Cardiac damage after vascular surgery procedures: a silent killer

G Galyfos*, F Sigala, G Zografos, K Filis

Abstract

Introduction
Perioperative myocardial ischaemia remains a major cardiovascular complication after non-cardiac, and especially vascular surgery. In this review, we try to identify the real significance of asymptomatic cardiac damage after vascular surgery and make conclusions regarding the proper perioperative management.

Discussion
The mechanism of perioperative myocardial ischaemia can be explained through the reactions of the heart functioning under conditions of stress. Regarding preoperative assessment of the patients, there is a large number of clinical risk indices available, although some of them have been proved useful for vascular patients in specific. A large number of studies and randomised trials have underlined the high incidence of asymptomatic myocardial damage after vascular procedures and its association with postoperative mortality. However, the results of studies so far show a high diversity regarding the impact of certain risk factors, such as the gender and the age of the patient.

Conclusion
Perioperative myocardial ischaemia deserves the classification as a ‘silent killer’. Cautious preoperative cardiac assessment and proper perioperative management could lead to optimal results.

Introduction
It is estimated that of the 230 million patients undergoing major surgery annually, approximately 1% (2,300,000 patients) suffer perioperative myocardial infarction (MI) with a cardiovascular mortality rate around 0.3% (690,000 patients)\(^1\). However, cardiac risk imbedded in surgical interventions can differ depending on the magnitude, duration, location, blood loss and fluid shifts related to the specific procedure. A major prognostic factor for occurrence of perioperative myocardial ischaemia is coronary artery disease (CAD)\(^2\). CAD defines the perioperative profile of the patient, especially in vascular surgery, and the risk for postoperative complications.

Perioperative myocardial ischaemia remains a major prognostic factor for early and long-term cardiac morbidity and mortality. Additionally, it increases the relative danger for early cardiac events, such as MI, almost nine times\(^3\). Furthermore, perioperative myocardial ischaemia increases the possibility for late (over 30 days to 2 years postoperatively) cardiac events almost 2.2 times\(^4\). The majority of high-risk patients have the tendency to present perioperative myocardial ischaemia on the day of the procedure, on the next day or during awakening after anaesthesia. It is estimated that almost 3% of patients with known CAD, undergoing non-cardiac procedures, present a perioperative MI. However, this value drops to 1% for patients without CAD\(^3,4\).

Therefore, this review aims at highlighting the role of perioperative cardiac damage as a major complication in vascular surgery patients and will try to make conclusions regarding the proper perioperative management of the vascular patient.

Discussion
The authors have referenced some of their own studies in this review. These referenced studies have been conducted in accordance with the Declaration of Helsinki (1964) and the protocols of these studies have been approved by the relevant ethics committees related to the institution in which they were performed. All human subjects, in these referenced studies, gave informed consent to participate in these studies.

Mechanism of perioperative myocardial ischaemia
The mechanism of perioperative myocardial ischaemia can be easily explained through the physiology of cardiac function under conditions of stress. The amount of oxygen supplied to the myocardium is determined by (1) the blood flow in the coronary arteries and (2) the oxygen-carrying capacity of the blood.

Therefore, an increased myocardial oxygen demand must be met by an increase in coronary blood flow. In addition, an imbalance between oxygen supply and oxygen demand results in myocardial damage, characterised by myocardial ischaemia and MI. This ischaemia results from reduction in oxygen supply due to constriction of coronary arteries or accumulation of platelets and formation of thrombi inside the arteries\(^5\).

In general, myocardial damage can be subdivided according to two pathological processes, described as type 1 and type 2 by the recent universal definition of MI\(^6\). Type 1 MI is defined as an acute coronary syndrome...
that occurs when a coronary plaque rupture, leading to thrombus formation, acute coronary thrombosis, supply ischaemia and MI. A reduction in arterial blood flow is the cause of myocardial damage in type 1 MI. In addition, myocardial damage may also be caused by a sustained myocardial oxygen supply–demand imbalance, or type 2 MI. In case of type 2 MI, myocardial damage is caused by an increased myocardial oxygen demand in response to stress, characterised by tachycardia and increased myocardial contractility, which is not met by a sufficient increase in coronary blood flow. It is obvious that in a patient with known CAD undergoing vascular surgery there is the risk for both type 1 and type 2 MI.

During surgery, high-catecholamine production is responsible for vasoconstriction and haemodynamic stress, associated with an increased oxygen demand of the myocardium. Perioperative myocardial damage may occur when the increased oxygen demand is not met by an adequate increase of oxygen supply. This is similar to MIs occurring in the non-surgical setting; however, surgery itself is a significant stress factor leading to an increased risk of plaque rupture. Next to surgical stress, haemodynamic fluctuations during surgery are an important cause of perioperative myocardial damage as well. Additionally, perioperative fluid administration increases the pre- and afterload in the left ventricle, making patients susceptible to perioperative myocardial damage. Conversely, perioperative preload reductions in the left ventricle can result in tachycardia with a concomitant reduction of coronary perfusion, leading to perioperative myocardial damage as well.

**Diagnosis of perioperative myocardial ischaemia**

Regarding the definition and detection of perioperative myocardial ischaemia, the utilisation of biomarkers in the past decade has been evolved to a useful diagnostic tool. The researchers have shown that almost 85% of the patient with perioperative MI will not present any chest pain, probably due to the high level of analgesia. Furthermore, according to Pastermak et al. even if patients show any atypical symptoms, the surgeons could attribute these symptoms to other causes (hypotension, pneumonia, bleeding, etc.). Many researchers have shown that cardiac troponin I (cTnI) remains the most suitable and efficient biomarker for detection of reversible and irreversible myocardial damage, with the highest sensitivity and specificity.

In the recent universal definition of MI, all contributors conclude that ‘...Most patients who have a perioperative MI will not experience ischemic symptoms. Nevertheless, asymptomatic perioperative MI is as strongly associated with 30-day mortality, as is symptomatic MI. Routine monitoring of cardiac biomarkers in high-risk patients, both prior to and 48–72 h after major surgery, is therefore recommended.’

**Preoperative cardiac assessment**

According to the latest Guidelines of American Heart Association (AHA)/American College of Cardiology (ACC) regarding preoperative cardiac assessment before non-cardiac surgical procedures, each procedure is classified into low, intermediate

---

**Table 1 Cardiac risk stratification for non-cardiac surgical procedures**

<table>
<thead>
<tr>
<th>Risk stratification</th>
<th>Procedure examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular (reported cardiac risk often more than 5%)</td>
<td>Aortic and other major vascular surgery</td>
</tr>
<tr>
<td></td>
<td>Peripheral vascular surgery</td>
</tr>
<tr>
<td></td>
<td>Intraperitoneal and intrathoracic surgery</td>
</tr>
<tr>
<td></td>
<td>Carotid endarterectomy</td>
</tr>
<tr>
<td>Intermediate (reported cardiac risk generally 1%–5%)</td>
<td>Head and neck surgery</td>
</tr>
<tr>
<td></td>
<td>Orthopaedic surgery</td>
</tr>
<tr>
<td></td>
<td>Prostate surgery</td>
</tr>
<tr>
<td></td>
<td>Endoscopic procedures</td>
</tr>
<tr>
<td>Low (reported cardiac risk generally less than 1%)</td>
<td>Superficial procedure</td>
</tr>
<tr>
<td></td>
<td>Cataract surgery</td>
</tr>
<tr>
<td></td>
<td>Breast surgery</td>
</tr>
<tr>
<td></td>
<td>Ambulatory surgery</td>
</tr>
</tbody>
</table>

*Combined incidence of cardiac death and non-fatal myocardial infarction.

*These procedures do not generally require further preoperative cardiac testing.

---

Licensee OA Publishing London 2014. Creative Commons Attribution License (CC-BY)

or high cardiac risk\textsuperscript{13}. (Table 1) As the authors underline, this classification is quite useful in perioperative management, although the individual clinical history, physical status and risk of each surgical patient remain the major determining factors. Therefore, a great number of clinical indices have been developed for preoperative cardiac risk assessment of surgical patients. The European Society of Cardiology and AHA/ACC Guidelines\textsuperscript{13,14} suggest the use of the Revised Cardiac Risk Index (RCRI) as the most appropriate stratification tool for the preoperative evaluation of a patient. Therefore, this risk index has prevailed lately and remains the most commonly used by surgeons and anaesthesiologists.

However, recently, there have been many studies questioning the performance of this index regarding vascular surgery procedures. In a recent study, Bursi et al.\textsuperscript{15} concluded that even after preoperative stratification according to ACC/AHA Guidelines, patients undergoing elective major vascular surgery remain at high risk of MI and death. Additionally, Bertges et al.\textsuperscript{16} designed and presented in 2010 the Vascular Study Group of New England – Cardiac Risk Index (VSG-CRI). The authors showed that this index predicts cardiac events after vascular surgery procedures better than the RCRI. Moreover, Ford et al.\textsuperscript{17} underlined in their review that the RCRI discriminated moderately well between patients at low versus high risk for cardiac events after mixed non-cardiac surgery, and it did not perform well at predicting cardiac events after vascular non-cardiac surgery or at predicting death. Finally, Carmo et al.\textsuperscript{18} evaluated all known clinical cardiac risk indices and concluded that RCRI performs inadequately in vascular surgery patients compared with VSG-CRI which is especially designed for this specific population\textsuperscript{19}.

Most importantly, the right selection of the proper cardiac risk index will define the following perioperative management of the patient. The appropriate strategy for the procedure can lead to minimisation of the risk for complications. Moreover, the proper risk evaluation of patients before surgery can help identify possible candidates for invasive or non-invasive cardiac stress testing preoperatively that could detect patients in need for coronary revascularisation as well.

### Prevalence of cardiac damage after vascular surgery

The prevalence of myocardial ischaemia/MI after vascular surgery has been a subject of research in the past decade. Kim et al.\textsuperscript{19} showed in a prospective trial that 28 patients undergoing vascular surgery (12% out of 229 patients) had postoperative cTnI > 1.5 ng/mL, which was associated with a 6-fold increased risk of 6-month mortality (adjusted OR, 5.9; 95% CI, 1.6 – 22.4) and a 27-fold increased risk of MI (OR, 27.1; 95% CI, 5.2 – 142.7). Furthermore, the authors observed a dose–response relation between cTnI concentration and mortality. In 2003, Landesberg et al.\textsuperscript{20} studied 447 patients undergoing major vascular surgery procedures. Detection of myocardial ischaemia in this study was based on the measurement of different markers (cTnI or T and creatine kinase-mB (CK-MB)) and electrocardiographic monitoring. Perioperative MI was observed in 14 (2.9%) – 107 (23.9%) patients, depending on the biomarkers’ criteria that were used. Postoperative CK-MB and troponin, even at low cutoff levels, proved to be independent and complementary predictors of long-term mortality after major vascular surgery. Hence, according to a larger-scale trial by Mohler et al.\textsuperscript{21}, there is a greater risk for cardiac events in the first 72 h after vascular surgery.

- Open abdominal aortic aneurysm (AAA) repair is a major vascular surgery procedure and therefore, it carries a greater risk for adverse cardiovascular events, as shown in Table 1. In 2005, Le Manach et al.\textsuperscript{22} studied a large series of open AAA repairs (n = 1136), where the authors consecutively measured cTnI levels before and after surgery. They observed a very high incidence of myocardial ischaemia (9%) and MI (5%). The interesting point about this trial was that the authors observed two types of MI (early and late), as far as the time of occurrence is concerned. Both types of MI and myocardial ischaemia showed increased in-hospital mortality. In another study, Ali et al.\textsuperscript{23} concluded that perioperative myocardial injury after elective open AAA repair predicts outcome after surgery, and therefore, routine TnI measurement should be considered in all patients, especially in those with high cardiovascular risk. Although endovascular aneurysm repair (EVAR) causes less surgical stress to the patient and probably the incidence of MI after EVAR is lower, several studies show that asymptomatic cardiac damage after EVAR is associated with poor long-term outcome as well\textsuperscript{24}.

- Carotid endarterectomy (CEA) has been associated with postoperative cardiac damage as well, although it is classified as an intermediate cardiac risk procedure according to AHA/ACC criteria\textsuperscript{13}. A recent analysis of the Carotid Revascularization Endarterectomy Versus Stenting Trial data by Blackshear et al.\textsuperscript{25} concluded that mortality 4 years after surgery was high in patients with postoperative MI (HR 3.40; 95% CI 1.67 – 6.92) or isolated increase of troponin levels (‘troponin leak’) (HR 3.57; 95% CI 1.46 – 8.68). The study concluded that patients showed more cardiac events (either MI or troponin leak) after CEA in comparison with carotid angioplasty and stenting (CAS). Additionally, several large...
Revascularisation procedures for peripheral artery disease in lower extremities are classified as high cardiac risk procedures as well. The majority of patients with critical limb ischaemia are elderly patients and of high operative risk due to severe co-morbidities, for example, CAD. However, the 30-day mortality rate in a large retrospective study from our institution was only 0.7%, suggesting that infrapopliteal percutaneous transluminal angioplasty even in high-risk patients is a safe procedure. In contrast, in patients with bypass the reported perioperative mortality (2.4% – 6% – 9%) and morbidity (9.3% – 31%) are high, resulting mainly from cardiac complications.

Finally, a large number of meta-analyses have been conducted in order to shed light on the true prevalence of postoperative myocardial damage after vascular surgery. In 2010, the European Society of Vascular Surgery published the large meta-analysis by Flu et al. The observed incidence of perioperative myocardial ischaemia ranged from 14% to 47% and that of perioperative MI from 1% to 26%. Moreover, the prognostic value of troponin T or I regarding the postoperative mortality or the occurrence of major cardiac complications ranged from 1.9 to 9.0. Hence, the majority of the events were asymptomatic. In 2011, Redfern et al. generated another large-scale meta-analysis including more than 66 studies from 1996 to 2010. The main subject of this review was the isolated increase in troponin levels (‘troponin leak’) after vascular procedures, without any symptoms or ECG findings. The related mortality within 30 days after surgery in patients with no troponin increase, with isolated troponin increase and postoperative MI was 2.3%, 11.6% and 21.6%, respectively ($P = 0.000001$).

### Gender and age

There is a great debate regarding the impact of gender on the early and late postoperative outcomes. As we have highlighted with two of our recently published comments, results so far...
are quite controversial and ambiguous regarding this matter\textsuperscript{11,12}. Most of the studies referring to the impact of gender on outcome after carotid and peripheral arteries revascularisation are observational or retrospective studies. Apparently, there is no consensus supporting the conviction that sex per se does not influence the outcome of peripheral arteries revascularisation. Or does it? Regarding AAA repair, things are not clear either. Lo et al.\textsuperscript{23} declare in their large-scale analysis that women are more likely to experience perioperative complications as a result of less favourable vascular anatomy. However, in another study by Grootenboer et al.\textsuperscript{34}, there were no differences observed between males and females after AAA repair. Only prospectively planned trials randomising patients according to gender could investigate the true impact on postoperative adverse events, including cardiac damage. Furthermore, only strictly planned protocols of detection can help avoid the possible underestimated of cardiac damage prevalence and miscalculating of risk for both genders.

As far as the impact of age is concerned, results of studies so far show a clear diversity as well. As highlighted in our recent review\textsuperscript{35} regarding outcomes after AAA repair in the elderly, older patients present with more co-morbidities, and therefore, major postoperative complications including MI show an incidence of almost 60%. Furthermore, O’Brien et al.\textsuperscript{36} showed, in a large-scale retrospective study ($n = 6140$), that age was a significant risk factor for death and MI for the open procedures of AAA repair, aortobifemoral reconstruction and lower limb bypass, although for endovascular procedures, age did not impact on MI rate for EVAR or death rates for EVAR, iliac angioplasty or lower limb angioplasty. However, Cadili et al.\textsuperscript{27} concluded that patients with AAA greater than 85 years of age are at a greater risk of mortality following endovascular repair. Finally, things are clearer for CEA. Octogenarians are classified as high-risk patients for CEA according to the criteria of the SAPPHIRE trial.\textsuperscript{27} Moreover, elderly patients >85 years of age are at increased risk for death or perioperative complications of stroke, death and MI, as shown in a retrospective cohort study of 4149 patients\textsuperscript{38}.

**Conclusion**

The high prevalence and asymptomatic nature of perioperative myocardial ischaemia, combined with a substantial influence on postoperative mortality of vascular surgery patients, justify the classification of this entity as a ‘silent killer’. All the aforementioned data underline the importance of early detection and adequate management of perioperative myocardial damage in vascular patients. The selection of the most appropriate cardiac risk index and the identification of the cardiovascular risk for each individual patient are crucial for the preoperative assessment in order to not underestimate the risk for presenting adverse cardiac events postoperatively. In this way complications and deaths could be minimised significantly. Moreover, early initiation of medical therapy to reduce possible cardiovascular risks, and the selection of ideal surgical and anaesthesiological techniques are strongly indicated to achieve optimal results.

**Abbreviations list**

AAA, abdominal aortic aneurysm; ACC, American College of Cardiology; AHA, American Heart Association; CAD, coronary artery disease; CAS, carotid angioplasty and stenting; CEA, carotid endarterectomy; CK-MB, creatine kinase-MB; cTnl cardiac troponin I; EVAR, endovascular aneurysm repair; MI, myocardial infarction; RCRI, revised cardiac risk index; SAPPHIRE, Stenting and Angioplasty in Patients with Protection in Patients at High Risk for Endarterectomy; VSG-CRI, Vascular Study Group of New England–Cardiac Risk Index.

**References**