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## THE PATIENT WITH HEART DISEASE

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Over the past six decades, mortality due solely to anaesthesia has decreased from approximately 1 in 1,500 to 1 in 150,000. However, death within 30 days of surgery remains a major issue. In the United Kingdom, over the past ten years, the number of such perioperative deaths has remained fairly constant at approximately 20,000 deaths per annum<sup>1</sup>, of which 9,000 are due to cardiac causes. For each cardiac death there are between 5 and 20 major cardiac complications, such as myocardial infarction, unstable angina, life-threatening arrhythmias, or acute left ventricular failure. Thus, the UK number of cardiac complications is expected to range from 45,000 to 180,000 per annum. These complications occur in patients with a compromised cardiovascular system, most frequently because of underlying coronary artery disease. Indeed, 60% of patients who die within 30 days of surgery have evidence of coronary heart disease<sup>2</sup>. Pre-existing valvular heart disease, hypertensive heart disease, and congestive cardiac failure also play an important role.

### Coronary heart disease

Angina causes only a moderate increase in perioperative morbidity provided it is well controlled and medication is continued throughout the perioperative period. Unstable, new and disabling angina are associated with a high post-operative morbidity. In such patients coronary angiography is usually necessary prior to major surgery in order to establish the severity of the disease and optimise treatment; this may include coronary angioplasty (with or without stenting) or coronary artery bypass surgery. When the angina is less severe and coronary bypass surgery is not indicated in its own right, prophylactic coronary artery revascularization may be performed, on occasion, in order to reduce the risk of postoperative myocardial infarction, but only in the face of major surgery<sup>3</sup>. However, where coronary revascularisation is indicated in its own right it should be carried out before non cardiac surgery.

Previous myocardial infarction. Myocardial infarction that has occurred less than three months before surgery is known to be associated with a very high risk of reinfarction<sup>4</sup>. In recent years this risk has become smaller<sup>5</sup>. The time that has elapsed between myocardial infarction and surgery is, therefore, only one of risk factors. Cardiologists consider that after uncomplicated myocardial infarction a delay of six weeks is acceptable. This view is endorsed in the American College of Cardiologists and American Heart association (ACC/AHA) guideline.<sup>6</sup>

Irrespective of the delay between infarction and surgery, risks remain high in patients presenting for major abdominal or thoracic surgery or for vascular surgery, and in patients who have suffered from acute left ventricular failure at the time of their infarction<sup>7</sup>, exhibit poor left ventricular function, or continue to suffer from angina. Therefore evaluation of left ventricular function is

essential especially before major surgery as there is an inverse relationship between left ventricular function and adverse cardiac outcome<sup>8</sup>. This evaluation includes clinical examination and exercise tolerance. Often, however, an objective test is needed as many patients minimise their disability, or are incapable of exercising for other reasons (arthritis, severe intermittent claudication) and, therefore, never "test" their cardiac reserve.

Silent myocardial ischaemia, as detected by ambulatory ECG (Holter) monitoring, is a feature of coronary heart disease. It is observed in patients who are totally asymptomatic (type 1), have suffered previous myocardial infarction (type 2), or suffer from angina (type 3). Up to 80% of ischaemic events are silent<sup>9</sup>. Silent myocardial ischaemia is associated with adverse prognosis<sup>10</sup>. Silent ischaemia occurs in up to 50% of adult surgical patients and is associated with postoperative cardiovascular complications<sup>11,12</sup>. It is more frequent and more prolonged during the postoperative period. This increased ischaemic burden (expressed as minutes of ischaemia per hour of monitoring) is responsible for the very strong association between postoperative silent ischaemia and adverse cardiac outcome<sup>11</sup>. Silent ischaemia may be caused by cardiovascular instability (tachycardia, hypertension, hypotension), coagulation disorders (microthrombosis and microlysis) and/or postoperative hypoxaemia<sup>13</sup>. A feature of perioperative silent myocardial ischaemia is that it is associated with short- and long-term adverse outcome thereby decreasing the event-free survival at two years from 90% to 76%<sup>14</sup>.

Patients with coronary grafts. Many patients undergo non-cardiac surgery after previous coronary bypass graft operation. The risk of postoperative myocardial infarction is low in this group of patients<sup>3,15</sup> provided they are not operated on less than six weeks to two months after coronary surgery, and do not have other risk factors such as angina or poor left ventricular function. Hypotension during the perioperative period must be avoided as it may cause thrombosis of the grafts. In some patients, significant increases in left ventricular function are observed after coronary artery bypass graft<sup>16</sup> or after angioplasty and stenting, because previously underperfused myocardium (hibernating myocardium) becomes more contractile after reperfusion.

Patients with previous angioplasty and stenting. Some benefits in terms of risk reduction can be expected in patients who have undergone coronary angioplasty more than three months before elective surgery<sup>17</sup>. If a stent is inserted, strong antiplatelets drugs are always given and surgery within a short period of insertion of the stent is extremely dangerous<sup>18</sup>; waiting six weeks is regarded as essential.

**Further investigations.** Often the medical history alone underestimates the severity of coronary heart disease. Before coronary angiography is performed, screening tests are useful.

Their aim is to identify patients with reversible ischaemia who should undergo coronary angiography.

Ambulatory ECG monitoring is valuable, however, it is now regarded as inferior to formal exercise testing.

Reversible ischaemia may be elicited by exercise testing and detected by electrocardiography, echocardiography, radionuclide angiography (technetium) or myocardial scintigraphy (thallium). Where patients are unable to exercise, a dobutamine infusion is an excellent pharmacological substitute to exercise. Reversible ischaemia is identified as ST-segment depression on the ECG, new wall motion abnormalities and/or a reduction of the ejection fraction on echocardiography or radionuclide angiography, and by a reversible defect (decreased uptake of the radioactive isotope) on myocardial scintigraphy. Presence of reversible ischaemia, strongly predicts perioperative cardiac events.<sup>19</sup>

Exercise echocardiography or echocardiography with dobutamine infusion are more widely available than myocardial scintigraphy, and allow relatively non-invasive screening for coronary artery disease. If exercise or dobutamine infusion elicit reversible ischaemia this indicates the presence of areas with compromised blood supply and the need for coronary angiography, bearing in mind that a high proportion of patients, particularly those presenting for vascular surgery, have correctable coronary artery lesions. The management strategy depends, to a large extent, upon the severity of the coronary artery disease as seen on coronary angiography. In addition, coronary angiography may reveal lesions that justify revascularisation in their own right.

Recently, the cardiac troponins I and T have been found to be helpful in the diagnosis of perioperative myocardial damage, including myocardial infarction.<sup>20</sup> Postoperative troponin elevation predicts adverse outcome<sup>21</sup> and, in some patients, preoperative elevation of troponins has been shown to predict the risk of perioperative myocardial infarction.<sup>22</sup>

### Arterial hypertension

Arterial hypertension is associated with an increase in the cardiovascular morbidity and mortality of anaesthesia and surgery<sup>23,24</sup>, even though hypertension was not found to be a significant predictor of cardiac complications of anaesthesia and surgery in several indices of cardiac risk in non-cardiac surgery.<sup>25,26</sup> In patients diagnosed as hypertensive, and on anti-hypertensive medication, treatment of hypertension should be maintained throughout the perioperative period; often the morning dose of ACE inhibitors is omitted because of the risk of hypotension. However, this policy may cause an increase in the risk of perioperative hypertension.<sup>27</sup> Treatment with angiotensin receptor antagonists needs to be stopped the day before surgery because of the risk of refractory hypotension after induction of anaesthesia and during surgery.<sup>28</sup> Where hypertension is poorly controlled, management of the patients should follow the principles applicable to untreated hypertension.

In untreated patients, mild hypertension (Stage 1: 140-159/90-99mmHg), does not constitute a major threat. Moderate hypertension (Stage 2: 160-179/100-109mmHg), constitutes a threat especially where it is associated with target organ involvement (coronary, cerebrovascular or renal disease), in

which case treatment prior to elective surgery is recommended. Severe hypertension (Stage 3: 180-201/110-119), and marked left ventricular hypertrophy (ECG and/or chest X-ray), increase the risk of complications. Such patients should be treated before surgery; this is also true of patients with malignant hypertension (Stage 4: > 210/>120).<sup>29</sup>

Professor Prys-Roberts, in an editorial published in 2001<sup>30</sup> took a different view of the management of hypertensive patients, suggesting that in untreated patients, postponement of surgery is unnecessary unless the diastolic pressure exceeds 120mmHg. For treated hypertension, cancellation in order to improve treatment may be justified if the diastolic pressure exceeds 110mmHg. Subsequently, Professor Prys-Roberts, in a letter<sup>31</sup>, adopted a position that is more in keeping with the generally agreed principles. Similarly, the AHA/ACC guideline suggest that patients with a diastolic blood pressure above 110mmHg should be treated before surgery.<sup>6</sup>

### Heart failure

Patients with heart failure are at risk of major postoperative cardiac events. Even incipient heart failure is a strong predictor of adverse outcome.<sup>25,26,32</sup> The number of patients with heart failure is increasing very rapidly because the mortality of myocardial infarction has been reduced and, therefore, more patients survive with impaired cardiac function.<sup>33</sup> Evaluation of cardiac function with echocardiography or radionuclide angiography is very useful because the risk of complications of anaesthesia and surgery is directly related to the severity of ventricular dysfunction. An ejection fraction less than 40% predicts adverse cardiac outcome.<sup>34</sup> The patient's drug therapy should be optimised before surgery. In some patients coronary bypass surgery<sup>16</sup> or coronary angioplasty and stenting improve left ventricular function to such an extent that even major surgery becomes considerably safer.

An increasing number of patients with heart failure are now receiving beta-blockers. The latter improve their long-term prognosis, especially where carvedilol is used. However, in all studies of beta-blockade in heart failure, treatment is initiated with extremely low doses, with increases in dosage over eight weeks or more.<sup>35</sup>

Recently the possible value of measuring natriuretic peptides has been emphasised.<sup>36</sup> In particular Brain Natriuretic Peptide (BNP) has been found to be elevated in patients with cardiac dysfunction.<sup>37</sup> It is a predictor of poor survival.<sup>38</sup> Measurement of BNP could be used as a screening test for cardiac dysfunction so that further tests would only be performed in selected patients.

### Anaesthetic management of patients with coronary or hypertensive heart disease

A major requirement is to avoid haemodynamic changes that may precipitate myocardial ischaemia. Tachycardia increases myocardial oxygen consumption and decreases coronary flow because of the shorter duration of diastole. Hypotension may reduce coronary flow more than myocardial oxygen consumption because of low coronary perfusion pressure. Hypertension can cause increases in oxygen demand that exceed the coronary reserve. This adverse effect is worsened when tachycardia is

present. However, many episodes of myocardial ischaemia occur in the absence of marked haemodynamic changes.<sup>39</sup> These may be caused by coronary artery spasm, transient spontaneous coronary occlusion (microthrombosis), or coronary steal. The latter may develop during the administration of dilators of the coronary resistance vessels. This has been reported with isoflurane (40). Another important contributor to the safety of these patients is the prevention of post-operative hypoxaemia.<sup>13</sup>

In high risk patients, invasive monitoring, including monitoring of the pulmonary occluded pressure (pulmonary capillary wedge pressure) is useful for major surgery, particularly vascular surgery of the thoracic or abdominal aorta. Transoesophageal echocardiography (TOE) may be useful for the detection of ischaemia and, more importantly, the assessment of ventricular filling. The new generation of ECG monitors are capable of displaying ST-segment trends, thus allowing better detection of perioperative myocardial ischaemia than visual inspection on an ECG monitor.

A prerequisite in the management of patients with coronary or hypertensive heart disease is to protect the myocardium. The first step is to maintain their treatment throughout the perioperative period. However, not all drugs used in the chronic management of these patients are equally effective in preventing cardiac complications of anaesthesia and surgery. A more active approach to ischaemia prevention has developed.

#### Active drug prevention of ischaemia

Over the past five years it has become clear that the management of surgical patients with coronary heart disease could be improved by the prophylactic administration of drugs in order to decrease oxygen demand, make the circulation more stable, or improve the distribution of coronary blood flow. Drugs having such effects include calcium antagonists, adenosine modulators, alpha2 adrenoceptor agonists, and beta-blockers.

Systematic studies of the perioperative prophylactic administration of calcium antagonists are lacking. However, observational studies do not show patients on calcium antagonists to be protected against silent myocardial ischaemia<sup>41,42</sup> even though calcium antagonists cause coronary vasodilatation, relieve exercise-induced coronary vasoconstriction, reduce left ventricular afterload, and improve the oxygen balance.

Adenosine modulation causes a selective augmentation of adenosine levels in tissues under ischaemic conditions but not in the non-ischaemic myocardium. This results in improved left ventricular function, enhanced collateral blood flow, reduced risk of ventricular dysrhythmias, and attenuated risk of stunning. Five trials of the adenosine modulator acadesine (total of 4,043 patients) were analysed together.<sup>43</sup> They showed a significant reduction in myocardial infarction (-27%), stroke (-26%), and cardiac death (-50%). Unfortunately, the development of this agent has been stopped.

Alpha2-adrenoceptor agonists decrease sympathetic activity by a central mechanism, this results in better haemodynamic stability, and decreased risk of silent ischaemia. In addition, there is sedation, and reduction in anaesthetic and opioid requirements. Clonidine has been shown to reduce the risk of perioperative

myocardial ischaemia.<sup>44</sup> In terms of cardiac outcome, a study of the alpha2-adrenoceptor agonist mivazerol showed significant reductions in cardiac death, myocardial infarction and cardiac death, and myocardial infarction and all causes of death, but only in vascular surgical patients.<sup>45</sup> Development of this promising agent has been stopped.

Beta-adrenoceptor blockers are known to reduce myocardial oxygen consumption, decrease the effects of sympathetic activation, and redistribute coronary blood flow. They may reduce overall sympathetic outflow. For more than twenty-five years, beta-blockers have been shown to minimise the risk of perioperative myocardial ischaemia.<sup>46-48</sup> More importantly, perioperative beta-adrenoceptor blockade has been shown to decrease the incidence of perioperative myocardial infarction.<sup>49,50</sup> More recently, atenolol given for one week perioperatively<sup>51</sup> was shown to result in lower mortality at two years by comparison with administration of a placebo (9% vs 20%).

In 1997, the American College of Physicians published a guideline for assessing and managing the perioperative risk from coronary artery disease associated with major non-cardiac surgery.<sup>52</sup> The important message was that for all patients, eligibility for beta-blocker use should be determined. Further evidence for beneficial effects of perioperative beta-blockade was obtained by Poldermans and colleagues.<sup>53</sup> They studied patients in whom coronary artery disease had been demonstrated by the presence of reversible ischaemia on dobutamine echocardiography. In their study, prolonged beta-blockade, started a week or more before surgery, was associated with a large reduction in cardiac death (3.4% vs 17% in the control group) and non-fatal myocardial infarction (0% vs 17% in the control group). The efficacy of beta-blockade was impressive. Moreover, as patients were maintained on beta-blockers, their long-term prognosis was also much improved.<sup>54</sup> However, as all patients had reversible ischaemia, they were at a particularly high risk for coronary events. Thus, the efficacy of beta-blockade cannot be extrapolated to patients at risk for, rather than with demonstrable coronary artery disease. However, based on published studies, and the efficacy of beta-blockade in patients with coronary heart disease, beta-blockers seem to be the logical answer to the perioperative drug management of patients with risk factors for, or with, coronary artery disease.

**Why are they not used much more frequently?** There are perceived risks to beta-blockade such as worsening of conduction disorders or airway obstruction in patients with reactive airway disease. There is also the risk of worsening of left ventricular dysfunction. Though beta-blockers are now used successfully in the treatment of patients with heart failure<sup>55</sup>, their introduction shortly before surgery may not be well tolerated, unless the initial dosage is very low and doses are increased slowly over several weeks.

Before using beta-blockers routinely in all at risk patients, it is necessary to consider that the studies of Mangano and colleagues<sup>51</sup>, and Poldermans and colleagues<sup>53,54</sup> were carried out in patients admitted to intensive care or high dependency units, not to ordinary wards. In ITU or HDU environments, any adverse effects can be easily prevented or treated. On the ward this may not be the case. Indeed, the most recent ACC/AHA

guideline<sup>6</sup> suggests that beta-blockers should be used in high risk patients and not necessarily in all patients at risk for coronary artery disease

Beta-blockers may still be the safest agents to use. The treatment should be started well ahead of surgery rather than just the day before surgery. More importantly, a prospective study of their safety on the ward is warranted. If they prove to be well tolerated then their use could be greatly increased.<sup>56</sup> Hopefully, this coupled with other measures could reduce substantially the number of cardiac complications of anaesthesia and surgery.

If acute beta-blockade is effective in reducing the risk of cardiac complications of anaesthesia and surgery, it is tempting to conclude that patients on chronic beta-blocker treatment are well protected. This is not the case. The incidence of perioperative silent myocardial ischaemia is not reduced in patients on chronic beta-blockade.<sup>42</sup> Similarly, chronic beta-blockade does not appear to reduce perioperative mortality.<sup>57</sup> Chronic beta-blockade may not offer the same degree of protection as acute beta-blockade because of beta-adrenoceptor up-regulation or other factors. Therefore, such patients must be considered to be at risk, and monitored especially carefully.

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