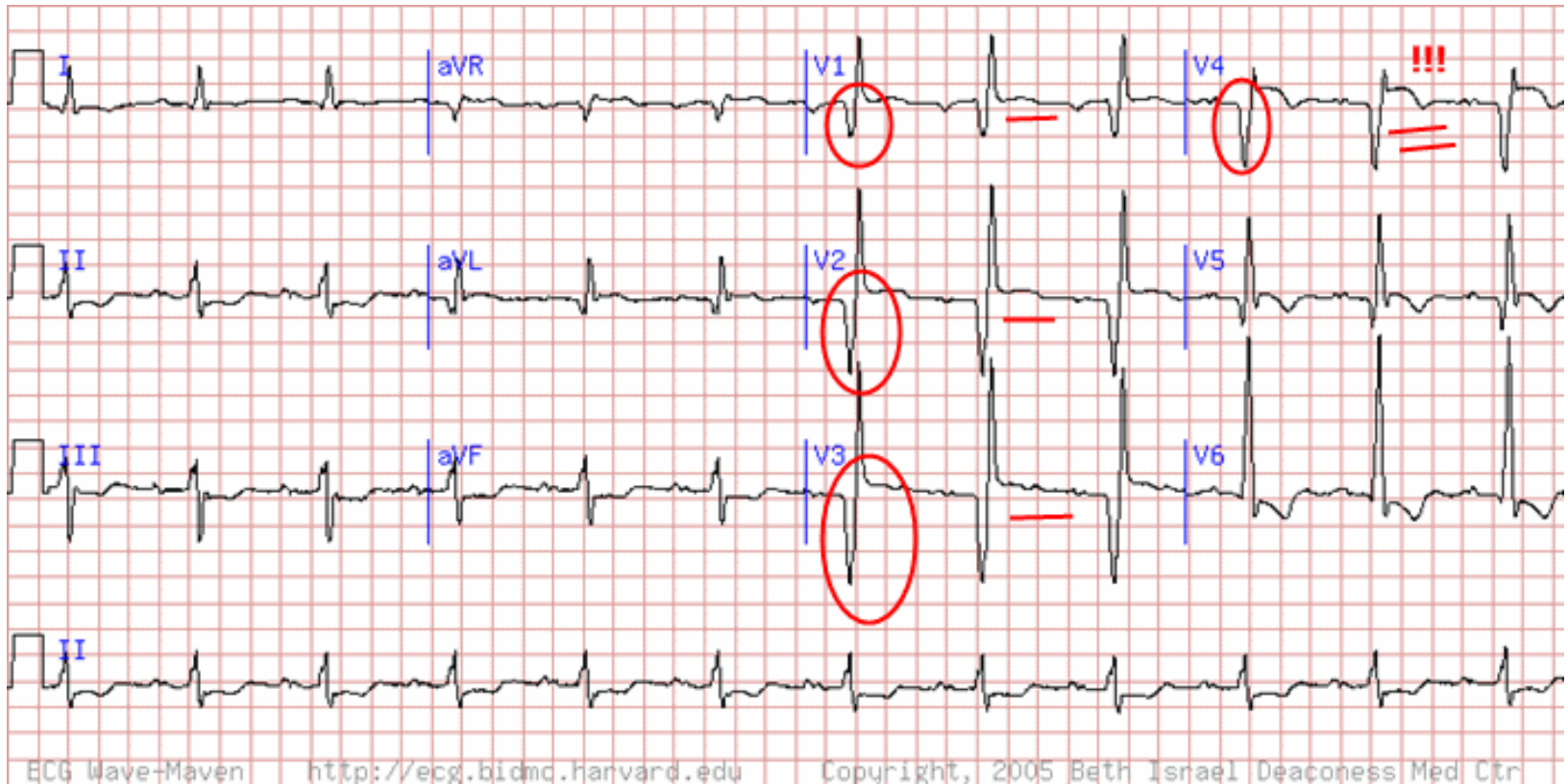
(Physical Examination 2)

- Cardiac auscultation may detect murmurs caused by aortic stenosis or hypertrophic cardiomyopathy, either of which can cause angina in the absence of IHD.
- Assessment of the abdominal aorta for an aneurysm or bruits and palpation of lower extremity pulses is necessary to evaluate for peripheral vascular disease.
- Careful palpation of all peripheral pulses and assessment of symmetry versus diminution are also valuable noninvasive approaches for assessing the integrity of the arterial circulation.
- Finally, examination for xanthelasmas, tendon xanthomas, retinal arterial abnormalities, and peripheral neuropathy can be helpful.

Diagnosis

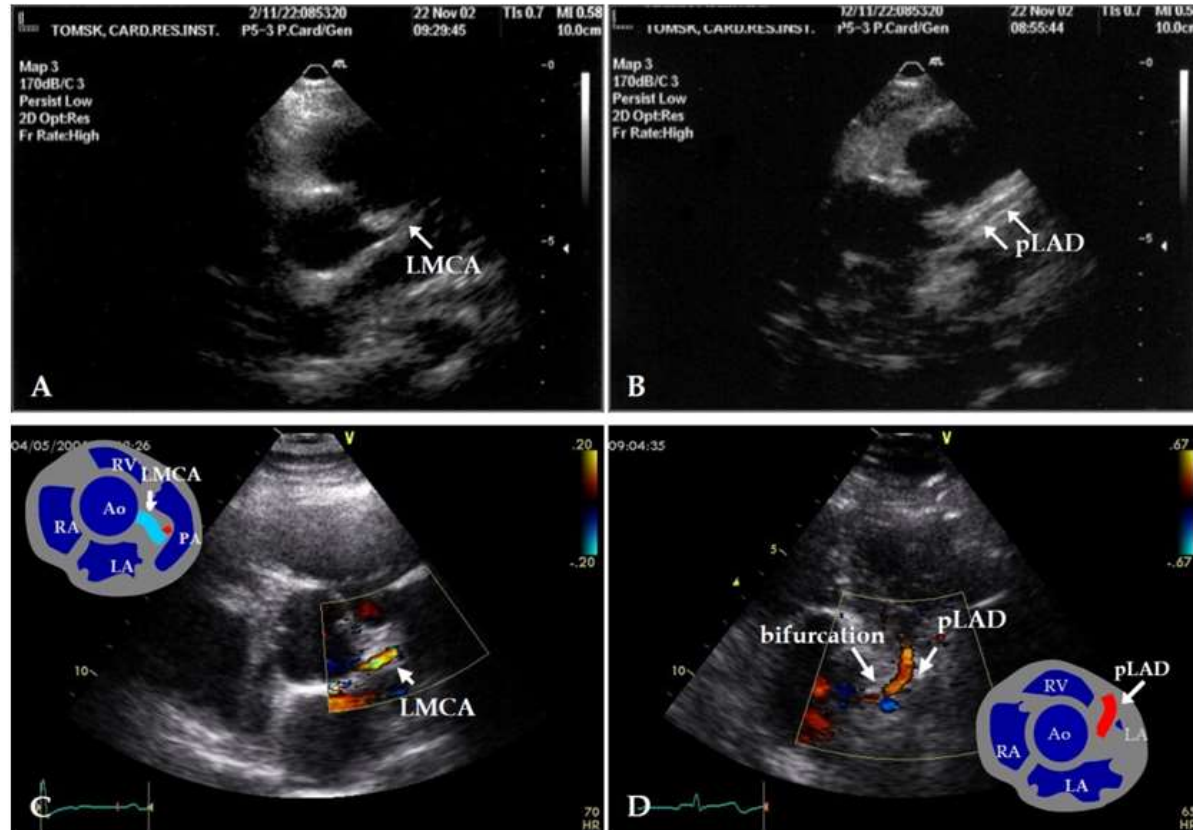
- Electrocardiogram (ECG): reveal evidence of a previous heart attacks
- B-mode, Doppler and intravascular ultrasound: degree of any blockages in arteries
- Ankle-brachial index: recognition of peripheral vascular disease, which is usually caused by atherosclerosis
- Stress test (including echocardiogram): reveal evidence of a chronic coronary artery disease
- Ambulatory ECG
- Vascular catheterization and angiogram: reveal evidence of narrowed, blocked or aneurismatic arteries
- Other imaging tests (CT, MRA, etc.): reveal evidence of narrowed or blocked arteries, as well as aneurysms and calcium deposits in the artery walls
- Blood tests: cholesterol and C-reactive protein levels, lipoproteinogram

Diagnosis (Electrocardiogram)



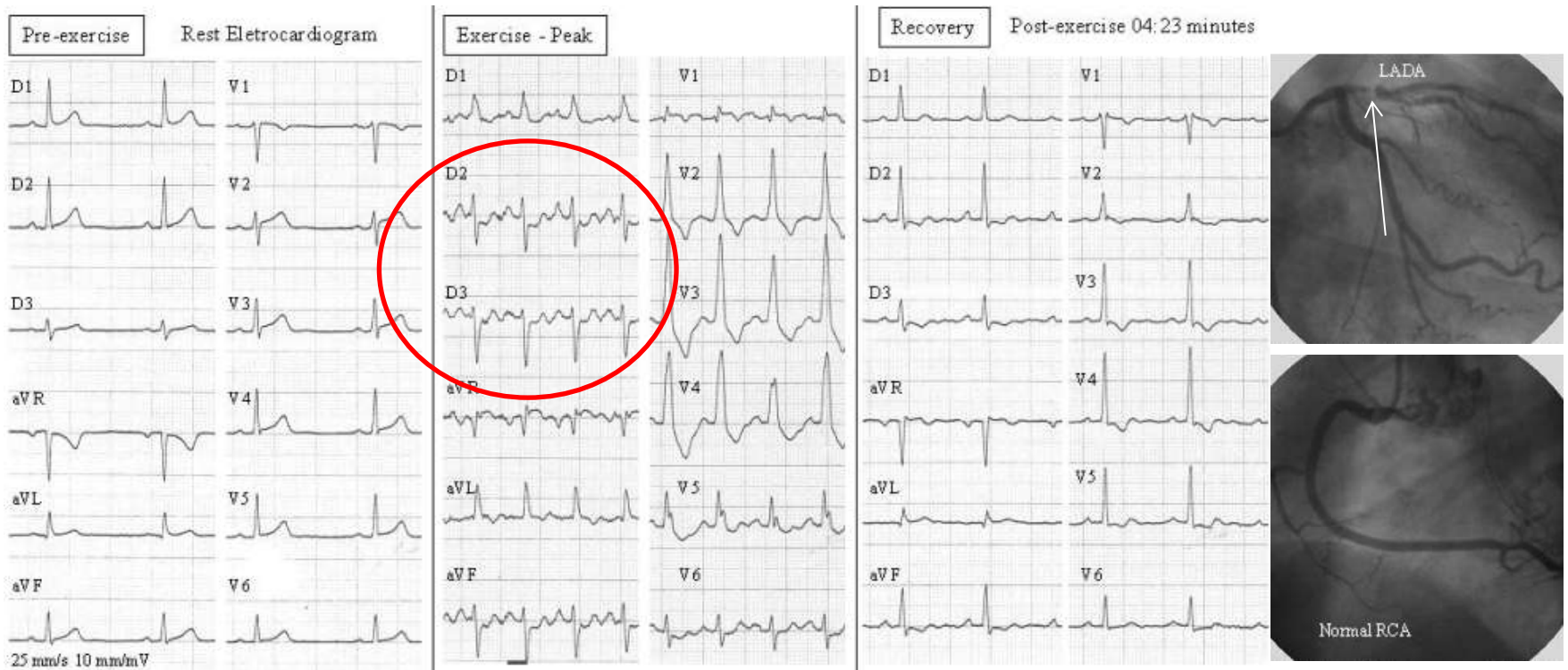
An old post-infarction scar of the front wall (deep Q in V1- V4). The situation is most probably complicated by a suspected ventricular aneurysm. ST sections for QRS in V1 -V4 are elevated, best seen in V4 where the elevation reminds the Pardee's wave (underlined in red).

Diagnosis (Ultrasound)



Images of the left main coronary artery (LMCA) and proximal the left anterior descending coronary artery (LAD - pLAD). The left parasternal position, a modified parasternal short axis view of great vessels, Nyquist limit is 20-67 cm/s. A – LMCA, B-mode; B – pLAD, B-mode; C – LMCA, Color Doppler mapping; D - bifurcation of the LMCA; Color Doppler mapping.

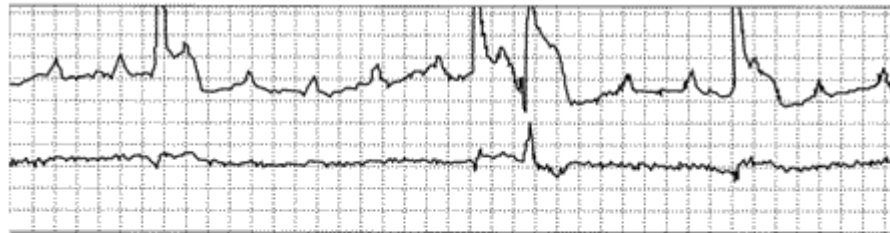
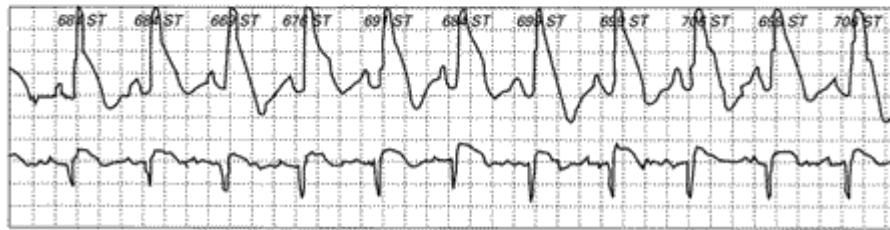
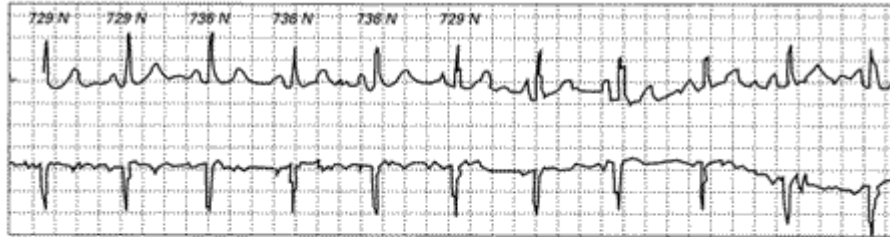
Diagnosis (Stress test)



54-year-old male, with a chest pain during exercise (II C CSA) underwent an exercise stress test. ECG demonstrated an increase in R wave amplitude from V1 to V4, and minor ST segment depression in DII, DIII and aVF. Coronary angiogram showed a critical proximal left anterior descending artery lesion.

Diagnosis

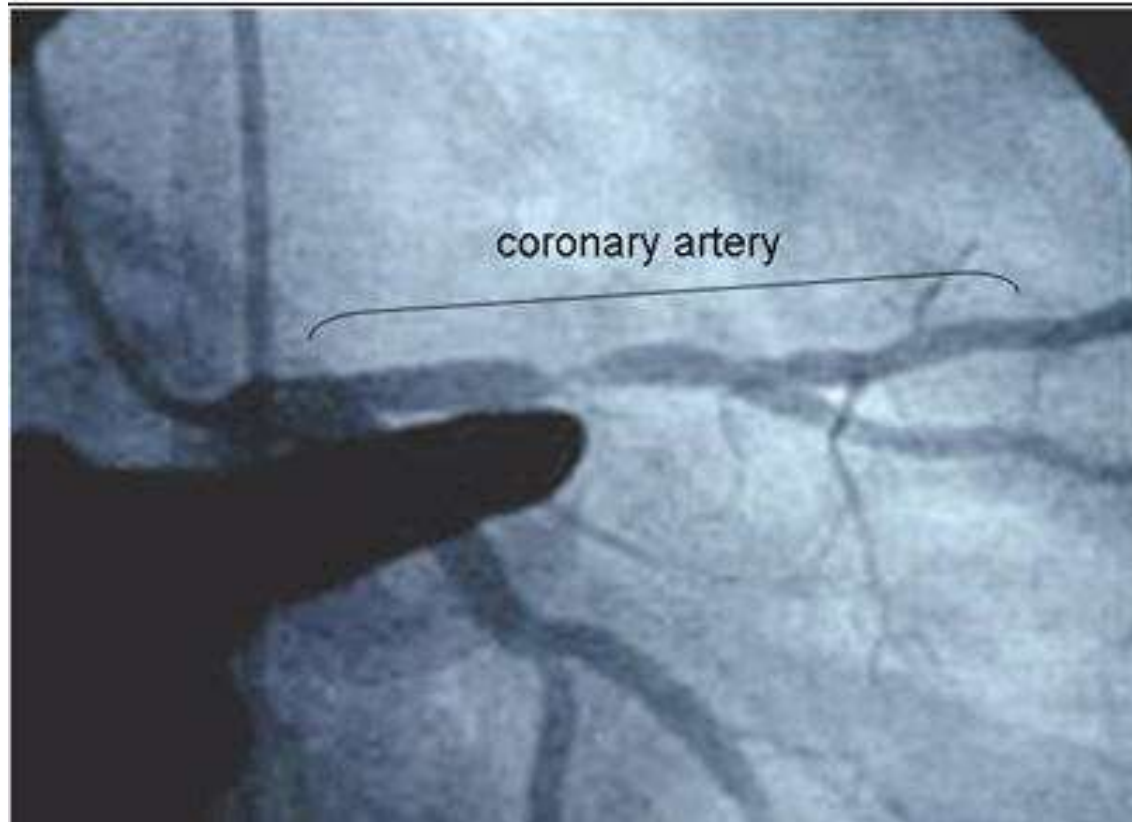
(Ambulatory ECG)



AECG recording in Prinzmetal angina. A. Control. Lead II (top), precordial lead (bottom). B. Marked ST-segment elevation, associated with mild angina. C. High-grade atrioventricular block and continued ST-segment elevation, associated with near syncope. D. Nonsustained ventricular tachycardia with continued ST-segment elevation associated with palpitations and light-headedness.

Diagnosis

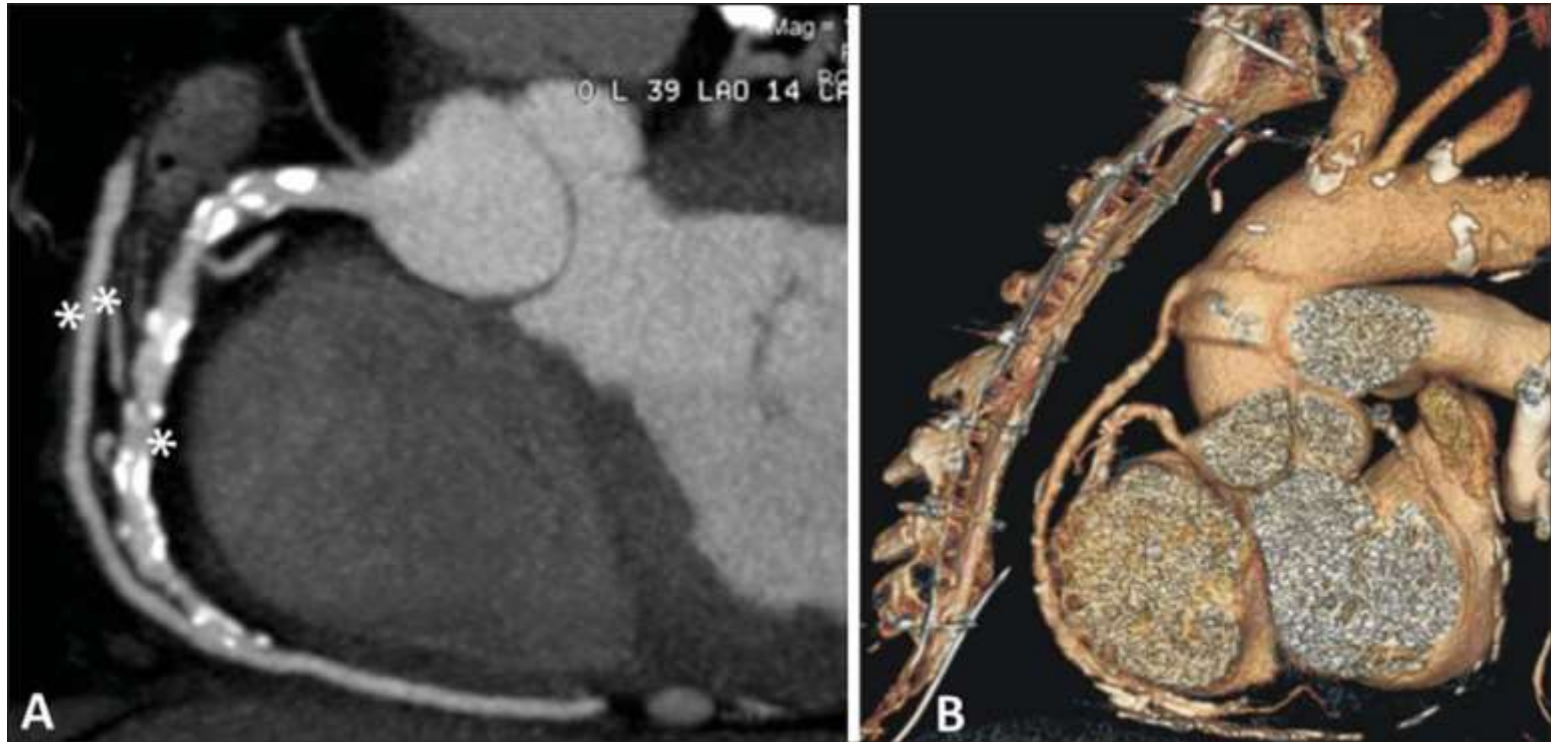
(Vascular catheterization and angiogram)



The finger (top left) is pointing to the narrowed region of a dye-filled coronary artery.

Diagnosis

(Coronary computed tomography angiography)



Evaluation of vena saphena graft to right coronary artery. Note the permeable graft (double asterisks) and the anastomosis with the right coronary artery (single asterisk) (A). 3D reconstruction (B).

Treatment

(Lifestyle Changes)

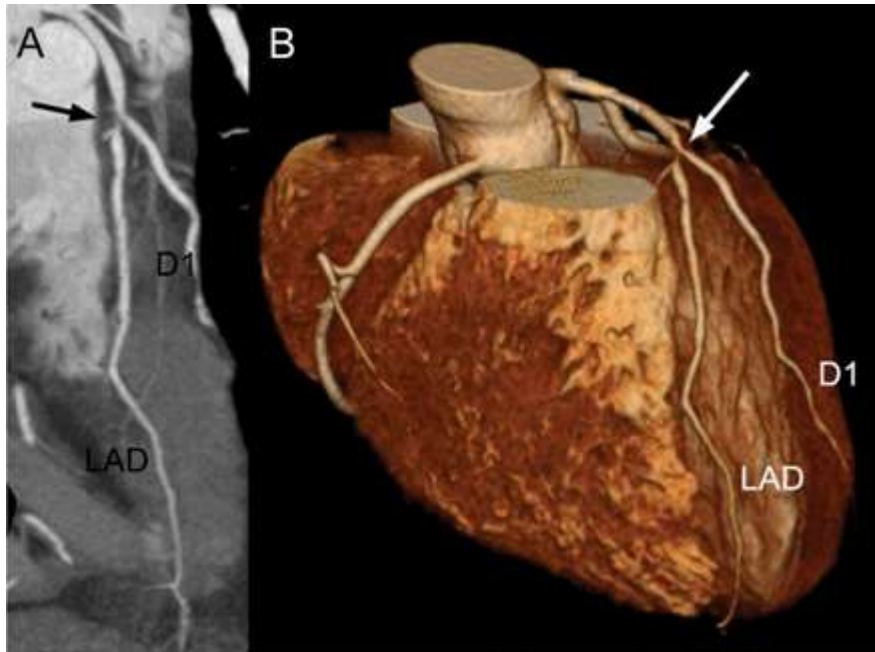
- Salt restriction
- Moderation of alcohol consumption
- Other dietary changes (vegetables, low-fat dairy products, dietary and soluble fibers, whole grains and protein from plant sources, reduced in saturated fat and cholesterol)
- Weight reduction
- Regular physical exercise
- Smoking cessation

Treatment (Education)

- There should be a change in focus in the education of all physicians to more strongly emphasize evidence based primary prevention of SIHD as a part of ASVD
- Education focused on school children, especially targeted to create sustainable healthy behavior and sustainable control of risk factors
- Telemedicine has been proven effective in selected world regions
- Engage the media to promote education for SIHD and ASVD prevention, and the need for rapid access to treatment
- Produce easily accessible (through medical journals and internet) guidelines for management of IHD and ASVD

Treatment

(Pharmacotherapy Aims)



The two aims of the pharmacotherapy of SIHD patients are to obtain relief of symptoms and to prevent cardiovascular (CV) events.

Treatment

(Pharmacotherapy Medications 1)

Medications for risk factors and ischemia management:

- Nitrates,
- Beta-blockers,
- Calcium channel blockers,
- ivabradine,
- Nicorandil,
- Trimetazidine,
- Ranolazine,
- Allopurinol,
- Molsidomine.

Treatment

(Nitrates 1)

Short-acting nitrates for acute effort angina:

- Sublingual nitroglycerin is the standard initial therapy for effort angina. When angina starts, the patient should rest sitting and take sublingual nitroglycerin (0.3–0.6 mg) every 5 min until the pain goes or a maximum of 1.2 mg has been taken within 15 min. Nitroglycerin spray acts more rapidly. Nitroglycerin can be used prophylactically when angina can be expected, such as activity after a meal, emotional stress, sexual activity and in colder weather.
- Isosorbide dinitrate (5 mg sublingually) helps to abort anginal attacks for about 1 h.

Treatment

(Nitrates 2)

- Long-acting nitrates (isosorbide dinitrate, mononitrates, transdermal nitroglycerin patches) for angina prophylaxis are not continuously effective if regularly taken over a prolonged period without a nitrate-free or nitrate-low interval of about 8–10 hours (tolerance).
- Worsening of endothelial dysfunction is a potential complication of long-acting nitrates, hence the common practice of the routine use of long-acting nitrates as first line therapy for patients with effort angina needs re-evaluation.

Treatment

(Beta-blockers)

Beta-blockers act directly on the heart to reduce heart rate, contractility, atrioventricular (AV) conduction and ectopic activity.

Additionally, they may increase perfusion of ischaemic areas by prolonging the diastole and increasing vascular resistance in non-ischaemic areas.

Treatment

(Calcium channel blockers)

- Calcium channel blockers (calcium antagonists) act chiefly by vasodilation and reduction of the peripheral vascular resistance.
- Calcium channel blockers can chemically be classified into the dihydropyridines and the non- dihydropyridines, their common pharmacological property being selective inhibition of L-channel opening in vascular smooth muscle and in the myocardium.
- The non- dihydropyridines, by virtue of nodal inhibition, tend to reduce the heart rate (heart rate-lowering agents, verapamil and diltiazem) and explain the anti-anginal properties.

Treatment

(Ivabradine)

- Ivabradine is a heart rate-lowering agent selectively inhibiting the sinus node I(f) pacemaking current, thereby decreasing the myocardial oxygen demand without effect on inotropism/
- The effect was predominant in patients with a heart rate ≥ 70 bpm.
- Ivabradine is an effective anti-anginal agent, alone or in combination with b-blockers.

Treatment (Nicorandil)

- Nicorandil is a nitrate derivative of nicotinamide that can be used for the prevention and long-term treatment of angina, and may be added after beta-blockers and calcium antagonists.
- Long-term use of oral nicorandil may stabilize coronary plaque in patients with stable angina.

Treatment (Trimetazidine)

- Trimetazidine is an anti-ischaemic metabolic modulator, with similar anti-anginal efficacy to propranolol in doses of 20 mg thrice daily.
- The heart rate and rate \times pressure product at rest and at peak exercise remained unchanged in the trimetazidine group, thus showing a non-mechanical anti-ischaemic action.

Treatment (Ranolazine)

- Ranolazine is a selective inhibitor of late sodium current with anti-ischaemic and metabolic properties.
- Ranolazine can be added to other well-established anti-anginal drugs, in particular in patients with higher HbA1c levels, who may also more often rely on medical management.

Treatment (Allopurinol)

- Allopurinol, an inhibitor of xanthine oxidase that reduces uric acid in persons with gout, is also anti-anginal.
- Allopurinol additionally reduced vascular oxidative stress.

Treatment (Molsidomine)

- This direct NO donor has anti-ischaemic effects similar to those of isosorbide dinitrate.
- The long-acting once-daily 16 mg formulation is as effective as 8 mg twice daily.

Treatment

(Pharmacotherapy Medications 2)

Medications for event prevention:

- Antiplatelet agents (low-dose aspirin, P2Y₁₂ inhibitors (thienopyridines) and their combinations).
- Lipid-lowering agents (statins).
- Renin-angiotensin-aldosterone system blockers.

Treatment

(Antiplatelet Agents)

- Antiplatelet agents decrease platelet aggregation and may prevent formation of coronary thrombus.
- Due to a favorable ratio between benefit and risk in patients with SIHD and its low cost, low-dose aspirin is the drug of choice in most cases and clopidogrel may be considered for some patients.
- The use of antiplatelet agents is associated with a higher bleeding risk.

Treatment

(Lipid-lowering Agents)

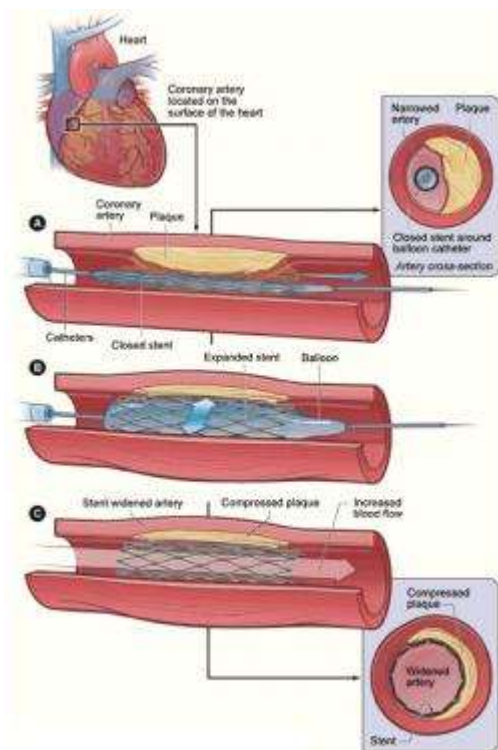
- Patients with documented CAD are regarded as being at very high risk and should be treated with statins.
- The treatment target is LDL-C ,1.8 mmol/L and/or more than 50% reduction if the target level cannot be reached.

Treatment

(Renin-Angiotensin-Aldosterone System Blockers)

- Angiotensin converting enzyme (ACE) inhibitors reduce total mortality, myocardial infarction, stroke and heart failure among specific subgroups of patients, including those with heart failure, previous vascular disease alone, or high-risk diabetes.
- Hence, it is appropriate to consider ACE inhibitors for the treatment of patients with SIHD, especially with co-existing hypertension, left ventricle ejection fraction $\leq 40\%$, diabetes or chronic kidney disease, unless contra-indicated.

Treatment (Revascularization)



- Percutaneous coronary intervention
- Coronary artery bypass surgery
- Revascularization vs. medical therapy

Prognosis

- Long-term prognosis in the individual patient is unpredictable.
- There are indications that the course of coronary heart disease may be modified, and that the pattern of survival may begin to approach that of the average population by controlling some of the predisposing factors, and by application of such measures as dietary restriction of fat and prolonged anticoagulation.

Prophylaxis

- Risk factor assessment and modification should begin early in life (childhood)
- Most risk factors can be modified by lifestyle changes as opposed to drug or device treatment
- Solidarity in primary prevention efforts will benefit both the individual and the society as a whole
- Effective treatment reduces the first clinical manifestations of SIHD and ASVD
- The role of Governments is crucial
- Aggregate risk factor reduction can decrease cardiovascular events by as much as 70%
- Adequate Secondary prevention measures can reduce vascular event recurrence by 75%

Abbreviations

- ACE - angiotensin converting enzyme
- ASVD – atherosclerotic vascular disease
- CT – computer tomography
- CV - cardiovascular
- CAD -coronary artery disease
- ECG – electrocardiography
- ICD - International Classification of Diseases
- IGT - impaired glucose tolerance
- IHD - ischemic heart disease
- HDL – high-density lipoprotein
- LDL - low-density lipoprotein
- MRA – magnetic resonance angiogram
- miRNAs - posttranscriptional regulators
- SIHD – stable forms of ischemic heart disease

Diagnostic and treatment guidelines

Europe

- [2013 ESC guidelines on the management of stable coronary artery disease](#)
- [Joint 2016 European Guidelines on Cardiovascular Disease Prevention in Clinical Practice](#)

North America

- [2014 ACC/AHA/AATS/PCNA/SCAI/STS Focused Update of the Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease](#)
- [2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease](#)