

## Peri-operative myocardial infarction

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Patients with, or at risk for, cardiac disease have a 3,9% (95% confidence interval (CI) 3,3% – 4,6%) chance of suffering a major peri-operative cardiac event.<sup>1</sup> This is associated with a significant in-hospital mortality of 15 - 25%, and subsequent cardiovascular death or myocardial infarction at 6 months (hazard ratio 18; 95% CI 6 – 57).<sup>1</sup>

This paper focuses on our understanding of the pathophysiology of peri-operative myocardial infarction, the flaws associated with the proposed definition of peri-operative myocardial infarction, and the management of peri-operative myocardial infarction.

### Presentation of peri-operative myocardial infarction

#### *Time of presentation*

The majority of peri-operative myocardial infarctions present within the first 24 hours of surgery.<sup>2</sup> A later presentation was associated with the use of the older biomarkers such as creatine phosphokinase. Nearly 90% present by seven days, although the range of presentation is throughout the entire hospital admission.<sup>3</sup>

#### **Pattern of presentation of troponin elevation**

Three patterns are recognised.<sup>4</sup> The first pattern is characterised by a rapid rise in troponins peaking at  $37 \pm 22$  hours postoperatively. The second pattern displays a delayed peak in troponins at  $74 \pm 39$  hours, following  $54 \pm 35$  hours of troponin elevation above the upper reference limit.<sup>4</sup> The third pattern of troponin elevation is characterised by troponins above the reference limit without a late peak, so-called 'myocardial damage'.<sup>4</sup> It has been proposed that coronary plaque rupture is associated with the first pattern, and a sustained myocardial oxygen supply-demand imbalance in the postoperative period is consistent with a delayed myocardial infarction (second pattern).<sup>4</sup> This conclusion is, however, probably incorrect and will be discussed.

#### **The pathophysiology of peri-operative myocardial infarction**

The pathophysiology of peri-operative myocardial infarction is poorly understood. In addition to troponin surveillance, other investigative approaches provide important information.

#### *Post-mortem studies*

Firstly, in patients that die, the peri-operative cardiac events appear to be approximately evenly distributed between myocardial oxygen supply-demand imbalance and plaque rupture, although plaque rupture may contribute proportionally less to fatal peri-operative myocardial infarction than myocardial supply-demand imbalance, as direct evidence of plaque rupture was found in only 7% of patients in one study.<sup>5,6</sup>

The second important characteristic identified was that of an absence of evidence of plaque rupture in 83% of patients who died within the first three postoperative days.<sup>6</sup> Thus myocardial oxygen-supply demand imbalance predominates in the first three to four postoperative days.

Thirdly, plaque rupture was evenly distributed over 17 postoperative days, suggestive of a random presentation throughout the postoperative period.<sup>6</sup>

Finally, post-mortem studies suggest that fatal peri-operative myocardial infarction occurs on the background of established coronary artery disease.<sup>5,6</sup>

#### *Pre-operative coronary angiography*

A matched case control study of pre-operative coronary angiographic findings in vascular surgical patients found that the only independent predictor of mortality was the number of lesions with > 30% stenosis, which supports the notion that established coronary artery disease with a degree of obstruction to flow is important in the pathophysiology of peri-operative myocardial infarction.<sup>7</sup>

#### *Pre-operative tests of inducible myocardial ischaemia*

The importance of significant coronary stenoses is evident when one examines the performance of pre-operative special investigations. The tests with the lowest negative likelihood ratios (of approximately 0,2) for major adverse cardiac events are pre-operative dynamic tests of inducible myocardial ischaemia.<sup>8-17</sup> This suggests that the patients in whom no inducible ischaemia is elicited are unlikely to have peri-operative cardiac complications.

While a negative test result for inducible myocardial ischaemia is clinically accurate (likelihood ratio 0,2), a positive test result is not as accurate at predicting an adverse outcome (positive likelihood ratios of approximately 4) suggesting that, once a patient has coronary pathology associated with an increased risk of peri-operative myocardial infarction, a number of other factors are necessary for these lesions to result in a peri-operative myocardial infarction.<sup>8-17</sup>

### *Peri-operative Holter studies*

The studies of peri-operative myocardial ischaemia have shown that, in vascular surgical patients, 20% of all patients have postoperative ST depression.<sup>18</sup> ST depression is nearly 40 times more common than ST elevation on peri-operative Holter monitoring.<sup>19</sup> This finding suggests that total coronary occlusion is less common than myocardial oxygen supply-demand imbalances in the peri-operative period. ST depression precedes troponin elevation in 83% of vascular surgical patients by approximately 18 hours.<sup>19</sup> 97% of vascular surgical patients present with ST depression within the first 72 hours of surgery, suggesting the predominance of oxygen supply-demand imbalance as opposed to complete coronary occlusion at this time.<sup>19</sup>

### **Summary of the pathophysiology of peri-operative myocardial infarction**

Based on these landmark studies, the following pathophysiological processes are probably responsible for peri-operative myocardial infarction. Peri-operative myocardial infarction is most likely to occur in patients with significant coronary artery stenoses. In the first three to four postoperative days, patients probably have a relative flow mediated hypoperfusion which precedes myocardial infarction, most commonly at the site of significant stenoses (>80%). This may be aggravated by hypotension or intracoronary thrombosis secondary to hypercoagulability and inflammation, and possibly further aggravated by an increased myocardial oxygen demand associated with surgery, pain and sympathetic stimulation. This precedes troponin elevation in 80% of patients by approximately 18 hours. Even a rapid rise in troponins within the first two postoperative days is more likely to represent a severe oxygen supply-demand imbalance than plaque rupture. Peri-operative myocardial infarctions following plaque rupture are more likely to resemble medical myocardial infarctions and are evenly distributed in the postoperative period.

### **The problem with the definition of a peri-operative myocardial infarction**

There are no standard criteria defining a peri-operative myocardial infarction in noncardiac surgical patients. In noncardiac surgery, of the patients suffering myocardial infarction, 14% (95% CI 3 - 25%) will have chest pain and only 53% (95% CI 38-68%) will have symptoms or signs which would alert the physician to the possibility of a peri-operative myocardial infarction.<sup>20</sup> It has been suggested that a peri-operative myocardial infarction should be defined by a

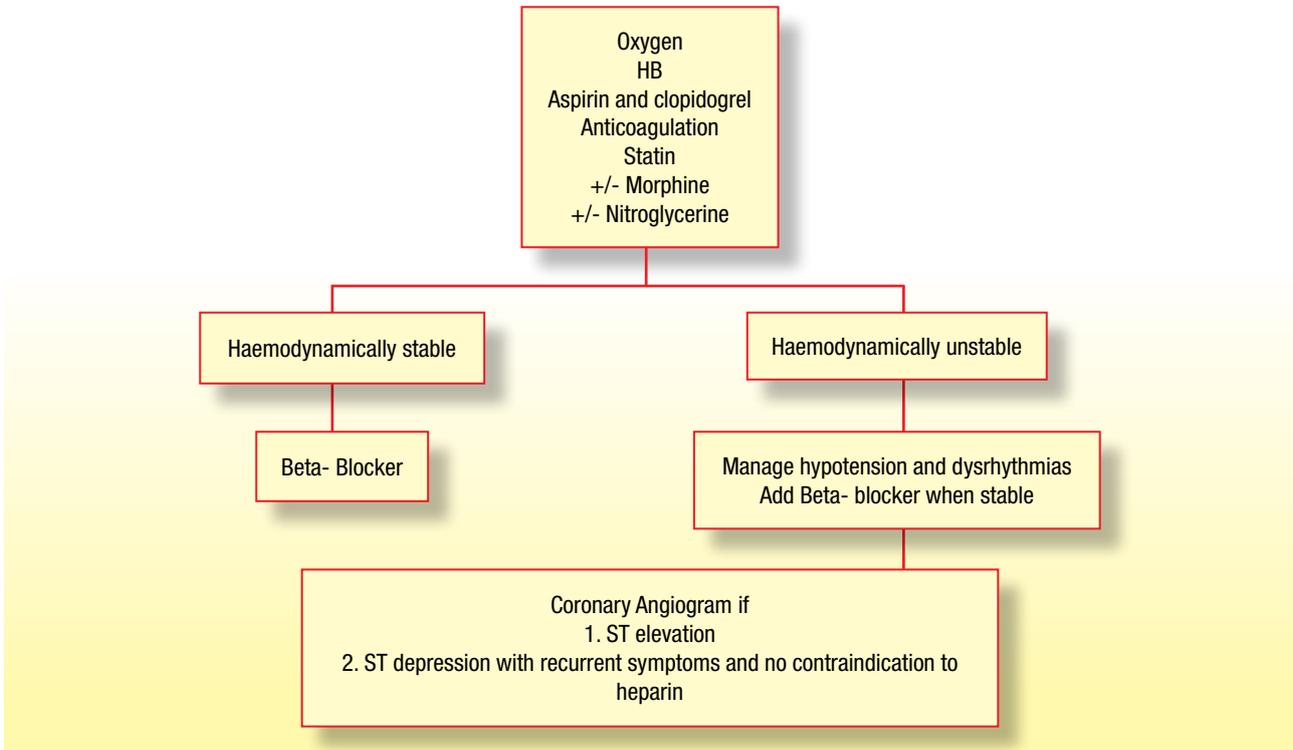
troponin rise above the upper reference limit, together with one of the following: ischaemic symptoms, ischaemia on ECG, new Q waves on ECG, coronary artery intervention, or new wall motion abnormalities or fixed defect on radionuclide scanning.<sup>20</sup>

The question that needs to be addressed is whether the prognosis of the patients with troponin elevation, but with insufficient signs to fulfil the diagnostic criteria for a peri-operative myocardial infarction, the so-called "myocardial damage" group, which may exceed 60% of all troponin positive vascular surgical patients, is significantly worse than troponin negative patients?<sup>4,21</sup> It certainly is. Troponin elevation has been associated with both significantly increased short- and long-term mortality.<sup>4,22,23</sup>

Early isolated postoperative troponin elevation is more likely to be associated with cardiac pathology, while other noncardiac presentations of troponin elevation present later.<sup>24</sup> One could improve the sensitivity for cardiac pathology when only considering troponin elevation by looking for myocardial ischaemia. The duration of myocardial ischaemia is highly correlated with the rise in troponins ( $r = 0,83$ ;  $p < 0,000 1$ ).<sup>19</sup> In patients with ST depression who do not fulfil the criteria for a peri-operative myocardial infarction, the duration of myocardial ischaemia is still  $38 \pm 26$  minutes, and observing these patients about twice in the first postoperative hour should identify  $2/3$  of patients at risk of myocardial damage.<sup>19</sup> This may be the reason why an immediate postoperative ECG in the recovery room with new ST depression or elevation or T wave inversion is an independent predictor of postoperative cardiac complications including acute myocardial infarction, pulmonary oedema, ventricular fibrillation, cardiac arrest and complete heart block (odds ratio 2,2; 95% CI 1,2 - 3,9;  $p < 0,01$ ).<sup>25</sup>

Therapy of a suspected peri-operative myocardial infarction

Figure 1: The proposed management algorithm.



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