

Angina pectoris: drug management

The management of stable angina comprises lifestyle changes, medication, percutaneous coronary intervention and surgery. NICE produced guidelines in 2011 covering the management of stable angina

Medication

- all patients should receive aspirin and a statin in the absence of any contraindication
- sublingual glyceryl trinitrate to abort angina attacks
- NICE recommend using either a beta-blocker or a calcium channel blocker first-line based on 'comorbidities, contraindications and the person's preference'
- if a calcium channel blocker is used as monotherapy a rate-limiting one such as verapamil or diltiazem should be used. If used in combination with a beta-blocker then use a long-acting dihydropyridine calcium-channel blocker (e.g. modified-release nifedipine). Remember that beta-blockers should not be prescribed concurrently with verapamil (risk of complete heart block)
- if there is a poor response to initial treatment then medication should be increased to the maximum tolerated dose (e.g. for atenolol 100mg od)
- if a patient is still symptomatic after monotherapy with a beta-blocker add a calcium channel blocker and vice versa
- if a patient is on monotherapy and cannot tolerate the addition of a calcium channel blocker or a beta-blocker then consider one of the following drugs: a long-acting nitrate, ivabradine, nicorandil or ranolazine
- if a patient is taking both a beta-blocker and a calcium-channel blocker then only add a third drug whilst a patient is awaiting assessment for PCI or CABG

Nitrate tolerance

- many patients who take nitrates develop tolerance and experience reduced efficacy
- the BNF advises that patients who develop tolerance should take the second dose of isosorbide mononitrate after 8 hours, rather than after 12 hours. This allows blood-nitrate levels to fall for 4 hours and maintains effectiveness
- this effect is not seen in patients who take modified release isosorbide mononitrate

Ivabradine

- a new class of anti-anginal drug which works by reducing the heart rate
- acts on the I_f ('funny') ion current which is highly expressed in the sinoatrial node, reducing cardiac pacemaker activity
- adverse effects: visual effects, particular luminous phenomena, are common. Bradycardia, due to the mechanism of action, may also be seen
- there is no evidence currently of superiority over existing treatments of stable angina

Heart failure: drug management

A number of drugs have been shown to improve mortality in patients with chronic heart failure:

- ACE inhibitors (SAVE, SOLVD, CONSENSUS)
- spironolactone (RALES)
- beta-blockers (CIBIS)
- hydralazine with nitrates (VHEFT-1)

No long-term reduction in mortality has been demonstrated for loop diuretics such as furosemide.

NICE issued updated guidelines on management in 2010, key points include:

- first-line treatment for all patients is both an ACE-inhibitor and a beta-blocker
- second-line treatment is now either an aldosterone antagonist, angiotensin II receptor blocker or a hydralazine in combination with a nitrate
- if symptoms persist cardiac resynchronisation therapy or digoxin* should be considered
- diuretics should be given for fluid overload
- offer annual influenza vaccine
- offer one-off** pneumococcal vaccine

*digoxin has also not been proven to reduce mortality in patients with heart failure. It may however improve symptoms due to its inotropic properties. Digoxin is strongly indicated if there is coexistent atrial fibrillation

**adults usually require just one dose but those with asplenia, splenic dysfunction or chronic kidney disease need a booster every 5 years

Myocardial infarction: secondary prevention

NICE produced guidelines on the management of patients following a myocardial infarction (MI) in 2007. Some key points are listed below

All patients should be offered the following drugs:

- ACE inhibitor
- beta-blocker
- aspirin
- statin

Clonidogrel

- ST-segment-elevation MI: patients treated with a combination of aspirin and clopidogrel during the first 24 hours after the MI should continue this treatment for at least 4 weeks
- non-ST segment elevation myocardial infarction (NSTEMI): following the 2010 NICE unstable angina and NSTEMI guidelines clopidogrel should be given for the first 12 months if the 6 month mortality risk is > 1.5%

Aldosterone antagonists

- patients who have had an acute MI and who have symptoms and/or signs of heart failure and left ventricular systolic dysfunction, treatment with an aldosterone antagonist licensed for post-MI treatment should be initiated within 3-14 days of the MI, preferably after ACE inhibitor therapy

Chest pain: assessment of patients with suspected cardiac chest pain

NICE issued guidelines in 2010 on the 'Assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin'.

Below is a brief summary of the key points. Please see the link for more details.

Patients presenting with acute chest pain

Immediate management of suspected acute coronary syndrome (ACS)

- glyceryl trinitrate
- aspirin 300mg. NICE do not recommend giving other antiplatelet agents (i.e. Clopidogrel) outside of hospital
- do not routinely give oxygen, only give if sats < 94%*
- perform an ECG as soon as possible but do not delay transfer to hospital. A normal ECG does not exclude ACS

Referral

- current chest pain or chest pain in the last 12 hours with an abnormal ECG: emergency admission
- chest pain 12-72 hours ago: refer to hospital the same-day for assessment
- chest pain > 72 hours ago: perform full assessment with ECG and troponin measurement before deciding upon further action

*NICE suggest the following in terms of oxygen therapy:

- do not routinely administer oxygen, but monitor oxygen saturation using pulse oximetry as soon as possible, ideally before hospital admission. Only offer supplemental oxygen to:
- people with oxygen saturation (SpO₂) of less than 94% who are not at risk of hypercapnic respiratory failure, aiming for SpO₂ of 94-98%
- people with chronic obstructive pulmonary disease who are at risk of hypercapnic respiratory failure, to achieve a target SpO₂ of 88-92% until blood gas analysis is available.

Patients presenting with stable chest pain

With all due respect to NICE the guidelines for assessment of patients with stable chest pain are rather complicated. They suggest an approach where the risk of a patient having coronary artery disease (CAD) is calculated based on their symptoms (whether they have typical angina, atypical angina or non-anginal chest pain), age, gender and risk factors.

NICE define anginal pain as the following:

1. constricting discomfort in the front of the chest, neck, shoulders, jaw or arms
2. precipitated by physical exertion

- 3. relieved by rest or GTN in about 5 minutes
- patients with all 3 features have typical angina
- patients with 2 of the above features have atypical angina
- patients with 1 or none of the above features have non-anginal chest pain

The risk tables are not reproduced here but can be found by clicking on the link.

If patients have typical anginal symptoms and a risk of CAD is greater than 90% then no further diagnostic testing is required. It should be noted that all men over the age of 70 years who have typical anginal symptoms fall into this category.

For patients with an estimated risk of 10-90% the following investigations are recommended. Note the absence of the exercise tolerance test:

| Estimated likelihood of CAD | Diagnostic testing |
|------------------------------------|--|
| 61-90% | Coronary angiography |
| 30-60% | Functional imaging, for example: <ul style="list-style-type: none"> • myocardial perfusion scan with SPECT • stress echocardiography • first-pass contrast-enhanced magnetic resonance (MR) perfusion • MR imaging for stress-induced wall motion abnormalities. |
| 10-29% | CT calcium scoring |

Atrial fibrillation: post-stroke

NICE issued guidelines on atrial fibrillation (AF) in 2006. They included advice on the management of patients with AF who develop a stroke or transient-ischaemic attack (TIA).

Recommendations include:

- following a stroke or TIA warfarin should be given as the anticoagulant of choice. Aspirin/dipyridamole should only be given if needed for the treatment of other comorbidities
- in acute stroke patients, in the absence of haemorrhage, anticoagulation therapy should be commenced after 2 weeks. If imaging shows a very large cerebral infarction then the initiation of anticoagulation should be delayed

ECG: coronary territories

- The table below shows the correlation between ECG changes and coronary territories:

| | ECG changes | Coronary artery |
|---------------------|--------------------|--------------------------|
| Anteroseptal | V1-V4 | Left anterior descending |
| Inferior | II, III, aVF | Right coronary |

| | | |
|----------------------|-------------------|--|
| Anterolateral | V4-6, I, aVL | Left anterior descending or left circumflex |
| Lateral | I, aVL +/- V5-6 | Left circumflex |
| Posterior | Tall R waves V1-2 | Usually left circumflex, also right coronary |

Heart failure: diagnosis

NICE issued updated guidelines on diagnosis and management in 2010. The choice of investigation is determined by whether the patient has previously had a myocardial infarction or not.

Previous myocardial infarction

- arrange echocardiogram within 2 weeks

No previous myocardial infarction

- measure serum natriuretic peptides (BNP)
- if levels are 'high' arrange echocardiogram within 2 weeks
- if levels are 'raised' arrange echocardiogram within 6 weeks

Serum natriuretic peptides

B-type natriuretic peptide (BNP) is a hormone produced mainly by the left ventricular myocardium in response to strain. Very high levels are associated with a poor prognosis.

| | BNP | NTproBNP |
|----------------------|-----------------------------------|------------------------------------|
| High levels | > 400 pg/ml (116 pmol/litre) | > 2000 pg/ml (236 pmol/litre) |
| Raised levels | 100-400 pg/ml (29-116 pmol/litre) | 400-2000 pg/ml (47-236 pmol/litre) |
| Normal levels | < 100 pg/ml (29 pmol/litre) | < 400 pg/ml (47 pmol/litre) |

Factors which alter the BNP level:

Increase BNP levels

Left ventricular hypertrophy
 Ischaemia
 Tachycardia
 Right ventricular overload
 Hypoxaemia (including pulmonary embolism)
 GFR < 60 ml/min
 Sepsis
 COPD
 Diabetes
 Age > 70
 Liver cirrhosis

Decrease BNP levels

Obesity
 Diuretics
 ACE inhibitors
 Beta-blockers
 Angiotensin 2 receptor blockers
 Aldosterone antagonists

Heart failure: NYHA classification

The New York Heart Association (NYHA) classification is widely used to classify the severity of heart failure:

NYHA Class I

- no symptoms
- no limitation: ordinary physical exercise does not cause undue fatigue, dyspnoea or palpitations

NYHA Class II

- mild symptoms
- slight limitation of physical activity: comfortable at rest but ordinary activity results in fatigue, palpitations or dyspnoea

NYHA Class III

- moderate symptoms
- marked limitation of physical activity: comfortable at rest but less than ordinary activity results in symptoms

NYHA Class IV

- severe symptoms
- unable to carry out any physical activity without discomfort: symptoms of heart failure are present even at rest with increased discomfort with any physical activity

Atrial fibrillation: cardioversion

Onset < 48 hours

If atrial fibrillation (AF) is of less than 48 hours onset patients should be heparinised and a transthoracic echocardiogram performed to exclude a thrombus. Following this patients may be cardioverted, either:

- electrical - 'DC cardioversion'
- pharmacology - amiodarone if structural heart disease, flecainide in those without structural heart disease

Following electrical cardioversion if AF is confirmed as being less than 48 hours duration then further anticoagulation is unnecessary

Onset > 48 hours

If AF is of greater than 48 hours then patients should have therapeutic anticoagulation for at least 3 weeks. If there is a high risk of cardioversion failure (e.g. Previous failure or AF recurrence) then it is recommend to have at least 4 weeks amiodarone or sotalol prior to electrical cardioversion

Following electrical cardioversion patients should be anticoagulated for at least 4 weeks. After this time decisions about anticoagulation should be taken on an individual basis depending on the risk of recurrence

Prescribing in patients with heart failure

The following medications may exacerbate heart failure:

- thiazolidinediones*: pioglitazone is contraindicated as it causes fluid retention
- verapamil: negative inotropic effect
- NSAIDs**/glucocorticoids: should be used with caution as they cause fluid retention
- class I antiarrhythmics; flecainide (negative inotropic and proarrhythmic effect)

*pioglitazone is now the only thiazolidinedione on the market

**Low-dose aspirin is an exception - many patients will have coexistent cardiovascular disease and the benefits of taking aspirin easily outweigh the risks

Heart Failure

Pharmacological Management (Heart failure with impaired left ventricular function ie <40% ejection fraction)

- For those with asymptomatic heart failure start treatment with either an ACE inhibitor or beta blocker. Both agents reduce morbidity and mortality and improve symptoms
- Symptomatic heart failure patients should start a combination of ACE inhibitor and beta blocker. Add a diuretic if there is fluid retention.
- Severe heart failure patients should be referred to a specialist.
- Additional treatment may include angiotensin receptor antagonists, digoxin and aldosterone antagonists. Angiotensin receptor antagonists may be used in combination with ACE inhibitors in this patient group if the patient remains symptomatic. Digoxin is used as an aid to rate control but does not improve mortality. Aldosterone antagonists (spironolactone, eplerenone) are advised for those with LVEF >35% and severe symptoms (NYHA class 3-4). They improve mortality (RALES study).
- Third line drugs include hydralazine, and amiodarone.
- Non drug treatment options include resynchronisation therapy, implantable cardiac defibrillators and cardiac transplant

Atrial Fibrillation

The risk of thromboembolic events in atrial fibrillation can be assessed using the CHADS VASC scoring system. The European Society for Cardiology recommends oral anticoagulation for those with a score of 2 or above. Currently warfarin is the preferred anticoagulant. This lady has a CHADS VASC score of 4 and therefore would benefit from anticoagulation. She scores 2 points for being over 75 years old, 1 point for a history of hypertension and one point for female sex. The CHADS VASC also scores the following risk factors; congestive heart failure (1 point), age 64-74 (1 point), pre-existing cardiovascular disease (1 point), diabetes (1 point) and previous stroke or TIA (2 points).

Definition

- Paroxysmal (up to 7 days in duration and self terminating)
- Persistent (> 7 days in duration and does not self terminate)

- Permanent (rhythm control interventions have been abandoned and the arrhythmia is accepted by the patient and physician)

Risk

- Double the mortality of patients in sinus rhythm

Epidemiology

- Atrial fibrillation is common
 - 1-3% of over 60's
 - 10% of over 80's

Complications

- Tachycardiopathy
- Thromboembolism

Risk Factors

- Thyroid disease
- Ischaemia
- Rheumatic disease
- Hypertension
- Mitral valve disease
- Alcohol
- Carcinoma of the lung
- Pericarditis
- Chronic obstructive lung disease

When To Admit

- Acute onset AF under 48 hours
- Haemodynamically unstable patients
- AF presenting with chest pain
- AF presenting with neurological signs

Management

1. **Anticoagulate the patient according to the CHADS VASC score**
2. **Choose an appropriate rate or rhythm control strategy**

Persistent/Permanent AF

- Rhythm Control is first choice for those in persistent/permanent AF who are;

- Under 65s
- Symptomatic
- First Presentations with lone AF
- Heart Failure patients
- Rate Control is first choice for those in persistent/permanent AF who are;
 - Over 65
 - Coronary heart disease patients
 - Not suitable for cardioversion due to contraindications
 - NB Rate control is with a beta blocker or rate limiting calcium channel blocker (verapamil or diltiazem)

Paroxysmal AF

- Manage paroxysmal AF with rhythm control
- Beta blockers are the first line treatment

CHADS VASC Score (Anticoagulation for patients with Atrial Fibrillation)

Patients with persistent or paroxysmal AF with a CHADS VASC Score of 2 or above require warfarinisation as the benefit of warfarin outweighs the risk of bleeding.

Acute onset AF requires anticoagulation if;

- Stable sinus rhythm is not restored with 48 hours
- There are long term risk factors for AF recurrence (failed previous cardioversions, mitral valve disease, enlarged left atrium) even if sinus rhythm is restored.

Chest Pain of Recent Onset

Immediate management of a suspected acute coronary syndrome

- management of ACS should start as soon as it is suspected, but should not delay transfer to hospital
- offer pain relief as soon as possible. This may be achieved with GTN (sublingual or buccal), but offer intravenous opioids such as morphine, particularly if an acute myocardial infarction (MI) is suspected
 - offer people a single loading dose of 300 mg aspirin as soon as possible unless there is clear evidence that they are allergic to it
 - if aspirin is given before arrival at hospital, send a written record that it has been given with the person
 - only offer other antiplatelet agents in hospital. **Follow appropriate management of unstable angina/NSTEMI or or local protocols for STEMI)**
- **do not routinely administer oxygen, but monitor oxygen saturation using**

pulse oximetry as soon as possible, ideally before hospital admission. Only offer supplemental oxygen to:

- people with oxygen saturation (SpO₂) of less than 94% who are not at risk of hypercapnic respiratory failure, aiming for SpO₂ of 94-98%
- people with chronic obstructive pulmonary disease who are at risk of hypercapnic respiratory failure, to achieve a target SpO₂ of 88-92% until blood gas analysis is available
- monitor people with acute chest pain, using clinical judgement to decide how often this should be done, until a firm diagnosis is made. This should include:
 - exacerbations of pain and/or other symptoms
 - pulse and blood pressure
 - heart rhythm
 - oxygen saturation by pulse oximetry
 - repeated resting 12-lead ECGs and
 - checking pain relief is effective
- manage other therapeutic interventions using appropriate guidance (**management of unstable angina/NSTEMI or local protocols for STEMI**).

Acute Coronary Syndrome and Antiplatelets

Prasugrel - Who needs prasugrel for secondary prevention of acute coronary syndrome?

Prasugrel in combination with aspirin is recommended for secondary prevention in people with acute coronary syndromes having percutaneous coronary intervention, when

- Immediate primary percutaneous coronary intervention for ST-segment-elevation myocardial infarction is necessary
- Stent thrombosis has occurred during clopidogrel treatment
- The patient has diabetes mellitus

Regular Antiplatelet Therapy After Acute Coronary Syndrome

- Clopidogrel in combination with aspirin is recommended for secondary prevention of acute coronary syndrome in all other groups (without contraindications).
- Dual treatment continues for 12 months. After the 12 month period aspirin is continued indefinitely as monotherapy.

Immediate Antiplatelet Therapy for Acute Coronary Syndrome

- Aspirin 300mg loading dose is given to all patients with acute coronary syndrome.
- In addition a 300mg loading dose of clopidogrel is given to those categorised as higher risk by a risk scoring system. This is not primary care management and so is not detailed further here.

Acute Coronary Syndromes

This patient has symptoms suggestive of an acute coronary syndrome (ACS). He currently has chest pain and should therefore be referred to hospital as an emergency. Whilst waiting for the emergency ambulance the patient should be advised to rest and take 300mg of Aspirin. If he has a supply he may take his GTN tablet or spray.

Symptoms suggestive of an acute coronary syndrome

- pain in the chest and/or other areas (i.e the arms, back or jaw) lasting longer than 15 minutes
- chest pain associated with nausea and vomiting, sweating, breathlessness, or particularly a combination of these
- chest pain associated with haemodynamic instability
- new onset chest pain, or deterioration in previously stable angina, with recurrent chest pain occurring frequently and with little or no exertion, and with episodes often lasting longer than 15 minutes

Refer people to hospital as an emergency if an ACS is suspected and

- they currently have chest pain or
- they are currently pain free, but had chest pain in the last 12 hours, and a resting 12-lead ECG is abnormal or not available.

Refer people for urgent same-day assessment if an ACS is suspected and

- they had chest pain in the last 12 hours, but are now pain free with a normal resting 12-lead ECG or
- the last episode of pain was 12 to 72 hours ago.
- the pain has resolved and there are signs of complications such as pulmonary oedema.

Blood Pressure Targets

NICE provides guidelines on target blood pressures for hypertensive patients in different categories. 140/85 is the optimal blood pressure target identified by the primary prevention trial HOT at which cardiovascular risk was found to be lowest. A rule of thumb is to aim for the lowest blood pressure achievable without side effects.

NICE targets

- Target for non diabetics 140/90
- Target for type 2 diabetics 140/80
- Target for type 2 diabetics with microalbuminuria or proteinuria 135/75
- Target for type 1 diabetics 135/85
- Target for type 1 diabetics with nephropathy 130/80

Peripheral Vascular Disease

Antiplatelet choice for people with established Peripheral Vascular Disease

- NICE recommend Clopidogrel as the optimal first choice antiplatelet for the

treatment of peripheral vascular disease (statement 4.2.23)

- Aspirin is the second choice

Managing Peripheral Vascular Disease

Assessment

- Ask about intermittent claudication and symptoms of critical limb ischaemia
- Examine the legs for ulceration and presence of foot pulses
- Measure the ankle brachial pressure index
 - Lie the patient down
 - Record the systolic blood pressure in both arms and in the foot pulses (dorsalis pedis, posterior tibial).
 - Use a doppler probe when measuring the foot pulses
 - Divide the highest arm pressure by the highest foot pulse pressure
 - If the systolic pressures are within 10mmHg of each other PVD is unlikely. Intermittent claudication occurs at ABPIs of 0.95 to 0.5. Below 0.5 patients experience rest pain. Below 0.2 gangrene and ulceration occur.

Management

- Secondary Prevention of Cardiovascular Disease in people with Arterial Disease
 - Offer all people advice and support regarding
 - smoking cessation
 - diet, weight management and exercise
 - the prevention, diagnosis and management of diabetes
 - the prevention, diagnosis and management of high blood pressure
 - antiplatelet therapy (clopidogrel)
- Specific Management for Intermittent Claudication
 - Offer a supervised exercise programme (2 hours of supervised exercise a week for 3 months encouraging people to exercise to the point of maximal pain).
 - Offer imaging for people who fail to achieve satisfactory improvement of symptoms on the exercise programme (to see if angioplasty may help).
 - Consider naftidrofuryl oxalate for people who do not want angioplasty or bypass surgery and remain symptomatic. Stop treatment if there is no benefit within 3 months.

