Coronary artery bypass graft surgery requires close peri-operative management

In our second learning points article this issue, the cardiac pharmacist team from Barts and the London Heart Centre bring us their specialist expertise to teach us about the management of one of the most common surgeries performed in the UK — coronary artery bypass grafting

Cardiovascular disease (CVD) is the single largest cause of mortality in the UK, accounting for 37% of all deaths in men and women.[1] Numerous strategies have been implemented to reduce the burden of coronary heart disease (CHD) and other CVD complications through the introduction of *National Service Frameworks*,[2] NICE[3] guidance, and more recently quality and outcome framework (QOF) targets for primary care. More than 30,000 coronary artery bypass grafts (CABGs) are carried out each year, making this form of treatment one of the most common — and expensive — surgeries in the UK.[1]

The aim of this article is to discuss CABG as a form of treatment for CHD and to describe strategies aimed at secondary prevention that will reduce the risk of further morbidity or mortality in these high risk patients.

Learning outcomes

After reading this article it is anticipated that you will:

- Have an understanding of coronary artery bypass grafts (CABGs).
- Know what pharmacological treatments should be given to patients following CABG.
- Understand the primary care role in continuation, optimisation or stopping medicines after CABG.

The Case

James Morrison is a 63-year-old man who was admitted to hospital after experiencing ongoing chest pain. Mr Morrison had noticed that he had been 'slowing down' a little and that he was finding normal activities, such as going to the corner shop, more difficult in recent months. Mr Morrison had initially put this down to signs of ageing.

Mr Morrison has an uneventful past medical history and does not take any regular medication. On admission, he was found to have unstable angina (see learning points, case 1).[4] An echocardiograph (an ultrasound image of the heart) showed there was no presence of any left ventricular dysfunction and no evidence of left ventricular hypertrophy. The following results were found:

- BP of 137/79 mmHg.
- Pulse of 84 beats per minute.
- Total cholesterol of 4.7mmol/L.

A diagnostic angiogram was performed and it was found that he had three vessel disease, showing that he had extensive occlusion in the three major vessels within the heart. These are the right coronary artery (RCA), the Circumflex (Cx) and the left anterior descending artery (LAD). An elective CABG was arranged and Mr Morrison was transferred to the local cardiac tertiary referral centre.

Post-operatively he made a good recovery. However, he developed atrial fibrillation (AF) on the third day after CABG and the cardiothoracic surgical team started him on amiodarone.

On the day of discharge Mr Morrison had a blood pressure of 110/72 mmHg with a pulse rate of 65 beats per minute and was in sinus rhythm. He was discharged on day 7 post-operatively with the following medicines:

- aspirin 75mg OM
- atenolol 25mg OM
- simvastatin 20mg ON
- amiodarone 200mg TDS for 7 days, then 200mg BD for 7 days then 200mg OD thereafter
- frusemide 40mg OM
- paracetamol 500-1g QDS prn.

What is CABG?

CABG is an operation aimed at treating coronary artery disease. The cardiothoracic surgeon will initially start by making an incision in the front of the chest, through the sternum, also known as a median sternotomy. The IMA (internal mammary artery) from under the sternum and the long saphenous vein from the leg are harvested to use as new 'arteries' to get across the

Learning points

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narrowed or blocked coronary artery (see Figure 1). The grafted blood vessel is attached from the aorta to the diseased coronary artery beyond the point of the blockage (Figure 1).

Post-operative AF Management

Mr Morrison's recovery was complicated by the occurrence of AF on the third post-operative day. The incidence of post-operative AF after cardiac surgery occurs in approximately 30%[5] of patients, and usually occurs on the second or third day. It is also associated with a 2–3 fold increased risk of post-operative stroke.[5,6]

The use of beta-blockers in the immediate post-operative period has been shown to reduce the risk of AF.[7,8] For patients already taking beta-blockers treatment should not be stopped pre-operatively but rather the dosage should be halved. This is to minimise the risk of post-operative AF caused by withdrawal of beta-blockers in the pre-operative period, which has been found to double the risk of AF.[5]

Other risk factors for the development of post-operative AF in Mr Morrison include advancing age and prolonged duration of operation.[5]

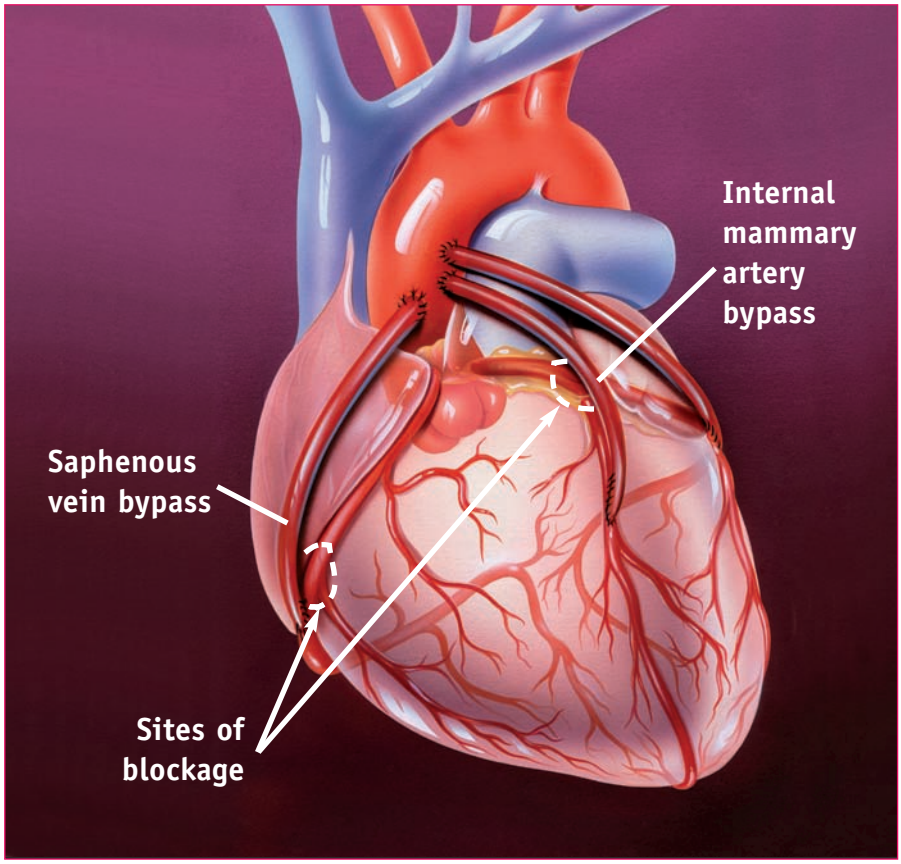

Figure 1. *Heart bypass grafts. Grafted vessels are attached from the aorta to the diseased coronary vessel at a point beyond the blockage (dotted areas) during coronary artery bypass surgery*

On the second day after Mr Morrison's CABG surgery, he was started on metoprolol 12.5mg TDS. Metoprolol is a short-acting beta-blocker that is used initially to stabilise the blood pressure and heart rate before switching to a suitable once-daily beta-blocker. Despite taking a beta-blocker he went on to develop AF for which the team prescribed amiodarone.

Anticoagulation with warfarin is indicated if the AF persists for more than 48 hours despite the patient taking appropriate rhythm or rate control therapy. Mr Morrison converted back to sinus rhythm after he started amiodarone and therefore did not require anticoagulation. NICE guidance suggests that post-operative AF after cardiothoracic surgery should be managed by a rhythm-control strategy, such as amiodarone in the first instance.[7]

All patients that have undergone CABG surgery are seen in an outpatient clinic 6-8 weeks after discharge. It is likely Mr Morrison will remain in sinus rhythm and amiodarone will be stopped. In the post-operative period the cells of the conduction system within the heart are generally oedematous because of surgical manipulation and the operation itself. This makes the cell membrane of the myocytes unstable for a period of time after the operation. For this reason patients continue to take amiodarone for a period of up to 6–8 weeks even though they are in sinus rhythm after discharge.

It is essential that Mr Morrison be appropriately counselled on the potential side-effects of amiodarone, such as the appearance of any visual disturbances (caused by corneal microdeposits), photo-toxicity, peripheral neuropathy or thyroid disorders. He should also be asked to report any signs of unexpected shortness of breath or cough (which may indicate pneumonitis or pulmonary fibrosis).

It should be noted that although amiodarone and beta-blockers may interact causing an increased risk of bradycardia, atrioventricular (AV) block and myocardial depression, in practice this is monitored in

the early dose titration phase while patients are in hospital and should not be problematic.

After CABG what medications need to be continued?

Aspirin

The use of aspirin in patients with cardiovascular disease is well established. In meta-analyses, the Antithrombotic Trialist's Collaboration showed clear evidence of a reduction in all cause mortality, vascular mortality, non-fatal reinfarction of the myocardium, and non-fatal stroke in people with acute coronary syndromes, stroke, transient ischaemic attacks (TIAs) or other vascular diseases.[9,10] For 1000 patients with a 5% risk of cardiac events in the next five years, low dose aspirin would prevent 6 to 20 myocardial infarctions (MIs), thus reducing the risk of MI by 30% in primary prevention.[11] There is no evidence that enteric coated aspirin reduces the risk of gastrointestinal bleeding episodes.

Aspirin should be started within 6 hours post-operatively to prevent graft occlusion (300mg loading dose followed by 75mg daily). The incidence of saphenous vein graft occlusion is highest during the first post-operative year.[5] Starting aspirin early is essential because its benefit on graft patency is lost when begun later. In truly aspirin allergic patients, clopidogrel is a suitable alternative.[5]

Atenolol

As discussed earlier, beta-blockers reduce the risk of post-operative AF after cardiothoracic surgery. Metoprolol, timolol and propranolol have all been shown to reduce mortality by 20–25%[12–14] after a MI. It is not known if the effects are a class effect or whether they are just seen with these specific beta-blockers. However, the NICE guidance of secondary prevention after a MI does not specify the beta-blocker to be used[15] and in practice a once-daily beta-blocker, such as atenolol is often used.

Simvastatin

Meta-analysis of lipid lowering in five trials showed that statins were associated with a 34% relative risk reduction in major coronary events in primary prevention and 30% in secondary prevention trials.[16] Regression analyses of randomised, controlled trials indicate that for every 10% reduction in total cholesterol with statin therapy there will be a 15% reduction in coronary mortality.[17] Trials such as WOSCOPS,[18] 4S[19] and the Heart Protection Study[20] have consistently shown the benefits of lowering low density lipoprotein (LDL) cholesterol and total cholesterol in primary and secondary prevention studies.

Statins have shown great benefits in reducing the cardiovascular risk and mortality of patients, regardless of their baseline LDL cholesterol levels. In recent years, more intensive cholesterol lowering strategies have been recommended by the British Hypertension Society and the Joint British Society Guidelines (BHS/JBS) on prevention of cardiovascular disease, with targets of:

- total cholesterol of <4 mmol/L or a 25% reduction, or whichever is the greater
- LDL cholesterol of <2 mmol/L or a 30% reduction, or whichever is the greater.

Although the BHS/JBS advocate intensive cholesterol lowering targets, the Department of Health has reiterated that national policy is still total cholesterol of <5 mmol/L and an LDL of <3mmol/L until NICE publishes detailed guidance on lipid management, which is expected in December 2007.[21] Until then locally agreed targets should be followed.

On admission, Mr Morrison had a total cholesterol level of 4.7 mmol/L. His cholesterol should be checked three months after starting simvastatin 20mg to ensure that cholesterol targets are achieved. Great care should be taken because amiodarone interacts with simvastatin resulting in an increased risk of myopathy and rhabdomyolysis when simvastatin doses of 40mg or above are used. This is especially important considering the atorvastatin to simvastatin switch that is currently becoming widespread among PCTs.

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The manufacturer recommends that simvastatin doses of no greater than 20mg be used when co-administering amiodarone.[17] Because amiodarone is likely to be stopped after the 8-week post-CABG surgery outpatient appointment with the cardiothoracic surgeon, optimisation of the simvastatin dose from 20mg to higher doses may be possible pending the patient's cholesterol level results.

Amiodarone

In line with NICE guidance for the management of post-operative AF, amiodarone was prescribed for Mr Morrison. Starting amiodarone soon after diagnosis of post-operative AF is essential in ensuring that patients return to sinus rhythm, allowing the possibility for it to be stopped after an outpatient assessment. It is essential that these patients are monitored on a regular basis and amiodarone discontinued or switched to another agent if possible. Prolonged administration of amiodarone after CABG in the absence of further complications should be reviewed.

As previously stated, because there is an interaction with simvastatin, doses greater than 20mg of simvastatin should not be concurrently used with amiodarone. However, review of amiodarone in the outpatient setting might indicate that it is better not to stop amiodarone but to optimise the simvastatin dose occasionally.

Learning points

Frusemide

After CABG surgery, patients may be up to 5Kg heavier than their pre-operative weight. This is predominantly caused by the intra-operative fluid load during cardio-pulmonary bypass. Once Mr Morrison's weight returns to his normal pre-operative weight, frusemide therapy should be reviewed and stopped if there are no additional indications for long-term diuretic therapy, such as concurrent heart failure. Inappropriately prolonged therapy with frusemide may result in electrolyte disturbances, dehydration or gout.

Further considerations

Angiotensin converting enzyme inhibitors

The HOPE and EUROPA trials showed the benefits of using angiotensin converting enzyme inhibitors (ACEi) in patients with coronary artery disease. These trials showed the relative risk reduction of the primary outcome of the composite of cardiovascular death, MI (non-fatal in the EUROPA trial) and stroke (in the HOPE trial) were reduced by 22% and 20% respectively.[22,23]

The SIGN guidelines suggest that all patients with existing coronary heart disease should be prescribed an ACEi as part of secondary prevention.[24] This is further endorsed by the recent NICE guidance on the secondary prevention of MI.[15] After CABG, the use of ACEi's is indicated and doses should be optimised to the maximum tolerated dose. In our case, it was decided to start an ACEi once the patient was discharged home and his blood pressure had stabilised. ACEi's have been shown to reduce the incidence of post-operative major adverse cardiac events.

Follow-up after discharge in primary care

After discharge advice should be provided to GPs about which cardiac medicines to continue, optimise or stop. The following is usual advice:

- continuation of aspirin and beta-blocker
- lipid lowering therapy should be optimised to locally agreed targets
- ACEi should be started and optimised to the maximum tolerated dose
- amiodarone should be reviewed and stopped within 6–8 weeks of surgery if no further complications arise
- frusemide should be stopped once the patient returns to his normal pre-operative weight.

Further advice on non-pharmacological therapy is essential. This includes advice on how to stop smoking, dietary advice, exercise, blood pressure monitoring and glucose monitoring in diabetic patients. The *NSF for coronary heart disease* suggests the following:[2]

- advice on how to stop smoking, including the use of nicotine replacement therapy
- advice on modifiable risk factors, such as physical activity, diet, alcohol consumption, weight and diabetes
- advice and therapy to maintain blood pressure below 140/85 mmHg
- meticulous control of blood pressure and glucose in patients with diabetes. ✣

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