Analysis of Risk Factors for Myocardial Infarction and Cardiac Mortality after Major Vascular Surgery

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Background: Patients undergoing vascular surgical procedures are at high risk for perioperative myocardial infarction (PMI). This study was undertaken to identify predictors of PMI and in-hospital death in major vascular surgical patients.

Methods: From the Vascular Surgery Registry (6,948 operations from January 1989 through June 1997) the authors identified 107 patients in whom PMI developed during the same hospital stay. Case-control patients (patients without PMI) were matched at a 1×:1 ratio with index cases according to the type of surgery, gender, patient age, and year of surgery. The authors analyzed data regarding preoperative cardiac disease and surgical and anesthetic factors to study association with PMI and cardiac death.

Results: By using univariable analysis the authors identified the following predictors of PMI: valvular disease (P = 0.007), previous congestive heart failure (P = 0.04), emergency surgery (P = 0.02), general anesthesia (P = 0.03), preoperative history of coronary artery disease (P = 0.001), preoperative treatment with β-blockers (P = 0.003), lower preoperative (P = 0.03) and postoperative (P = 0.002) hemoglobin concentrations, increased bleeding rate (as assessed from increased cell salvage; P = 0.025), and lower ejection fraction (P = 0.02). Of the 107 patients with PMI, 20.6% died of cardiac cause during the same hospital stay. The following factors increased the odds ratios for cardiac death: age (P = 0.001), recent congestive heart failure (P = 0.01), type of surgery (P = 0.04), emergency surgery (P = 0.02), lower intraoperative diastolic blood pressure (P = 0.001), new intraoperative ST-T changes (P = 0.01), and increased intraoperative use of blood (P = 0.005). Patients who underwent coronary artery bypass grafting, even more than 12 months before index surgery, had a 79% reduction in risk of death if they had PMI (P = 0.01). Multivariable analysis revealed preoperative definitive diagnosis of coronary artery disease (P = 0.001) and significant valvular disease (P = 0.03) were associated with increased risk of PMI. Congestive heart failure less than 1 yr before index vascular surgery (P = 0.0002) and increased intraoperative use of blood (P = 0.007) were associated with cardiac death. The history of coronary artery bypass grafting reduced the risk of cardiac death (P = 0.04) in patients with PMI.

Conclusions: The in-hospital cardiac mortality rate is high for patients who undergo vascular surgery and experience clinically significant PMI. Stress of surgery (increased intraoperative bleeding and aortic, peripheral vascular, and emergency surgery), poor preoperative cardiac functional status (congestive heart failure, lower ejection fraction, diagnosis of coronary artery disease), and preoperative history of coronary artery bypass grafting are the factors that determine perioperative cardiac morbidity and mortality rates. (Key words: Anesthesia; cardiac death; myocardial ischemia.)

RELATIVELY higher incidence of perioperative myocardial infarction (PMI) and cardiac death in patients undergoing vascular surgery may be attributed to the high prevalence of coronary artery disease (CAD) in vascular
surgical patients and to the higher surgical stress of some vascular procedures.\textsuperscript{1–4} Aggressive medical and surgical treatments during the past 2 decades contributed to the reduction in morbidity and mortality rates in these patients. Significant perioperative cardioprotective effects can be achieved by improving myocardial blood supply by performing percutaneous transluminal angioplasty (PTCA) near the time of surgery.\textsuperscript{6} Coronary artery bypass graft (CABG) surgery also reduces the perioperative cardiac morbidity rate, because patients who undergo this procedure experience fewer complications after subsequent vascular operations.\textsuperscript{7}

Since 1978, the cardiology workup and medical clearance for vascular surgery at The Cleveland Clinic Foundation have been very aggressive, and early trends to perform coronary angiography in patients being considered for elective aortic reconstruction\textsuperscript{8} eventually were replaced with newer and less invasive tests. Currently, dobutamine stress echocardiography is the most frequently performed cardiac screening test at our institution, especially before elective aortic reconstruction or elective infringuinal revascularization. Dobutamine stress echocardiography is less expensive than other tests and has good positive (33%) and high negative (100%) predictive values for perioperative cardiac complications.\textsuperscript{9,10} Additional cardiac risk assessment and preoperative improvement of cardiac performance (medical and surgical) usually are tailored according to the findings of the initial test, the individual patient's functional capacity, and the level of surgery-specific risk.\textsuperscript{11}

The objective of the current study was to evaluate predictors for perioperative PMI and PMI-related cardiac deaths in a highly specialized referral center for patients with cardiovascular disease. We identified all patients who had myocardial infarction (MI) after major vascular surgery during the same hospital stay, as diagnosed by clinical symptoms or changes in the electrocardiogram (ECG) or serum enzyme levels, and we analyzed associations among the patient, anesthetic, and surgical risk factors for PMI by comparing data with patients who underwent the same surgical procedures but who did not experience PMI.

Materials and Methods

Vascular Surgery Registry

The Cleveland Clinic Vascular Surgery Registry is a comprehensive, prospectively recorded database describing clinical and surgical characteristics of all patients undergoing vascular surgery at the institution since 1989. We reviewed the database of surgeries performed from January 1989 through June 1997 and identified patients who had PMI during the same hospital stay. We also identified all patients who died during the same hospital stay after vascular surgery and reviewed their records for possible MI. This information was verified against the Cleveland Clinic Medical Records database for the same time period using the International Classification of Diseases codes for MI (410 - 410.9), heart failure (428.1 - 428.9), cardiogenic shock (785.51), and cardiac complications during or resulting from any surgical procedure (complications include cardiac arrest, cardiac insufficiency, and heart failure [997.1]).

Inclusion and Exclusion Criteria

We included all patients who underwent abdominal or thoracic aortic reconstructive surgery, carotid endarterectomy, or peripheral vascular surgery inclusive of lower extremity amputations (for details see the ANESTHESIOLOGY Web site at www.anesthesiology.org). Only operations performed during general or neuraxial anesthesia were included (6,948 operations). We excluded all patients who underwent minor vascular procedures (e.g., creation of arteriovenous fistula, arterial thrombectomy) performed during monitored anesthesia care or upper extremity regional blocks, patients in whom MI was developing at admission and who required emergency vascular surgery during the same hospital stay, patients with vascular complications after PTCA (i.e., brachial or inguinal hematoma or emergency thrombectomy), and patients who underwent combined CABG–carotid endarterectomy surgery.

Preoperative, Demographic, and Clinical Variables

In addition to gender, age, duration of hospital stay, and time of MI and death, we collected information regarding preoperative cardiac history and comorbid conditions: treated diabetes mellitus, previous stroke, preoperative angina (stable or unstable), preoperative definite presence of CAD (as identified by history of at least one of the following: MI, CABG, PTCA, angina, or positive electrocardiographic changes consistent with myocardial ischemia), presence of significant valvular disease, preoperative invasive treatments (CABG or PTCA), and medical treatments (aspirin, \(\beta\)-blockers, angiotensin-converting enzyme [ACE] inhibitors, calcium antagonists). Only the preoperative medications the patient was taking until the day of surgery were considered for review. History of hypertension was included as a risk factor if a diagnosis was present in the medical
patients. Fresh frozen plasma, platelets, albumin, and hydroxyethyl starch use were combined in a single category (i.e., colloid administration) and, for the purpose of analysis, combined with crystalloid use. Intraoperative hemodynamic variables also were recorded: lowest and highest systolic and diastolic blood pressures, highest heart rate, and duration of these hemodynamic end points (these parameters were obtained from the handwritten anesthesia record; recording interval was 5 min). Intraoperative hemodynamic variables and their potential effects on PMI were analyzed only for MIIs that occurred during postoperative days 0 and 1 (n = 80). The rationale for this last analysis was to establish whether PMI that occurred during or shortly after surgery could be associated with extremes of intraoperative hemodynamics. By the same token, if the PMI occurred beyond the first 48 h after surgery, causes other than unfavorable intraoperative hemodynamics must be suspected (such as pain-induced catecholamine release or fluid shifts). Duration and urgency of surgery also were recorded.

**Intraoperative Monitoring**

All patients underwent standard intraoperative monitoring, which consisted of five-lead electrocardiography with ST-segment trend analysis (leads II and V5), pulse oximetry, and noninvasive and invasive blood pressure measurements. A pulmonary artery catheter was used, depending on the type of surgical procedure: In the aortic surgery group, only one patient in the index group and five patients in the control group were not monitored with use of pulmonary artery catheters.

**Criteria for Diagnosis of Myocardial Infarction**

The confirmation of MI was based on the presence of at least one of the following criteria: an elevated total CPK concentration and a ratio of CPK-MB isoenzyme to total CPK of 5% or greater; electrocardiography changes consistent with MI (new Q waves or ST-segment changes); and postoperative physician notes indicating a diagnosis of MI. Intraoperative records and postoperative notes were reviewed by two staff anesthesiologists, an anesthesia resident, student nurse anesthetists, and senior medical students, all supervised by staff anesthesiologists.

**Perioperative Myocardial Infarction Surveillance**

In all patients undergoing aortic reconstructive surgery in our institution three sets of cardiac enzymes are checked postoperatively. In other vascular surgery pa-
tients, cardiac enzyme testing is performed during cer-
tain perioperative circumstances (new ECG changes, intraoperative hypotension or tachycardia, or other signs or symptoms that may indicate that the patient experi-
enced an adverse cardiac event). One hundred patients in
the PMI group had enzymatic confirmation of MI. In the
remaining seven patients the diagnosis of MI was
established without enzymatic confirmation and was
based on electrocardiographic changes consistent with
MI (in all seven) and autopsy confirmation (in five of
seven). Sixty-five patients in the control group under-
went postoperative cardiac enzyme measurements, and
all analyses were negative for MI. All our patients under-
went preoperative and postoperative electrocardiogra-
phy. Furthermore, no patient in the control group showed
electrocardiographic or clinical evidence of MI (absence of
such a note in the medical record). Several patients were
excluded from the index group because of sustained car-
diac arrest (sudden intraoperative dysrhythmia) that might
have been caused by MI; however, the ECG showed no
evidence that PMI was the cause of death.

Analysis of Myocardial Infarction Timing and
Mortality Rate after Perioperative Myocardial
Infarction
Cardiac death was defined as death as a result of
dysrhythmia, congestive heart failure (CHF), cardiogenic
shock, or multisystem organ failure that occurred after
MI. The timing of MI or cardiac death in relation to
surgery was considered to be postoperative day 0 if it
occurred 0–24 h after surgery, postoperative day 1 if it
occurred between 25 and 48 h after surgery, postopera-
tive day 2 if it occurred 49–72 h after surgery, and so
forth. After MI occurred, we also noted the use of either
vasopressor or intraaortic balloon pump support to
maintain hemodynamic stability. We also analyzed the
predictive value of cardiopulmonary resuscitation as an
indicator of adverse outcome; only cardiopulmonary re-
suscitation performed shortly after PMI was considered.

Identification of Case-Control Patients
To identify the risk factors for PMI, we compared
patients in whom MI developed (index group) with
patients in whom MI did not occur (control group). The
control group was selected from the Vascular Surgery
Registry by random 1×:×1 computer matching to the
index group according to age (within 5 yr), gender, type
of surgery, and year of surgery.

Statistical Analysis
Two primary analyses were conducted: identification
of risk factors for PMI (case-control patients vs. PMI
patients) and analysis of predictors of mortality (patients
who died vs. those who survived MI).

Univariable Analyses. For categorical variables, poten-
tial univariable predictors of MI were identified using
the McNemar test. Potential univariable predictors of
cardiac death among PMI patients were identified using
chi-square analysis, the Fisher exact test, or the Mantel-
Haenszel chi-square test (for ordinal data) as appropriate.
All categorical variables were summarized as counts and
percentages. Results for categorical variables were sum-
morized by the P value, odds ratio (OR), and 95% confi-
dence interval (CI) for the OR. Such values were calcu-
lated using exact methods if appropriate. For continuous
variables, univariable logistic regression models were
developed to assess the association between each poten-
tial predictor and perioperative death. To assess the
association of these predictors with MI, conditional lo-
gistic regression modeling for case-control matching
was used. Continuous variables were summarized by the
mean and standard deviation or by the median and in-
terquartile range. A significance level of P < 0.05 was
used for all analyses.

Multivariable Analyses. The associations between
combinations of explanatory variables and the odds of
perioperative death were analyzed with use of multiple
logistic regression. Forward stepwise model selection
was used to find a set of predictors that could be used
simultaneously to predict death. A significance level of
0.05 was used as the inclusion criterion in the stepwise
procedure. For PMI, the same analysis was used, but
with conditional multiple logistic regression, adjusting
for the case-control pairing.

All analyses were performed using either SAS soft-
ware (version 6.12; SAS Institute, Cary, NC) or S-PLUS soft-
ware (version 3.4; MathSoft, Seattle, WA).

Results
We identified 107 patients with PMI during their same
hospital stays after vascular surgery; 22 died (20.6%). In
the control group, four patients (3.7%) died, all from
noncardiac causes (for details see the ANESTHESIOLOGY
Web site at www.anesthesiology.org). The risk of death
after PMI was 10 (95% CI: 3.1–32.4) times greater than
the risk from all other noncardiac postoperative complica-
tions (P = 0.001). The overall incidence of PMI was
1.54% (107 of 6,948), and the overall post-MI mortality
VASCULAR SURGERY, PERIOPERATIVE MYOCARDIAL INFARCTION, CARDIAC DEATH

Table 1. Univariable Analysis of Association of Coexisting Disease with Perioperative Myocardial Infarction

<table>
<thead>
<tr>
<th>Coexisting disease</th>
<th>Control Group n (%)</th>
<th>PMI Group n (%)</th>
<th>OR (95% CI)</th>
<th>P* Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>35 (32.7)</td>
<td>42 (39.3)</td>
<td>1.47 (0.76, 2.82)</td>
<td>0.25</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>21 (19.6)</td>
<td>29 (27.1)</td>
<td>1.50 (0.80, 2.81)</td>
<td>0.21</td>
</tr>
<tr>
<td>Hypertension</td>
<td>84 (78.5)</td>
<td>86 (80.4)</td>
<td>1.11 (0.59, 2.10)</td>
<td>0.75</td>
</tr>
<tr>
<td>Poorly controlled hypertension†</td>
<td>26 (25)</td>
<td>28 (27)</td>
<td>0.95 (0.51, 1.76)</td>
<td>0.87</td>
</tr>
<tr>
<td>Valvular disease</td>
<td>24 (23.1)</td>
<td>43 (41.4)</td>
<td>2.25 (1.26, 4.09)</td>
<td>0.007</td>
</tr>
<tr>
<td>Preoperative ECG: Dysrhythmias</td>
<td>29 (27.1)</td>
<td>25 (23.4)</td>
<td>0.79 (0.40, 1.55)</td>
<td>0.49</td>
</tr>
<tr>
<td>Preoperative definite CAD</td>
<td>64 (59.8)</td>
<td>91 (85.0)</td>
<td>3.47 (1.84, 6.49)</td>
<td>0.001</td>
</tr>
<tr>
<td>Preoperative ECG: Ischemic changes</td>
<td>41 (38.7)</td>
<td>47 (44.3)</td>
<td>1.27 (0.73, 2.22)</td>
<td>0.40</td>
</tr>
<tr>
<td>Preoperative angina</td>
<td>17 (15.9)</td>
<td>27 (25.2)</td>
<td>1.83 (0.92, 3.67)</td>
<td>0.09</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>41 (38.3)</td>
<td>49 (45.8)</td>
<td>1.30 (0.79, 2.14)</td>
<td>0.31</td>
</tr>
<tr>
<td>History of congestive heart failure</td>
<td>18 (16.8)</td>
<td>30 (28.0)</td>
<td>2.09 (1.04, 4.22)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

*P* values are from the McNemar test; all odds ratios (OR) represent the perioperative myocardial infarction (PMI) group (control group is reference with OR 1.0).
†Poorly controlled hypertension (for details, see Methods).
Cl = confidence interval; ECG = electrocardiogram; CAD = coronary artery disease.

The median duration of hospital stay was 13 days (interquartile range: 8-17) for survivors of PMI and 8 days (interquartile range: 5-10) for control patients who survived. The median period between surgery and cardiac death was 3 days (interquartile range: 1 to 24). Demographic, clinical, surgical, anesthetic, and laboratory characteristics of PMI and control patients are summarized in tables 1-7 (univariable analysis). Table 8 summarizes risk factors for PMI and cardiac death (multivariable analysis).

Risk Factors for Myocardial Infarction

The following factors were associated significantly \((P < 0.05\) for all) with a greater risk of PMI: valvular disease, previous CHF, emergency surgery, general anesthesia, preoperative diagnosis of CAD, lower preoperative and postoperative hemoglobin concentrations, and increased intraoperative bleeding as judged by the amount of cell-salvaged blood (tables 1-3). The risk of PMI increased with decrease in preoperative ejection fraction: For each decrease in ejection fraction for one category (see Materials and Methods), the risk of PMI increased by 39% \((\text{OR} = 0.61, 95\% \text{ CI}: 0.40-0.91; P = \text{0.04)}\).
Table 3. Univariable Analysis of Association of Surgical (Duration of Surgery, Fluid Balance), Anesthetic (Intraoperative Hemodynamics), and Laboratory Characteristics with Perioperative Myocardial Infarction

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control Group (mean ± SD)</th>
<th>PMI Group (mean ± SD)</th>
<th>OR (95% CI)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of surgery (hr)</td>
<td>6.95 ± 2.5</td>
<td>6.93 ± 2.8</td>
<td>1.00 (0.89, 1.12)</td>
<td>0.96</td>
</tr>
<tr>
<td>Intraoperative fluid balance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estimated blood loss (l)††‡</td>
<td>1.08 ± 1.64</td>
<td>1.19 ± 1.56</td>
<td>1.04 (0.92, 1.18)</td>
<td>0.53</td>
</tr>
<tr>
<td>Cell-salvaged blood (l)††‡</td>
<td>0.23 ± 0.56</td>
<td>1.32 ± 2.79</td>
<td>1.70 (1.07, 2.72)</td>
<td>0.025</td>
</tr>
<tr>
<td>Blood given (units)§</td>
<td>1.2 ± 3.9</td>
<td>1.8 ± 3.5</td>
<td>1.08 (0.98, 1.25)</td>
<td>0.18</td>
</tr>
<tr>
<td>Crystalloid and colloid given (l)†</td>
<td>5.0 ± 3.4</td>
<td>5.0 ± 3.8</td>
<td>1.00 (0.94, 1.06)</td>
<td>0.98</td>
</tr>
<tr>
<td>Intraoperative hemodynamics∥</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lowest SBP (mmHg)†</td>
<td>50.3 ± 11.1</td>
<td>52.2 ± 12.6</td>
<td>1.11 (0.97, 1.15)</td>
<td>0.20</td>
</tr>
<tr>
<td>Lowest DBP (mmHg)†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of lowest SBP (min)†</td>
<td>7.9 ± 6.0</td>
<td>7.1 ± 4.9</td>
<td>0.89 (0.68, 1.15)</td>
<td>0.36</td>
</tr>
<tr>
<td>Maximal heart rate (beats/min)‡</td>
<td>91 ± 15</td>
<td>91 ± 16</td>
<td>1.02 (0.92, 1.13)</td>
<td>0.73</td>
</tr>
<tr>
<td>Highest SBP (mmHg)∥</td>
<td>174 ± 22</td>
<td>179 ± 25</td>
<td>1.04 (0.99, 1.11)</td>
<td>0.20</td>
</tr>
<tr>
<td>Highest DBP (mmHg)∥</td>
<td>82 ± 13</td>
<td>79 ± 16</td>
<td>0.92 (0.82, 1.02)</td>
<td>0.13</td>
</tr>
<tr>
<td>Laboratory parameters</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative hemoglobin (g/dl)</td>
<td>13.3 ± 3.1</td>
<td>12.5 ± 1.8</td>
<td>0.82 (0.69, 0.96)</td>
<td>0.03</td>
</tr>
<tr>
<td>Postoperative hemoglobin (g/dl)</td>
<td>11.3 ± 2.3</td>
<td>10.3 ± 2.0</td>
<td>0.76 (0.64, 0.90)</td>
<td>0.002</td>
</tr>
<tr>
<td>Preoperative creatinine (mg/dl)</td>
<td>1.29 ± 0.8</td>
<td>1.35 ± 0.5</td>
<td>1.14 (0.77, 1.82)</td>
<td>0.52</td>
</tr>
</tbody>
</table>

* P values are from univariable logistic regression analysis. All odds ratios (OR) represent the perioperative myocardial infarction (PMI) group (control group is reference with OR 1.0). ORs are expressed in terms of 1 unit increase, unless otherwise noted (e.g., the odds of having an MI for patients with preoperative hemoglobin of 13.3 g/dl are estimated to be 18% less than the odds of having an MI for patients with hemoglobin level of 12.5 g/dl).
† ORs expressed as a result of a variable change of 500 ml or 5 units (beats per minute [bpm], min, mmHg).
‡ This analysis is performed only for patients who underwent aortic reconstructive surgery (n = 37).
§ Includes allogeneic and cell-salvaged blood (data for the entire group, n = 107).
∥ Includes invasive monitoring (data for the entire group, n = 107).
CI = confidence interval; SBP = systolic blood pressure; DBP = diastolic blood pressure; MI = myocardial infarction.

0.02). Hypertension, even uncontrolled, and previous MI were not predictors for PMI. Invasive hemodynamic monitoring did not reduce the risk of PMI (table 2). Surprisingly, patients receiving β-blockers were more likely to experience PMI (P = 0.003).

Table 4. Univariable Analysis of the Association between Preoperative Coexisting Disease and In-hospital Cardiac Mortality

<table>
<thead>
<tr>
<th>Coexisting Disease</th>
<th>Patients with PMI (n)</th>
<th>In-hospital Death n (%)</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>42</td>
<td>10 (23.8)</td>
<td>1.38 (0.54, 3.56)</td>
<td>0.50</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>29</td>
<td>7 (24.1)</td>
<td>1.34 (0.48, 3.71)</td>
<td>0.58</td>
</tr>
<tr>
<td>Hypertension</td>
<td>86</td>
<td>17 (19.8)</td>
<td>0.79 (0.23, 3.15)</td>
<td>0.76†</td>
</tr>
<tr>
<td>Poorly controlled hypertension‡</td>
<td>26</td>
<td>5 (19)</td>
<td>0.85 (0.28, 2.60)</td>
<td>0.78</td>
</tr>
<tr>
<td>Valvular disease</td>
<td>43</td>
<td>11 (25.6)</td>
<td>1.56 (0.61, 4.03)</td>
<td>0.35</td>
</tr>
<tr>
<td>Preoperative ECG: Dysrhythmias</td>
<td>25</td>
<td>5 (20.0)</td>
<td>0.96 (0.31, 2.92)</td>
<td>0.94</td>
</tr>
<tr>
<td>Preoperative definite CAD</td>
<td>91</td>
<td>18 (19.8)</td>
<td>1.74 (0.19, 3.53)</td>
<td>0.74‡</td>
</tr>
<tr>
<td>Preoperative ECG: Ischemic changes</td>
<td>51</td>
<td>11 (21.6)</td>
<td>1.13 (0.44, 2.87)</td>
<td>0.81</td>
</tr>
<tr>
<td>Preoperative angina</td>
<td>27</td>
<td>5 (18.5)</td>
<td>0.84 (0.28, 2.55)</td>
<td>0.76</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>49</td>
<td>8 (16.3)</td>
<td>0.61 (0.23, 1.61)</td>
<td>0.32</td>
</tr>
<tr>
<td>History of congestive heart failure§</td>
<td>30</td>
<td>11 (36.7)</td>
<td>3.47 (1.31, 9.25)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

* P values are from chi-square tests, except † Fisher exact test.
‡ Poorly controlled hypertension (for details, see Methods).
§ If CHF was present at surgery, the odds ratio for death was 12.0 (P = 0.008), and if the patient had history of CHF more than 12 months before index surgery, the odds ratio for mortality was 1.4 (P = 0.70).
PMI = perioperative myocardial infarction; CI = confidence interval; ECG = electrocardiogram; CAD = coronary artery disease; CHF = congestive heart failure.

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Table 5. Univariable Analysis of the Association between Preoperative Treatments and In-hospital Cardiac Mortality

<table>
<thead>
<tr>
<th>Preoperative Medications or Other Therapies</th>
<th>Patients with PMI (n)</th>
<th>In-hospital Death n (%)</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>38</td>
<td>9 (23.7)</td>
<td>1.34 (0.51, 3.50)</td>
<td>0.55</td>
</tr>
<tr>
<td>β-Blockers</td>
<td>39</td>
<td>5 (12.8)</td>
<td>0.44 (0.15, 1.31)</td>
<td>0.13</td>
</tr>
<tr>
<td>Calcium antagonists</td>
<td>25</td>
<td>3 (12.0)</td>
<td>0.45 (0.12, 1.68)</td>
<td>0.23</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>25</td>
<td>3 (12.0)</td>
<td>0.45 (0.12, 1.68)</td>
<td>0.23</td>
</tr>
<tr>
<td>Previous PTCA</td>
<td>12</td>
<td>1 (8.3)</td>
<td>0.32 (0.01, 2.47)</td>
<td>0.45†</td>
</tr>
</tbody>
</table>

* P values are from chi-square tests, except † Fisher exact test.

PMI = perioperative myocardial infarction; CI = confidence interval; ACE = angiotensin converting enzyme; CABG = coronary artery bypass grafting; PTCA = percutaneous transluminal coronary angioplasty.

Table 6. Univariable Analysis of the Association between Surgical and Anesthetic Features and In-hospital Cardiac Mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total PMI (n)</th>
<th>In-hospital Death n (%)</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery type</td>
<td></td>
<td></td>
<td></td>
<td>0.04*</td>
</tr>
<tr>
<td>Carotid endarterectomy</td>
<td>34</td>
<td>2 (5.9)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Aortic reconstructive surgery</td>
<td>37</td>
<td>10 (27.0)</td>
<td>5.93 (1.19, 29.4)</td>
<td></td>
</tr>
<tr>
<td>Peripheral vascular surgery</td>
<td>36</td>
<td>10 (27.8)</td>
<td>6.15 (1.24, 30.6)</td>
<td></td>
</tr>
<tr>
<td>Surgery urgency status</td>
<td></td>
<td></td>
<td></td>
<td>0.02†</td>
</tr>
<tr>
<td>Elective</td>
<td>95</td>
<td>16 (16.8)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Emergency</td>
<td>12</td>
<td>6 (50.0)</td>
<td>4.94 (1.14, 20.8)</td>
<td></td>
</tr>
<tr>
<td>Anesthesia type</td>
<td></td>
<td></td>
<td></td>
<td>0.22†</td>
</tr>
<tr>
<td>General</td>
<td>88</td>
<td>16 (18.2)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Regional</td>
<td>19</td>
<td>6 (31.6)</td>
<td>2.08 (0.56, 6.98)</td>
<td></td>
</tr>
<tr>
<td>Intraoperative ST-T changes</td>
<td></td>
<td></td>
<td></td>
<td>0.01†</td>
</tr>
<tr>
<td>No</td>
<td>88</td>
<td>14 (15.9)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>18</td>
<td>8 (44.4)</td>
<td>4.23 (1.20, 14.2)</td>
<td></td>
</tr>
<tr>
<td>Monitoring with pulmonary artery catheter</td>
<td></td>
<td></td>
<td></td>
<td>0.42*</td>
</tr>
<tr>
<td>No</td>
<td>71</td>
<td>13 (18.3)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>36</td>
<td>9 (25.0)</td>
<td>1.49 (0.57, 3.90)</td>
<td></td>
</tr>
<tr>
<td>POD when PMI and death occurred</td>
<td></td>
<td></td>
<td></td>
<td>0.03‡</td>
</tr>
<tr>
<td>POD 0</td>
<td>25</td>
<td>9 (36.0)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>POD 1</td>
<td>55</td>
<td>10 (18.2)</td>
<td>0.40 (0.14, 1.15)</td>
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</tr>
<tr>
<td>POD ≥ 2</td>
<td>27</td>
<td>3 (11.1)</td>
<td>0.22 (0.05, 0.95)</td>
<td></td>
</tr>
</tbody>
</table>

* P values are from * chi-square tests, † Fisher exact test, and ‡ Mantel-Haenszel chi-square test.

CI = confidence interval; PMI = perioperative myocardial infarction; POD = postoperative day.
Previous CABG significantly lowered the risk of death after PMI (27.9 vs. 7.7%; \( P = 0.01 \); table 5). Although previous PTCA did not significantly protect against death (\( P = 0.45 \)), only 1 of 12 patients with PTCA died, and the OR for cardiac death was low for patients who had PTCA (0.32). Previous CHF increased the risk of death after MI almost 3.5-fold (\( P = 0.01 \); see footnote in table 4). Decrease in ejection fraction was not a significant risk factor for cardiac death (OR = 1.42, 95% CI: 0.77–2.63; \( P = 0.26 \)). Preoperative abnormalities seen on the ECG (see Materials and Methods) did not predict MI death (\( P = 0.81 \)).

Preoperative medical therapy for hypertension or heart disease (table 5) did not decrease the risk of inhospital death after PMI, even though death tended to occur less frequently among patients who were receiving \( \beta \)-blocker or ACE inhibitor therapy (13 vs. 12%, respectively) than among those not receiving these therapies (25 vs. 23%, respectively). In contrast, death tended to occur more often in patients receiving calcium antagonists than in those not receiving calcium antagonists (27.5 vs. 14.3%, respectively; \( P = 0.09 \)).

### Surgical and Anesthetic Features as Predictors of In-hospital Cardiac Death

Patients who underwent peripheral vascular or aortic reconstructive surgery were at a greater risk of death than those who underwent carotid endarterectomy (\( P = 0.04 \); table 6). The risk for cardiac death after aortic surgery was almost sixfold higher than for carotid endarterectomy. The likelihood of cardiac death was not associated with the type of anesthesia (general vs. regional), duration of anesthesia, or extent of invasive intraoperative monitoring. If MI occurred, the estimated
risk of death after emergency surgery were 4.9 times higher than after elective surgery \((P = 0.02)\). Mortality rate was not associated with intraoperative tachycardia, systolic hypotension, or hypertension (table 7). Lower mean intraoperative diastolic pressure \((P = 0.001)\) and increased intraoperative administration of blood \((P = 0.005)\), however, were associated with greater mortality rates. Although in absolute terms both the estimated blood loss and the amount of cell-salvaged blood (and therefore the rate of bleeding) appeared to be higher in patients who died, these differences were not statistically significant compared with survivors (table 7).

**Laboratory Features and Time of Perioperative Myocardial Infarction as Predictors of Cardiac Death**

Preoperative and postoperative hemoglobin concentrations \((P = 0.81)\), preoperative creatinine concentrations \((P = 0.12)\), and the magnitudes of CPK \((P = 0.61)\) and CPK-MB \((P = 0.26)\) increases were not associated with greater risk of cardiac death. PMI occurred most frequently on postoperative day 1 (51.4%) and postoperative day 0 (23.4%). The mortality rate, however, was highest on postoperative day 0 (36%), a significantly higher rate than for those who had MI on postoperative day 2 or later (fig. 1; \(P = 0.03\)).

**Predictors of Cardiac Death Based on Post-Myocardial Infarction Course**

The clinical course after MI was a significant predictor of mortality. Patients who were immediately unstable and required vasoactive support were 13 times more likely to die than those who were hemodynamically stable after MI \((P = 0.001)\). Death was 6.6 times more likely in patients who required intraaortic balloon pump support immediately after MI compared with those who did not need it \((P = 0.06)\). Not surprisingly, the need for cardiopulmonary resuscitation during or shortly after MI predicted an approximately 34-fold greater risk of death \((P = 0.001)\).

**Predictors of Perioperative Myocardial Infarction and In-hospital Cardiac Death Based on Multivariable Analysis**

Table 8 summarizes the final model from stepwise multiple logistic regression, which identified a preoperative diagnosis of CAD \((P = 0.001)\) and significant aortic or mitral valvular disease \((P = 0.03)\) as predictors of PMI. In the final regression model, CHF less than 1 yr before the index vascular surgery \((P = 0.0002)\) and increased intraoperative administration of blood \((P = 0.007)\) were both associated with cardiac death. After controlling for the presence of CHF and CABG, we estimated that for every unit of blood administered (within a range of 0 to 21 units), the risk of death increased by 24\% \((P = 0.007)\). Finally, figure 2 shows the probability of death in patients who did or did not have histories of CABG, CHF, or both. After controlling for CHF and number of blood units administered (held constant at 1.8 per patient), we found that a history of CABG reduced the risk of cardiac death in all patients \((P = 0.04)\).

**Discussion**

The incidence of CAD is substantially higher in patients requiring vascular surgery than in the general surgical population. Hertz et al.\(^5\) found that only 8% of those undergoing elective vascular surgery had normal coronary arteries; therefore, it is not surprising that this group of surgical patients represents those at highest risk for PMI. It is also not surprising that other cardiovascular risk factors (e.g., hypertension, diabetes mellitus) were not risk factors for PMI in our patient cohort, because these comorbid conditions are widely present in the entire patient population undergoing vascular surgery.

Reported perioperative reinfarction rates today are lower compared with early reports,\(^{13}\) probably because of better perioperative treatments, including CABG or PTCA. PMI today is identified more frequently in areas...
with good collateral blood flow that, although preoperatively assessed as sufficient, may be functionally inadequate during surgical stress.\(^3\) We found that previous MI was not a significant risk factor for reinfarction or cardiac death; of control patients, 38.3% had previous MI and underwent vascular surgery without reinfarction. Of patients with PMI, 45.8% had previous MI; 6.5% (7 of 107, none of whom died) had MI within 12 months of the index surgery. Patients who have had recent successful PTCA\(^6,14\) or CABG\(^15\) have lower rates of MI and death after major surgery. Our study did not find that CABG protected against reinfarction. The mortality rate after PMI, however, was 7.7% in patients with previous CABG, compared with 27.9% in patients without prior CABG. The majority of our PMI patients with CABG (34 of 39) underwent CABG more than 1 yr before the index vascular surgery, and these patients had a 79% reduction in mortality rate compared with patients with PMI but no CABG; therefore, CABG protection against fatal cardiac complications appears to extend beyond 12 months. In the current study, prior PTCA was not cardioprotective in terms of reinfarction rate. However, 22.1% of patients (21 of 95) who did not have PTCA died after PMI, compared with 8.3% (1 of 12) of those with previous PTCA; the single patient with PTCA who died had undergone PTCA more than 12 months before surgery, and this patient might have developed coronary restenosis, which occurs in 25–40% of patients within 8 months of PTCA.\(^16\) The surprising finding that CABG did not reduce the incidence of PMI may be explained by the fact that CABG may be a marker of more severe CAD. To make a definitive conclusion, however, one would need to know the actual coronary pathology at reinfarction, particularly the patency of the bypass grafts. We do not know if reinfarction occurred in the bypassed areas, or if these areas were still protected and less severe MI (which presumably resulted in a lower mortality rate) occurred in other areas that had become stenotic. Alternatively, smaller coronary artery branches that give collateral blood flow to the infarcted area may not have been functionally adequate during surgical stress. This theory appears to be supported by Ellis et al.,\(^3\) who found that, if patients with high-grade coronary stenosis underwent coronary revascularization before peripheral vascular surgery, most perioperative reinfarctions appeared to be caused by inadequate collateralization. This finding causes concern, because today many patients are cleared for surgery based on angiographically visible collaterals that are assumed to provide adequate protection from MI.

Recently, Badner et al.\(^17\) reported a 17% post-PMI mortality rate after noncardiac surgery. The overall in-hospital mortality rate after PMI in our study was 20.6%. PMI was an early postoperative event, with the highest mortality rate on postoperative day 0 (36%). The mortality rate also was higher if the ST-segment and T-wave changes occurred intraoperatively. This suggests that some anesthesia or surgery factors may be responsible not only for PMI but also for cardiac death. In patients with CAD, the myocardial oxygen supply–demand relation may be affected grossly by how the anesthesiologist controls preload, afterload, contractility, and heart rate. Although patients who had general anesthesia had a 3.3-fold increase in the risk of PMI, the duration of surgery and invasive monitoring of intraoperative hemodynamics did not affect the risk of MI or cardiac death after PMI. Lower diastolic blood pressure (43 mmHg) in PMI patients was the only hemodynamic variable associated with increased risk of cardiac death.

Diehl et al.\(^18\) determined that increased perioperative blood loss and transfusion during vascular surgery were associated with the incidence of postoperative complications and death. In our study, the patients who suffered PMI had lower preoperative and postoperative hemoglobin concentrations than survivors. The total amount of salvaged blood in patients undergoing aortic
surgery (and therefore, the rate of bleeding) was significantly higher in patients who experienced PMI than in the control group. Furthermore, the patients who died received more blood than survivors. For perioperative blood loss that required transfusion of one blood unit in our patients with PMI, the risk of cardiac death increased by 24%. All these findings indicate that perioperative bleeding may play an important role in pathogenesis of PMI and cardiac death.

The risk of cardiac complications for patients undergoing noncardiac or peripheral vascular surgery sharply increases after the age of 70 yr. We found that the patients who died were almost 7 yr older than survivors, and that the women who died were an average of 7.3 yr older than the men who died.

Perioperative use of β-blockers reduces the incidence of PMI, the frequency of postoperative ischemia, and the risk of death at 2 yr after the operation, but not of cardiac death during the same hospital stay. In our study, patients who were receiving β-blockers were more likely to experience PMI; post hoc analyses showed that the intraoperative extremes of heart rates did not differ between patients on β-blocker therapy and those not receiving therapy. These findings suggest inadequate effects of β-blockade. In addition, β-blocker therapy might have been an indicator of more severe CAD and therefore a higher risk for PMI. Patients using β-blockers, however, tended to have lower in-hospital cardiac mortality rates. Slogoff and Keats demonstrated that patients with CAD and using β-blockers experience myocardial ischemia intraoperatively, despite better heart rate control. Preoperative therapy with calcium antagonists has not been shown to reduce the incidence of perioperative ischemia and even may increase the risk of major adverse cardiac events and death. Our results show a trend of increased cardiac risk in patients on calcium antagonists. At the same time, ACE inhibitor therapy showed a trend toward reducing the cardiac morbidity and in-hospital mortality rates.

Left ventricular hypertrophy and ST-segment depression seen on the preoperative ECG are important markers of increased risk for MI or cardiac death after major vascular surgery. We found no increased risk of PMI in patients with preexisting electrocardiographic changes consistent with myocardial ischemia. We also have found that preoperative change in an ECG or even a combination of changes consistent with CAD did not increase the risk of death after PMI. New intraoperative ST-segment or T-wave changes, however, were associated with a greater risk of perioperative cardiac death.

Mangano et al. demonstrated that current CHF is a risk factor for perioperative cardiac morbidity. We confirmed that history of CHF was associated with higher risk of MI. CHF less than 1 yr before the index surgery increased the cardiac mortality risk, and if CHF was present at surgery the OR of death was 12 times that of patients without CHF. CHF that occurred more than 1 yr before surgery was not associated with an increased cardiac mortality rate. Although a lower ejection fraction was associated with increased risk of PMI, it was not associated with increased risk of cardiac death. Halm et al. found that myocardial contractility assessed by echocardiography has limited prognostic value for assessment of cardiac risks; however, they assessed the outcomes based on small number of MI and cardiac fatalities.

The overall incidence of PMI and cardiac death increases with the urgency of vascular surgery. We confirmed that emergency surgery increased the risk for PMI and death. In the current study, the risks of death during peripheral vascular surgery and aortic reconstruction were similar, and much higher than after carotid endarterectomy. Krupski et al. demonstrated that the risk for postoperative cardiac ischemic events in lower extremity vascular operations is at least as great as for aortic operations. This may be explained by the finding that the peripheral vascular surgery is performed more often on an urgent basis in patients who otherwise face amputation, and therefore the cardiac evaluation and preoperative medical or surgical therapies of CAD may be less complete.

Our study has several limitations. The design is retrospective case-control; therefore, we could show only whether risk factors were associated with cardiac injury and death rather than establish a cause-effect relation. Hemodynamic variables were assessed from the handwritten anesthesia records, which may not reflect the extent and duration of hemodynamic variations accurately. The perioperative surveillance of MI was not done prospectively, was not performed on all patients, and was not always performed in a systematic manner. Therefore, the low incidence of PMI in this study may be an underestimate of the true infarction rate; it is possible that some patients with PMI were asymptomatic and therefore were not tested. We are confident, however, that we captured all patients who had clinically significant PMI. If there were patients with undiagnosed PMI, our reported cardiac mortality rate may be somewhat overestimated. We believe, however, that our reported incidence of overall perioperative cardiac mortality rate is accurate, because death is an unmistakable outcome.

In conclusion, the in-hospital cardiac mortality rate is
References