BMJ Best Practice

Stable ischaemic heart disease

Straight to the point of care

Last updated: Jun 09, 2023

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Summary

Initial assessment of stable ischaemic heart disease involves a thorough history, including chest discomfort and related symptoms as well as risk factors, in order to assess the likelihood of coronary artery disease. This is followed by appropriate non-invasive testing guided by the probability of disease.

Management should focus on lifestyle modification, with emphasis on smoking cessation, weight management, physical activity, lipid control, and blood pressure control.

Antiplatelet therapy should be prescribed for all patients, and dual antiplatelet therapy may be considered in selected patients.

Beta-blockers may improve survival in selected patients. Addition of short- and long-acting nitrates, beta-blockers, and calcium-channel blockers can reduce chronic anginal symptoms.

Patients with persistent angina despite lifestyle modification and guideline-directed medical therapy may warrant percutaneous or surgical revascularisation for reduction of symptoms.

It is possible that for carefully selected patients, revascularisation in addition to lifestyle modification and medical therapy may improve survival.

Definition

Ischaemic heart disease, an inability to provide adequate blood supply to the myocardium, is primarily caused by atherosclerosis of the epicardial coronary arteries. For this reason the terms ischaemic heart disease, chronic coronary syndrome, coronary heart disease, and coronary artery disease are often used interchangeably, although the true pathophysiology is more complex.[1] [2]

Complications of ischaemic heart disease include myocardial infarction, ischaemic cardiomyopathy, and sudden cardiac death. Exertional angina is the classic symptom of ischaemic heart disease, but patients may have atypical or no symptoms. Although routine screening is discouraged, testing may reveal ischaemic heart disease in patients without symptoms or complications.

Ischaemic heart disease is said to be stable when symptoms, if any, are manageable and not rapidly progressive; there must also be no recent infarction, procedural intervention, or signs of significant ongoing cardiac necrosis. Stable ischaemic heart disease (SIHD) stands in contrast to acute coronary syndrome (ACS), a term that encompasses unstable angina, ST-elevation myocardial infarction, and non-ST-elevation myocardial infarction. Although ACS is a manifestation of the same general disease process as SIHD, risk stratification, diagnostic testing, and medical and procedural management usually differ significantly between the two conditions. In some circumstances patients with low-risk unstable angina may be managed similarly to patients with SIHD.[3] [4]

Epidemiology

Ischaemic heart disease (IHD) is the leading cause of morbidity and mortality in the US and worldwide.[6] [7] IHD is common, particularly among older adults; in the US, the prevalence rises from 7.5% in men and 6.5% in women aged 40 to 59 years to 30.6% in men and 20.6% in women aged 80 years and older.[8] In the US, the lifetime risk of developing IHD at age 40 years is one in two for men and one in three for women.[9] Globally, it was estimated that 197.2 million people had IHD in 2019, and it was more prevalent in men (113.7 million) than in women (83.6 million).[10] Despite a male predominance and roughly 10-year lag in incidence in women, IHD is the leading cause of mortality for women worldwide.[11] [12]

In the US, Canada, and much of Europe, mortality from IHD has been declining since at least 1990.[13] [14] This decline is likely caused by improvements in treatment as well as reductions in risk factors including smoking, hypertension, and hyperlipidaemia.[15] There is concern that these improvements may be offset by increases in obesity, physical inactivity, and diabetes.[16] Globally, IHD mortality is increasing in lower- and middle-income countries such that it is now the leading cause of premature mortality in all but the least sociodevelopmentally advantaged nations.[7]

Prevalence of IHD varies widely both between and within countries.[6] [13] [14] IHD and many of its risk factors (e.g., hypertension and hyperlipidaemia) have both genetic and environmental influences. On the basis of a study of Swedish twins, the overall heritability of IHD is often cited as 40% to 60%.[17] Family history of IHD, particularly premature IHD, is a risk factor for ischaemic events in middle-aged adults.[18] Socioeconomic inequalities are predispositions to IHD, and there is increasing attention to social determinants of health including social support, culture, language, access to care, neighbourhood environment, and exposure to adversity.[14][19] [20] [21]

Aetiology

Ischaemic heart disease is primarily caused by atherosclerosis.

Less common, non-atherosclerotic causes include vasospasm, endothelial and microvascular dysfunction, spontaneous thrombosis or embolism, coronary artery dissection, extrinsic compression, systemic vasculitis/arteritis, and damage from radiation.[22] [2] [23] [24] These aetiologies are more common in younger patients, women, and those without traditional ischaemic heart disease risk factors.[23] [24]

Pathophysiology

Atherosclerosis is the development of lipid-rich plaques in the arterial wall. Plaque development is the result of an inflammatory process that can involve not only lipids but also altered smooth muscle cells, matrix proteins, calcification, necrosis, and haemorrhage. Plaques do not occur uniformly through the arterial tree and tend to occur at bends, branch points, and other areas of turbulent flow.[25]

A traditional model suggests two means of plaque progression. Large thick-walled plaques are thought to slowly obstruct the lumen of coronary arteries, thereby causing decreased perfusion and chronic intermittent exertional symptoms when they reach 70% to 80% stenosis. Thin-walled 'vulnerable plaques' may not cause meaningful obstruction until the wall is disrupted, at which point acute haematoma and thrombus formation cause sudden myocardial infarction by occluding the arterial lumen locally or embolising distally into the coronary circulation. This model explains two clinically important phenomena: 1) myocardial infarction may occur in patients at anatomical sites without baseline flow limitation; 2) therapies that reduce chronic

intermittent angina (improve flow) may be different from those that reduce ischaemic heart disease mortality (stabilise plaque, prevent thrombosis).

The actual process is more varied and complex. In many cases arteries can expand outwards, meaning that plaque size may not correlate with luminal stenosis, which in turn may not correlate with functional flow limitation.[26] [27] Additionally, plaque development is not linear; plaques may move repeatedly through development, regression, and erosion/rupture.[26]

Classification

The Canadian Cardiovascular Society grades angina by the extent of limitation of physical activity.[5]

Grade I: Ordinary physical activity (walking, climbing stairs) does not cause angina. Angina occurs with strenuous or rapid or prolonged exertion at work or recreation.

Grade II: Slight limitation of ordinary activity. Angina may occur with moderate exertion, such as walking or climbing stairs rapidly, walking uphill, walking or climbing stairs after meals, in cold or wind, under emotional stress, or during the few hours after awakening, or walking more than two blocks on level ground, or climbing more than one flight of ordinary stairs at a normal pace and in normal conditions.

Grade III: Marked limitation of ordinary physical activity. Angina occurs with mild exertion, such as walking one or two blocks on level ground and climbing one flight of stairs in normal conditions and at normal pace.

Grade IV: Inability to carry on any physical activity without discomfort, anginal syndrome may be present at rest.

Case history

Case history #1

A 50-year-old man presents with a complaint of central chest discomfort of 2 weeks' duration, occurring after walking for more than 5 minutes or climbing more than one flight of stairs. The chest discomfort resolves with rest within several minutes. He is obese, has a history of hypertension, and smokes 10 cigarettes a day. His father died from a myocardial infarction at the age of 54 years. On examination, his blood pressure is 144/92 mmHg with a heart rate of 82 bpm. The remainder of his examination is normal.

Case history #2

A 60-year-old man with a history of a myocardial infarction presents for follow-up. He was started on aspirin, beta-blocker, and statin therapy after his heart attack. In the past 2 weeks the patient has noted return of chest pressure when he walks rapidly. The chest pressure resolves with sublingual glyceryl trinitrate or a decrease in his activity level. He is a former smoker and has modified his diet and activity to achieve his goal body weight. He is normotensive on examination with a heart rate of 72 bpm. The remainder of his examination is normal.

THEORY

Other presentations

Atypical locations of anginal pain include the epigastrium, neck, jaw, or arms. Exertional dyspnoea, fatigue, nausea, indigestion, and light-headedness are alternative symptoms sometimes called anginal equivalents. Women, older people, and patients with diabetes may be more likely to present with atypical angina or anginal equivalents.

Approach

Evaluation of a patient with suspected stable ischaemic heart disease (SIHD) typically begins with assessment of symptoms and risk factors. Symptoms and risk factors together determine a patient's pre-test probability of SIHD. Whether calculated formally using risk tables or informally with clinical judgement, pre-test probability is the basis for further diagnostic testing.[3] [4]

An important first step is to ensure that symptoms are stable. Chronic or subacute symptoms that are intermittent and exertional are characteristic of SIHD. Acute onset or rapidly progressive chest pain or dyspnoea can be signs of acute coronary syndrome or other emergent conditions. Evaluation and risk stratification of these patients is different and usually done in emergency departments or acute care settings.

Clinical history

Angina pectoris, chest discomfort caused by cardiac ischaemia, is the cardinal symptom of ischaemic heart disease. Patients often describe pressure, tightness, heaviness, or squeezing discomfort rather than 'pain'. Angina is classically substernal although it may radiate to the neck, jaw, epigastrium, and left or possibly right arm. It is unusual to present above the mandible, below the umbilicus, or localised to a small area of the chest wall. Pain that is sharp, positional, or pleuritic is less characteristic. Anginal symptoms are usually gradual in onset and last minutes rather than being fleeting or prolonged for hours.[57]

Angina is defined by three features:

- Substernal chest discomfort of characteristic quality and duration
- Provoked by exercise or emotional stress
- Relieved with rest or glyceryl trinitrate.

Patients with more of these features are at greater likelihood of having ischaemic heart disease.[58] [59] [60] However, patients with ischaemic heart disease may have different or additional symptoms including anginal 'equivalents', such as dyspnoea, fatigue, nausea, numbness, indigestion, and light-headedness.[57]

In the US there is evidence that women and Black, Hispanic, and South Asian patients are less likely to receive appropriate diagnostic testing for coronary disease. Although women often experience typical symptoms, they are also more likely to experience dyspnoea, nausea, and fatigue.[57]

Chest pain has traditionally been described as ‘typical’ if it has all three features of angina, ‘atypical’ if it has two, and ‘non-anginal’ if it has one or none of the features of angina. Some guidelines avoid the term 'atypical' and instead suggest ‘cardiac’, ‘possibly cardiac’, and ‘non-cardiac’ pain, although symptoms alone can not determine the cause of chest pain.[57] [61]

Physical examination

The physical examination is often normal or non-specific in patients with stable angina but may reveal signs of associated conditions such as heart failure, valvular disease, or hypertrophic cardiomyopathy. Findings suggestive of non-coronary atherosclerotic disease, such as diminished pedal pulses, pulsatile abdominal mass, or carotid bruit, increase the likelihood of ischaemic heart disease.[58] [62] Presence of a rub suggests pericardial or pleural disease as the source of pain. Pain that is reproduced by palpation of the chest reduces the likelihood of angina.[63] Fundoscopy may demonstrate presence of increased light

reflexes and arteriovenous nicking, providing evidence of hypertension and associated risk of coronary disease. Presence of xanthomas or xanthelasma suggests severe hypercholesterolaemia.

Laboratory testing

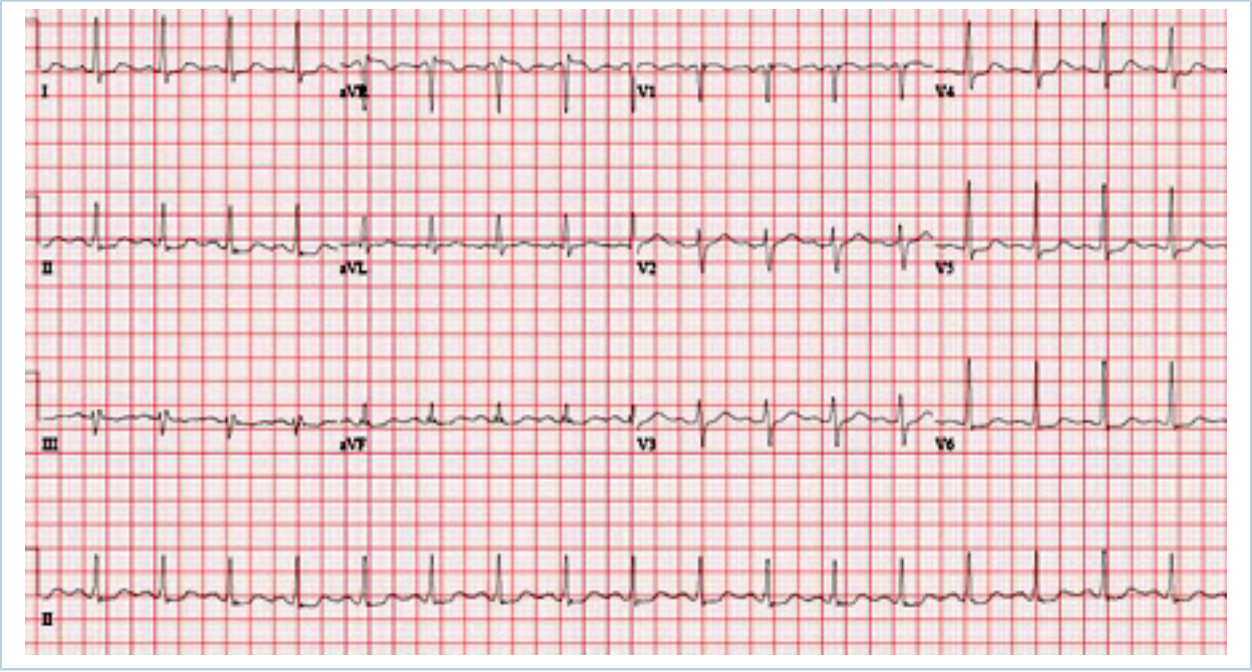
Initial laboratory testing should include haemoglobin and lipid panel, and testing for diabetes mellitus.

Angina is caused by an imbalance of myocardial oxygen supply and demand. It is important to evaluate for anaemia as a contributor or alternative cause of anginal pain. Metabolic abnormalities associated with risk factors (diabetes, hypercholesterolaemia) should be investigated as part of the evaluation of patients with angina.

Other causes of increased metabolic demands on the heart (e.g., thyrotoxicosis) or past medical history such as hypothyroidism (associated with dyslipidaemia) should be investigated, if warranted by the history and physical examination.[3] [4]

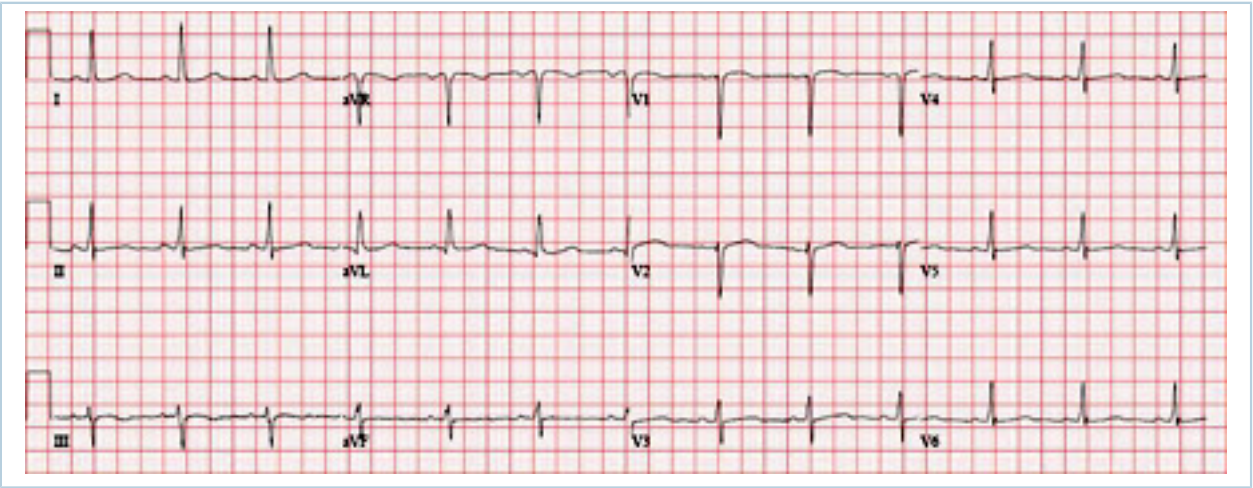
Resting ECG

Resting ECG is recommended for all patients without an obvious non-cardiac cause of chest pain.[57] It will be normal in >50% of patients, but may reveal abnormalities such as arrhythmias, Q waves, or ST changes that may increase the likelihood of ischaemic heart disease. Furthermore, it can determine baseline abnormalities that may preclude use of exercise ECG for non-invasive stress testing. These include complete left bundle branch block, >1 mm of ST depression, and paced rhythm or pre-excitation syndrome. An ECG taken during an episode of chest pain may demonstrate ST-segment depression suggestive of ischaemia.[3] [4]



ECG showing non-specific ST depressions in V5 and V6, which may indicate ischaemia. There are non-specific ST-segment changes in III and aVF

From the collection of Dr S.D. Fihn; used with permission



Normal ECG

From the collection of Dr S.D. Fihn; used with permission

Resting echocardiography

Resting echocardiography can identify prior myocardial infarction (MI); suggest alternative myocardial, valvular, or pericardial causes of chest symptoms; and provide prognostic information in patients with SIHD. For patients with known or suspected SIHD, US guidelines recommend resting echocardiography only in the presence of prior MI or pathological Q waves on ECG (or the more conventional indications of signs of heart failure, complex ventricular arrhythmias, or undiagnosed murmur).[3] European guidelines endorse echocardiography in all cases of suspected SIHD and consideration of adding carotid ultrasound to identify peripheral atherosclerosis.[4] However, the value of this additional testing is not well established. Both guidelines advise against repeat echocardiography in the absence of a change in clinical status.

Estimating pre-test probability

When the clinical evaluation is complete, the practitioner must determine whether the probability of ischaemia warrants further testing.

Pre-test probability has typically been estimated from age, sex, and the clinical classification of chest pain: typical (cardiac), atypical (possibly cardiac), or non-cardiac.[3] [64] [65] Updated pre-test probabilities using contemporary data sets also include estimates for patients presenting with dyspnoea rather than angina.[4] [60] These updated data sets suggest lower rates of SIHD for most groups. It is not known whether the lower pre-test probabilities in contemporary studies are due to changes in population-level prevention efforts (e.g., statins), patient reporting, or study design. US and European guidelines suggest use of the new, lower pre-test probabilities.[4] [57] European guidelines also suggest adjusting the calculated pre-test probability for additional factors (e.g., family history, smoking) as well as other data that may be available (e.g., resting ECG changes, coronary calcium score).[4] However, there is no algorithmic way to make such adjustments.

	Typical (%)		Atypical (%)		Non-anginal (%)		Dyspnoea as only/primary symptom	
Age (years)	Men	Women	Men	Women	Men	Women	Men	Women
30-39	3	5	4	3	1	1	0	3
40-49	22	10	10	6	3	2	12	3
50-59	32	13	17	6	11	3	20	9
60-69	44	16	26	11	22	6	27	14
70+	52	27	34	19	24	10	32	12

Pre-test probabilities of obstructive coronary artery disease in symptomatic patients according to age, sex, and nature of symptoms in pooled analysis

Juarez-Orozco et al. Eur Heart J Cardiovasc Imaging. 2019 Nov 1;20(11):1198-207; used with permission

Note: typical angina indicates presence of all three features of angina (substernal chest pain/discomfort; provoked by exercise or emotional stress; relieved with rest or nitroglycerin); atypical angina indicates presence of two of the three features; non-anginal pain indicates presence of one or none of the features.

US and European guidelines recommend diagnostic testing for stable patients with a pretest probability of 15% or higher.[4] [57] In patients at lower risk, testing may be deferred, although European guidelines consider testing reasonable for patients with a pretest probability of 5 to 15% and US guidelines consider select testing (CAC score or exercise ECG) reasonable for patients at lower risk. At very low pretest probability, providers should keep in mind that a positive result is more likely to be a false positive (low positive predictive value).

Types of diagnostic test

Tests for SIHD generally can be divided into two main types: anatomical and functional. Anatomical tests identify atherosclerosis and/or luminal narrowing in epicardial coronary arteries. Functional tests assess myocardial function and/or perfusion at rest and during stress.

Traditionally, the only anatomical test was invasive coronary angiography and the only functional test was non-invasive stress testing. Therefore, functional tests were usually the initial choice for stable disease. Anatomical testing was usually second line and considered the reference standard. However, advances in cardiac imaging now allow for non-invasive anatomical testing. In addition, new procedures in the catheterisation laboratory can now provide functional information as part of an invasive assessment.

These developments have prompted questions about the relative importance of total atherosclerotic burden, focal luminal narrowing, and impaired function in SIHD. Emerging research now directly compares the ability of anatomical and functional testing to predict cardiac events and improve clinical outcomes.[66] [67] [68] [69] [70]

Stress tests

Non-invasive functional tests, also called stress tests, remain a key diagnostic modality. Stress tests can be further categorised by the type of stress and the outcome used to assess cardiac function/perfusion.

Exercise is generally preferred as a means of stress because it can provide higher levels of physiological stress as well as prognostically valuable information about patients' functional status. Use of pharmacological stress rather than exercise is typically reserved for patients unable to perform moderate exercise due to orthopaedic, pulmonary, or other comorbidities. Options for pharmacological stress testing include vasodilators (adenosine, dipyridamole, or regadenoson) or a beta-agonist (dobutamine).

The outcome measures for stress testing include ECG alone or ECG plus imaging. The most common imaging options are echocardiography and nuclear imaging (SPECT). Positron-emission tomography (PET) and cardiac magnetic resonance imaging (CMR) may also be available. The use of imaging as an outcome for stress testing is required when baseline ECG findings preclude identification of inducible ischaemia (such as left bundle-branch block, ventricular pacing, or baseline ST-segment depressions ≥0.5 mm). Imaging is also usually required when a pharmacological stress is used. The addition of imaging to ECG stress testing provides more precise anatomical localisation as well as information about the magnitude of inducible ischaemia and irreversibly infarcted tissue. Once the decision is made to add imaging, choice of modality depends on the indication for the test (diagnosis, risk stratification, assessment of myocardial viability), and patient-related factors (obesity, concerns about radiation), as well as local expertise and availability. If a patient has undergone one type of testing in the past, repeating the same test can facilitate comparison.

Exercise ECG may have a lower sensitivity in women, although it is not clear that this difference should alter diagnostic strategy.[3] [71] [72]

In addition to predicting the likelihood of obstructive lesions on angiogram, functional testing can stratify patients in relation to risk of cardiovascular mortality. The Duke treadmill score is a well-validated model derived from the duration of exercise, ST-segment changes, and angina on a standard treadmill exercise ECG.[73] Models with additional variables may improve the ability to identify patients at low risk.[74] The addition of imaging to stress ECG can also add prognostic information.[75] [76]

Coronary computed tomography angiography

Coronary computed tomography angiography (CCTA), a contrast-enhanced computed tomography (CT) study, can identify coronary plaque and stenosis. CCTA has advanced to achieve high concordance with invasive angiography in identifying significant stenoses and thus offers a non-invasive anatomical test. Like invasive angiography, CCTA can also identify lesser, non-obstructive atherosclerotic lesions. As even these non-obstructive plaques are associated with increased cardiac risk, CCTA can add some predictive power beyond functional testing.[77] In particular, the absence of any atherosclerosis on CCTA is associated with very low rates of cardiovascular events for at least 5 years.[78] [79]

Emerging CT technologies aim to add functional information to the anatomical data provided by CCTA. CT myocardial perfusion (CTP) and fractional flow reserve CT (FFRCT) both appear to increase specificity of CCTA with a small loss of sensitivity, although variations in test protocol produce slightly different results.[80] [81] [82]

CT scans without contrast enhancement are not able to show the lumen of epicardial arteries but can identify the extent of coronary artery calcification (CAC). As calcification is associated with atherosclerotic plaque, CAC screening can identify many patients with atherosclerosis. However, as it is not able to distinguish between obstructive and non-obstructive lesions, the role of CAC testing in diagnosis is limited. In symptomatic patients, CAC screening adds predictive power to typical clinical risk factors.[83] At typical thresholds it has higher sensitivity but lower specificity than functional testing for identification of

SIHD and in identifying risk for future events.[84] However, not all atheromatous plaques are calcified, and especially in younger, symptomatic patients a negative CAC score may not effectively rule out SIHD.[85]

Coronary angiography

Coronary angiography uses catheters to inject contrast directly into epicardial coronary arteries, providing visualisation of the artery lumen and degree of stenosis. Risks of invasive angiography include those from contrast and radiation, thrombosis or haemorrhage related to vascular access, arrhythmia, and atheroembolism. Traditionally, lesions causing stenosis greater than 50% to 70% are considered significant, although the presence of lesser degrees of stenosis are also associated with worse cardiac outcomes.[86] Because of the variability in length and irregularity of plaques, estimates of the degree of stenosis may be imperfect, and measurements of luminal narrowing do not necessarily correlate with the level of symptomatic or functional impairment.[87]

One of several techniques to overcome the limits of conventional angiography, fractional flow reserve (FFR) is increasingly used to guide decisions about procedural intervention. FFR - the direct measurement of pressure gradients across a stenosis after administration of adenosine - provides functional information about blood flow with a pharmacological stress. It correlates with stress testing in small studies and predicts the likelihood of future cardiac events.[88] [89]

Choosing a test modality

Comparing tests for SIHD is complicated by verification bias, a paucity of head-to-head trials, and uncertainty about the optimal reference standard.[90] That said, it is useful to roughly compare the ability of non-invasive tests to predict significant stenosis on invasive angiography.

	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)
Stress ECG	58 (46-69)	62 (54-69)
Stress echo	85 (80-89)	82 (72-89)
CCTA	97 (93-99)	78 (67-86)
SPECT	87 (83-90)	70 (63-76)
PET	90 (78-96)	85 (78-90)
Stress CMR	90 (83-94)	80 (69-88)

Sensitivity and specificity of tests for anatomically significant coronary artery disease

Adapted from Knuuti et al. The performance of non-invasive tests to rule-in and rule-out significant coronary artery stenosis in patients with stable angina: a meta-analysis focused on post-test disease probability. Eur Heart J. 2018 Sep 14;39(35):3322-30; used with permission. (CCTA, coronary computed tomography angiography; CI, confidence interval; CMR, stress cardiac magnetic resonance; PET, positron emission tomography; SPECT, single-photon emission computed tomography [exercise stress SPECT with or without dipyridamole or adenosine]; Stress echo, exercise stress echocardiography)

For initial diagnosis, current US and European guidelines recommend either CCTA or stress testing with imaging. Exercise ECG has a limited role.[4] [57] UK guidelines emphasise CCTA as the initial diagnostic test for SIHD and advise against exercise ECG.[91] [92]

Use of CCTA as an initial diagnostic test is likely to identify patients with subclinical atherosclerosis that would not be identified on functional testing. The risks and benefits of this approach have not been fully defined. A major US trial randomising patients to functional testing versus CCTA showed an increased rate of invasive catheterisation in the CCTA group but no difference in clinical outcomes.[66] A Scottish randomised trial adding CCTA to routine care (including exercise ECG for most patients) showed increased rates of preventative and symptomatic SIHD treatments with no difference in overall rates of angiography or revascularisation at 5 years.[93] There may be advantages to using CCTA for younger, lower-intermediate risk patients and stress testing for older, higher-risk patients. However, local expertise, availability, as well as patient specific factors may weigh heavily in the choice between CCTA and stress testing with imaging.

Tests for vasospasm and microcirculatory dysfunction

Some patients have symptoms consistent with angina but lack the classic stenosis of epicardial coronary arteries. For these patients, invasive and non-invasive testing for vasospasm and microcirculatory dysfunction can be considered.[4] [57] Limited evidence shows improved symptoms with tailored therapy.[94]

History and exam

Key diagnostic factors

presence of risk factors (common)

- Key risk factors include smoking, hypertension, hyperlipidaemia, isolated low HDL cholesterol, diabetes, inactivity, obesity, family history of coronary heart disease, male sex, and illicit drug use.

typical angina symptoms (common)

- Typical angina is: 1) chest pressure or squeezing lasting several minutes, 2) provoked by exercise or emotional stress, and 3) relieved by rest or glyceryl trinitrate. This symptom complex is most consistently associated with ischaemic heart disease.[58] [59]

atypical angina symptoms (common)

- Atypical angina is defined as chest discomfort with only two characteristics of typical angina. It is less predictive of coronary disease than typical angina, but may be more frequent in women, people with diabetes, or older people.[95] [96] [97] [98] Some guidelines avoid the term 'atypical' and instead suggest ‘cardiac’, ‘possibly cardiac’, and ‘non-cardiac’ pain, although symptoms alone can not determine the cause of chest pain.

symptoms of low-risk unstable angina (common)

- Features of low-risk unstable angina include pain from exertion lasting less than 20 minutes, pain not rapidly increasing, and normal/unchanged ECG.

normal examination (common)

- Typically, normal in chronic stable angina.

Other diagnostic factors

known medical history of exacerbating factor (common)

- As anginal pain results from an imbalance between myocardial oxygen supply and myocardial oxygen demand, patient history should also be evaluated for problems that may exacerbate this imbalance. Thyroid disease, anaemia, hyperviscosity syndrome, arteriovenous fistula, and underlying lung disease are known exacerbating factors.

non-anginal chest pain (common)

- Non-anginal chest pain is defined as chest discomfort with only one or none of the characteristics of typical angina. It is less predictive of coronary disease than typical or atypical angina, but should be evaluated with consideration of the patient's age and other risk factors.[58] [62]

epigastric discomfort (uncommon)

- An alternate location for anginal discomfort, more commonly in women, people with diabetes, or older people.

jaw pain (uncommon)

- An alternate location for anginal discomfort.

arm pain (uncommon)

- An alternate location for anginal discomfort, more commonly the left arm.

dyspnoea on exertion (uncommon)

- This may suggest exercise-induced left ventricular dysfunction; coronary disease should be considered among the differential diagnosis in this setting. It may be an anginal equivalent (e.g., in patients with diabetes). Additionally, dyspnoea may suggest underlying lung disease or anaemia that can contribute to anginal symptoms.

nausea/vomiting (uncommon)

- May be associated with angina.

perspiration (diaphoresis) (uncommon)

- This may be associated with angina, but should also raise suspicion for illicit drug use (cocaine) or thyrotoxicosis.

fatigue (uncommon)

- May be associated with angina, but should also raise suspicion for anaemia.

hypoxia (uncommon)

- Hypoxia may exacerbate anginal symptoms as a result of poor oxygen delivery to ischaemic myocardium. Evaluation for underlying pulmonary processes should be considered.

tachycardia (uncommon)

- Tachycardia should raise suspicion for alternative or exacerbating causes of angina, including thyrotoxicosis, anaemia, sympathomimetic drug use, arteriovenous fistula, or primary atrial or ventricular tachycardia.

S3 (uncommon)

- If present in the setting of chest discomfort, this suggests ischaemia-induced left ventricular dysfunction and high-risk coronary disease.[63]

mitral regurgitation murmur (uncommon)

- If present in the setting of chest discomfort, this suggests ischaemia-induced papillary muscle dysfunction.[63]

bibasilar rales (uncommon)

- If present in the setting of chest discomfort, this suggests ischaemia-induced left ventricular dysfunction and high-risk coronary disease.

aortic outflow murmur (uncommon)

- This suggests aortic stenosis or hypertrophic cardiomyopathy as an alternative aetiology of anginal pain.[99]

carotid bruit (uncommon)

- Presence of peripheral vascular disease increases the likelihood of atherosclerotic coronary disease.[64]

diminished peripheral pulses (uncommon)

- Presence of peripheral vascular disease increases the likelihood of atherosclerotic coronary disease.

signs of abdominal aortic aneurysm (uncommon)

- Presence of peripheral vascular disease increases the likelihood of atherosclerotic coronary disease.

retinopathy seen on fundoscopic examination (uncommon)

- Presence of increased light reflexes and arteriovenous nicking provide evidence of hypertension and associated risk of coronary disease.

xanthomas or xanthelasma (uncommon)

- Presence of xanthomas or xanthelasma suggests severe hypercholesterolaemia.

Risk factors

Strong

advancing age

- Advancing age is the single most powerful risk for ischaemic heart disease. It is important to have a high index of suspicion in older patients even if they have atypical chest pain or exertional symptoms.

smoking

- Aside from advanced age, smoking is the most important risk factor for coronary disease. In the case-control INTERHEART study, smoking accounted for 36% of global risk for myocardial infarction. Risk was dose-dependent and started at as little as 1 to 5 cigarettes per day.[28]

hypertension

- There is robust observational evidence of a linear association between systolic and diastolic blood pressure and ischaemic heart disease mortality.[29] Randomised controlled trials support the benefit of blood pressure control in reducing ischaemic heart disease outcomes.[30] [31]

elevated LDL cholesterol

- Multiple cohort studies have established elevated LDL cholesterol as a strong risk factor in the development of coronary disease.[32]
- Studies of LDL cholesterol reduction have demonstrated that lowered LDL levels are associated with decreased risk of coronary events in patients with pre-existing coronary disease and in selected patients for primary prevention.[33] [34] [35] [36]

isolated low HDL cholesterol

- A strong inverse relationship exists between the serum level of HDL cholesterol and vascular risk. The likely mechanism involves the role of HDL in reverse cholesterol transport, thus extracting LDL cholesterol from the vessel wall. In addition, HDL cholesterol may help to reduce the level of oxidised phospholipids in the arterial wall.[37]

diabetes

- Patients with diabetes have up to fourfold higher rates of future cardiovascular events. This risk is magnified in patients with other concomitant risk factors.[38]

inactivity

- Prospective studies have demonstrated a strong association between levels of physical activity and rates of cardiovascular disease. Physical activity exerts cardioprotective effects through lowered blood pressure, improvement in lipid profile, and reduced adiposity and diabetes incidence, as well as direct effects on vascular inflammation and endothelial function.[39]

obesity

- The role of obesity as an independent risk factor for coronary disease is unclear due to its associations with hypertension, diabetes, hyperlipidaemia, and physical inactivity. It is a strong marker for increased risk of coronary disease.[40]
- Cardiovascular risk is increased in patients with central obesity. Abdominal obesity (waist-to-hip ratio >0.85) is a particularly strong marker for increased risk of coronary disease.[41]

illicit drug use

- Use of sympathomimetic agents (cocaine, methamphetamine) increases myocardial oxygen demand and may provoke ischaemic symptoms. Additionally, cocaine may promote vasospasm of the epicardial arteries, resulting in angina.[42]

male sex

- Male sex is a risk factor for ischaemic heart disease, although rates of ischaemic heart disease rise rapidly in women after menopause such that sex differences are attenuated with increasing age.[11]

Weak

family history of ischaemic heart disease

- Family history is a risk factor for ischaemic heart disease but adds little prognostic information when combined with other common risk factors.[28] This finding suggests that whether through genes or shared lifestyle, much of the effect of family history is mediated through known risk factors including hyperlipidaemia, hypertension, diabetes, obesity, smoking, and diet.

hypertriglyceridaemia

- It is difficult to determine the independent effects of elevated triglycerides due to its tight inverse correlation with HDL cholesterol and the incomplete assessment of daily triglyceride exposure through measurement of fasting lipid profiles.[43]

mental stress/depression

- Mental stress and depression are independent risk factors for disease progression.[44]

plasma biomarkers

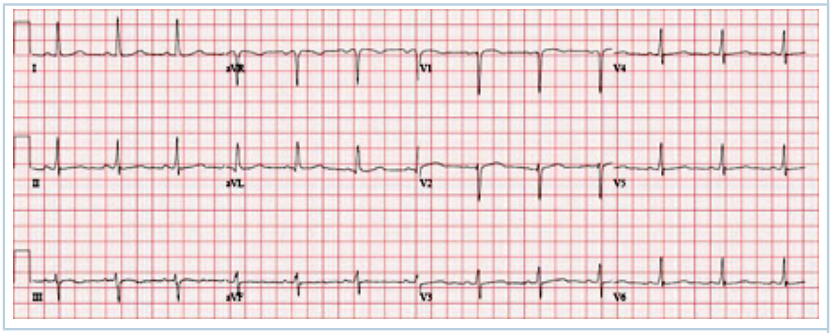
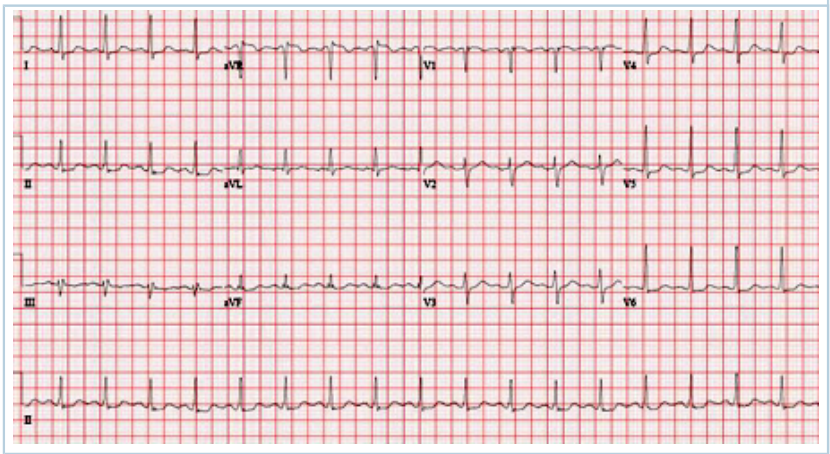
- Plasma biomarkers of inflammation (high-sensitivity CRP, soluble intercellular adhesion molecule [sICAM-1], serum amyloid A, interleukin [IL]-6/IL-18, myeloperoxidase, soluble CD40 ligand), altered thrombosis (tissue plasminogen activator [tPA]/plasminogen activator inhibitor type 1 [PAI-1], fibrinogen, homocysteine, d-dimer), and altered lipids (lipoprotein-a, LDL particle size, apolipoprotein A [ApoA]) have been proposed in the risk stratification of patients with coronary disease. There is insufficient evidence to support routine use of these biomarkers in risk stratification.[45] [46] [47]

polluted air

- Greater concentration of fine particulates in the air has been associated with increasing coronary artery calcium measured by CT as well as cardiovascular risk.[48] [49]

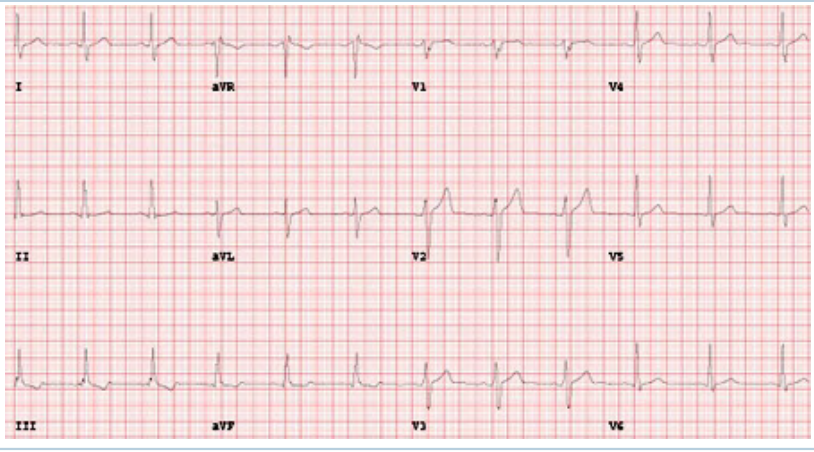
Investigations

1st test to order

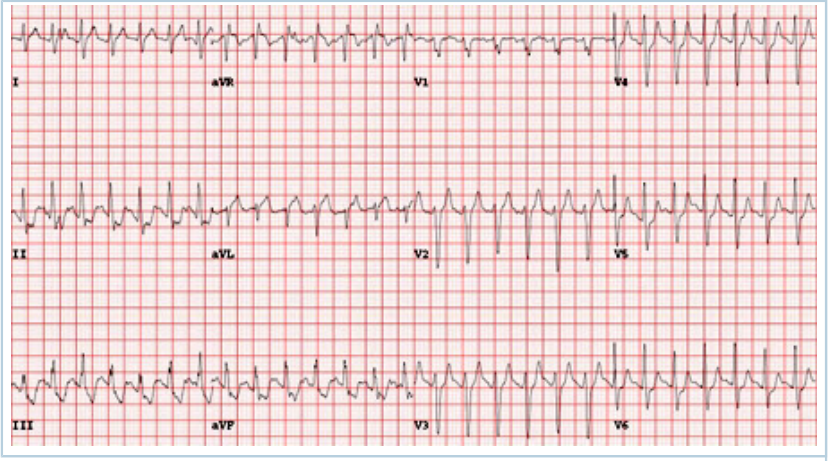
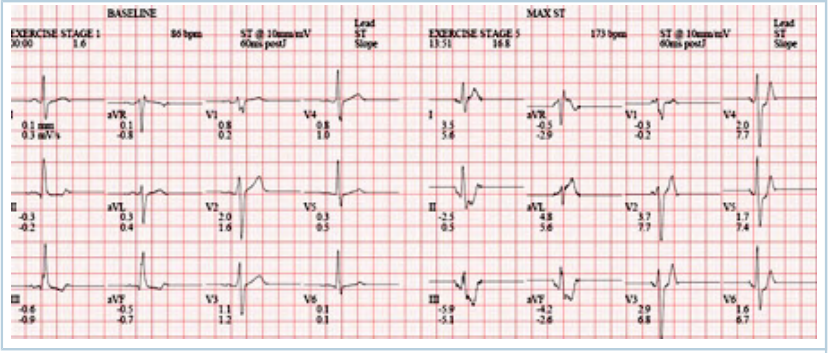
Test	Result
resting ECG • Resting ECG is appropriate for initial evaluation of all patients with known or suspected ischaemic heart disease.[57] • In addition to providing diagnostic and prognostic information, the presence of baseline ECG abnormalities may also guide use of further testing such as echocardiography and stress testing.  *Normal ECG* *From the collection of Dr S.D. Fihn; used with permission*  *ECG showing non-specific ST depressions in V5 and V6, which may indicate ischaemia. There are non-specific ST-segment changes in III and aVF* *From the collection of Dr S.D. Fihn; used with permission*	**often normal, but may reveal ST-T changes suggestive of ischaemia or Q waves indicative of prior infarction**
haemoglobin • Anaemia results in additional cardiac workload and reduced oxygen delivery to the heart, which can exacerbate angina. Severe anaemia may cause angina without obstructive coronary lesions.[3]	**reduced in anaemia**
lipid profile • Dyslipidaemia is an important risk factor for ischaemic heart disease.	**elevated LDL cholesterol is associated with increased risk; elevated HDL is protective**
fasting blood glucose or HbA1c • Diabetes is an important risk factor for ischaemic heart disease.	**elevated in diabetes**

Other tests to consider

Test	Result
exercise ECG (without imaging) • Patients use a treadmill, stationary cycle, or other device at increasing levels of speed and resistance while under medical supervision. In addition to ECG before, during, and in recovery from exercise, interpretation should include exercise capacity and heart rate achieved, as well as symptoms and haemodynamic response during and after exercise. • Scores such as the Duke treadmill score aid in determination of cardiac risk. • Risks are primarily related to inducing cardiac stress. • Not routinely recommended in European, UK or current US guidelines.[4] [57] [91] [92] • Inappropriate for patients with baseline ECGs that make interpretation of exercise ST-segment changes difficult (left bundle branch block, baseline ST depression >1 mm, paced rhythm, digitalis use, pre-excitation). • Inappropriate for patients who have limited exercise capacity (i.e., <4-5 METS) due to poor conditioning, obesity, physical impairments, or co-existing illness.[3]	**ST-segment elevation and depression identify ischaemia**



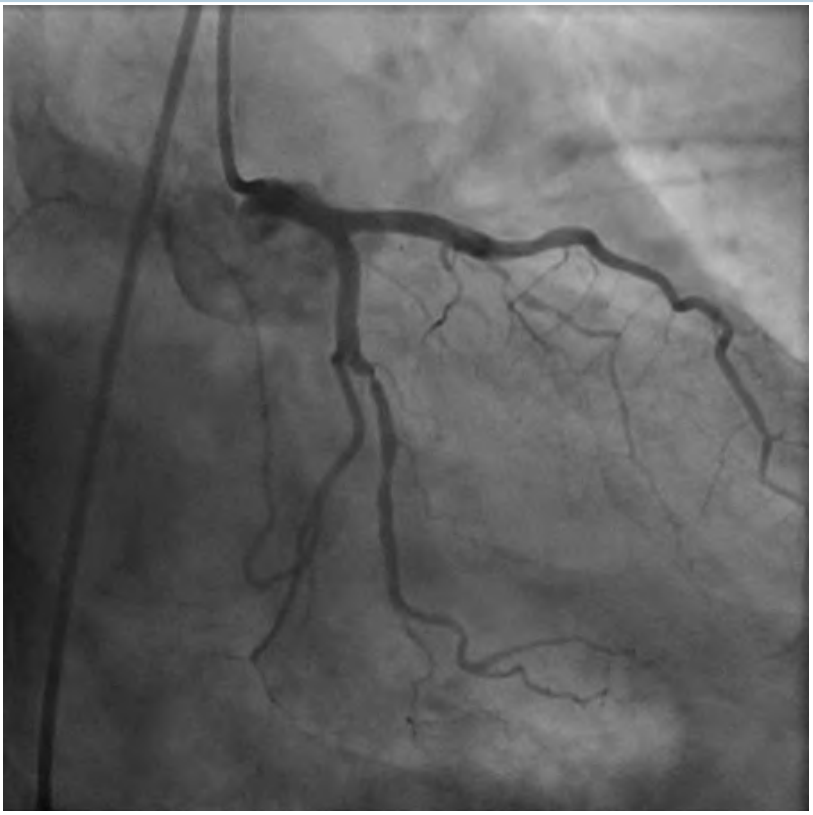
Baseline exercise ECG in a 55-year-old man with a 1-month history of angina on exertion
From the collection of Dr S.D. Fihn; used with permission

Test	Result
 *Maximal exercise ECG in a 55-year-old man with a 1-month history of angina on exertion with ST depressions in II, III, aVF diagnostic of ischaemia, and normal ST changes in V4-6 (rapid upsloping)* *From the collection of Dr S.D. Fihn; used with permission*  *Computerised summary of exercise ECG in a 55-year-old man with a 1-month history of angina on exertion* *From the collection of Dr S.D. Fihn; used with permission*	
exercise or pharmacological stress with imaging • Imaging options include single photon emission CT (SPECT), echocardiography, cardiac magnetic resonance (CMR), and positron-emission tomography (PET). • Imaging identifies the extent and distribution of inducible ischaemia or irreversible infarct. The difference in summed scores for perfusion/wall motion from rest to stress adds prognostic information from ECG which is also recorded. • The addition of imaging improves sensitivity and perhaps specificity over exercise ECG. Imaging is required when patients' baseline ECG precludes the detection of ischaemia or when a pharmacological rather than exercise stress is used. Stress testing with imaging is also used for prognosis or to guide revascularisation decisions in patients with known SIHD. Risks include inducing cardiac stress and (for SPECT and PET) the use of radiation. • Choice of imaging modality may be influenced by patient factors, and the exact questions being asked, as well as local availability and expertise. Stress echocardiography and SPECT are the best studied and most available. Echocardiography provides more detailed information about cardiac anatomy but is more operator dependent.	**ST-segment elevation and depression on the ECG identify ischaemia, as do wall motion or perfusion abnormalities on the imaging component**

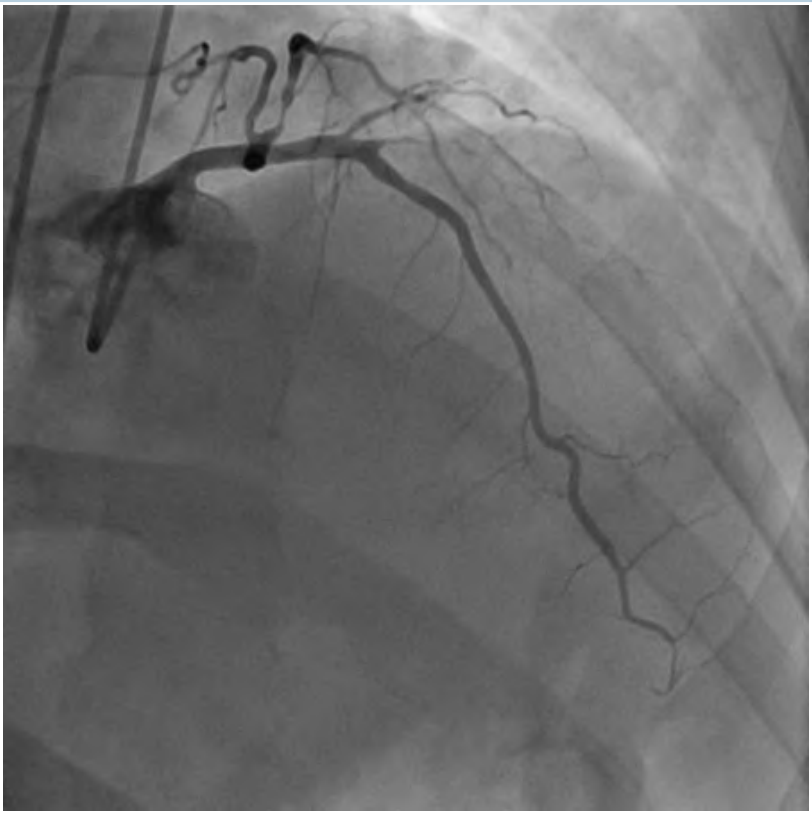
DIAGNOSIS

Test	Result
US guidelines suggest a possible preference for PET over SPECT due to fewer non-diagnostic studies.[57]	
coronary CT angiography (CCTA) • CCTA has high sensitivity and specificity and an increasing evidence base for prognosis and risk stratification. Severe coronary calcification can limit diagnostic quality. Risks are primarily related to contrast and radiation, although administration of beta-blockers or nitrates may also be required during the test.	**typically luminal narrowing of >50% is considered positive, although the presence of lesser lesions is prognostically relevant; identification of 'soft plaques' is also considered positive**
invasive coronary angiography • Coronary angiography is the conventional reference standard for diagnosis of coronary artery disease. Angiography also provides details about the overall coronary anatomy. Fractional flow reserve (FFR) is increasingly used to clarify the functional significance of stenoses, particularly when intervention is being considered without prior functional testing. • Risks include the use of radiation and administration of contrast, as well as thrombosis or haemorrhage related to vascular access, arrhythmia, and atheroembolism. • Invasive angiography is not typically used for initial diagnosis of SIHD, although in patients with a high pre-test probability it may be used for confirmation of the diagnosis, risk stratification, and to identify appropriate candidates for revascularisation. It may also be used for diagnosis when initial non-invasive testing is inconclusive.[100]	**50% to 70% luminal diameter narrowing is considered coronary obstruction, although presence of lesser lesions is prognostically relevant**

Test	Result



Angiogram (right anterior oblique caudal projection) in a 55-year-old man with a 1-month history of angina on exertion. A 90% proximal stenosis of obtuse marginal 1 is present, explaining the patient's lateral ischaemia
From the collection of Dr S.D. Fihn; used with permission

Test	Result
 *Angiogram (right anterior oblique cranial projection) in a 55-year-old man with a 1-month history of angina on exertion. The image shows a 90% proximal stenosis of obtuse marginal 1 (explaining the patient's lateral ischaemia), 90% proximal stenosis of the first diagonal, and 99% subtotal occlusion of the second diagonal (explaining the patient's anterior and anterolateral ischaemia)* *From the collection of Dr S.D. Fihn; used with permission*	
thyroid-stimulating hormone • Hyperthyroidism increases metabolic demands and cardiac workload, which can exacerbate angina.[3] • Hypothyroidism is associated with dyslipidaemia and ischaemic heart disease.	**below normal range (hyperthyroidism); elevated (hypothyroidism)**
CXR • X-ray may reveal alternate causes of chest symptoms.	**usually normal in SIHD**
rest echocardiography • European guidelines recommend routine echocardiography in patients with known or suspected SIHD.[4] US guidelines recommend resting echocardiography only in the presence of known prior myocardial infarction or pathological Q waves on ECG (or the more conventional indications of heart failure, complex ventricular arrhythmias, or undiagnosed murmur).[3] Both guidelines advise against repeat echocardiography in the absence of a change in clinical status.	**often normal in SIHD; focal wall motion abnormalities may indicate prior myocardial infarction and the extent of any impact on cardiac function; other findings may indicate alternative valvular, myocardial, or pericardial causes of chest symptoms**

Emerging tests

Test	Result
CT myocardial perfusion (CTP) and fractional flow reserve CT (FFRCT) • Both techniques add to coronary CT angiography and are designed to improve specificity by identifying functionally significant stenoses.[80] [81] [101] • CTP assesses myocardial uptake of contrast on CT scans with and without a pharmacological stress. FFRCT uses computational fluid dynamics to assess flow in vessels based on data from coronary CT angiography without a pharmacological stress phase.	**CTP shows perfusion in areas of myocardium, FFRCT shows flow in vessels**
coronary artery calcium (CAC) scoring • Calcium scoring can identify the overall burden of atherosclerosis without characterising the severity of specific stenoses. Involves radiation but no contrast or induced cardiac stress. • Although the use of age and sex norms and choice of an appropriate cut-off value may allow for sensitivity and specificity similar to that for functional tests, CAC is not currently recommended for diagnosis of SIHD or risk stratification in symptomatic patients. CAC may have a role in cardiovascular risk stratification for selected patients without symptoms or with such a low pretest probability that no other testing would be indicated.[19] [54] [57] There are not yet any trials evaluating the use of CAC scores to guide intensification or de-escalation of medications to reduce cardiac risk.	**overall calcification is usually reported in ranges from 0 to >400**
tests for vasospasm and microcirculatory dysfunction • Some patients have symptoms consistent with angina but lack the classic stenosis of epicardial coronary arteries. Patients with non-exertional symptoms suggestive of vasospastic angina may undergo ambulatory ECG monitoring and/or intracoronary acetylcholine testing. Patients with mixed exertional and non-exertional symptoms suggestive of microvascular dysfunction may undergo invasive or non-invasive assessment of coronary flow reserve and microcirculatory resistance as well as intracoronary acetylcholine testing.[4] Limited evidence shows improved symptoms with tailored therapy.[94]	**may show arteriolar dysregulation or increased microcirculatory resistance**

Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Aortic dissection	• The pain of aortic dissection is typically severe, sudden in onset, and often described as tearing, sharp, or stabbing. The pain may be retrosternal, interscapular, abdominal, or in the neck, lower back, or lower extremities. Hypertension is common with distal aortic dissections. Pulse deficits are common, particularly in proximal dissections.[102]	• Chest radiograph may show a widened mediastinum, leading to initial suspicion. • Contrast-enhanced CT or transoesophageal echocardiogram will demonstrate the presence of a true and false lumen with dissection flap.[102]
Pericarditis	• The pain of acute pericarditis is typically severe, sudden in onset, and retrosternal or left precordial in location. The chest pain is often pleuritic, aggravated by supine positioning and relieved by sitting upright. A pericardial friction rub may be appreciated on examination.[103]	• ECG will show diffuse ST-segment elevation and PR-segment depression.[103]
Pulmonary embolism	• Dyspnoea is the most common symptom of acute pulmonary embolus. History may reveal symptoms of lower extremity venous thrombosis (erythema, warmth, pain, or swelling). Tachypnoea and tachycardia are the most common signs.[104]	• D-dimer: normal value is useful to rule out pulmonary embolism in patients with low clinical probability of pulmonary embolism.[104] • An ECG is useful to exclude alternate diagnosis. • Non-specific findings seen with pulmonary embolism include ST abnormalities, T-wave changes, and right or left axis deviation.
Pneumothorax	• Typically, presents with acute chest pain, dyspnoea, and cough. Examination reveals decreased breath sounds and hyperresonance over the area of pneumothorax.[105]	• The chest radiograph will show a visceral pleural line at the apex in an upright film; caution is advised in interpretation of supine films.[105]
Pneumonia with pleurisy	• Pleurisy results in localised chest pain that is worsened by deep breathing.[106] • In the setting of pneumonia, patients will commonly	• A pulmonary infiltrate with or without an effusion is typically seen on chest radiograph.

Condition	Differentiating signs / symptoms	Differentiating tests
	complain of dyspnoea, fevers, cough, and sputum production. • On examination, bronchial breath sounds and dullness to percussion may be appreciated in focal lung region.	
Oesophagitis	• Dysphagia and odynophagia are the predominant complaints of oesophagitis. • Infectious oesophagitis typically occurs in immunocompromised patients.[107] • Medications should be reviewed for common offenders of pill-induced oesophagitis.[108] • History of radiotherapy may raise suspicion for radiation oesophagitis.	• The results of barium swallow and endoscopy are dependent on the cause of oesophagitis. • *Candida albicans* will appear as a shaggy mucosa on barium swallow and numerous small white-yellow plaques on endoscopy. • Herpes simplex virus appears as small ulcers on barium swallow and oesophagogastroduodenoscopy, whereas large, deep, and linear ulcers suggest cytomegalovirus.[107] • In suspected pill oesophagitis, endoscopy may be indicated to exclude infectious causes.[108] • Barium swallow and endoscopy can demonstrate the severity of mucosal damage with radiation oesophagitis.
Oesophageal spasm	• Patients may complain of intermittent chest pain and dysphagia in the setting of oesophageal spasm. Glyceryl trinitrate can improve oesophageal spasm by inducing smooth muscle relaxation.[109] This can make oesophageal spasm difficult to differentiate from angina.	• Barium swallow may show prominent non-propulsive contractions leading to a corkscrew appearance. • Oesophageal manometry may demonstrate repetitive and aperistaltic contractions.[109]
GORD	• Oesophageal reflux typically presents as an epigastric or retrosternal burning pain, with radiation towards the throat. Patients may report resolution of the pain with a trial of antacids.[110]	• Typically managed empirically with acid-suppressive therapy. Oesophageal pH monitoring can be performed to demonstrate episodes in which the oesophageal pH drops to below 4.[110]

Condition	Differentiating signs / symptoms	Differentiating tests
Biliary colic	• The pain of biliary colic is localised to the right upper quadrant, occurring 15 to 30 minutes after a meal and persisting for 3 to 4 hours. It is often associated with nausea, vomiting, and bloating.[111] [112] [113]	• Ultrasound or hepatobiliary iminodiacetic acid scan will reveal gallstones.[111]
Cholecystitis	• Similar to the pain of biliary colic, the pain of cholecystitis is localised to the right upper quadrant and is often associated with nausea and vomiting. Unlike biliary colic, patients with cholecystitis also have fever, abdominal tenderness, and leukocytosis.[112]	• Ultrasound will demonstrate gallstones and/or thickening of the gallbladder wall. Hepatobiliary iminodiacetic acid scan will not fill the gallbladder due to obstruction of the cystic duct.[112]
Choledocholithiasis	• Similar to the pain of biliary colic, the pain of choledocholithiasis is localised to the right upper quadrant and is often associated with nausea and vomiting.[113]	• Ultrasound generally shows dilated bile ducts and occasionally identifies a biliary stone. Endoscopic retrograde cholangiopancreatography is the gold standard for the diagnosis of common bile duct stones and can be helpful in relieving the biliary obstruction.[113]
Cholangitis	• Similar to the pain of choledocholithiasis, the pain of cholangitis is localised to the right upper quadrant and is often associated with nausea and vomiting. Unlike choledocholithiasis, patients with cholangitis typically present with fever and jaundice in addition to abdominal pain.[112] [113]	• Ultrasound generally shows dilated bile ducts and occasionally identifies a biliary stone. Endoscopic retrograde cholangiopancreatography is the most sensitive and specific test for the diagnosis of common bile duct stones and can be helpful in relieving the biliary obstruction.[112] [113]
Peptic ulcer disease	• Recurrent episodes of pain in the epigastrium with radiation to the back are common in peptic ulcer disease. The pain may temporarily improve with ingestion of food.[114]	• Oesophagoduodenoscopy: visualisation of ulceration in the gastric or duodenal mucosa.[114]
Pancreatitis, acute	• The pain of pancreatitis is located in the epigastrium	• The diagnosis is most supported by an elevation

Condition	Differentiating signs / symptoms	Differentiating tests
	and commonly radiates to the mid back. It is constant, lasting for hours to days, and not relieved by vomiting or bowel movements. A history of alcohol use or gallstones may provide a specific cause. Abdominal examination varies with the severity of the attack.[115]	in serum amylase and lipase 3 times the upper limit of normal. Ultrasound is useful to evaluate for cholelithiasis, while CT is useful to evaluate the extent of pancreatic inflammation or findings suggestive of pancreatic necrosis.[115]
Costochondritis	• The pain of costochondritis is typically localised to one or more of the costochondral or costosternal junctions, with reproduction of the pain on palpation.	• Diagnosed solely on reproduction of the pain with palpation of the tender areas.
Fibromyalgia	• Tender points of fibromyalgia can be located to near the sternum along the second intercostal space. Additionally, patients may complain of fatigue and chest heaviness. Patients with fibromyalgia will typically have multiple additional tender points localised to the neck, buttocks, shoulders, arms, and upper back.[116]	• Diagnosis is on clinical grounds by identifying point tenderness areas (typically, patients will have at least 11 of the 18 classic tender points) with no accompanying tissue swelling or inflammation, and by excluding other medical conditions as a cause.[116]
Rib fracture	• Rib fractures are often preceded by a history of traumatic injury to the area and pain is often localised to the area of fracture.	• Chest radiograph may show rib fractures. Pain with palpation of the tender area also suggests the diagnosis.
Sternoclavicular arthritis	• The pain of sternoclavicular arthritis is usually maximal immediately over the sternoclavicular joint. A history of osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, or psoriatic arthritis should raise suspicion for this diagnosis.[117]	• Diagnosis is usually on clinical grounds as the joint is poorly visualised by conventional radiography.[117]
Herpes zoster virus infection	• The majority of patients with herpes zoster will have a prodromal pain in the dermatome that will become affected. Before the development of vesicles, it can be difficult to differentiate this chest pain	• Dermatomal distribution and presence of vesicular skin lesions.[118]

Condition	Differentiating signs / symptoms	Differentiating tests
	from other causes of chest pain.[118]	
Anxiety disorders and panic attacks	• The increased tension and autonomic hyperactivity of anxiety disorders and panic attacks may lead to feelings of fatigue, muscle aches, palpitations, and chest pain that may lead to concern of heart disease.[119] [120]	• Diagnosis is on clinical grounds.

Screening

Screening of asymptomatic patients for ischaemic heart disease is not recommended. However, all adults should be routinely screened for cardiovascular risk factors including smoking, dyslipidaemia, hypertension, diabetes, overweight and obesity, physical inactivity, unhealthy diet, and family history of premature ischaemic heart disease. Calculated estimates of patients' 10-year risk of atherosclerotic cardiovascular disease may guide implementation of some preventive interventions such as medications for dyslipidaemia. [Atherosclerotic cardiovascular disease (ASCVD) risk estimator] (http://tools.acc.org/ldl/ascvd_risk_estimator/index.html#!/calulate/estimator) [QRISK calculator] (https://qrisk.org) In select cases, testing such as CAC score may be reasonable to refine risk stratification.[19] [54]

Approach

General approach

The treatment goals of patients with stable ischaemic heart disease (SIHD) are to:

- Improve quality of life by eliminating or reducing symptoms and restoring level of activity
- Improve outcomes by reducing complications including myocardial infarction (MI) and death.

Education and lifestyle modification

Patients with SIHD should have an individualised education plan to optimise care and promote wellness. It is important to educate patients on the importance of medication adherence for managing symptoms and retarding disease progression.[3] The patient should be made aware of medication management strategies that reduce cardiovascular risk in a manner that respects his or her level of understanding, reading comprehension, and ethnicity. The patient and provider together should review all therapeutic options including a discussion of appropriate levels of exercise, with encouragement to maintain recommended levels of daily physical activity, self-monitoring skills, and information on how to recognise worsening cardiovascular symptoms, and how to take appropriate action.

Physical activity

- The patient should be encouraged to participate in 30 to 60 minutes of moderate-intensity aerobic activity, such as brisk walking, at least 5 days and preferably 7 days per week. This should be supplemented by an increase in daily lifestyle activities (e.g., walking breaks at work, using the stairs, gardening, household work) to improve cardiorespiratory fitness.
- systematic review found that exercise-based cardiac rehabilitation in people with coronary heart disease likely reduces the risk of all-cause mortality, hospitalisation, and myocardial infarction, and improves health-related quality of life compared with no exercise; however, the population studied consisted mainly of people post-MI and post-revascularisation.[121] The authors of the review concluded that more evidence is required in people with stable angina.
- Medically supervised programmes (cardiac rehabilitation) and physician-directed, home-based programmes have demonstrated benefit in at-risk patients when initiated at time of diagnosis.[122] [123]

Diet

- Dietary therapy for all patients should include reduced intake of saturated fats (to <7% of total calories) and trans-fatty acids (to <1% of total calories).[124] [125] Encouraging intake of omega-3 fatty acids from fish or supplements, and/or fibre (>10 g/day) may be reasonable dietary interventions.

Weight management

- Specifically, patients should demonstrate understanding of weight control goals with maintenance of a body mass index of 18.5 kg/m² to 24.9 kg/m² and a waist circumference less than 102 cm for men and less than 89 cm for women (less for certain racial groups).[3]

Smoking cessation

- Smoking cessation and avoidance of exposure to environmental tobacco smoke at work and home should be encouraged for all patients with SIHD. Follow-up, referral to special programmes, and pharmacotherapy are recommended, as is a step-wise strategy for smoking cessation.[3] [124] Observational studies show that smoking cessation is associated with a greater than one third reduction in ischaemic heart disease mortality.[126] The benefits appear within a few years. After 10 to 15 years of abstinence, risk is similar to or minimally higher than that of people who have never smoked.[127]

Stress and depression recognition and management

- Depression is common in patients with ischaemic heart disease, particularly after acute infarction. It is associated with worse health behaviours and possibly worse cardiovascular outcomes.[128] Although treatment of depression has not been shown to improve cardiac outcomes, it is reasonable to screen patients and treat as indicated.[3] [4]

Vaccine recommendations

- Annual influenza vaccine is recommended for all patients.[124]

Guideline-directed medical therapy to improve outcomes

This should be instituted in all patients and may include:

- Antiplatelet therapy
- Beta-blockers
- Renin-angiotensin-aldosterone antagonists
- Lipid management
- Blood pressure control
- Diabetes management.

Antiplatelet therapy

- Antiplatelet therapy protects against platelet activation and acute thrombosis, and thereby reduces the risk of MI and sudden death.
- Low-dose aspirin should be prescribed indefinitely in most patients with SIHD, although European guidelines make a less strong recommendation for patients with SIHD without prior infarction or revascularisation.[3] [4] Aspirin reduces the relative risk of non-fatal MI by 20%.[129]
- Low doses of aspirin are as effective as higher doses and have a lower risk of gastrointestinal, major, and life-threatening bleeding.[130]
- Clopidogrel is at least as effective as aspirin in reducing vascular events.[131] However, its use as monotherapy is generally reserved for patients with contraindications to aspirin.[3] [4]
- Dual antiplatelet therapy (DAPT) - the use of aspirin combined with P2Y12-receptor inhibitors such as clopidogrel - increases the risk of bleeding and is not universally beneficial for patients with SIHD.[132] [133] [134] European guidelines endorse consideration of long-term DAPT for patients with particularly high risk of ischaemic events but not high risk of bleeding.[4]
- After an episode of acute coronary syndrome, US and European guidelines recommend DAPT for 1 year. This recommendation applies whether the acute coronary syndrome is treated medically, percutaneously, or surgically. Shorter or longer durations of DAPT may be reasonable in patients at high or low bleeding risk, respectively. Outside of the acute pre-procedural period, clopidogrel

is recommended in all scenarios; alternative P2Y12 inhibitors may be appropriate in selected cases.[134] [135]

- After percutaneous coronary intervention (PCI), DAPT can prevent the rare but morbid complication of in-stent thrombosis as well as reduce the risk of MI unrelated to the stent. US guidelines recommend 6 months of DAPT following placement of contemporary drug-eluting stents and 1 month of DAPT following placement of a bare metal stent. European guidelines recommend 6 months of DAPT regardless of stent type. Both guidelines acknowledge that shorter or longer duration of DAPT may be reasonable depending on bleeding risk.[134] [135]
- Scoring systems (such as Precise DAPT or the American College of Cardiology DAPT risk calculator) can assist clinicians in weighing the antithrombotic benefit and bleeding risk of extended DAPT.
- DAPT poses markedly increased bleeding risk in patients taking vitamin K antagonists or direct oral anticoagulants. For patients taking anticoagulation for indications such as atrial fibrillation, mechanical heart valves, or venous thromboembolism, triple therapy is generally avoided or used for as short a period as possible.[134] [135]
- European guidelines recommend routine use of proton-pump inhibitors (PPI) with DAPT to reduce the risk of gastrointestinal haemorrhage.[135] US guidelines recommend PPI therapy only for patients with risk factors.[134]

Beta-blocker therapy

- Beta-blockers decrease heart rate and myocardial contractility and, in turn, reduce myocardial oxygen demand and anginal symptoms. These agents have been shown to significantly improve mortality rates among patients with prior MI and, in combination with ACE inhibitors, among those with reduced left ventricular (LV) function.[136] [137] [138] [139] However, no large randomised trials have assessed the effects of beta-blockers on survival or coronary event rates in patients with SIHD. There is little evidence to support long-term beta-blockade in patients without angina or LV dysfunction.[140]
- US and European guidelines recommend beta-blocker therapy for patients with systolic dysfunction.[3] [4] US guidelines recommend starting beta-blocker therapy and continuing for 1 to 3 years in all patients after MI or acute coronary syndrome.[3] European guidelines suggest consideration of long-term therapy after ST-elevation MI.[4]

Renin-angiotensin-aldosterone antagonist therapy

- ACE inhibitors result in a reduction in angiotensin II with an increase in bradykinin. These changes in the physiological balance between angiotensin II and bradykinin could contribute to the reductions in LV and vascular hypertrophy, atherosclerosis progression, plaque rupture, and thrombosis through favourable changes in cardiac haemodynamics and improved myocardial oxygen supply and demand. Clinical studies have demonstrated significant reductions in the incidence of acute MI, unstable angina, and need for coronary revascularisation in patients after MI with LV dysfunction, independent of aetiology.[141] [142] [143] Similar benefits have been seen in patients without LV dysfunction who have atherosclerosis, vascular disease, diabetes, and additional risk factors for ischaemic heart disease.[144] [145] [146]
- US and European guidelines recommend ACE inhibitors (or angiotensin-II receptor antagonists) primarily for patients with SIHD who also have hypertension, systolic dysfunction, diabetes mellitus, or chronic kidney disease. Use can also be considered for those with SIHD who have other vascular disease or are at very high risk of cardiovascular events.[3] [4]

Statins and other lipid-lowering medications

- Statins are the mainstay of lipid pharmacotherapy and appropriate for all patients with SIHD (unless clearly contraindicated). High-intensity statin therapy is indicated for most patients.[55] [147] [148]
- Meta-analysis of placebo-controlled and higher-versus-lower dose trials show that statin therapy reduces coronary death and non-fatal MIs regardless of baseline low-density lipoprotein (LDL) cholesterol. In placebo-controlled trials, lower-potency statins reduce the relative risk of these major coronary events by 27%. Although there have not been large placebo-controlled studies of high-potency statins in the SIHD population, the degree of benefit appears proportional to the intensity of statin therapy, with a relative reduction of major coronary events of approximately 25% per 1.04 mmol/L (40 mg/dL) reduction in LDL-cholesterol achieved.[149] On the basis of these data, some authorities suggest approximating the benefit of statin therapy as a relative risk reduction of 1% for each 1% reduction in LDL achieved, more for higher baseline LDL and less for lower baseline LDL.[147]
- Statins, particularly high-dose statins, have been less well studied in patients aged over 75 years but meta-analysis suggests similar efficacy for patients with existing vascular disease irrespective of age.[150] Moderate-to-high-intensity statin therapy is still generally recommended, taking into consideration patient frailty and preferences.[147]
- There have been no treat-to-target trials of lipid management. For patients less than 75 years old with clinical ischaemic heart disease, US guidelines suggest using high-intensity statins with an aim of achieving a 50% or greater reduction in LDL-cholesterol levels.[147] European guidelines recommend targeting both a reduction in LDL cholesterol of 50% or more and a value below 1.42 mmol/L (55 mg/dL).[148]
- Statins are usually well tolerated. Serious adverse events including liver injury, myonecrosis, and rhabdomyolysis are rare.[151]
- When patients develop possible adverse effects, such as myalgias, every effort should be undertaken to ascertain whether these are actually related to the medication. Alternative statins, lower doses, or alternative dosing schedules may be tried.
- The evidence supporting statin therapy in SIHD far exceeds that of other lipid-lowering medications. However, for patients unable to take statins, or who have a less than expected reduction in LDL despite adherence at the highest tolerated dose, ezetimibe monotherapy or combination therapy with ezetimibe and a statin may be considered.[99] [147] For patients at very high risk with persisting elevations in LDL, a proprotein convertase subtilisin-kexin type 9 (PCSK9) inhibitor may be added (although cost may remain a barrier). Newer non-statin therapies are approved (e.g., bempedoic acid, inclisiran); however, evidence-based guidelines do not recommend their use as yet, and you should consult your local protocols.[152] See Emerging treatments .
- The decision to add non-statin therapies should be shared between patient and clinician following a discussion on the risks and benefits, and taking into account patient preferences. Lifestyle modifications should be optimised, in addition to reviewing adherence to statins.

Blood pressure control

- Lifestyle modification including physical activity, weight reduction, reduction of sodium intake, and moderation of alcohol consumption will help many patients adequately control blood pressure.[153] [154] [155] [156] [157] [158] [159]
- There is some variability between hypertension guidelines as to blood pressure goals.[160] [161] [162] [163]

- There is consensus that antihypertensive medications are warranted for patients with SIHD whose blood pressure is >140/90 mmHg.[124]
- Intensive blood pressure lowering remains controversial. Recent data suggest decreased cardiovascular events and mortality by targeting systolic blood pressure <120 mmHg in high-risk patients without a history of stroke or diabetes.[164] It remains unclear if these results apply to patients with diabetes.[165]
- US guidelines now recommend that patients with SIHD be treated to a target below 130/80 mmHg.[162] European guidelines recommend 120-130 mmHg systolic for most patients with SIHD and 130-140 mmHg for those over 65 years old.[4]
- Although the ideal antihypertensive agent depends on individual patient characteristics, beta-blockers and ACE inhibitors or angiotensin-II receptor antagonists are used as indicated for patients with LV dysfunction, recent MI, or stable angina. The addition of other drugs may be needed to achieve target blood pressures.[124] [162]

Management of diabetes

- Patients with ischaemic heart disease and diabetes mellitus are at high risk of morbidity and mortality from cardiovascular events. In type 1 diabetes, glycaemic control reduces the risk of macrovascular complications including angina, MI, and need for revascularisation.[166]
- In type 2 diabetes, the effects of glycaemic control on macrovascular complications are less clear.[167] Observational studies show an association between hyperglycaemia and increased risk of ischaemic heart disease.[168] Randomised trials of more intensive glycaemic control over 3 to 6 years have not shown consistent reductions in MI nor cardiac death. Meta-analyses suggest a reduction in the former but not the latter.[169] [170] [171] [172] [173] [174] Longer term follow-up may be required.[175]
- For older medications, there is weak evidence of cardiovascular benefit with metformin compared with sulfonylureas.[176] Following concerns about adverse cardiac effects of rosiglitazone, US and European regulators require specific evaluation of cardiovascular outcomes for new diabetes medications.[177] [178] Since then, studies of several new hypoglycaemic medications for type 2 diabetes have shown cardiovascular benefit in trials with large numbers of patients with SIHD. These include the sodium glucose transporter-2 (SGLT-2) inhibitors empagliflozin and canagliflozin, as well as the glucagon-like peptide-1 (GLP-1) agonists liraglutide and semaglutide.[167] [179] [180] [181] [182] For patients with SIHD and diabetes, joint US/European diabetes standards recommend lifestyle modification and metformin followed by a medication specifically approved for cardiovascular risk reduction such as a GLP-1 receptor agonist (preference: liraglutide) or SGLT-2 inhibitor.[183]

Anti-anginal pharmacotherapy to reduce symptoms

- Sublingual glyceryl trinitrate (delivered by either a tablet or spray formulation) is the therapy of choice to terminate acute episodes of angina or for prophylaxis before activities known to induce anginal symptoms. Onset of action is within minutes. Failure to resolve anginal symptoms with a reduction in physical activity and a trial of sublingual glyceryl trinitrate should prompt emergency evaluation for an acute coronary syndrome (unstable angina or MI).[3] [4]
- For those with recurrent angina, several medications can be used chronically to reduce symptoms and increase exercise tolerance. Although few studies have directly compared anti-anginals, beta-blockers (titrated to a heart rate of 55-60 beats per minute), calcium-channel blockers, and long-acting nitrates are the mainstays of treatment.[184] US guidelines suggest beta-blockers followed

by either of the other classes.[3] European and UK guidelines suggest general use of beta-blockers and calcium-channel blockers but note that medication choice may be influenced by baseline haemodynamics (particularly heart rate, blood pressure, and systolic function).[4] [185]

- A key component of therapy with long-acting nitrates is ensuring an adequate nitrate-free period every day to avoid tolerance and loss of effect. Phosphodiesterase-5 inhibitors for erectile dysfunction should be avoided in patients using nitrates as the combination may precipitate an unsafe drop in blood pressure.[3] [4]
- Patients with vasospastic (Prinzmetal variant) angina may note greater reduction of symptoms with use of calcium-channel blockers or nitrates due to their effect on coronary vasospasm.[186]
- Second-line anti-anginal medications include ranolazine, nicorandil, ivabradine, and trimetazidine.[4] The Medicines and Healthcare products Regulatory Agency (MHRA) in the UK has issued warnings concerning advice on the use of nicorandil and ivabradine.[187] [188] [189] More investigation is needed to clarify the safety and efficacy of ivabradine in treatment of angina and to investigate the occurrence of bradycardia and atrial fibrillation observed with its use.[190] [191] There is limited evidence supporting the use of trimetazidine and it is not included in UK guidelines.[192]

Coronary revascularisation

Revascularisation, either by coronary artery bypass graft (CABG) surgery or by percutaneous coronary intervention (PCI), may be indicated to improve either the quality or quantity of life: to improve SIHD symptoms refractory to medical therapy or to improve survival.

US, European, and UK guidelines all recommend revascularisation for patients with limiting symptoms despite maximal medical therapy.[99] [185] [193] [194] The guidelines also recommend revascularisation in carefully selected cases to improve survival or other cardiac outcomes but disagree about exactly which patients qualify and the roles for CABG and PCI. There is consensus in favor of revascularisation for patients with significant disease of the left main coronary artery but varying recommendations regarding patients with other anatomy, reduced ejection fraction, and high ischaemic burden.[99] [185] [193] [194] Some European guidelines suggest the possibility of a less restrictive approach to revascularisation but do not offer specific recommendations.[4]

European guidelines and US Appropriate Use Criteria emphasise the role of FFR in revascularisation decisions.[4] [195] There is consensus that complex cases should be evaluated by a 'heart team' including interventional cardiology and cardiothoracic surgery.[99] [185] [193] [194]

Revascularisation for refractory symptoms:

- Revascularisation is indicated in patients with unacceptable symptoms despite maximal medical therapy. Symptoms may be classic angina or anginal equivalents such as dyspnoea on exertion. Randomised trials have shown that CABG and PCI improve anginal symptoms over medical therapy.[196] [197] [198]
- Of note, the only blinded trial comparing PCI to a placebo procedure did not show benefit of PCI in relieving angina or enhancing exercise capacity.[199] The trial involved very aggressive medical management in both groups and was limited by small sample size and brief follow-up; however, it raises questions about the extent to which the apparent symptomatic benefits of PCI are due to the placebo effect.

Revascularisation for survival benefit:

- While the benefits of revascularisation in the setting of acute coronary syndrome are clear, for patients with SIHD large trials have not shown reductions in cardiovascular mortality or MI when revascularisation is added to medical therapy. The classic COURAGE trial and the contemporary ISCHEMIA trial showed no benefit from revascularisation on mortality or MI.[200] [201] [202] Notably, patients with obstruction of the left main coronary artery were excluded from both large trials. Questions remain about the definition and clinical significance of peri-procedural infarcts in the ISCHEMIA trial.[198]
- Trials focused solely on the mortality benefits of CABG in SIHD are more dated butshowed benefit in certain subgroups of patients with ischemic heart disease.[196] [203] [204] [205] The evolution of both surgical techniques (e.g., arterial grafts, off-pump CABG) and the comparison medical therapies (e.g., statins, beta-blockers) potentially limits the relevance of these older trials to contemporary practice. PCI has not been shown to improve mortality but smaller studies and meta-analyses have suggested possible benefit from fractional flow reserve (FFR)-guided PCI in other cardiac outcomes.[57] [206] [207] [208]

Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Ongoing			(summary)
all patients			
		1st	**lifestyle education**
		plus	**antiplatelet therapy**
		plus	**statin**
		adjunct	**antihypertensive therapy**
		adjunct	**blood sugar control**
		adjunct	**additional lipid-lowering therapy**
		adjunct	**revascularisation**
	with anginal symptoms	**plus**	**sublingual glyceryl trinitrate**
		plus	**beta-blocker ± calcium-channel blocker ± long-acting nitrate**
		adjunct	**consider other anti-anginal therapies**

Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Ongoing

all patients

1st **lifestyle education**

» All patients should be provided with individualised patient education and guideline-directed medical therapy with the goals of reducing the risk of future cardiovascular events and reducing anginal symptoms.

» Patient education includes ongoing assessments and recommendations to help patients achieve weight management, increased physical activity, dietary modifications, lipid goals, and smoking cessation.[3] [4] [124] [Evidence C]

» Additionally, helping patients understand their medication regimens is a key component of patient education and medication adherence.[3]

plus **antiplatelet therapy**

Treatment recommended for ALL patients in selected patient group

Primary options

» aspirin: 75-150 mg orally once daily

Secondary options

» clopidogrel: 75 mg orally once daily

OR

» aspirin: 75-150 mg orally once daily
-and-
» clopidogrel: 75 mg orally once daily

» All patients should be started on aspirin and this should be continued indefinitely. For patients with a contraindication to aspirin therapy, it is reasonable to use clopidogrel.[3] [4] [131] [209] [210]

» After an episode of acute coronary syndrome or placement of cardiac stents, combination therapy with aspirin plus a P2Y12 inhibitor is indicated. Duration of dual therapy depends on the bleeding risk and antithrombotic benefit; minimum durations are particularly important to prevent thrombosis within cardiac stents.

Ongoing

plus **statin**

Treatment recommended for ALL patients in selected patient group

Primary options

» atorvastatin: moderate intensity: 10-20 mg orally once daily; high intensity: 40-80 mg orally once daily

OR

» rosuvastatin: moderate intensity: 5-10 mg orally once daily; high intensity: 20-40 mg orally once daily

OR

» simvastatin: moderate intensity: 20-40 mg orally once daily
Due to increased risk of rhabdomyolysis, doses of 80 mg/day are not recommended.

OR

» pravastatin: moderate intensity: 40-80 mg orally once daily

OR

» lovastatin: moderate intensity: 40-80 mg orally (immediate-release) once daily

OR

» fluvastatin: moderate intensity: 40 mg orally (intermediate-release) twice daily; 80 mg orally (extended-release) once daily

OR

» pitavastatin: moderate intensity: 1-4 mg orally once daily

» Statins are the mainstay of lipid pharmacotherapy and appropriate for all patients with SIHD (unless clearly contraindicated). Most patients with SIHD should receive high-intensity statin treatment.

» Statins, particularly high-dose statins, have been less well studied in patients aged over 75 years, but moderate-to-high-intensity statin therapy is still generally recommended,

Ongoing

taking into consideration patient frailty and preferences.[147]

adjunct **antihypertensive therapy**

Treatment recommended for SOME patients in selected patient group

Primary options

» metoprolol: 50-200 mg orally (immediate-release) twice daily; 25-400 mg orally (extended-release) once daily
-or-
» nadolol: 40-80 mg orally once daily
-or-
» timolol: 10-30 mg orally twice daily
-or-
» bisoprolol: 10-20 mg orally once daily
-or-
» carvedilol: 6.25 to 25 mg orally twice daily

--AND/OR--

» benazepril: 10-40 mg orally once daily
-or-
» captopril: 25-100 mg orally twice daily
-or-
» enalapril: 5-40 mg orally once daily
-or-
» fosinopril: 10-40 mg orally once daily
-or-
» lisinopril: 10-40 mg orally once daily
-or-
» perindopril: 4-8 mg orally once daily
-or-
» quinapril: 10-40 mg orally twice daily
-or-
» ramipril: 2.5 to 20 mg orally once daily
-or-
» trandolapril: 1-8 mg orally once daily
-or-
» losartan: 25-100 mg orally once daily
-or-
» telmisartan: 20-80 mg orally once daily
-or-
» olmesartan: 10-40 mg orally once daily
-or-
» azilsartan: 40-80 mg orally once daily

» US guidelines now recommend that patients with SIHD be treated to a target below 130/80 mmHg.[162] European guidelines recommend 120-130 mmHg systolic for most patients with SIHD and 130-140 mmHg for those over 65 years old.[4]

» Beta-blockers and ACE inhibitors or angiotensin-II receptor antagonists are indicated regardless of blood pressure for some SIHD

Ongoing

patients (i.e., those with left ventricular dysfunction, myocardial infarction in the past 3 years, or stable angina). These agents may also be considered as treatments for hypertension in other patients with SIHD, although beta-blockers are generally less potent and therefore less preferred in the absence of another indication. Calcium-channel blockers also have anti-anginal properties and may be used in conjunction with beta-blockers. Additional medications, including diuretics, may be required to achieve blood pressure targets.

» Atenolol and beta-blockers with intrinsic sympathomimetic activity are inferior to other beta-blockers, especially in older patients.[211] Consider alternatives to atenolol, labetalol, acebutolol, or pindolol.

adjunct **blood sugar control**

Treatment recommended for SOME patients in selected patient group

» For patients with SIHD and concomitant type 2 diabetes, joint US/European standards recommend lifestyle modification and metformin followed by a medication specifically approved for cardiovascular risk reduction such as a glucagon-like peptide-1 (GLP-1) receptor agonist (preference: liraglutide) or sodium glucose transporter-2 (SGLT-2) inhibitor.[183]

adjunct **additional lipid-lowering therapy**

Treatment recommended for SOME patients in selected patient group

Primary options

» ezetimibe: 10 mg orally once daily

Secondary options

» alirocumab: 75-150 mg subcutaneously every 2 weeks; or 300 mg subcutaneously every 4 weeks

OR

» evolocumab: 140 mg subcutaneously every 2 weeks; or 420 mg subcutaneously once monthly

» The evidence supporting statin therapy in SIHD far exceeds that of other lipid-lowering medications. However, for patients unable to take statins, or who have a less than expected reduction in LDL despite adherence at the highest tolerated dose, ezetimibe monotherapy

Ongoing

or combination therapy with ezetimibe and a statin may be considered.[99] [147]

» For patients at very high risk with persisting elevations in LDL, a proprotein convertase subtilisin-kexin type 9 (PCSK9) inhibitor (e.g., alirocumab, evolocumab) may be added (although cost may remain a barrier).

» Newer non-statin therapies are approved (e.g., bempedoic acid, inclisiran); however, evidence-based guidelines do not recommend their use as yet, and you should consult your local protocols.[152] See Emerging treatments .

» The decision to add non-statin therapies should be shared between patient and clinician following a discussion on the risks and benefits, and taking into account patient preferences. Lifestyle modifications should be optimised, in addition to reviewing adherence to statins.

adjunct **revascularisation**

Treatment recommended for SOME patients in selected patient group

» Coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI) is recommended to relieve anginal symptoms in patients with continued unacceptable angina despite maximal medical therapy. Revascularisation is also recommended in selected patients for whom it is thought to improve survival or other cardiac outcomes. This includes patients with significant stenosis of the left main coronary and, depending on the guideline, patients with other anatomy, reduced ejection fraction or large ischaemic burden.[3] [185] [193] [194]

» Some European guidelines suggest a less restrictive approach to revascularisation of lesions that are functionally significant on invasive or non-invasive testing, although evidence for this approach is limited.[4] It is recommended that a multidisciplinary team of general cardiologists, interventional cardiologists, and cardiac surgeons (a 'heart team') assemble to discuss and make recommendations on the optimal management strategy. This may include guideline-directed medical therapy, PCI, CABG, or a combination of all three.

» Revascularisation does not obviate the need for aggressive risk-factor modification to reduce risk of future myocardial infarction.

Ongoing

with anginal symptoms **plus** **sublingual glyceryl trinitrate**

Treatment recommended for ALL patients in selected patient group

Primary options

» glyceryl trinitrate: 0.3 to 0.6 mg sublingually every 5 minutes when required, maximum 3 doses

» Sublingual glyceryl trinitrate is the preferred therapy to terminate acute episodes of angina or for prophylaxis before activities known to induce anginal symptoms.

» The mechanism of action is to reduce left ventricular wall stress and associated myocardial oxygen demand through systemic vasodilation. Coronary blood flow is also increased by coronary vasodilation. Onset of action is within minutes.[212]

» Failure to resolve anginal symptoms with a reduction in physical activity and a trial of sublingual glyceryl trinitrate should prompt emergency evaluation for an acute coronary syndrome (unstable angina or myocardial infarction).[3]

» Concurrent use of phosphodiesterase-5 inhibitors (e.g., sildenafil, tadalafil, or vardenafil) is contraindicated as the combination may result in a precipitous drop in blood pressure.

plus **beta-blocker ± calcium-channel blocker ± long-acting nitrate**

Treatment recommended for ALL patients in selected patient group

Primary options

» metoprolol: 50-200 mg orally (immediate-release) twice daily; 100-400 mg orally (extended-release) once daily
-or-
» nadolol: 40-80 mg orally once daily
-or-
» timolol: 10-30 mg orally twice daily
-or-
» bisoprolol: 10-20 mg orally once daily
-or-
» carvedilol: 25 to 50 mg orally twice daily

--AND/OR--

» nifedipine: 30-90 mg orally (extended-release) once daily
-or-
» amlodipine: 5-10 mg orally once daily

Ongoing

--AND/OR--

» isosorbide mononitrate: 20 mg orally (immediate-release) twice daily
-or-
» isosorbide dinitrate: 5-80 mg orally (immediate-release) two to three times daily
-or-
» glyceryl trinitrate transdermal: 5-15 mg/24 hour patch once daily

» Primary therapies for patients with chronic anginal symptoms may include beta-blockers, calcium-channel blockers (particularly dihydropyridines, although non-dihydropyridines may be considered), and long-acting nitrates.

» US guidelines favour beta-blockers as the initial choice. European guidelines generally encourage beta-blockers or calcium-channel blockers but also emphasise that choice of agent may be affected by the patient's baseline pulse, blood pressure, and comorbidities including systolic dysfunction.[3] [4]

adjunct **consider other anti-anginal therapies**

Treatment recommended for SOME patients in selected patient group

Primary options

» ranolazine: 500-1000 mg orally twice daily

OR

» ivabradine: 2.5 to 7.5 mg orally twice daily

OR

» nicorandil: 10-20 mg orally twice daily

OR

» trimetazidine: consult specialist for guidance on dose

» Other anti-anginal therapies, such as ranolazine, ivabradine, nicorandil, and trimetazidine may be considered for angina that persists despite use of primary therapies.

Emerging

Combination antiplatelet and anticoagulant therapy

There is interest in using low doses of direct oral anticoagulants in combination with antiplatelet agents to reduce recurrent events. However, reductions in vascular risk appear to be driven more by stroke than myocardial infarction, and bleeding risk is increased.[213]

Colchicine

One systematic review and meta-analysis evaluating the efficacy and safety of colchicine in patients with coronary artery disease found that it reduced cardiovascular events and inflammatory markers, high-sensitivity C-reactive protein, and interleukin 6, in patients with coronary disease compared with controls, but that more research is needed on the impact on cardiovascular and all-cause mortality.[214] One randomised controlled trial found that colchicine reduced a combined cardiovascular endpoint in patients with SIHD; however, almost 10% of potential participants were excluded after experiencing side effects during an open-label run-in period.[215]

Other LDL-lowering therapies

Bempedoic acid and inclisiran are newer non-statin therapies approved for use with diet and maximally tolerated statin therapy in adults who require additional lowering of LDL-C.[152] They may be selectively considered for high risk patients with severely or persistently elevated LDL despite use of (or for those unable to use) better established alternatives. Trials assessing clinical outcomes are ongoing. In the CLEAR Outcomes trial, statin-intolerant patients receiving bempedoic acid had a 21.7% reduction in LDL-C at 6 months, compared with 0.6% reduction with placebo, and also had a lower risk of major adverse cardiovascular events (e.g., death from cardiovascular causes, non-fatal myocardial infarction, non-fatal stroke, or coronary revascularisation).[216]

Coronary-sinus-reducing device

A coronary-sinus-reducing device has shown some promise in the small COSIRA trial, improving symptoms and quality of life in patients with refractory angina who were not candidates for revascularisation.[217]

Primary prevention

The American Heart Association defines eight key measures for improving and maintaining cardiovascular health, 'Life's Essential 8', these are: healthy diet, participation in physical activity, avoidance of nicotine, healthy sleep, healthy weight, and healthy levels of blood lipids, blood glucose, and blood pressure.[50] Prevention of ischaemic heart disease includes community- and patient-level interventions to encourage exercise, healthy diet, and ideal body weight while discouraging smoking. The US Preventive Services Task Force (USPSTF) recommends that adults at increased risk of cardiovascular disease are offered behavioural counselling interventions to promote a healthy diet and physical activity; those not at high risk may also be selectively considered for behavioural counselling interventions, while recognising that the net benefit is smaller.[51] [52] Treatment targets for antihypertensive therapy and use of statin medications are typically guided by individual risk for cardiovascular disease, usually estimated with a 10-year risk calculator, such as the Pooled Cohort Equations (US), QRISK (Europe), and SCORE (Europe). [Atherosclerotic cardiovascular disease (ASCVD) risk estimator] (http://tools.acc.org/ldl/ascvd_risk_estimator/index.html#!/calulate/estimator) [QRISK calculator] (https://qrisk.org) [SCORE2 and SCORE2-OP risk assessment models] (https://www.escardio.org/Education/Practice-Tools/CVD-prevention-toolbox/SCORE-Risk-Charts) The USPSTF recommends that adults aged 40 to 75 years who have one or more cardiovascular risk factors (i.e., dyslipidaemia, diabetes, hypertension, or smoking) and an estimated 10-year cardiovascular disease risk of 10% or greater should be started on a statin. Those with 10-year risk of 7.5% to less than 10% may selectively be offered a statin.[53]

Aspirin is no longer routinely recommended for primary prevention but may be considered in selected patients for whom the absolute cardiovascular benefit outweighs the absolute risk of increased bleeding.[19] [54] [55] [56]

Secondary prevention

All patients with known SIHD should be provided with individualised patient education, risk factor modification, and guideline-directed medical therapy with the main goals of reducing the risk of future cardiovascular events and death.

Patient discussions

Patient education should include some explanation of the disease process in addition to individualised discussion of lifestyle, medical, and procedural treatment options. To allow for shared decision-making, patients should be apprised of potential benefits and risks. Patient education may be particularly important in promoting uptake of lifestyle and pharmacological interventions that improve prognosis without immediately altering symptoms.

Education should also include complications of SIHD, concerning symptoms, and when to seek care for these (e.g., to seek emergency care for angina that does not resolve rapidly with rest and/or glyceryl trinitrate as it may be indicative of myocardial infarction).

It can also be valuable to ask patients about any fears, lest the diagnosis of SIHD cause excess worry or needlessly limit important activities. Patients with stable angina should be educated on the appropriate use of as-needed sublingual glyceryl trinitrate before or during exertion.

Patient education is endorsed by guidelines.[3] [4] When education is delivered as part of cardiac rehabilitation, there is limited evidence of improvement in quality of life as well as selected health behaviours and outcomes.[218] [219]

FOLLOW UP

Monitoring

Monitoring

Patients should have periodic follow-up to assess for changes in symptoms and physical activity as well as complications such as heart failure and arrhythmia. When patients have new or worsening angina, clinicians must determine whether these can be safely managed as progressive SIHD or whether they reflect higher risk unstable angina requiring management as acute coronary syndrome. Patients with progressive SIHD symptoms may benefit from repeat functional or anatomical testing and/or additional medical or procedural treatment.

Follow-up visits should also include ongoing attention to risk factors and lifestyle, including smoking, exercise, diet, weight, and blood pressure. Adherence to medications and any side effects should be assessed. Laboratory work should include routine screening for diabetes and monitoring of lipids and renal function. For stable, asymptomatic patients, US guidelines recommend routine rest ECG no more than annually and in response to changes in symptoms.[3] Repeat functional and anatomical testing is recommended only for changes in symptoms. European guidelines discuss adding routine echocardiography and/or functional testing every 3-4 years but caution against routine anatomical testing with coronary computed tomography angiography.[4]

Initially, patients might be seen every 4 to 6 months with annual visits for patients with stable regimens and minimal symptoms.[3] [4] Annual influenza vaccine is recommended.[3] [4]

Complications

Complications	Timeframe	Likelihood
ischaemic cardiomyopathy/heart failure	**long term**	**medium**
Patients are at risk of systolic heart failure either by irreversible loss of myocardium after myocardial infarction or by transient dysfunction in hypoperfused tissues at times of increased activity.		
myocardial infarction	**variable**	**high**
Occurs as a result of unstable atherosclerotic plaque with acute thrombosis and closure of the affected coronary artery. Patients with SIHD are at risk due to atherosclerotic disease. Close adherence to secondary prevention measures reduces the likelihood of this complication. Patients with new severe chest pain or accelerating chest pain should seek emergency evaluation for this possible complication.[99]		
sudden cardiac death	**variable**	**medium**
Sudden cardiac death is the rapid cessation of cardiac activity and haemodynamic collapse with little or no symptomatic prodrome. When reversed by defibrillation and other resuscitative measures it may also be called sudden cardiac arrest. Ischaemic heart disease can lead to sudden cardiac death through acute ischaemia and infarction or through arrhythmia related to scar or other damage from ischaemic events.		
stroke	**variable**	**medium**
The same risk factors that predispose to ischaemic heart disease increase the risk of non-coronary atherosclerotic diseases including stroke and peripheral artery disease. Although not strictly complications of SIHD, measures taken to treat SIHD may also reduce these adverse outcomes.		
peripheral arterial disease	**variable**	**medium**
The same risk factors that predispose to ischaemic heart disease increase the risk of non-coronary atherosclerotic diseases such as stroke and peripheral artery disease. Although not strictly complications of SIHD, measures taken to treat SIHD may also reduce these adverse outcomes.		

Prognosis

With aggressive lifestyle modification and guideline-directed medical therapy, patients can expect a reduction in anginal symptoms. With guideline-directed management, 58% of patients can expect to be free of angina within 1 year.[200]

Ischaemic heart disease is a dynamic process. Even with aggressive medical management and lifestyle changes, some patients may experience recurrence or worsening of anginal symptoms due to progression of atherosclerotic disease. Upwards titration of anti-anginal medications may resolve these symptoms; however, some patients may require revascularisation to improve anginal symptoms and exercise tolerance.

Diagnostic guidelines

United Kingdom

Risk estimation and the prevention of cardiovascular disease (https://www.sign.ac.uk/our-guidelines)

Published by: Scottish Intercollegiate Guidelines Network **Last published:** 2017

Recent-onset chest pain of suspected cardiac origin: assessment and diagnosis (https://www.nice.org.uk/guidance/CG95)

Published by: National Institute for Health and Care Excellence **Last published:** 2016

Europe

2019 ESC guidelines for the diagnosis and management of chronic coronary syndromes (https://www.escardio.org/Guidelines)

Published by: European Society of Cardiology **Last published:** 2019

International

Non-invasive imaging in coronary syndromes: recommendations of the European Association of Cardiovascular Imaging and the American Society of Echocardiography, in collaboration with the American Society of Nuclear Cardiology, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance (https://www.asecho.org/guideline/non-invasive-imaging-in-coronary-syndromes/)

Published by: European Association of Cardiovascular Imaging, American Society of Echocardiography **Last published:** 2022

North America

2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR guideline for the evaluation and diagnosis of chest pain (https://professional.heart.org/en/guidelines-and-statements/guidelines-and-statements-search)

Published by: American Heart Association, American College of Cardiology **Last published:** 2021

ACR appropriateness criteria: chronic chest pain - high probability of coronary artery disease (https://www.acr.org/Clinical-Resources/ACR-Appropriateness-Criteria)

Published by: American College of Radiology **Last published:** 2021

Guidelines for performance, interpretation, and application of stress echocardiography in ischemic heart disease (https://www.asecho.org/guidelines/guidelines-standards)

Published by: American Society of Echocardiography **Last published:** 2020

ACR appropriateness criteria: chronic chest pain - noncardiac etiology unlikely: low to intermediate probability of coronary artery disease (https://www.acr.org/Clinical-Resources/ACR-Appropriateness-Criteria)

Published by: American College of Radiology **Last published:** 2018

ACCF/AHA/ASE/ASNC/HFSA/HRS/SCAI/SCCT/SCMR/STS 2013 multimodality appropriate use criteria for the detection and risk assessment of stable ischemic heart disease (https://www.acc.org/guidelines#/tab4)

Published by: American College of Cardiology Foundation; American Heart Association; American Society of Echocardiography; American Society of Nuclear Cardiology; Heart Failure Society of America; Heart Rhythm Society; Society for Cardiovascular Angiography and Interventions; Society of Cardiovascular Computed Tomography; Society for Cardiovascular Magnetic Resonance; Society of Thoracic Surgeons **Last published:** 2014

Role of noninvasive testing in the clinical evaluation of women with suspected ischemic heart disease (https://professional.heart.org/en/guidelines-and-statements)

Published by: American Heart Association **Last published:** 2014

2014 ACC/AHA/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease (https://professional.heart.org/en/guidelines-and-statements)

Published by: American College of Cardiology; American Heart Association; American Association for Thoracic Surgery; Preventive Cardiovascular Nurses Association; Society for Cardiovascular Angiography and Interventions; Society of Thoracic Surgeons **Last published:** 2014

North America

ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease (https://professional.heart.org/en/guidelines-and-statements)

Published by: American College of Cardiology; American Heart Association; American Association for Thoracic Surgery; Preventive Cardiovascular Nurses Association; Society for Cardiovascular Angiography and Interventions; Society of Thoracic Surgeons

Last published: 2012

Treatment guidelines

United Kingdom

Management of stable angina (https://www.sign.ac.uk/our-guidelines)

Published by: Scottish Intercollegiate Guidelines Network

Last published: 2018

Risk estimation and the prevention of cardiovascular disease (https://www.sign.ac.uk/our-guidelines)

Published by: Scottish Intercollegiate Guidelines Network

Last published: 2017

Stable angina: management (https://www.nice.org.uk/guidance/CG126)

Published by: National Institute for Health and Care Excellence

Last published: 2016

Europe

2022 ESC guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for therapeutic radiology and oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS) (https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Cardio-oncology-guidelines)

Published by: European Society of Cardiology **Last published:** 2022

2019 ESC guidelines for the diagnosis and management of chronic coronary syndromes (https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines)

Published by: European Society of Cardiology **Last published:** 2019

2018 ESC/EACTS guidelines on myocardial revascularization (https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines)

Published by: European Society of Cardiology; European Association for Cardio-Thoracic Surgery **Last published:** 2018

2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS (https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines)

Published by: European Society of Cardiology; European Association for Cardio-Thoracic Surgery **Last published:** 2017

North America

2022 ACC expert consensus decision pathway for integrating atherosclerotic cardiovascular disease and multimorbidity treatment: a framework for pragmatic, patient-centered care: a report of the American College of Cardiology Solution Set Oversight Committee (https://www.acc.org/guidelines)

Published by: American College of Cardiology **Last published:** 2023

2022 ACC expert consensus decision pathway on the role of nonstatin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk (https://www.acc.org/guidelines)

Published by: American College of Cardiology **Last published:** 2022

2021 ACC/AHA/SCAI guideline for coronary artery revascularization (https://professional.heart.org/en/guidelines-and-statements)

Published by: American College of Cardiology; American Heart Association **Last published:** 2021

AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol (https://professional.heart.org/en/guidelines-and-statements)

Published by: American Heart Association; American College of Cardiology; American Association of Cardiovascular and Pulmonary Rehabilitation; American Association Academy of Physician Assistants; Association of Black Cardiologists; American College of Preventive Medicine; American Diabetes Association; American Geriatrics Society; American Pharmacists Association; American Society for Preventive Cardiology; National Lipid Association; Preventive Cardiovascular Nurses Association **Last published:** 2018

ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS 2017 appropriate use criteria for coronary revascularization in patients with stable ischemic heart disease (https://www.acc.org/guidelines#/tab4)

Published by: American College of Cardiology; American Heart Association; American Association for Thoracic Surgery; American Society of Echocardiography; American Society of Nuclear Cardiology; Society for Cardiovascular Angiography and Interventions; Society of Cardiovascular Computed Tomography; Society of Thoracic Surgeons **Last published:** 2017

2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease (https://www.acc.org/guidelines)

Published by: American College of Cardiology; American Heart Association **Last published:** 2016

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 (https://professional.heart.org/en/guidelines-and-statements)

Published by: American College of Cardiology Foundation; American Heart Association; American Association for Thoracic Surgery; Preventive Cardiovascular Nurses Association; Society for Cardiovascular Angiography and Interventions; Society of Thoracic Surgeons

Last published: 2014

ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease (https://professional.heart.org/en/guidelines-and-statements)

Published by: American College of Cardiology Foundation; American Heart Association; American Association for Thoracic Surgery; Preventive Cardiovascular Nurses Association; Society for Cardiovascular Angiography and Interventions; Society of Thoracic Surgeons

Last published: 2012

AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease (https://professional.heart.org/en/guidelines-and-statements)

Published by: American Heart Association; American College of Cardiology Foundation.

Last published: 2011

Effectiveness-based guidelines for the prevention of cardiovascular disease in women (https://www.ahajournals.org/doi/10.1161/CIR.0b013e31820faaf8)

Published by: American Heart Association

Last published: 2011

Online resources

1. Atherosclerotic cardiovascular disease (ASCVD) risk estimator (http://tools.acc.org/ldl/ascvd_risk_estimator/index.html#!/calulate/estimator) *(external link)*

2. QRISK calculator (https://qrisk.org) *(external link)*

3. SCORE2 and SCORE2-OP risk assessment models (https://www.escardio.org/Education/Practice-Tools/CVD-prevention-toolbox/SCORE-Risk-Charts) *(external link)*

Evidence tables

What are the effects of patient education on management of coronary heart disease?

This table is a summary of the analysis reported in a Cochrane Clinical Answer that focuses on the above important clinical question.

Cochrane Clinical Answers

View the full source Cochrane Clinical Answer (https://www.cochranelibrary.com/cca/doi/10.1002/cca.1777/full)

Evidence C *

Confidence in the evidence is very low or low where GRADE has been performed and there may be no difference in effectiveness between the intervention and comparison for key outcomes. However, this is uncertain and new evidence could change this in the future.

Population: Adults aged 51-73 years with coronary heart disease

Intervention: Patient education [a]

Comparison: Usual medical care (typically referral to an outpatient cardiologist, primary care physician, or both)

Outcome	Effectiveness (BMJ rating)†	Confidence in evidence (GRADE)‡
Total mortality at the end of the follow-up period (median 18 months)	No statistically significant difference	Moderate
Fatal and/or non-fatal MI at the end of the follow-up period (median 33 months)	No statistically significant difference	Very Low
Total revascularisations (including CABG and PCI) (median follow-up 36 months)	No statistically significant difference	Very Low
Cardiac hospitalisations (median follow-up 12 months)	No statistically significant difference	Very Low
All-cause withdrawal/drop-out (median follow-up 12 months)	No statistically significant difference	Low
Quality of life (median follow-up 12 months)	See note [b]	Moderate

Note

The Cochrane review which underpins this Cochrane Clinical Answer (CCA) notes that due to the limited quality and lack of certainty of the evidence, patient education should be used only as part of a comprehensive programme which includes exercise and psychological support, which reflects international guidance.

[a] Education interventions varied in what was delivered, who delivered it, and the intensity and duration of the intervention. See the CCA for more details.

[b] Results were inconsistent with most finding no difference although some favoured the intervention; a number of different scales were used to measure quality of life so results could not be meta-analysed and are therefore reported narratively. See the CCA for more details.

* Evidence levels

The Evidence level is an internal rating applied by BMJ Best Practice. See the EBM Toolkit (https://bestpractice.bmj.com/info/evidence-tables/) for details.

Confidence in evidence

A - High or moderate to high

B - Moderate or low to moderate

C - Very low or low

† Effectiveness (BMJ rating)

Based on statistical significance, which demonstrates that the results are unlikely to be due to chance, but which does not necessarily translate to a clinical significance.

‡ Grade certainty ratings

High	The authors are very confident that the true effect is similar to the estimated effect.
Moderate	The authors are moderately confident that the true effect is likely to be close to the estimated effect.
Low	The authors have limited confidence in the effect estimate and the true effect may be substantially different.
Very Low	The authors have very little confidence in the effect estimate and the true effect is likely to be substantially different.

BMJ Best Practice EBM Toolkit: What is GRADE? (https://bestpractice.bmj.com/info/toolkit/learn-ebm/what-is-grade/)

Key articles

- Fihn SD, Gardin JM, Abrams J, et al; American College of Cardiology Foundation/American Heart Association Task Force. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease. Circulation. 2012 Dec 18;126(25):e354-471. Full text (https://www.ahajournals.org/doi/10.1161/CIR.0b013e318277d6a0) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/23166211?tool=bestpractice.bmj.com)

- Knuuti J, Wijns W, Saraste A, et al. 2019 ESC guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J. 2020 Jan 14;41(3):407-77. Full text (https://academic.oup.com/eurheartj/article/41/3/407/5556137) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/31504439?tool=bestpractice.bmj.com)

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- Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Thorac Cardiovasc Surg. 2016 Nov;152(5):1243-75. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/27751237?tool=bestpractice.bmj.com)

- Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019 Jun 18;139(25):e1082-143. Full text (https://www.ahajournals.org/doi/10.1161/CIR.0000000000000625) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/30586774?tool=bestpractice.bmj.com)

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3. Fihn SD, Gardin JM, Abrams J, et al; American College of Cardiology Foundation/American Heart Association Task Force. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the

diagnosis and management of patients with stable ischemic heart disease. Circulation. 2012 Dec 18;126(25):e354-471. Full text (https://www.ahajournals.org/doi/10.1161/CIR.0b013e318277d6a0) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/23166211?tool=bestpractice.bmj.com)

4. Knuuti J, Wijns W, Saraste A, et al. 2019 ESC guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J. 2020 Jan 14;41(3):407-77. Full text (https://academic.oup.com/eurheartj/article/41/3/407/5556137) Abstract (http://www.ncbi.nlm.nih.gov/pubmed/31504439?tool=bestpractice.bmj.com)

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Images

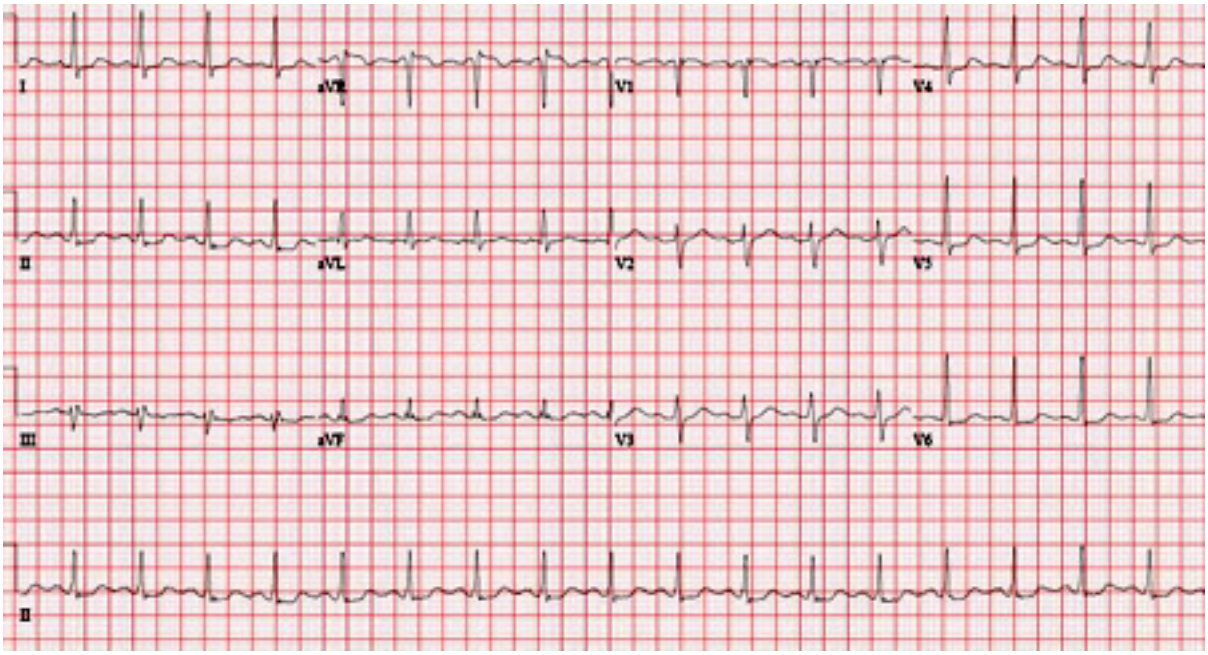

Figure 1: ECG showing non-specific ST depressions in V5 and V6, which may indicate ischaemia. There are non-specific ST-segment changes in III and aVF

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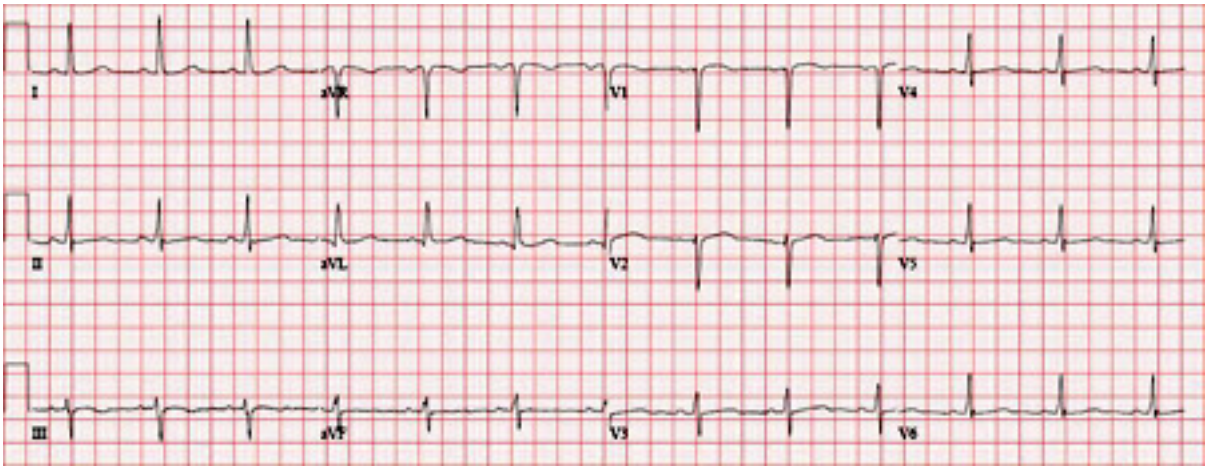

Figure 2: Normal ECG

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	Typical (%)		Atypical (%)		Non-anginal (%)		Dyspnoea as only/primary symptom	
Age (years)	Men	Women	Men	Women	Men	Women	Men	Women
30-39	3	5	4	3	1	1	0	3
40-49	22	10	10	6	3	2	12	3
50-59	32	13	17	6	11	3	20	9
60-69	44	16	26	11	22	6	27	14
70+	52	27	34	19	24	10	32	12

Figure 3: Pre-test probabilities of obstructive coronary artery disease in symptomatic patients according to age, sex, and nature of symptoms in pooled analysis

Juarez-Orozco et al. Eur Heart J Cardiovasc Imaging. 2019 Nov 1;20(11):1198-207; used with permission

	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)
Stress ECG	58 (46-69)	62 (54-69)
Stress echo	85 (80-89)	82 (72-89)
CCTA	97 (93-99)	78 (67-86)
SPECT	87 (83-90)	70 (63-76)
PET	90 (78-96)	85 (78-90)
Stress CMR	90 (83-94)	80 (69-88)

Figure 4: Sensitivity and specificity of tests for anatomically significant coronary artery disease

Adapted from Knuuti et al. The performance of non-invasive tests to rule-in and rule-out significant coronary artery stenosis in patients with stable angina: a meta-analysis focused on post-test disease probability. Eur Heart J. 2018 Sep 14;39(35):3322-30; used with permission. (CCTA, coronary computed tomography angiography; CI, confidence interval; CMR, stress cardiac magnetic resonance; PET, positron emission tomography; SPECT, single-photon emission computed tomography [exercise stress SPECT with or without dipyridamole or adenosine]; Stress echo, exercise stress echocardiography)

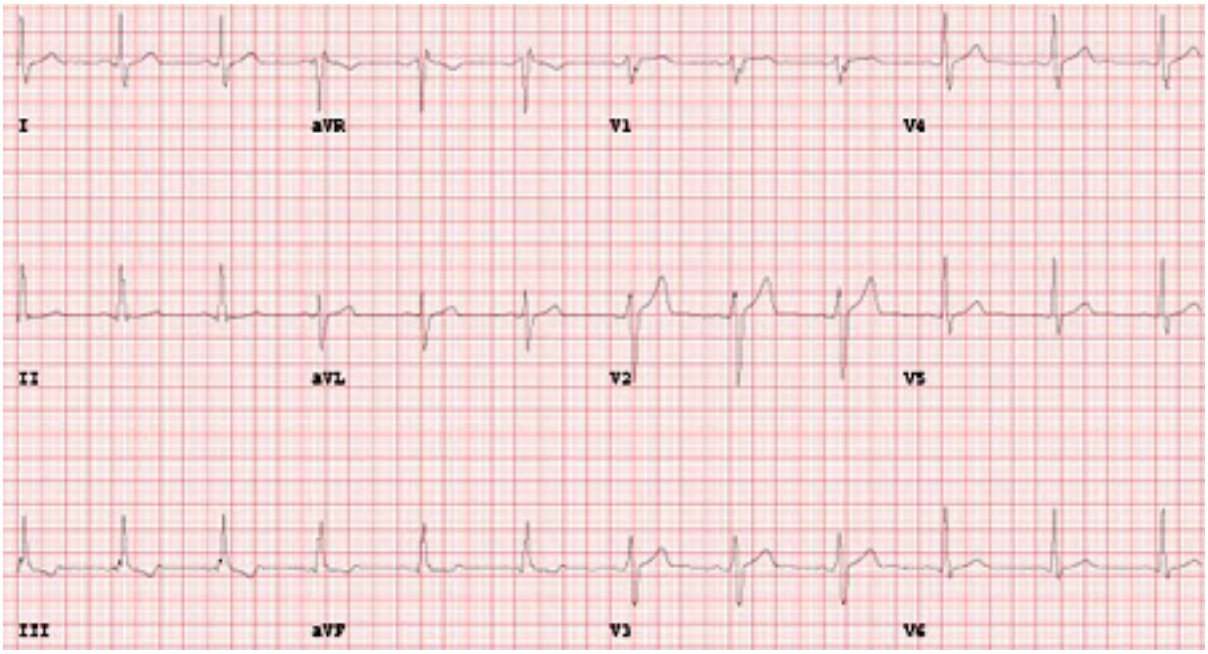

Figure 5: Baseline exercise ECG in a 55-year-old man with a 1-month history of angina on exertion

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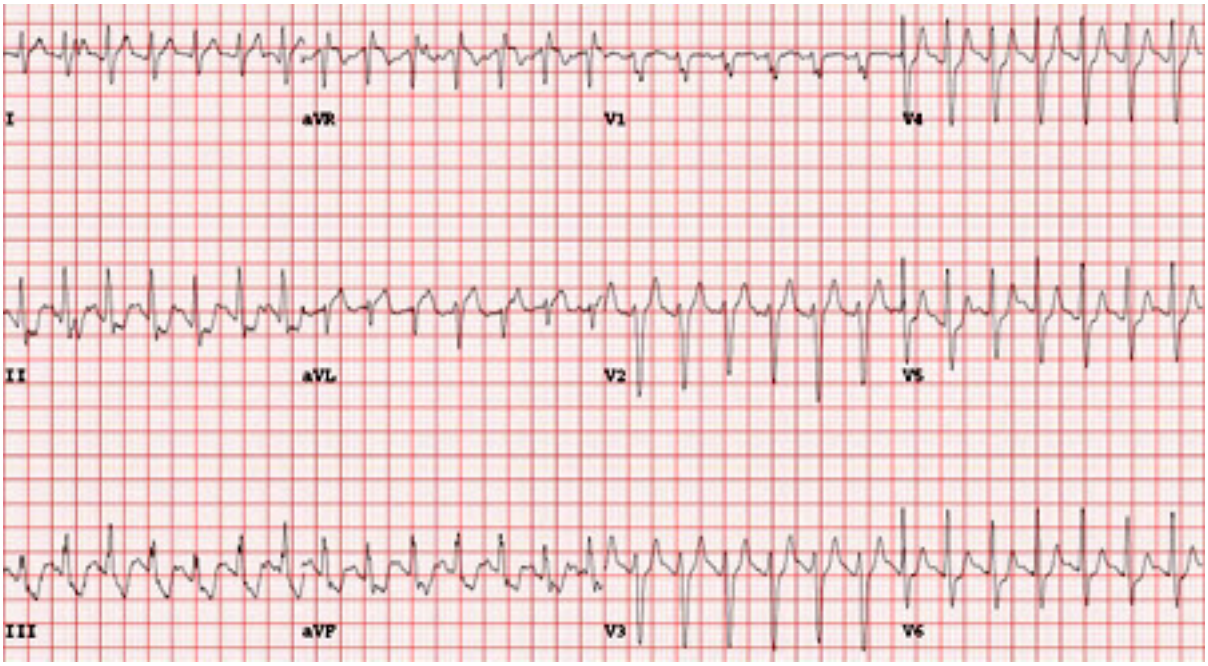

Figure 6: Maximal exercise ECG in a 55-year-old man with a 1-month history of angina on exertion with ST depressions in II, III, aVF diagnostic of ischaemia, and normal ST changes in V4-6 (rapid upsloping)

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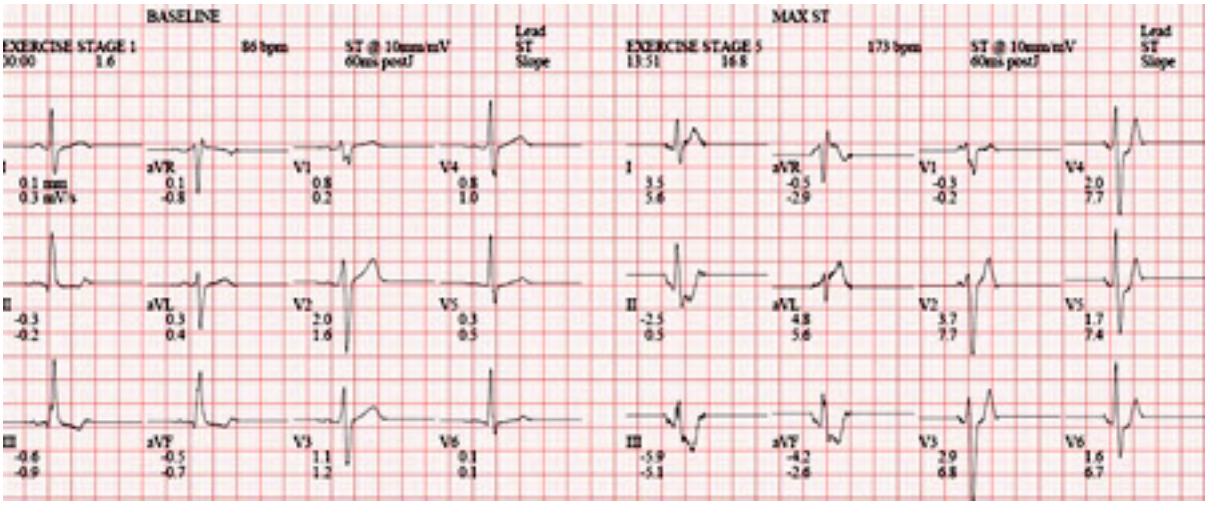

Figure 7: Computerised summary of exercise ECG in a 55-year-old man with a 1-month history of angina on exertion

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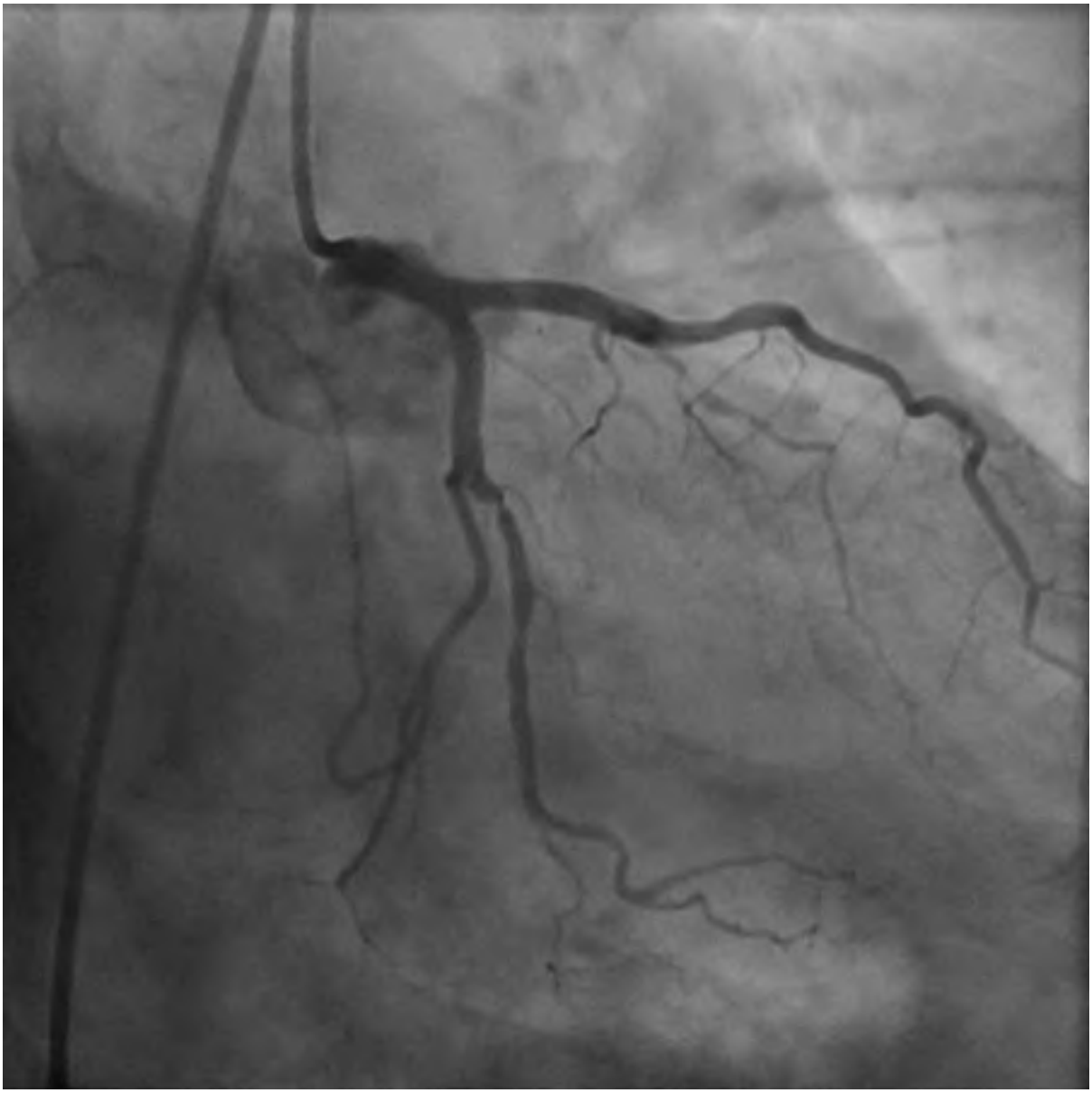

Figure 8: Angiogram (right anterior oblique caudal projection) in a 55-year-old man with a 1-month history of angina on exertion. A 90% proximal stenosis of obtuse marginal 1 is present, explaining the patient's lateral ischaemia

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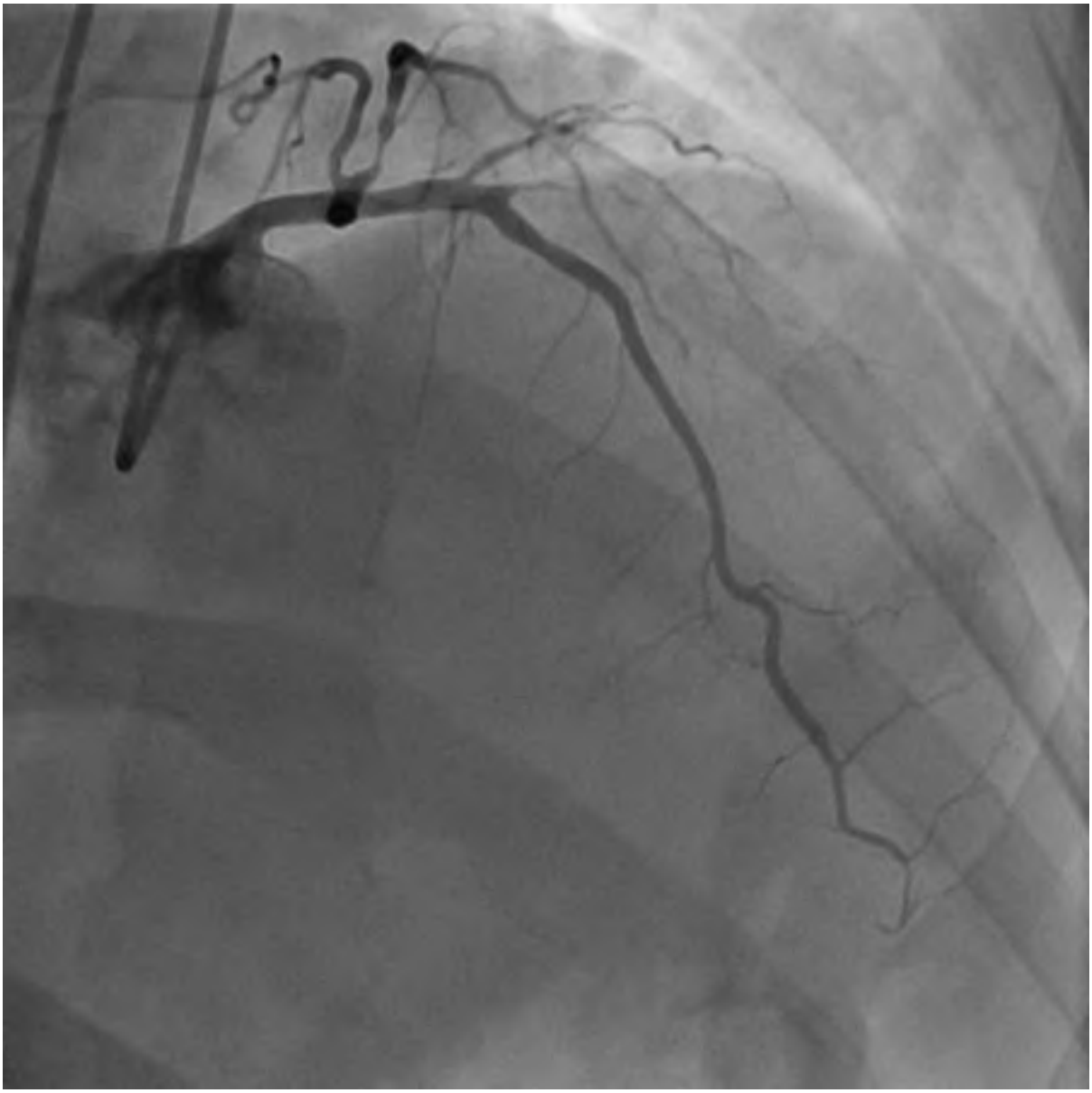

Figure 9: Angiogram (right anterior oblique cranial projection) in a 55-year-old man with a 1-month history of angina on exertion. The image shows a 90% proximal stenosis of obtuse marginal 1 (explaining the patient's lateral ischaemia), 90% proximal stenosis of the first diagonal, and 99% subtotal occlusion of the second diagonal (explaining the patient's anterior and anterolateral ischaemia)

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Figure 1 – BMJ Best Practice Numeral Style

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// Acknowledgements:

Dr Douglas Berger and Dr Stephan D. Fihn would like to gratefully acknowledge Dr Karen E. Segerson, Dr Mark C. Zaros, Dr Joy Bucher, and Dr Steven M. Bradley, previous contributors to this topic.
DISCLOSURES: KES, MCZ, JB, and SMB declare that they have no competing interests.

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