

## EDUCATIONAL ARTICLE

# Perioperative Management of Patients Undergoing Non-cardiac Vascular Surgery

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*Patients undergoing non-cardiac vascular surgery have arterial disease affecting more than one vascular bed and commonly have multiple significant co-morbidities. The surgical and anaesthetic teams are asked to address pre-, peri- and postoperative management issues relating not only to the surgery but arising from these co-morbidities. Here we review the strategies and rationale for the optimisation of these high risk patients.*

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### Introduction

Patients presenting for major non-cardiac vascular surgery (NCVS) represent a dynamic challenge for the anaesthetist and the surgeon that extends beyond the intricacies of the planned operation. These patients frequently have arterial disease affecting several vascular beds and suffer from other significant co-morbidities such as diabetes, respiratory and renal disease. The management of these patients has to address not only immediate perioperative management issues but also prevent the deterioration of coexisting disease.

### Assessing Perioperative Risk

Scoring systems such as POSSUM and P-POSSUM use pre- and peri-operative data to calculate the probability of an adverse outcome thus are of no value for pre-operative risk prediction. The ASA (American Society of Anaesthesiologists) score is shown in [Table 1](#). This seemingly crude score offers a means of formalising the clinician's subjective pre-operative assessment

and is intended not for risk prediction but to describe the patient's preoperative status. However, it has been shown to correlate well with the incidence of post operative complications and death.<sup>1</sup>

Cardiovascular complications are a particular concern in patients undergoing major NCVS. There are a number of scoring systems directed towards estimating the risk of perioperative cardiovascular complications. Amongst the first was developed by Goldman *et al.* which included 9 specific risk factors.<sup>2</sup> However this index has statistical flaws due to the number of risk factors studied and a study population which suffered a small number of cardiovascular complications.

Subsequent studies have attempted to refine the original Goldman Risk Index but has been superseded by the revised Cardiac Risk Index Score published in 1999.<sup>3</sup> This was derived from a study of 2893 patients and validated in a further 1422 patients. It includes the risk factors listed in [Table 2](#). Each risk factor is allocated 1 point. The total points score gives an estimate of perioperative cardiac risk. It is more robust than the Goldman Risk Index as the study population had a larger number of cardiac events and the authors were more general in their definition of cardiac risk factors.

Although a substantial step forward the revised Cardiac Risk Index remains an imperfect tool and does not perform well in certain subsets of patients

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**Table 1. The American Society of Anesthesiologists (ASA) physical status classification system**

ASA Score	
1	A normal healthy patient
2	A patient with mild systemic disease
3	A patient with severe systemic disease
4	A patient with severe systemic disease that is a constant threat to life
5	A moribund patient who is not expected to survive without the operation
6	A declared brain-dead patient whose organs are being removed for donor purposes

undergoing NCVS, in particular those undergoing aortic surgery. This issue is addressed by the Customised Probability Index developed in a cohort of 2310 patients undergoing elective NCVS over a ten year period.<sup>4</sup> The resulting predictive model is more complex but appears to be specifically applicable to patients undergoing vascular surgery (Fig. 1).

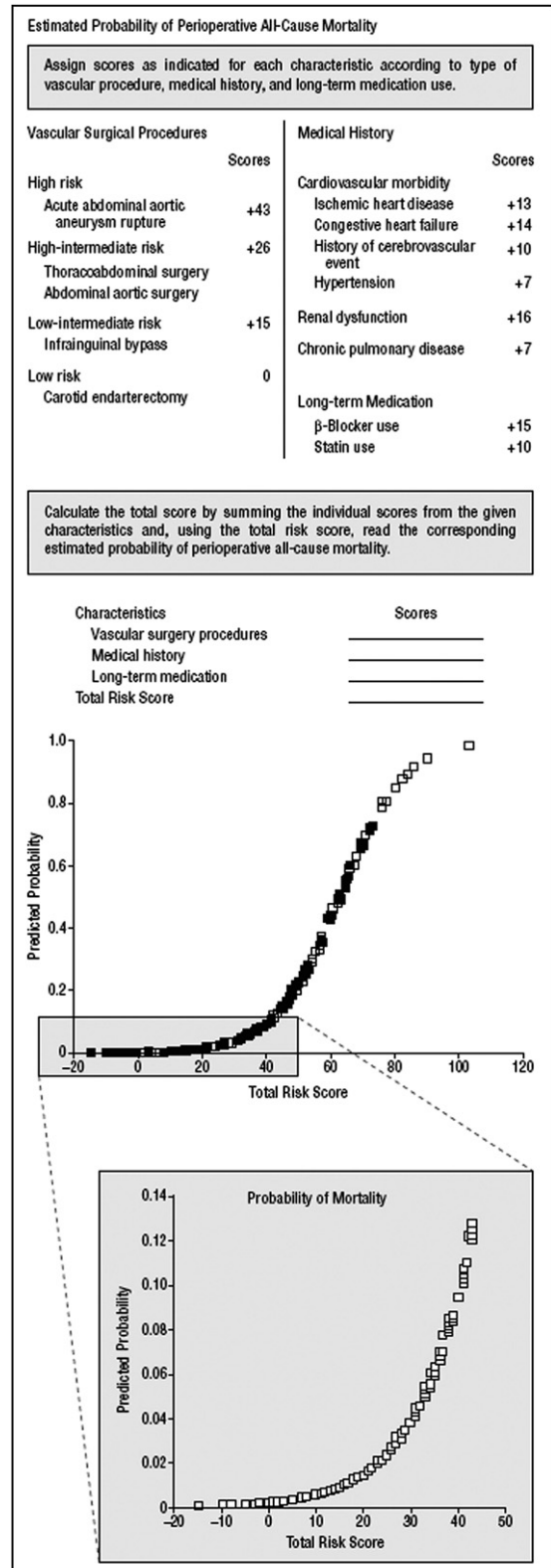
It should be noted that these tools are valuable for adjusting for case mix when studying outcomes in surgical populations but are of limited value for individual risk predication. Unfortunately the perfect tool to predict individual risk does not exist. The experienced clinical team should not depend on statistics alone but trust their own judgement and experience.

**Perioperative Cardiac Complications**

Cardiac complications are common in patients undergoing NCVS. This is in part related to the high incidence of coronary artery disease in these patients.<sup>5</sup> However the precise aetiology of perioperative myocardial injury remains unclear. Studies in NCVS patients have demonstrated perioperative myocardial infarction (MI) is associated with perioperative myocardial ischemic burden as detected by Holter monitoring.<sup>6</sup> This would suggest that perioperative MI is the result of protracted myocardial ischemia. On the

**Table 2. The Lee Risk Index. The risk factors (high-risk type of surgery; history of ischemic heart disease; history of congestive heart failure; history of cerebrovascular disease; preoperative insulin treatment and preoperative serum creatinine >2.0 mg/dl (177 µmol/l)) were validated in a study population of 1422**

Revised cardiac risk index class	Number of risk factors	Cardiac event rate in the validation cohort of the study population N = 1422 Events/Population	Risk of cardiac complications Rate (95% Confidence interval)
I	0	2/488	0.4% (0.05–1.5)
II	1	5/567	0.9% (0.3–2.1)
III	2	17/258	6.6% (3.9–10.3)
IV	3 or more	12/109	11% (5.6–18.4)



**Fig. 1. Customized probability model for perioperative all-cause mortality. The sum of the assigned scores relates to predicted mortality based on this index. Taken from Kertai et al. 2005.**

other hand post mortem data indicate that in over half of patients who suffer perioperative MI there is evidence of coronary artery plaque fissuring and rupture with the development of coronary thrombosis.<sup>7</sup> Whilst these pathological changes were not found in all the patients studied, their incidence was similar to that seen in patients that presented with clinical evidence of MI and subsequent death. It has been proposed that these two mechanisms may not occur in isolation.<sup>8</sup> Periods of protracted myocardial ischemia at emergence from anaesthesia may be associated with increased shear stress across the atherosclerotic plaque in the coronary arteries leading to plaque injury and coronary thrombosis.

Just as acute coronary syndromes (ACS) display a spectrum of myocardial injury; a similar continuum exists in the context of perioperative myocardial injury. Many patients who do not suffer a clinically evident perioperative event do display a degree of perioperative cardiac troponin release following NCVS. Six-month and five-year follow up of these patients show a significantly worse prognosis<sup>9,10</sup> (Fig. 2). In addition prognosis appears to correlate with the level of cardiac troponin release.

It should be emphasised that not every patient who displays perioperative cardiac troponin release can be labelled as having suffered a perioperative MI. Cardiac troponin release is not itself a diagnostic test for MI.<sup>11</sup> However, it is clear that perioperative troponin release has prognostic implications and an aim of perioperative management should be to attenuate or avoid perioperative myocardial injury.

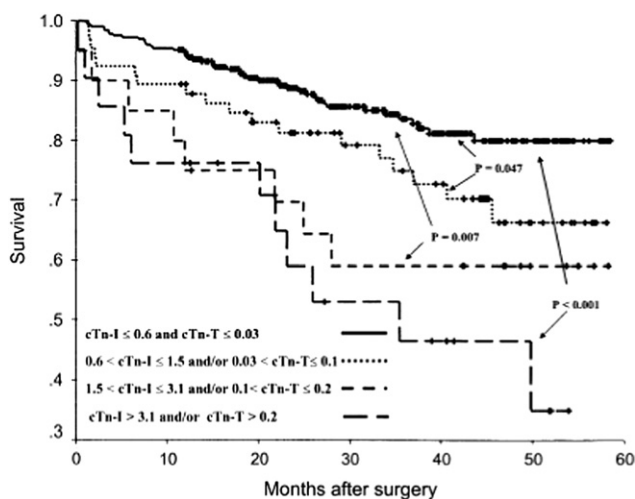


Fig. 2. Kaplan-Meier survival curves of NCVS patients divided according to postoperative troponin level (cTn-I – cardiac troponin-I; cTn-T – cardiac troponin-T). Taken from Landesberg *et al.* 2003.

### Cardiovascular Stability

One would expect high risk patients with underlying coronary artery disease to be at increased risk of myocardial ischemia if they suffer perioperative cardiac instability. In a study of 100 high risk patients approximately a quarter of ischemic episodes were preceded by significant increases in heart rate, 15% proceeded by increases in blood pressure and 8% by acute decreases in blood pressure.<sup>12</sup> Even an optimistic interpretation of these data would suggest that the majority of intraoperative episodes of myocardial ischemia cannot be attributed to haemodynamic changes. However historical data from Slogoff and Keats offer a warning regarding cardiovascular instability.<sup>13</sup> In a study of patients undergoing coronary artery by-pass grafting these authors demonstrated a significant association between perioperative myocardial ischemia and marked perioperative MI. In this study one anaesthetist paid little regard to heart rate control. This individual's patients had a 9-fold increased risk of myocardial infarction. Thus, whilst not all perioperative myocardial ischemia can be attributed to cardiovascular instability, these data suggests that marked instability may have significant adverse effects.

### Perioperative Beta-blockade

Two trials of perioperative beta-blockade are widely quoted. Mangano and colleagues randomised 200 patients undergoing vascular and other major surgery to receive atenolol or placebo pre-operatively and for 7 days post-operatively. Patients enrolled into the study either had proven cardiovascular disease or two or more risk factors for cardiovascular disease. The study demonstrated an improved outcome at 6 months amongst patients who received atenolol.<sup>14</sup> In the study by Poldermans *et al.* patients were randomised to receive bisoprolol or standard care. In the group who received bisoprolol this was started one to two weeks prior to surgery and the dose was increased to achieve adequate heart rate control. There was a 10-fold reduction in the perioperative cardiovascular event rate amongst the patients who received bisoprolol.<sup>15</sup>

Conclusive as the results appear both studies have significant weaknesses. Mangano and colleagues excluded 6 patients who died in hospital from their analysis and, despite randomisation, there was a higher incidence of pre-existing cardiovascular disease in the placebo group than in the atenolol group.<sup>14</sup> The Poldermans study was conducted in an extremely high-risk subset of vascular surgery patients. The

inclusion criteria included 2 or more clinical risk factors, new inducible wall motion abnormality on dobutamine stress echocardiography and no pre-existing beta-blockade. Only some 110 patients out of an initial study population of over 1300 patients were randomised. This was an unblinded study that did not use a placebo and the study was stopped early because of the very large benefit seen from beta-blockade. Some authorities have argued that this benefit was implausibly large and the study was terminated too early. Importantly subsequent studies have not been able to reproduce the benefits seen in these initial two studies.<sup>16,17</sup>

A recent meta-analysis examined the effects of beta-blockade in over 2000 patients randomised in 8 trials and found no overall benefit of perioperative beta blockade (odds ratio 0.78(95% CI: 0.33–1.78)).<sup>18</sup> Furthermore, an observational study in over 900,000 patients suggested that low risk patients with a revised Cardiac Risk Index score of 0 or 1 may actually be at increased risk of post-operative complications if they receive beta-blockers.<sup>19</sup>

However, it may be unwise to completely dismiss the role of perioperative beta-blockade. Evidence supports that good heart rate control with beta-blockade below the patients ischemic threshold leads to a substantial reduction in perioperative myocardial ischemia and perioperative cardiac troponin release.<sup>20</sup>

Whilst the evidence for initiating perioperative beta-blockade is equivocal there are clear data indicating that the withdrawal of beta-blockers prior to major surgery is associated with an increased incidence of cardiovascular morbidity and mortality.<sup>21</sup>

We suggest that patients with a primary indication for beta-blockade regardless of surgery should be considered for beta-blockade on the strength of this medical indication. This should be initiated at least 1 to 2 weeks before surgery to allow adequate heart rate control and to allow adverse effects to become evident and should be continued beyond the perioperative period in order to offer long term survival benefit. Recently published guidelines of the American College of Cardiology and American Heart Association recommend that:

1. Beta blockers should be continued in patients undergoing surgery who are receiving beta-blockers to treat angina, symptomatic arrhythmias, hypertension, or other ACC/AHA Class I guideline indications.
2. Beta blockers should be given to patients undergoing vascular surgery with proven cardiac ischemia on preoperative testing.<sup>22</sup>

## Statins

There are a number of recent studies that suggest statin therapy may reduce the risk of perioperative MI. In a small group of NCVS patients commenced on atorvastatin versus placebo showed a significant reduction in immediate post-operative events.<sup>23</sup> This is further supported by a retrospective analysis of a larger cohort of NCVS patients and a meta-analysis of 8 studies.<sup>24,25</sup> This evidence, whilst promising, is not conclusive. Many of these studies are small and the data collected over a long period during which practices have changed significantly. This is an area in which the results of large randomised control trials are required to guide therapy.

Data from medical patients suggest that the withdrawal of statin therapy may itself be associated with adverse consequences. Heesch and colleagues studied patients admitted to hospital following ACS.<sup>26</sup> Interestingly cessation of statins pre-event was associated with significantly poorer outcomes when compared to those patients who continued on statin therapy or those who had never been on a statin. It is important to be cautious in extrapolating from medical to surgical patients but these data mitigate against withdrawing statins from patients undergoing NCVS.

## Anti-platelet Therapy

Aspirin is indicated as secondary cardiovascular prevention in patients presenting with occlusive arterial disease.<sup>27</sup> While there is concern that anti-platelet agents may exacerbate surgical bleeding there is no evidence that this translates to an increased incidence of adverse outcome in NCVS patients or preventing the use of local anaesthetic techniques.<sup>28</sup> Again evidence from medical patients admitted to hospital following ACS suggest that those patients who had aspirin withdrawn prior to the event had worse outcomes than those who either continued on aspirin or who had never received aspirin therapy.<sup>29</sup> Taken together this data suggest that withdrawing aspirin is inappropriate in the context of patients undergoing NCVS.

The most appropriate course of action in patients who are receiving the ADP antagonist clopidogrel is unclear. This potent anti-platelet agent is associated with an increased risk of surgical bleeding and in patients undergoing cardiac surgery its use increases the transfusion requirement but does not itself have a direct effect on outcome.<sup>30</sup> The indication for clopidogrel use varies and in practice the judgement as to

whether clopidogrel should be discontinued has to be made on a case-by-case basis. It may certainly be appropriate to continue clopidogrel in patients undergoing carotid endarterectomy and lower limb re-vascularisation if strongly indicated. However, clopidogrel precludes the use of spinal or epidural anaesthesia or regional blockade techniques such as deep cervical plexus blockade.

### Coronary Artery Disease

There is unequivocal evidence that patients who have undergone coronary re-vascularisation have a reduced incidence of perioperative MI.<sup>31</sup> However, it does not follow that patients should undergo coronary re-vascularisation to simply reduce perioperative risk. Indeed the cumulative risk of coronary angiography, coronary artery by-pass grafting and then NCVS outweighs the risk of simply preceding to NCVS.<sup>32</sup> A recent interventional study showed no benefit to randomised patients who had undergone operative or percutaneous coronary re-vascularisation prior to surgery compared to those who proceeded straight to surgery.<sup>33</sup> The current consensus is that it is inappropriate to undertake coronary revascularisation simply to reduce the risk of subsequent non-cardiac surgery. These interventions should be considered only where there are indicated on their own merits.

Coronary angioplasty has been revolutionised by the advent of coronary stents. However, the insertion of a metal stent leaves a thrombogenic surface within the coronary artery. There is evidence that NCVS conducted soon after stent insertion is associated with a significantly increased risk of perioperative MI<sup>34</sup> and data suggested that this risk persisted for at least 6 weeks after percutaneous coronary intervention.<sup>35</sup> Recent data suggests that a patient may still remain at risk of perioperative myocardial infarction for several months after stent insertion. Certainly patients who have had a bare metal stent inserted in the 3 months prior to surgery should have clopidogrel continued if at all possible.<sup>36</sup> Re-endothelialization of drug eluting stents takes longer and patients with a drug eluting stent inserted in the previous 12 months should remain on clopidogrel throughout the perioperative period if at all possible. Aspirin should be continued throughout the perioperative period in these patients unless very strongly contra-indicated. The perioperative management of surgical patients who have undergone recent coronary artery stenting is examined in depth in an excellent review by Howard-Alpe and colleagues.<sup>37</sup>

### Temperature

Perioperative hypothermia is associated with catecholamine release and may produce tachycardia and vasoconstriction producing increased afterload. It is now well established that the active pursuit of normothermia is associated with a reduced incidence of perioperative myocardial ischemia.<sup>38</sup> This has been simplified by the advent of modern warming technologies such as forced air warming blankets, fluid warmers and a covering of the exposed bowel where this is possible.

### Anaesthetic Technique: General Anaesthesia

There is no evidence that favours one anaesthetic technique over another for the prevention of perioperative complications including MI. There is laboratory evidence that suggests that volatile anaesthetic agents may offer cardioprotection by ischemic preconditioning<sup>39</sup> and opening of the K-ATP channel in mitochondria.<sup>40</sup> There is now some translational evidence that this effect is seen in small cardiac surgery cohorts but considerably more work is required.<sup>41</sup>

### Anaesthetic Technique: Neuroaxial Blockage

Despite numerous studies there is no evidence that epidural or spinal anaesthesia reduces mortality in patients undergoing NCVS. A meta-analysis did suggest a significant benefit from neuroaxial blockade.<sup>42</sup> However, subsequent examination of these data revealed that this effect rested on 3 small studies with adverse event rates in the control group of between 20 and 30%. If these studies were excluded the benefit from neuroaxial blockade was lost.

### Pre-operative Testing

There is no evidence that any static test of cardiovascular function adds significantly to the predictive value to clinical risk factors to patients undergoing NCVS. There is an association between a poor ejection fraction measured by echocardiography and adverse outcomes following surgery.<sup>43</sup> However this test has a high false negative rate and does not preclude left ventricular dysfunction under stress.

Dynamic tests are more predictive but are resource hungry. These include exercise ECG, resting and stress myoview scans and stress echocardiography. The ACC/AHA guidelines recommend the selective use of these tests in patients who are undergoing

NCVS, have cardiovascular risk factors and have a limited functional capacity.<sup>43</sup>

There is an unequivocal association between poor lung function tests and post operative pulmonary complications. However poor performance on lung function testing does not preclude major NCVS.<sup>44</sup> Indeed it is well reported that abdominal aortic surgery may be performed on patients with a FEV1 or less than 1 metre. At least as important as lung function testing is the clinical status of the patient.<sup>45</sup>

Presently there are no clear guidelines for pre-operative carotid artery imaging in patients undergoing NCVS. The prevalence of asymptomatic internal carotid artery stenosis (>70%) in patients with peripheral arterial disease or abdominal aortic aneurysms is about 10%.<sup>46</sup> However the incidence of stroke following NCVS is less than 1%.<sup>47</sup> The decision to image the internal carotid artery is left to the clinicians discretion and further work needs to be done on this area.

### Conclusions

Patients presenting for vascular surgery have a complex array of medical problems. The careful management of these problems can improve outcome for these patients and is part of the fascination of this speciality. Put simply there is more to vascular surgery than vascular surgery.

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