

# Ischaemic Heart Disease/Chest Pain

## Part 2: Clinical management

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*[Editor: The following is primarily an abridged summary of technical notes on the investigation and management of chronic stable angina. Investigations have been given a rating of their use and value in different settings of IHD management. A class 1 indication implies there is substantial evidence and expert agreement supporting the use of these investigations.]*

*There is some overlap with Ischaemic Heart Disease Part 3: Chronic IHD, which covers the burden of ischaemic heart disease, epidemiology and evidence base for recommended interventions all in some detail. For more detail on the management of acute coronary syndromes, see Ischaemic Heart Disease Part 1: Acute chest pain.*

### **Pathophysiology**

IHD is a complication of atherosclerosis. Atherosclerosis is a chronic inflammatory disease of the arterial wall resulting from initial injury to the endothelial cells lining the artery. Injury is due to combination of chemical and mechanical stress. Mechanical stress is from elevated blood pressure. Chemical stress results from smoking, elevated cholesterol, and the alteration of proteins as a consequence of elevated blood glucose (glycosylated proteins).

### **Clinical manifestations**

#### **Angina**

Clinical syndrome is characterised by chest, jaw, shoulder, back and/or arm discomfort. It is typically aggravated by exertion or emotional stress and relieved by anginine.

#### **Chronic stable angina**

- Exertional/emotional-induced discomfort in the chest, jaw, shoulder, back and/or arm
- Exertional/emotional-induced dyspnoea

#### **Acute coronary syndromes**

- Unstable angina
- Non-ST infarction
- Non-Q wave infarction
- Q wave infarct
- Sudden death

### **History and clinical examination**

In patients presenting with chest pain a detailed symptom history, physical examination and directed risk factor assessment needs to be performed. Need to determine the probability of significant coronary artery disease and assess whether symptoms are chronic and stable or patient has an acute coronary syndrome which requires immediate attention and intervention.

#### Low risk

- Non-cardiac pain
- No risk factors

#### Intermediate risk

- Atypical pain (probable angina)
- 1–2 risk factors

#### High risk

- >2 risk factors
- Typical pain
- Previous known coronary artery disease

#### Recent:

<30 days post myocardial infarction (heart attack)

<6 months post PTCA (balloon angioplasty with or without stent)

<6 months post CABG (bypass surgery).

Patients with rest symptoms, recent onset of chest pains or increasing frequency of symptoms need to be considered as potentially having an acute coronary syndrome and need to be treated accordingly.

#### **Definition of angina symptoms**

##### Typical angina (definite)

- Substernal chest discomfort with a characteristic quality and duration that is provoked by exertion or emotional stress and relieved by rest or nitroglycerin

##### Atypical angina (probable)

- Meets two of the above characteristics

##### Noncardiac chest pain

- Meets one of the typical angina characteristics

##### Risk factors

- Family history
- Smoking
- Hypertension
- Diabetes
- Dyslipidaemia, elevated cholesterol
- Post menopause

#### **Investigations**

ECG (Class 1 indication)

Rest ECG.

Rest ECG with pain:

- To determine cardiac rhythm, previous AMI, acute ST changes, evidence of left ventricular hypertrophy
- Performed immediately if patient presents with chest pain, even if atypical; fax ECG for doctor's review
- 50% of patients with chronic stable angina will have a normal ECG; suggests normal rest left ventricular function
- Repeat ECG with each visit

## **Blood chemistry**

FBC (Class I indication)

Anaemia with haemoglobin less than 90 may result in angina at rest.

EUC (Class I indication)

Renal function

Electrolytes (potassium and magnesium); risk of arrhythmias.

Fasting blood sugar levels (Class I indication)

Diabetes is a major risk factor for coronary artery disease.

HbA1c in patients with known diabetes to assess diabetic control.

Lipids (Class I indication), total cholesterol, HDL, calculated LDL, triglycerides.

Thyroid function (Class II indication)

Hyperthyroidism may lead to increase in angina due to increased metabolism.

Patients with hypothyroidism may experience worsening of angina control with commencement of thyroid replacement therapy.

## **Imaging**

Chest X-Ray (Class I indication): Patients with signs and/or symptoms suggestive of: heart failure, valve disease, aortic dissection.

Chest X-Ray (Class IIa indication): Patients with lung disease.

## **Cardiac investigations**

Echocardiogram

- Assesses LV size, function, and presence of wall motion abnormalities suggesting previous AMI
- Valve disease, including aortic stenosis that can cause angina
- LV hypertrophy with associated outflow obstruction that can also cause angina

Not routinely required for the investigation of patient with stable angina.

Patients with: (Class I indication) LV failure, Q waves, ventricular arrhythmia, systolic murmur suggestive of aortic stenosis, mitral regurgitation, HOCM.

Patients with: (Class IIb indication) click or murmur suggestive of mitral valve prolapse.

## **Stress testing**

**Exercise ECG test**

- Treadmill or bicycle exercise with ECG monitoring with or without imaging
- In the NT these test are only available in Darwin and Alice Springs
- Should be used in initial assessment, as important in risk assessment
- Without imaging (e.g. without echocardiography or nuclear scanning)

Class I indications

- For investigation of patients with intermediate pre-test probability of obstructive coronary artery disease
- Includes patients with: complete RBBB, <1 mm ST depression at rest
- For risk assessment and prognosis during initial assessment

Class IIb indications

Patients with: high or low pre-test probability of obstructive coronary artery disease for age, gender and symptoms

Patients taking digoxin with baseline ECG ST depression <1 mm

Patients with ECG criteria for LV hypertrophy and baseline ST depression of <1 mm

## **Cardiac stress imaging**

Stress nuclear cardiac perfusion scan (previously called thallium scans, now myoview is used) or stress echocardiography. Wherever possible exercise testing should be used as the most appropriate form of stress as it provides the most information. The inability to perform an exercise test is a strong negative prognostic factor in patients with chronic coronary artery disease. Other forms of stress that are available in the NT are dobutamine or persantin. Nuclear cardiac perfusion scans are available in Darwin. Stress echocardiography is not routinely available

**Class I indications** for exercise nuclear cardiac perfusion scan (or stress echo)

- To identify the extent, severity and location of ischaemia in patients who do not have LBBB or ventricular paced rhythm who have an abnormal rest ECG or are on digoxin
- Patients with previous revascularisation with either angioplasty or CABG
- Patients with intermediate pre-test probability of CAD with >1 mm ST depression at rest or pre-excitation (WPW syndrome)

**Class I indications** for persantin nuclear cardiac perfusion scan.

- Patients with LBBB or ventricular paced rhythm

**Class IIb** indications for stress imaging

- Exercise or dobutamine echocardiography in patients with LBBB
- Any form of stress imaging as initial stress test in patients with normal resting ECG and are not taking digoxin

## **Angiography**

Gives the most accurate anatomical assessment of coronary arteries as well as assessment of LV function and mitral and aortic valve function. Is now available in Darwin as day procedure.

**Class I** indications

- Patients with disabling symptoms CCS symptoms Class III–IV
- Patients with high risk criteria on clinical assessment or after non-invasive testing regardless of angina severity
- Patients who have survived sudden cardiac death or serious arrhythmia
- Patients with angina and symptoms and signs of heart failure

**Class IIa** indications

- Patients with an uncertain diagnosis after non-invasive testing in whom the benefit of a more certain diagnosis outweighs the risk and cost of angiography
- Patients who are unable to undergo non-invasive testing due to disability, illness or morbid obesity
- Patients with an occupational requirement for a definitive diagnosis
- Patients with inadequate prognostic information after non-invasive testing

## **CT calcium score**

High resolution CT scan assessment of levels of coronary artery calcium is a good negative predictor of cardiac events. This is a new technology and is not yet available in the NT.

## **Management of chronic angina**

### **Acute management**

See chapter on acute coronary syndromes.

## **Chronic management**

The two primary objectives of treatment are to maximise survival by preventing heart attack and death and to control symptoms (patient's adequate quality of life). Treatment therefore involves revascularisation where appropriate, control of symptoms with medication and secondary prevention by targeting risk factors. Secondary prevention relates to patients who have already had cardiac events (either exertional angina or acute coronary syndromes) and have had cardiac investigation (such as angiography or revascularisation, such as angioplasty or coronary bypass surgery). Management therefore involves identifying risk factors, lifestyle modification (including education with regards to smoking, diet and exercise), intervention with medication and/or revascularisation and ongoing monitoring of outcomes.

## **Control of risk factors**

Risk modification significantly reduces primary and secondary events.

## **Smoking**

Provide education and advice on the dangers of smoking. Consider use of patches, nicotine chewing gum or other medications such as zyban. (Cessation of smoking has to be a priority.)

## **Hypertension**

Normalising blood pressure significantly reduces cardiac events. Needs both lifestyle modification and pharmacological intervention.

Recent trials have shown that in diabetic patients BP <130/80 improves survival.

## **Hypercholesterolaemia**

Several trials have now shown a benefit, both primary and secondary prevention, of cardiac events. For patients with highest risk (known coronary artery disease or previous cardiac) event aim for: total cholesterol <4.0 mmol/L, LDL cholesterol <2.5 mmol/L

## **Diabetes**

Prevention and early appropriate treatment of type 2 diabetes is important for both primary and secondary care. (See diabetes chapter)

## **Medication**

### **Antiplatelet medication**

#### Aspirin

- 100–150 mg daily. Post angioplasty and stent 300 mg daily for four weeks
- Inhibitor of thromboxane induced platelet activation
- Non-reversible effect on platelets, therefore effect lasts up to 10 days until adequate numbers of platelets have been naturally replaced
- Standard treatment in all patients with coronary artery disease
- Contraindications: allergy to aspirin, serious bleeding disorders, low platelet count

#### Clopidogrel

- 75 mg daily. Initial loading dose of 300 mg. The loading dose is given with aspirin in patients suspected of having an acute coronary syndrome, usually within 24 hour of presentation
- Inhibits ADP-mediated platelet activation. Recent studies have shown improved survival in combination with aspirin post-acute coronary syndrome
- Is used in combination with aspirin 300 mg daily for four weeks post-angioplasty with stent
- There is a slight increase in bleeding when used with aspirin
- Preferred alternative to aspirin if this medication is contraindicated

Ticlopidine

No longer in use due to drug-induced neutropenia.

### **β-blockers**

- Cardio-selective beta-blockers primarily affect B1 receptors and reduce angina by reducing cardiac oxygen demand. Reduces heart rate, force and rate of contraction
- All patients with angina should be on a beta-blocker unless contraindicated or unable to tolerate

Atenolol

- Once-a-day medication, 25 mg up to 100 mg daily
- Hydrophilic, therefore has better bioavailability than metoprolol, but dosage may have to be altered in renal failure

Metoprolol

- Twice-daily dosage 12.5 mg BD up to 100 mg BD
- Lipophilic, therefore variable bioavailability
- Proven benefit in heart failure

Carvedilol

- Twice-daily dosage 3.125 mg BD up to 25 mg BD
- Has alpha 1-, as well as beta 1- and 2-, blocking effects
- Has proven benefit on survival in patients with heart failure (mainly used in this group)

### **Nitrates**

GTN

- All patients with suspected obstructed coronary artery disease should have access to either medication and be educated in their use
- Sublingual anginine 600 mcg 1–3 tablets/30mins
- Sublingual GTN spray 400 mcg 1–4 puffs/30mins

Isordil

Imdur

Long-acting mononitrate.

- 60–120 mg/day. Do not use as a BD dose as patients will develop tolerance and medication will become ineffective

Nitrate patches

Long-acting 25–50 mg, eight hour medication-free, otherwise develop tolerance.

### **Calcium antagonists**

Do not use short-acting dihydropyridines as may induce tachycardia and angina.

Diltiazem, Verapamil, Amlodipine, Nifedipine Oros.

### **ACE inhibitors**

- Essential in treatment of patients with previous cardiac events, especially if impaired LV function, diabetes and/or hypertensive. Also should continue to be used in renal failure, especially diabetic nephropathy
- Ramipril, 1.25–10 mg daily
- Perindodril, 2–8 mg daily, long acting

## **Cholesterol-lowering medication**

- HMG Co enzyme A reductase inhibitors:
- Atorvastatin, Simvastatin, Pravachol, Fibrinates, Gemfibrozil

## **Other anti-anginal medications**

### **1. Perhexiline**

Starting dose 100 mg daily (recommend only started by visiting physician or cardiologist).

Increases intracellular oxygen and ATP coupling (e.g. improves heart muscle use of oxygen) and is used in patients with intractable angina and aortic stenosis. However, perhexiline has a long half-life (1–40 days) and is subject to saturable (non-linear) pharmacokinetics, so that small changes in dosage can produce disproportionate changes in plasma concentrations.

Perhexiline is also subject to genetic polymorphism (CYP2D6), and 5–10% of Caucasian patients are poor metabolisers, achieving high plasma perhexiline concentrations with usual doses. Monitoring is therefore recommended one week following commencement of dosing to detect poor metabolisers with rapidly rising plasma perhexiline concentrations, followed up within 14 days to ensure concentrations are not continuing to rise, and then at three-monthly intervals, as required.

If symptomatic response is inadequate using the above therapeutic range, increasing the dose to achieve plasma perhexiline concentrations in the range 0.60–1.20 mg/L may provide additional beneficial response. However, at this higher range monitoring for signs of toxicity (e.g. nausea, dizziness and elevated liver function tests) is recommended.

Significant interactions include fluoxetine, paroxetine (possibly other CYP2D6 substrates), amiodarone (increased risk of hepatotoxicity) and hypoglycaemic medications (increased insulin sensitivity).

### **2. Nicorandil**

Dose: 10–20mg daily. A nicotinamide nitrate with potassium channel-opening activity, is a vasodilator used as an additional therapy in the treatment of angina pectoris. This compound has been shown to possess several properties that have been proposed to be part of its antianginal efficacy, including reductions in preload and overload, an increase in large coronary artery diameter and an increase in coronary collateral blood flow.

Nicorandil has been described as a hybrid between nitrates and potassium channel activators. Potassium channel activators cause smooth muscle relaxation and subsequent vasodilation by increasing potassium flux through sarcolemma ATP-sensitive potassium channels. The drug is therefore capable of acting as a balanced arterial dilator and venodilator; potassium channel activation indirectly leads to calcium channel blockade and dilation of arterial resistance vessels, while the nitrate moiety dilates venous capacitance vessels. In the clinical setting, the nitrate's activity is probably predominant. In association with the decrease in afterload following nicorandil, the contractile responses during isovolumic contraction and relaxation improved significantly, indicating that nicorandil does not demonstrate negative inotropic actions

## **Revascularisation**

### **Class I indications**

- CABG (coronary artery bypass surgery) or PTCA
- Left main stenosis
- Three vessel disease (benefit greater if EF <50%)

- Two vessel disease with significant proximal left anterior descending CAD and either abnormal LV function (ejection fraction <50%) or demonstrable ischaemia on noninvasive testing
- PTCA for patients with two or three vessel disease with significant proximal left anterior descending CAD, who have anatomy suitable for catheter-based therapy, normal LV function, and who do not have treated diabetes
- PTCA or CABG for patients with one or two vessel without proximal left anterior descending CAD but with a large area of viable myocardium and high-risk criteria on noninvasive testing
- In patients with prior PTCA, CABG or PTCA for recurrent stenosis associated with a large area of viable myocardium and/or high-risk criteria on noninvasive testing
- PTCA or CABG for patients who have not been successfully treated (see text) by medical therapy and can undergo revascularization with acceptable risk

#### Class IIa indications

- Repeat CABG for patients with multiple saphenous vein graft stenoses, especially when there is: (i) significant stenosis of a graft supplying the left anterior descending coronary artery. PTCA may be appropriate for focal saphenous vein graft lesions or multiple stenoses in poor candidates for reoperative surgery, or (ii) PTCA or CABG for patients with one vessel disease with significant proximal left anterior descending CAD

#### Class IIb indications

Compared with CABG, PTCA for patients with three or two vessel disease with significant proximal left anterior descending CAD who have anatomy suitable for catheter-based therapy and who have treated diabetes or abnormal LV function.

#### Class III Indications

- PTCA or CABG for patients with one or two vessel CAD without significant proximal left anterior descending CAD who: (i) have mild symptoms that are unlikely due to myocardial ischemia; or (ii) have not received an adequate trial of medical therapy and (a) have only a small area of viable myocardium or (b) have no demonstrable ischemia on noninvasive testing
- PTCA or CABG for patients with borderline coronary stenoses (50–60% diameter in locations other than the left main) and no demonstrable ischemia on noninvasive testing
- PTCA or CABG for patients with insignificant coronary stenosis (<50% diameter)
- PTCA in patients with significant left main CAD who are candidates for CABG

Note: PTCA is used in these recommendations to indicate PTCA and/or other catheter-based techniques such as stents, atherectomy, and laser therapy.

#### **Exercise program**

Regular exercise has been proven to improve functional capacity and can have beneficial effects on lipid profile as well.