Perioperative Cardiac Damage in Vascular Surgery Patients

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Abstract  Background: Patients undergoing vascular surgery are at increased risk for developing cardiac complications. Majority of patients with perioperative myocardial damage are asymptomatic. Our objective is to review the available literature addressing the prevalence and prognostic implications of perioperative myocardial damage in vascular surgery patients. Methods: An Internet-based literature search was performed using MEDLINE to identify all published reports on perioperative myocardial damage in vascular surgery patients. Only those studies published from 2000 to 2010 evaluating myocardial damage using troponin I or T, with or without symptoms of angina pectoris were included. Results: Thirteen studies evaluating the prevalence of perioperative myocardial ischaemia or infarction were included in the study. The incidence of perioperative myocardial ischaemia ranged from 14% to 47% and the incidence of perioperative myocardial infarction ranged from 1% to 26%. In addition, 10 studies evaluating the prognostic value of perioperative myocardial ischaemia towards postoperative mortality or the occurrence of major adverse cardiac events were included. In the retrieved studies, hazard ratios varied from 1.9 to 9.0. Conclusion: The high prevalence and asymptomatic nature of perioperative myocardial damage, combined with a substantial influence on postoperative mortality of vascular surgery patients, underline the importance of early detection and adequate management of perioperative myocardial damage.

This article provides an extended overview regarding the prevalence and prognostic value of perioperative myocardial ischaemia and infarction in vascular surgery patients. In addition, treatment options to reduce the risk of perioperative myocardial damage are provided based on the current available literature.

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Introduction

In the present article, an extended overview is provided regarding the prevalence and prognostic value of perioperative myocardial ischemia and infarction in vascular surgery patients. In addition, treatment options in order to reduce the risk of perioperative myocardial damage are provided based on the current available literature.

Perioperative myocardial damage: ischaemia and infarction

The heart is an organ with a high metabolic demand, even at rest, and requires a continuous high level of oxygen supply to the myocardium. 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 increase of 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 myocardial infarction (MI).

In general, myocardial damage can be subdivided according to two pathological processes, described as type 1 and 2 by the universal definition of MI. Type 1 MI is defined as an acute coronary syndrome that occurs when a coronary plaque ruptures, leading to thrombus formation, acute coronary thrombosis, supply ischaemia and MI. A reduction of 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 of coronary blood flow.

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. Two retrospective studies investigated the coronary pathology of fatal perioperative MI. As demonstrated in the autopsy study by Dawood et al., 55% of the fatal perioperative MIs have direct evidence of plaque disruption, defined as fissure or rupture of plaque and haemorrhages into the plaque cavity. Similar autopsy results were found in the study of Cohen and Aretz, who observed that plaque rupture was present in 46% of patients with postoperative MI.

Next to surgical stress, haemodynamic fluctuations during surgery are an important cause of perioperative myocardial damage as well. 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.

It is estimated that of the 230 million patients undergoing major surgery annually, approximately 1% (2,300,000 patients) suffer perioperative MI with a cardiovascular mortality rate around 0.3% (690,000 patients). 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. In 2005, Boersma et al. developed a model to risk stratify surgical procedures, based on the occurrence of 30-day cardiac death and MI. Surgical procedures were classified low cardiac risk (<1%), intermediate cardiac risk (1–5%) or high cardiac risk (>5%) for the development of 30-day adverse cardiac outcome. High-cardiac-risk surgery is considered to be open lower extremity revascularisation and open abdominal aortic surgery. In addition, percutaneous transluminal angioplasty, endovascular aortic aneurysm repair and carotid surgery are considered as intermediate cardiac risk because they are associated with reduced myocardial stress and the need for lower fluid administration compared with open lower extremity revascularisation and open abdominal aortic surgery.

Methods

A systematic Medline search was undertaken to identify studies addressing perioperative cardiac damage, assessed with troponin I or T, in patients undergoing elective peripheral vascular surgery published between 2000 and 2010. The keywords used were ‘cardiac troponin, vascular surgery’, ‘perioperative ischaemia, vascular surgery’, ‘cardiac ischaemia, vascular surgery’ in combination with ‘prevalence’, ‘incidence’, ‘prognostic value’, ‘long term outcome’, ‘long-term mortality’ and ‘major adverse cardiac events’. The retrieved articles were also searched for any relevant references. The current study included solely studies addressing the prognostic value of increased troponin T or I levels when using regression analyses or contingency table analyses.

Results

Vascular surgery patients are at increased risk for developing perioperative cardiac complications, especially patients undergoing open lower extremity revascularisation and open abdominal aortic surgery. In 1981, Brown et al. described that about 40% of the patients undergoing elective abdominal aortic aneurysm resection had a history of either MI or angina pectoris. In addition, Hertzer et al. performed routine coronary angiography in more than 1000 patients to detect uncorrected coronary artery disease in patients with advanced peripheral vascular disease. They found coronary artery disease to be highly present in these patients with a prevalence of severe three-vessel disease in 18% of the patients and left main disease in 4% of patients. In 1989, Oeyang et al. observed that episodes of perioperative myocardial damage in patients having peripheral vascular surgery are most often silent. Utot et al. performed routine coronary angiography in patients
undergoing abdominal aneurysm repair and demonstrated that the incidence of silent ischaemia was 20%. In addition, the authors concluded that the number of coronary risk factors and resting electrocardiograms were not worthwhile for predicting silent coronary artery disease.17

Perioperative myocardial damage is difficult to diagnose due to its silent nature. In 1994, Adams 3rd et al. demonstrated that the measurement of cardiac troponin I is a sensitive and specific method for the diagnosis of perioperative MI in vascular surgery patients.18 Hereafter, several studies have correlated serial cardiac troponin measurements with continuous 12-lead ST-segment analysis after major vascular surgery.19 Troponin elevations occurred after prolonged, transient, postoperative ST-segment depression, and peak troponin elevations correlated with the duration of ST depression.20 Landesberg et al. demonstrated that 85% of postoperative cardiac complications were preceded by prolonged ST-segment depression.21 In addition, Fleisher et al. found that 78% of patients with cardiac complications had at least one episode of prolonged myocardial ischaemia (i.e., >30 min) either before or during the cardiac event.22 The hypothesis that ST-depression can lead to perioperative MI is further supported by increased troponin T levels during or shortly after prolonged ST-depression ischaemia.23 Episodes of perioperative ST-depression, indicating endocardial (non-transmural) myocardial ischaemia, has been described in up to 41% of vascular surgery patients and mostly occur within the first 2 days after surgery.24 ST-elevation-type ischaemia is considered relatively uncommon, confirmed by the incidence (12%) of intra-operative ST-elevation in a study performed by London et al.25 Recent studies using highly sensitive troponin essays demonstrated that low-level (>0.03 ng ml⁻¹) troponin elevations postoperatively are common in high-cardiac-risk patients, even with little or no evidence of ischaemia with electrocardiogram monitoring.26

In the current study, we performed a systematic Medline search to evaluate the prevalence of myocardial ischaemia or infarction in vascular surgery patients detected with troponin I or T measurement whether or not in combination with electrocardiogram changes or symptoms of angina pectoris. As demonstrated in Table 1, the incidence of perioperative myocardial ischaemia ranged from 14% to 47% and that of perioperative MI ranged from 1% to 26%. The wide range of incidence might be related to (1) different cut-off values of troponin I or T used in the study, (2) a variety of vascular procedures included in the studies and (3) that patient-specific cardiac risk factors differed between the studies. For example, in the study performed by Ali et al. the highest incidence of perioperative myocardial damage was found (both ischaemia and infarction), probably related to the fact that this study only included patients undergoing open abdominal aortic repair. In addition, Schouten et al. included only included patients with three or more cardiac risk factors (age >70 years, angina pectoris, MI, congestive heart failure, stroke, renal dysfunction and diabetes mellitus). In the study performed by Abraham et al., about 75% of the patients underwent endovascular abdominal aortic aneurysm repair and patients with increased cardiac troponin T in combination with a significant postoperative increase in serum creatinine (>50%) were excluded from the study. Importantly, Abraham et al. report the highest incidence of perioperative myocardial damage within the first 3 days after surgery.27

Prognosis after perioperative myocardial damage

In order to put the significance of perioperative myocardial damage into perspective, it is pivotal to address the influence of perioperative myocardial damage on long-term postoperative outcome. Multiple studies have been performed over the years to evaluate this issue. In 1982, Jamieson et al. were among the first to describe the influence of ischaemic heart disease on early and late mortality after surgery for peripheral occlusive vascular disease. The authors concluded that coronary artery disease is a major determinant of both early and late mortality after arterial reconstruction and that selective myocardial revascularisation may improve survival of these patients.28 Because perioperative myocardial damage is most often silent, the great majority of patients (95%) with perioperative myocardial damage remain untreated. This might contribute to an increased risk of long-term cardiovascular mortality as well.16,29,30

From 2000 to 2010, perioperative myocardial damage, defined as postoperative troponin elevations whether or not in combination with ST-segment alterations, has been related to adverse short-, mid- and long-term cardiovascular morbidity and mortality as well in multiple studies, outlined in Table 2.20,27,31–38 In the current study, hazard ratios describing the prognostic value of troponin T or I towards postoperative mortality or the occurrence of major adverse cardiac events varied from 1.9 to 9.0.

In patients undergoing vascular surgery, asymptomatic elevated troponin T levels were associated with an increased risk, of more than four- to six-fold, for cardiac events during a 6-month follow-up period, as demonstrated by Kim et al.39 Landesberg et al. and Kertai et al. studied the prognostic value of low- and intermediate-to-high cut-off levels of troponin T elevations on long-term mortality after vascular surgery. These studies demonstrated that postoperative troponin elevations even at low cut-off levels are independent and complementary predictors of long-term mortality.20,37 In addition, early mortality after perioperative MI ranges between 3.5% and 25% and is higher in patients with an intermediate- to high-level troponin elevation, compared with patients with a low-level troponin elevation.20,32,34

Endovascular surgery is associated with a reduced incidence of perioperative myocardial damage, compared with open vascular surgery, possibly explained by reduced myocardial stress during endovascular procedures.13 However, Winkel et al. recently demonstrated that asymptomatic perioperative myocardial damage, defined as cardiac troponin T elevations in the absence of ischaemic symptoms or electrocardiogram abnormalities, was associated with an increased mortality risk of patients undergoing endovascular abdominal aortic aneurysm repair.40 During a 2.9-year follow-up of 220 patients, they found that patients with asymptomatic myocardial damage had a mortality rate of 49%, compared with 15% for patients without perioperative myocardial damage (P < 0.001).
Discussion

Prevention of perioperative myocardial damage

In general, the management of perioperative myocardial damage is focussed on (1) coronary plaque stabilisation to reduce acute coronary syndromes, with subsequent supply ischaemia (type I MI), that occurs when a coronary plaque ruptures and (2) limiting surgical stress, which is the cause of sustained myocardial oxygen supply—demand imbalance (type 2 MI). The high incidence of perioperative myocardial damage reflects the high prevalence of underlying ischaemic heart disease in the vascular surgery population. Therefore, adequate preoperative evaluation is inevitable to: (1) identify patients at increased cardiac risk, (2) initiate risk reduction therapy and (3) select optimal surgical and anaesthesia techniques. In conventional preoperative cardiac risk indices (Revised Cardiac Risk index and Adapted Lee index), age, heart failure, ischaemic heart disease, cerebrovascular disease, renal dysfunction, diabetes mellitus and high-risk surgery (such as vascular surgery) have been identified as independent predictors of perioperative cardiovascular events.

Pharmacological treatment

The unpredictable progression of an unstable coronary plaque during surgical stress is the most important target for systemic pharmacological therapy to reduce the incidence of perioperative myocardial damage.

In the non-surgical setting, β-blockers are widely used for the prevention and treatment of ischaemic heart disease and heart failure, all major determinants of adverse postoperative outcome. Proposed mechanisms by which β-blockers exert intra-operative cardioprotective effects include heart rate control, reduction of systolic pressure and ventricular contractile force and its anti-arrhythmic properties. In the long term, β-blockers reduce mechanical stress imposed on coronary plaques preventing plaque rupture. In addition, the anti-inflammatory properties of β-blockers exert a beneficial effect towards coronary plaque stabilisation as well. In addition, β-blockers are known to reduce the process of adverse cardiac remodeling in patients with impaired left ventricular function, which is highly prevalent in the vascular surgery population, by inhibiting the sympathetic nervous system and hormone activation (A-type and B-type natriuretic peptides and norepinephrine).

In the most recent European Society of Cardiology (ESC) guidelines, β-blockers are recommended (Class I, Level of evidence B) in patients scheduled for high-risk surgery. In addition, β-blockers should be considered (Class IIa, level of evidence B) in patients undergoing intermediate-risk surgery, such as percutaneous transluminal angioplasty, endovascular aortic aneurysm repair and carotid surgery. Factors that influence the effectiveness of perioperative β-blockers treatment are the patients with underlying...
cardiac risk factors and variations in treatment protocols, such as β-blocker type, β-blocker dose and timing of β-blocker initiation before surgery. As recommended in the ESC guidelines, β-blocker treatment should be initiated optimally between 30 days and at least 1 week before surgery with a target heart rate between 60 and 70 beats per minute and systolic blood pressure >100 mmHG.

**Statins**

Statins are widely used to decrease low-density lipoprotein cholesterol in patients. Furthermore, statins seem to stabilise atherosclerotic plaques during surgery through pleiotropic effects and therefore have a beneficial influence on cardiovascular outcome. Multiple studies have not only shown beneficial effects of statins in patients with coronary artery disease, but in patients undergoing vascular surgery as well. In the most recent ESC guidelines, initiation of statins is recommended in patients undergoing high-risk surgery, optimally between 30 days and at least 1 week before surgery (Class I, Level of evidence B).

**Anti-platelet agents**

The perioperative surgical stress results in a hypercoagulable state, which is in combination with atherosclerotic plaques, the perfect substrate for the development of perioperative cardiac damage. Anti-platelet drugs are established agents in the prevention of cardiovascular and cerebrovascular ischaemic events. Treatment with aspirin or clopidogrel is recommended in patients with stable coronary artery disease to prevent cardiovascular events.

Aspirin irreversibly blocks platelet cyclo-oxygenase-1 known to decrease the tromboxane-A2 synthesis. Therefore aspirin reduces platelet activation and vasoconstriction. Aspirin reduces the risk of non-fatal MI by 34% and, in the setting of secondary prevention, reduces cardiovascular events by 27% and cardiovascular deaths by 18%. The most recent ESC guidelines addressing perioperative care state that continuation of aspirin should be considered in the perioperative period of patients previously treated with aspirin (Class IIa, level of evidence B). The thienopyridine derivative clopidogrel is an anti-platelet agent that inhibits the adenosine diphosphate-mediated platelet aggregation. Randomised controlled studies are needed to investigate the role of clopidogrel as a preventive treatment in patients with asymptomatic cardiac damage.

**Prophylactic revascularisation**

Preoperative cardiac risk evaluation by means of risk factor assessment and non-invasive testing may identify vascular surgery patients with asymptomatic coronary artery disease. Two randomised, controlled trials have evaluated the potential benefit that may be expected from preoperative revascularisation in these patients. The Coronary Artery Revascularisation Prophylaxis (CARP) trial randomised 510 patients with significant coronary artery stenosis to receive either revascularisation or no revascularisation prior to vascular surgery. The main finding of the CARP trial were obtained. Although the study population in the DECREASE-V trial reflected vascular surgery patients at
highest cardiac risk, revascularisation did not improve cardiovascular outcomes. The incidence of the composite endpoint of 30-day cardiovascular mortality and MI was 43% versus 33% (odds ratio (OR) 1.4, 95% CI: 0.7–2.8). Furthermore, no benefit was observed during 1-year follow-up after coronary revascularisation (49 vs. 44%; OR 1.2, 95% CI: 0.7–2.3; P = 0.48). The results from these trials indicate that prophylactic coronary revascularisation of cardiac-stable patients provides no benefit for postoperative outcome, with an exception for patients with left main coronary artery stenosis. The reasoning behind this apparent lack of benefit could be related to the fact that perioperative myocardial damage is not only caused by a significant blood-flow-limiting coronary artery stenosis (Type 1 MI). The perioperative stress response (evoking type 2 MI) may cause non-flow-limiting coronary plaques to rupture during surgery and to become flow limiting after all. This may explain why surgical or percutaneous treatment of flow-limiting coronary plaques apparently provides insufficient extra protection in addition to pharmacological treatment. In the most recent ESC guidelines addressing insufficient extra protection in addition to pharmacological treatment, it is only recommended to consider prophylactic revascularisation in patients undergoing high-risk surgery, such as lower extremity revascularisation or open abdominal aortic surgery, with proven ischaemic heart disease (Class IIb, level of evidence B).42

Future perspective: is there a role for remote ischemic preconditioning?

Because prophylactic coronary revascularisation had not proven to be successful, there remains a need for alternative strategies to protect the myocardium during vascular surgery. Research performed by Przyklenk et al. in a canine heart models demonstrated that brief occlusions of a coronary artery may protect the myocardial bed supplied by that coronary artery from prolonged ischemia.56 In addition, Gho et al. demonstrated that brief ischemia in “remote” organs (i.e. after occlusion of the anterior mesenteric artery or left renal artery) protects the myocardium against infarction as effectively as myocardial preconditioning, described by Przyklenk et al.57 Therefore, brief ischemia followed by reperfusion in one organ may provide systemic protection from prolonged ischemia in another organ. In the patients undergoing abdominal aneurysm repair remote ischemic preconditioning has been evaluated as well. Ali et al. included eighty-two patients which were randomized to conventional abdominal aortic aneurysm repair (control) and abdominal aortic aneurysm repair with remote ischemic preconditioning.58 Two cycles of intermittent cross clamping of the common iliac artery with 10 minutes ischemia followed by 10 minutes reperfusion served as the remote ischemic preconditioning stimulus. The authors found that remote ischemic preconditioning reduced the incidence of postoperative myocardial injury, MI, and renal impairment. In addition, in a small pilot study, Walsh et al. demonstrated that remote ischemic preconditioning reduced urinary biomarkers of renal injury in patients undergoing elective endovascular abdominal aneurysm repair.59 However, the authors point out that future large scale trials are needed to determine the effect of remote ischemic preconditioning on the occurrence of major adverse cardiac events.

Conclusion

The high prevalence and asymptomatic nature of perioperative myocardial damage, combined with a substantial influence on postoperative mortality of vascular surgery patients, underlines the importance of early detection and adequate management of perioperative myocardial damage. With the use of preoperative cardiac risk indices, high-cardiac-risk patients at risk for developing perioperative myocardial damage during vascular surgery can be unveiled. Routine assessment of perioperative cardiac troponin levels and/or continuous electrocardiogram monitoring can detect perioperative myocardial damage in patients at risk. In order to reduce the risk of developing perioperative myocardial damage, pharmacological treatment with β-blockers, statins and aspirin has demonstrated to exert beneficial effects. In addition, prophylactic coronary revascularisation does not seem to provide sufficient extra protection in addition to pharmacological treatment. Future randomised, controlled trials are needed to evaluate if remote ischaemic preconditioning or treatment with clpoidogrel may serve as novel preventive treatment strategies to reduce asymptomatic myocardial damage during vascular surgery.

Conflict of Interest/Funding

None

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42 Winkel TA, Schouten O, van Kuijik JP, Verhagen HJ, Bax JJ, Poldermans D. Perioperative asymptomatic cardiac damage


