Clinical presentation and diagnosis of coronary artery disease: stable angina

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Angina pectoris is a clinical syndrome of discomfort in the chest, jaw, arm, or other sites which is associated with myocardial ischaemia. The nature of angina has many individual variations, and it is easier first to consider the typical syndrome. It is hard to better the descriptions of William Heberden:

There is a disorder of the breast, marked with strong and peculiar symptoms, considerable for the danger belonging to it.... Those who are afflicted with it are seized, while they are walking, and more particularly when they walk soon after eating, with a painful and most disagreeable sensation in the breast ... the moment they stand still all this uneasiness vanishes.... After it has continued some months, it will not cease so instantaneous upon standing still ... (most) whom I have seen, who are at least twenty, were men, and almost all above 50 years old, and most of them with a short neck, and inclining to be fat.... But the natural tendency of this illness be to kill the patients suddenly.... The os sterni is usually pointed to as the seat of this malady ... and sometimes there is with it a pain about the middle of the left arm.

The usual cause of myocardial ischaemia is coronary atherosclerosis. Other diseases of the coronary arteries (emboli, spasm, vasculitis, Kawasaki disease, congenital anomalies), other cardiac diseases (hypertrophic cardiomyopathy, severe hypertension, severe aortic valve disease), and high output states (severe anaemia, thyrotoxicosis) are all uncommon or rare causes of angina. However, while angina is usually associated with atherosclerotic coronary artery disease, the converse is not always true. The condition of coronary atherosclerosis is very common (fatty streaks and more advanced plaques are almost universal in adults in industrialised countries) but it does not always cause myocardial ischaemia. Furthermore, myocardial ischaemia may present other than with angina – for each presentation there is a wide differential diagnosis.

Angina

Approximately 50% of cases are recognised because of chest pain. Cardiac ischaemic pain is thought to arise from stimulation of nerve
endings near the endocardium by factors such as adenosine, lactate, and H+. These afferent fibres run predominantly with sympathetic fibres through the stellate ganglion to thoracic roots T1 to T5. The pain is typically described as tight, squeezing, like a weight on the chest, or like indigestion; as with any visceral pain, the localisation is vague and there is considerable individual variation between patients.

There are many other causes of chest pain, and the differential diagnosis is summarised in Table 1. The characteristics of angina are well known, and the points of differentiation from non-cardiac pain are summarised in Table 2.

### Table 1 The differential diagnosis of chest pain

<table>
<thead>
<tr>
<th>Cardiac causes</th>
<th>Other vascular causes</th>
<th>Respiratory causes</th>
<th>Gastrointestinal causes</th>
<th>Other causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina</td>
<td>Discrete thoracic aortic aneurysm</td>
<td>Pulmonary embolism, pulmonary infarction</td>
<td>Oesophagitis, oesophageal spasm, hiatus hernia</td>
<td>Chest wall syndromes, costochondritis (Tietze's syndrome)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>Aortic dissection</td>
<td>Pneumonia</td>
<td>Oesophageal rupture, mediastinitis (Boerhaave's syndrome)</td>
<td>Cervical spondylosis, thoracic disk problems, thoracic outlet syndrome</td>
</tr>
<tr>
<td>Variant angina (Prinzmetal angina)</td>
<td></td>
<td>Viral pleurisy, e.g. Bornholm disease</td>
<td>Peptic ulcer</td>
<td>Herpes zoster</td>
</tr>
<tr>
<td>Microvascular angina (syndrome X)</td>
<td></td>
<td>Pneumothorax, pneumomediastinum</td>
<td>Biliary colic, pancreatitis, splenic infarct</td>
<td>Psychogenic</td>
</tr>
<tr>
<td>pericarditis, myocarditis</td>
<td></td>
<td>Acute asthma</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 2 The characteristics of cardiac and non-cardiac chest pain

<table>
<thead>
<tr>
<th>Cardiac pain (Usually angina)</th>
<th>Non-cardiac pain (Usually musculoskeletal or gastro-oesophageal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Descriptors of pain</td>
<td>Site</td>
</tr>
<tr>
<td>Heavy, tight, pressure, dull</td>
<td>Central anterior</td>
</tr>
<tr>
<td>Band, squeezing</td>
<td>Left arm, right arm, teeth</td>
</tr>
<tr>
<td></td>
<td>Interscapular, epigastric</td>
</tr>
<tr>
<td>Precipitants</td>
<td>Precipitants</td>
</tr>
<tr>
<td>Exercise, emotion</td>
<td>Stress</td>
</tr>
<tr>
<td>Cold</td>
<td>Stress, locally tender</td>
</tr>
<tr>
<td>Post-prandial</td>
<td>Posture, particular movements of arms or neck</td>
</tr>
<tr>
<td></td>
<td>Swallowing (odynophagia)</td>
</tr>
</tbody>
</table>
The diagnosis of strengthened by recognition of precipitating factors (exertion, emotion, extremes of temperature), relieving factors (rest, sublingual nitrates), associated symptoms (sweating, pallor, nausea, alarm), and some special patterns (diurnal rhythm, walk-through, warm-up).

Difficulty arises because angina can cause atypical pains, for example interscapular or epigastric without any anterior chest discomfort. Individual patients often have more than one type of chest pain, and musculoskeletal and gastro-oesophageal pains commonly co-exist with angina as well as forming part of the differential diagnosis. Often, a detailed accurate history will clarify the diagnosis or diagnoses. However, the frequency and severity of angina provides only an approximate guide to the severity of the underlying coronary artery atherosclerosis and to the prognosis; some patients with myocardial ischaemia are asymptomatic.

Acute myocardial infarction

In some patients, coronary artery disease is first diagnosed when they present with the severe pain and haemodynamic disturbance of acute infarction, usually as a result of sudden thrombotic occlusion of an atherosclerotic coronary artery. On close questioning, there may be a history of some chest discomfort prior to the infarct, but in some cases no warning at all.

Dyspnoea

For some patients, dyspnoea is the only sensation experienced during myocardial ischaemia, so-called ‘angina equivalent’. The mechanisms are thought to be the same as for angina, but with a different central appreciation of the afferent stimuli. More often, dyspnoea occurs together with angina – many patients experience their tightness across the chest both as a pain and as a sense of restriction in breathing. It is important to avoid asking leading questions in order to obtain an accurate description from the patient.

Dyspnoea may also arise in patients with coronary artery disease if there is ischaemic left ventricular dysfunction causing pulmonary venous congestion or pulmonary oedema, if there is papillary muscle dysfunction causing mitral regurgitation, or in a chronic low output state (see below). The mechanisms of dyspnoea in these cases may involve hypoxia, pulmonary receptors, and a sense of the effort made by the respiratory muscles.

Cardiac failure

The triad of dyspnoea, fatigue, and dependent oedema suggests overt cardiac failure. In industrialised countries, coronary atherosclerosis is
the commonest cause of cardiac failure\textsuperscript{4,5}. This presentation suggests advanced coronary artery disease with myocardial infarction, or with diffuse myocardial fibrosis as a result of previous ischaemic episodes.

**Arrhythmias**

Atrial fibrillation is seen in 20\% of patients with coronary artery disease. Serious ventricular arrhythmias such as ventricular tachycardia may also occur. Atroventricular block may result from myocardial infarction, and sometimes transiently during exercise-related ischaemia. These arrhythmias are usually detected during the investigation of a patient with chest pain or dyspnoea, and it is less common for patients to present with palpitation or dizzy spells as the primary symptom.

**Sudden death**

It is now recognised that in a proportion of patients the first manifestation of coronary artery disease is sudden collapse and death, due to acute myocardial infarction and/or ventricular arrhythmias. The absence of premonitory symptoms emphasises the need for a population approach to primary prevention. A family history of sudden collapse and death is relevant when taking the history of a patient, but there are other cardiovascular causes including cardiomyopathies, long QT syndromes and cerebrovascular aneurysms and malformations.

**Other presentations**

Many other symptoms can occur with coronary artery disease, but it is rare for them to be the main presentation in the absence of one of the above symptom complexes. Fatigue is common in coronary artery disease, possibly related to its psychological effects, but also when there is cardiac failure\textsuperscript{4}. Coronary artery disease may present with peripheral arterial embolism and with embolic stroke, usually when there has been myocardial infarction and mural thrombus within the left ventricle.

**Clinical diagnosis of chest pain**

**General considerations**

Given a clinical history of chest discomfort suggestive of angina, the diagnosis depends as much upon the probability that the given individual has coronary artery disease as upon the exact nature of the symptoms. The main predictors of coronary artery disease are age, male gender,
family history, tobacco smoking, diabetes mellitus, and hyperlipidaemia. Thus somewhat atypical chest pain in a 60-year-old male smoker with a strong family history is more likely to represent angina than is typical exertional pain in a 20-year-old woman with no risk factors.

**Symptoms**

The differing presentations of coronary artery disease have been listed above, and the differential diagnosis of chest pain is given in Table 1. The distinction of angina from other chest pains is not always as easy as one might suppose, and a good history is important, with particular regard to the characteristics of the pain outlined in Table 2.

It is also important to ask how symptoms affect the patient’s daily activities including their ability to work, and the nature of their work. The level of angina (and of dyspnoea) can be graded on the NYHA or Canadian Cardiovascular Society scales, which both run from I (very mild) to IV (symptoms at rest or on minimal exertion). Although crude, these scales are useful in clinical trials and in following changes over time in a given patient.

At this stage, the clinician uses the information which he has obtained to form a judgement whether the pain is angina or not. There are a number of simple scores to assist with this\textsuperscript{6,7}, but they are not widely used in clinical practice.

**Physical examination**

The physical examination is usually normal, and is most useful in providing evidence of alternative diagnoses such as chest wall pain and other musculoskeletal pains. The physical examination may give indirect clues to coronary artery disease such as evidence of severe hyperlipidaemia (xanthomas, premature corneal arcus) or evidence of left ventricular impairment (third heart sound, signs of overt cardiac failure such as dependent oedema).

**Role of investigations**

Investigations may be used to confirm the diagnosis, to detect associated conditions (such as heart failure, diabetes mellitus), and for the assessment of prognosis to guide further investigation and treatment – so-called ‘risk stratification’. Here we will consider the diagnostic value of investigations (risk stratification will be discussed elsewhere in this volume).
Basic investigations

Resting electrocardiogram
The ECG is often normal. Pathological Q waves almost always indicate myocardial infarction and other causes are uncommon. Finding Q waves, therefore, has considerable specificity but it is insensitive for the diagnosis of coronary artery disease. The ECG may also show changes suggestive of other diagnoses including pericarditis, LV hypertrophy, right heart strain, and atrial fibrillation.

Chest X-ray
This is usually normal, but if there is cardiac failure there may be increased cardiothoracic ratio and/or pulmonary venous congestion. The aortic contour may give a clue to aortic dissection or thoracic aortic aneurysm, but is not reliable in this regard. Other causes of chest pain may be suggested by pleural shadowing, radiographic features of pulmonary hypertension, masses in the lung fields or mediastinum, and the fluid level of a hiatus hernia behind the heart.

Blood tests
Full blood count to detect any anaemia, thyroid function tests to detect thyrotoxicosis (high output state, angina) or hypothyroidism (hyperlipidaemia and coronary disease), and urea and electrolytes to assess renal function are usually performed. A lipid profile including HDL, LDL, triglycerides, and glucose measurement are also routine as they may require management in their own right. Additionally, a very high cholesterol or a new finding of impaired glucose tolerance would sway the diagnostic probabilities towards coronary artery disease.

Optional cardiac and non-cardiac investigations for alternative diagnoses

Upper GI endoscopy, barium studies or abdominal ultrasound may be indicated, as may be a lateral chest X-ray of the thoracic or cervical spine. CT or MRI of the chest is useful to examine the aorta, lung fields, and mediastinum. An echocardiogram is useful: (i) if there is a murmur or other specific reason; (ii) for a general assessment of left ventricular function; and (iii) following myocardial infarction to document LV function, regional wall motion abnormalities, any mitral regurgitation, ischaemic septal defect, or LV thrombus.

Non-invasive coronary assessment
The four most common non-invasive tests are:

Exercise test
This focuses on abnormal ST segment depression but also offers the opportunity to assess the patient's overall exercise capacity, the symptoms
limiting exertion, and heart rate and blood pressure responses to exercise.

Radio-isotope myocardial perfusion scanning

This provides imaging of myocardial perfusion, with reversible perfusion deficits indicating ischaemia, and fixed perfusion deficits indicating infarction or sometimes attenuation by overlying tissue. Modern methods may also allow the definition of hibernating and stunned myocardium, helping the planning of revascularisation.

Coronary calcification score

The use of fast electron-beam CT scanning allows non-invasive calculation of a coronary calcification score, much more accurately than the old method of fluoroscopy to detect coronary calcification.

Stress echocardiography

This observes changes in regional wall motion and overall LV function during exercise and/or pharmacological stress. It may also be possible to observe dynamic LV outflow tract gradients as in hypertrophic cardiomyopathy, and ischaemic papillary muscle dysfunction causing mitral regurgitation

Other methods

Other methods used occasionally include 24-hour ambulatory ST-segment monitoring, and PET scanning for myocardial perfusion and metabolism. MRI and MR angiography of the coronary arteries is a developing field likely to be of great value in future. Currently, available MRI technology is well able to define LV function regional wall motion abnormalities and may be more accurate than stress echocardiography.

These will be discussed in more detail elsewhere in this volume, but we should make some general points. All the above non-invasive tests are inaccurate to some degree. If we use coronary angiography as the gold standard to define the presence a stenosis of 50% or greater in a major epicardial vessel, then typically the sensitivity is 70–90% and specificity 70–90% for the above methodologies. Each method has further specific weaknesses – for example, the treadmill exercise ECG is poor at reflecting disease in the circumflex territory.

If more than one non-invasive test is performed in a given patient, one may give a result indicating normality and the other indicate coronary disease. When there are discrepant data, the clinician has to make a decision on the overall situation as to whether there is likely to be
coronary artery disease or not. Performing additional tests is also of limited usefulness because ‘predictive redundancy’ – the incremental information offered by performing a second non-invasive test is less than would be expected if they were independently predictive. Patients who have an equivocal test with one modality are more likely to have an equivocal test with another modality, and those who are false positives with one are also more likely to be false positive with another – the reasons for this are unclear, but it is of practical importance. If the most appropriate non-invasive test has been correctly selected for the individual patient, then if the result is borderline or does not fit with the clinical picture, performing a different non-invasive test in addition may not be helpful. However, all of the non-invasive tests have considerable prognostic value, aside from their ability to detect structural coronary artery disease – this will be discussed below.

**Diagnosis in special groups**

*Silent ischaemia*

During an episode of myocardial ischaemia, there is a sequence of events often termed the ‘ischaemic cascade’. Perfusion and metabolic abnormalities are followed by abnormalities of regional wall motion, changes in global LV diastolic function, then changes in LV systolic function, about which time there are changes in the resting ECG, and finally anginal pain. It is, therefore, possible to have considerable myocardial ischaemia and changes in LV function before any pain is manifest. Indeed Herrick in 1912 described autopsies revealing myocardial infarction in patients with no history of chest pain whatever. Ambulatory ST-segment ECG monitoring in patients with extensive coronary artery disease has shown that whilst only 5–10% of these patients have no angina whatever, about 40% of all episodes of ST depression are asymptomatic. Episodes of so-called ‘silent myocardial ischaemia’ are more common in the elderly and in patients with diabetes mellitus.

The sequence of the ischaemic cascade may help explain why different non-invasive tests may give discrepant data, as they depend upon different disturbances in cardiac function. For example, the thallium scan detects changes in perfusion, the PET scan detects changes in metabolism, but the stress echo will only detect a later stage when there are wall motion abnormalities, and the exercise ECG may be the last to change. We should also consider the interpretation of a patient without chest pain who has abnormal non-invasive tests for coronary artery disease – possibly undertaken because of pain in the past, or as a pre-operative assessment. The possible interpretations include: (i) the test is...
incorrect, in other words a false positive result; or (ii) silent ischaemia, where the stress was of insufficient intensity or duration to cause pain as the last change in the ischaemic cascade.

The elderly

The incidence of coronary artery disease rises rapidly with age in men and also in women following the menopause. It is important to exclude contributory factors such as anaemia, thyrotoxicosis, and fast atrial fibrillation or severe bradycardias. They may present a difficult challenge in knowing how far to investigate, and there may be practical difficulties with undertaking simple non-invasive tests such as treadmill or cycle exercise. The elderly are also more likely to have silent ischaemia and to suffer silent myocardial infarcts.

Diabetes mellitus

Type II diabetes mellitus is of increasing prevalence in non-industrialised countries, and a major association of coronary artery disease and of a poor prognosis. These patients are more likely to have diffuse coronary artery disease, and more likely to have silent myocardial infarction and episodes of silent ischaemia.

Patients following myocardial infarction

These patients have already declared themselves as having significant coronary artery disease and of being at increased risk unless treated vigorously. There is a strong evidence base for secondary prevention which involves more stringent targets for blood pressure and lipids than does primary prevention. There is also considerable randomised controlled trial data for the benefits of aspirin, clopidogrel, β-blockers, ACE inhibitors, and statins. In this area where the treatment guidelines are well worked out, the main problem is ensuring implementation and the provision of adequate healthcare resources.

Patients following cardiac transplantation

Angina can occur in patients some years after transplantation, implying re-innervation of the transplanted heart. However most angina in transplant recipients is painless or atypical; hence, most transplant centres have a
programme of regular non-invasive testing and, in some cases, of annual coronary arteriography starting 5 years after transplantation.

**International differences**

It is estimated that cardiovascular disease is responsible for 30% of mortality world-wide, about half of which is attributable to coronary artery disease. It is much more prevalent in industrialised countries with established market economies, but there is a rapid increase in prevalence in many of the former socialist economies, the lowest prevalence being in non-industrialised countries\(^\text{10}\). Although the prevalence has always been low in some industrialised countries (such as Japan) and is slowly declining in others (USA, Canada, Australia, France), the prevalence of coronary artery disease world-wide is predicted to increase. This is partly because of demographic changes with increasing proportions of the elderly, overall population growth, and ethnic differences. Certain groups such as those from South Asia (India, Bangladesh, Pakistan, Sri Lanka) and from China have a very high incidence of coronary artery disease if they migrate to industrialised countries or adopt a Western lifestyle. It has been speculated that this is due to a ‘thrifty gene’ and impaired glucose tolerance\(^\text{10}\).

Healthcare resources are the major determinant of the technologies for investigation, the range of treatments, and healthcare personnel numbers per head of population available locally. In some regions, it may only be practical to make a clinical diagnosis unsupported by investigation, to treat symptomatically with GTN, and to give advice on diet and other aspects of life-style. In well-funded healthcare systems such as the US the majority of patients would have at least an echocardiogram to assess LV function plus a non-invasive test for coronary artery disease, such as a myocardial perfusion scan or exercise ECG; a large number would go on to invasive angiography.

**Key points for clinical practice**

- Myocardial ischaemia is usually caused by coronary artery atheroma and thrombosis – other pathologies are rare
- The most common symptom of myocardial ischaemia is angina (50% of cases); other symptoms include dyspnoea, fatigue, and arrhythmias
- In some patients with coronary artery disease, episodes of myocardial ischaemia can occur without symptoms; ‘silent ischaemia’ is more common in the elderly and in diabetics
Most patients describe angina as a pressure, a tightness, or a discomfort, rather than as a pain. The perception of angina varies between individuals, and atypical pains may, nonetheless, represent angina in a patient with coronary risk factors.

The clinical diagnosis of angina depends upon an appreciation of the probability that the individual patient has coronary artery disease (age, male, family history, smoking, diabetes mellitus, hyperlipidaemia) as well as on a detailed account of the symptoms.

The physical examination is usually normal, but may give clues to coronary risk factors (signs of hyperlipidaemia) or clues to an alternative diagnosis (musculoskeletal pain).

Simple investigation such as the chest X-ray and the resting ECG are usually normal, but are useful as a baseline in the majority of patients, and in a minority show specific abnormalities informing the diagnosis (enlarged heart, pathological Q waves).

References


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