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Cardiac Outcome after Peripheral Vascular Surgery

Comparison of General and Regional Anesthesia

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Background: **Despite evidence that regional anesthesia may be associated with fewer perioperative complications than general anesthesia, most studies that have compared cardiac outcome after general or regional anesthesia alone have not shown major differences. This study examines the impact of anesthetic choice on cardiac outcome in patients undergoing peripheral vascular surgery who have a high likelihood of associated coronary artery disease.**

Methods: **Four hundred twenty-three patients, between 1988 and 1991, were randomly assigned to receive general (n = 138), epidural (n = 149), or spinal anesthesia (n = 136) for femoral to distal artery bypass surgery. All patients were monitored with radial artery and pulmonary artery catheters. Postoperatively, patients were in a monitored setting for 48–72 h and had daily electrocardiograms for 4–5 days and creatine phosphokinase/isoenzymes every 8 h × 3, then daily for 4 days. Cardiac outcomes recorded were myocardial infarction, angina, and congestive heart failure.**

Results: **Baseline clinical characteristics were not different between anesthetic groups. Overall, the patient population included 86% who were diabetic, 69% with hypertension, 36% with a history of a prior myocardial infarction, and 41% with a history of smoking. Cardiovascular morbidity and overall mortality were not significantly different between groups when analyzed by either intention to treat or type of anesthesia received. In the intention to treat analysis, incidences of cardiac event or death for general, spinal, and epidural groups were 16.7%, 21.3%, and 15.4%, respectively. The absolute risk difference observed between general and all regional anesthesia groups for cardiac event or death was −1.6% (95% confidence interval −9.2%, 6.1%) This reflected a nonsignificant trend for lower risk of postoperative events with general anesthesia.**

Conclusions: **The choice of anesthesia, when delivered as described, does not significantly influence cardiac morbidity and overall mortality in patients undergoing peripheral vascular surgery. (Key words: Anesthesia. Diabetes. Outcome: angina; congestive heart failure; myocardial infarction; peripheral vascular surgery.)**

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PERIPHERAL vascular surgery is associated with greater cardiac morbidity and overall mortality than other forms of noncardiac surgery.[1,2] Perioperative myocardial infarction is reported to occur in 4–15% of patients undergoing peripheral vascular surgery and accounts for more than 50% of perioperative mortality.[2–4] This incidence is not surprising given that coronary artery disease exists in as many as 70% of patients with peripheral vascular disease[5] and that the majority of such patients will die from cardiovascular related causes.[6] History of a previous myocardial infarction, congestive

heart failure, valvular heart disease, and diabetes are risk factors that have been associated with increased perioperative cardiac morbidity and mortality for both vascular and nonvascular surgical procedures.[2,7–10]

Type of anesthesia represents another variable that may have an impact on cardiac outcome. Recent evidence suggests that regional anesthesia alone or in combination with general anesthesia may be associated with less perioperative cardiac morbidity than general anesthesia alone.[11–15] However, studies that have examined this question in patients undergoing vascular surgery have reported no significant difference in cardiac morbidity or mortality between regional anesthesia alone and general anesthesia.[13,16–18] There remains, therefore, no uniform preference for one form of anesthesia over another for patients undergoing peripheral vascular surgery.[19] Given the high incidence of cardiac disease in vascular surgery patients, this is an ideal group in which to further examine the effects of anesthesia on cardiac outcome. The purpose of this randomized trial was to evaluate whether type of anesthesia is an important factor that may influence perioperative cardiac outcomes in patients undergoing peripheral vascular surgery.

Methods and Materials

After written informed consent was obtained, patients scheduled for elective peripheral vascular surgery (femoral to distal artery) were randomly assigned to receive general, spinal, or epidural anesthesia in a protocol approved by the Institutional Review Board of the New England Deaconess Hospital. Assignments for randomization to type of anesthesia were generated by computer program and placed in sealed envelopes. The envelopes were picked sequentially as patients accrued and not opened until after eligible patients had consented to participate in the study. Of 705 consecutive patients scheduled to undergo femoral to distal artery bypass surgery, 423 were randomly assigned. Patients excluded from randomization included those in whom regional anesthesia was contraindicated and those who refused to participate. Contraindications for regional anesthesia included preexisting coagulopathy (*i.e.*, patients receiving preoperative infusions of heparin or urokinase), operations requiring arm veins, and prior lower back surgery.

Demographic data, medications, and surgical and medical history were obtained from the patient and the medical record. All patients underwent preoperative 12-lead electrocardiography.

Anesthesia

Intraoperative monitoring was carried out with radial artery and pulmonary artery catheters, pulse oximetry, noninvasive blood pressure measurements, and dual-channel electrocardiographic monitoring (leads II and V5). Additional monitoring for general anesthesia included capnography, mass spectrometry, and nerve stimulation. Pulmonary artery catheters were inserted in the operating room before surgical incision. Premedication consisted of oral diazepam (5–10 mg) or intramuscular midazolam (1–3 mg) often supplemented with either intramuscular meperidine (25–50 mg) or intravenous fentanyl (25–50 μg).

Spinal anesthesia was performed with hyperbaric tetracaine 1% (16–20 mg) combined with 3–5 mg phenylephrine. This was administered *via* a 22-G spinal needle at L4–L5 or L3–L4 with the patient in the lateral decubitus position, operative side down. Patients were kept in this position for 10 min after the intrathecal injection. Epidural anesthesia was performed at either L2–L3 or L3–L4 using a 17-G Weiss needle. Blockade was induced with 2% lidocaine and maintained with 0.5% bupivicaine, titrated to maintain a dermatome level between T8 and T10. Regional anesthesia was supplemented with intravenous midazolam and/or fentanyl to maintain conscious sedation. Inadequate regional anesthesia was defined as either a spinal or an epidural anesthetic that could not technically be performed or was not sufficient to provide adequate anesthesia and/or motor blockade for surgery.

General anesthesia was induced, after preoxygenation, with intravenous thiopental (2–4 mg/kg), intravenous fentanyl (1–5 μg/kg), and intravenous succinylcholine (1–1.5 mg/kg) or intravenous vecuronium (0.1 mg/kg). After tracheal intubation, anesthesia was maintained with intravenous fentanyl (20–50 μg/h), isoflurane or enflurane (0.5–1.5 MAC), nitrous oxide (50–70%), and neuromuscular blockade. Positive pressure ventilation was adjusted to maintain a $PaCO_2$ of 30–40 mmHg, a PaO_2 of >100 mmHg, and a *p*H of 7.35–7.45 as assessed by arterial blood gas analysis and end-tidal carbon dioxide monitoring.

Intravenous nitroglycerin (0.5–1.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was typically administered intraoperatively and postoperatively for the first 6–12 h to aid in controlling blood pressure and pulmonary artery pressures and to provide prophylaxis against myocardial ischemia. The

administration and dosing of intravenous nitroglycerin was left to the discretion of the anesthesia care team. Generally, intravenous nitroglycerin was not administered to patients with blood pressures lower than 100 mmHg systolic or to patients whose blood pressure decreased to lower than 100 mmHg systolic after initiating the nitroglycerin infusion. Indications for the use of nitroglycerin did not differ for patients assigned to the general anesthesia group *versus* the spinal or epidural anesthesia groups.

Intraoperative fluid therapy was guided by pulmonary artery catheter monitoring and generally was limited to approximately 2 l of crystalloid solution. The decision to administer additional fluids was based on various factors, including the presence of low central and pulmonary artery pressures in conjunction with a low blood pressure, a low cardiac index (less than 1.5 to 2 l/M^2), or associated blood loss. No protocol or algorithm was used to dictate fluid management. Postoperatively, patients were managed in the postanesthesia care unit for the first 12–24 h with continuous electrocardiographic and pulmonary artery pressure monitoring. After discharge from the postanesthesia care unit, patients were transferred to a vascular intensive care unit, where the pulmonary artery pressures were monitored for an additional 12–24 h. Intravenous morphine (2–5 mg) and/or meperidine (12.5–50 mg) were given for analgesia as needed while the patient remained in a monitored care setting. The patients' pain control regimens were changed to subcutaneous morphine, intramuscular meperidine, or oral analgesics on transfer to a general patient care floor. At the discretion of the anesthesia care team, some patients in the epidural group received morphine sulfate, 3 mg in 10 ml of preservative-free normal saline, *via* the epidural catheter. All epidural catheters were removed on discharge from the postanesthesia care unit. On the 1st postoperative day, patients were given subcutaneous heparin (5,000 units every 12 h) until ambulating; oral aspirin (81 mg) was then given daily until discharge.

Endpoints

Patients were examined and interviewed daily until discharge for the presence of symptoms suggestive of angina pectoris and/or congestive heart failure. A 12-lead electrocardiogram was taken on arrival to the postanesthesia care unit and then daily for 4 days. Creatine phosphokinase (CK) isoenzymes were drawn every 8 h for the first 24 h, then daily for 3 days. All electrocardiograms were interpreted by two cardiologists blinded to the type of anesthesia received.

A myocardial infarction was defined as: (1) development of new Q waves longer than 0.03 s in duration, associated with ST elevation of at least 1 mm in two or more leads, or (2) new ST segment depression of at least 1 mm in two or more leads associated with an increase in CPK with a greater than 5% MB fraction. Congestive heart failure was defined as new dyspnea associated with clinical signs of pulmonary edema and was confirmed by consistent findings on chest x-ray.

The major endpoints of this study were to determine whether general anesthesia was associated with more cardiovascular morbidity and overall mortality than regional anesthesia in high-risk patients undergoing peripheral vascular surgery. Mortality was defined as death occurring during the patient's hospitalization. Cardiovascular morbidity was defined by specific cardiac events, which included myocardial infarctions, angina, and congestive heart failure. Secondary outcomes also were recorded and included operating room time, maximum pulmonary artery and central venous pressures, operative fluids, and length of stay in a monitored care setting and in the hospital.

Statistical Analysis

Initial power calculations based on estimates concerning differential mortality rates across anesthesia types indicated a required sample size of 200 patients in each treatment group.

The study data were examined by an independent committee after 400 patients were accrued. Power calculations based on the observed overall mortality rates (3.1%) indicated that more than 24,000 patients would be required to have an 80% power to detect a 50% reduction in mortality between anesthesia types. Because of the practical limitations of such a large sample size requirement at a single institution, the trial was stopped after 423 patients were enrolled.

Data were analyzed (1) by intention to treat (anesthesia randomly assigned) and (2) by type of anesthetic used in the procedure (anesthesia received). Baseline characteristics and outcomes were compared between randomly assigned patients using chi-squared or Fisher's exact tests for categorical data and independent *t*-tests for continuous data. Length of stay comparisons were made using Wilcoxon's rank-sum test. Comparisons carried out between the three anesthesia groups initially were made with analysis of variance. Where significant differences existed, detailed individual

comparisons between the specific regional anesthetic and general anesthesia were made by two-sided *t*-tests. Statistical calculations were performed using SYSTAT (Evanston, Ill), absolute risk differences were calculated using STATA (release 3.1, 1993, College Station, TX).

Results

Figure 1 outlines the flow of randomly assigned patients throughout the study. An intention to treat analysis was performed on the entire cohort of 423 randomly assigned patients, and a separate analysis according to type of anesthesia received was performed in the later group of 315 patients.

Intention to Treat Analysis

There were no significant differences between randomly assigned groups for any of the baseline characteristics analyzed (table 1). Table 2 compares postoperative outcomes and secondary outcomes among the three anesthesia groups by intention to treat analysis. There were no significant differences among the three groups in the incidence of adverse cardiac events or death. Separate analyses of single cardiac events, which included myocardial infarctions, angina, and congestive heart failure, also revealed no significant differences among the three groups (table 2). There were also no significant differences among the three groups in operating room time, time spent in a monitored care setting, or hospital length of stay (table 2). The maximum pulmonary artery diastolic pressures and maximum central venous pressures were significantly lower in the spinal and epidural groups when compared to the general anesthesia group. The spinal group received significantly less operative fluid (approximately 400 ml) than the general anesthesia group. The percentage of patients given intravenous nitroglycerin was not significantly different between groups (78% general, 68% spinal, 69% epidural).

The absolute risk difference observed in our data between general and all regional anesthesia groups is presented in table 3. There was a nonsignificant trend in most major outcomes for general anesthesia to be superior to regional anesthesia. This trend was most pronounced when general was compared to spinal anesthesia. Spinal anesthesia was associated with 4.7% more cardiac morbidity and mortality than general anesthesia. However, the 95% confidence limits indicate the true difference could have been between 13.9% fewer to 4.6% more cardiac events or death. Similar results were found in almost all of the individual categories.

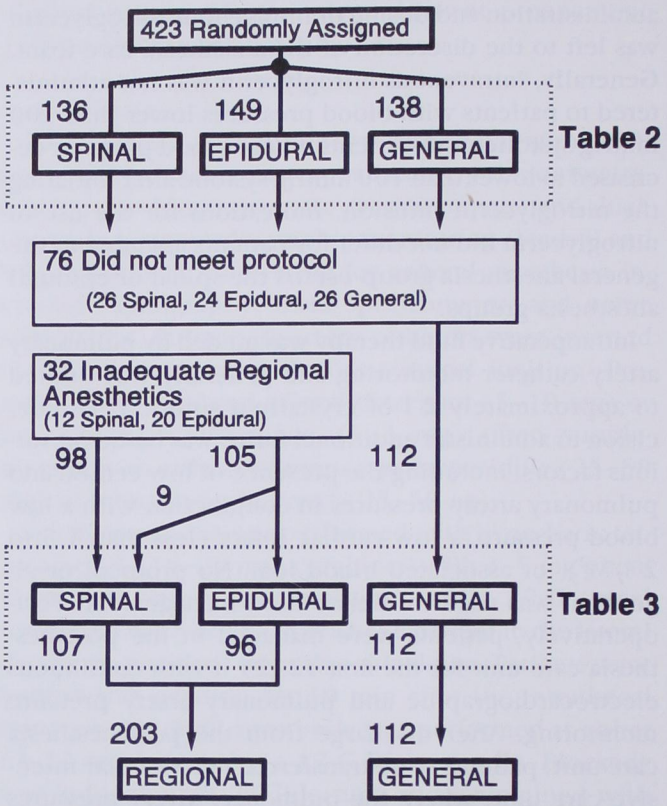

Fig. 1. Flow diagram for randomly assigned patients.

Nineteen myocardial infarctions occurred in the cohort. Thirteen (68%) of these myocardial infarctions were silent. Three (16%) of those patients suffering from a myocardial infarction died as a consequence of that myocardial infarction. Of those patients who had a perioperative myocardial infarction, nine (47%) had a history of a previous myocardial infarction. Nine patients (6%) with a history of a previous myocardial infarction had a perioperative myocardial infarction. All detected myocardial infarctions occurred within 4 days of surgery with an average time of occurrence of 1.5 days.

Thirteen patients in the entire cohort of the patients studied died during their hospitalization. The causes of death included myocardial infarction (23%), fatal dysrhythmia (15%), cerebral vascular accidents (23%), and multisystem failure (38%).

The in-hospital death rate for patients who had an inadequate regional anesthetic was significantly greater

Table 1. Clinical Characteristics

	General (n = 138)	Spinal (n = 136)	Epidural (n = 149)	*P*
Age (yr)	68 ± 12	68 ± 11	68 ± 11	0.95
Proportion male	58.7	60.3	59.1	0.96
Diabetes	81.9	86.0	89.3	0.20
Cardiac history				
Prior hypertension	72.2	70.0	65.5	0.47
Prior angina	22.7	25.2	29.9	0.39
Prior CHF	18.8	27.3	28.0	0.16
Prior MI	32.6	35.9	38.6	0.56
Prior PTCA	4.8	5.3	9.2	0.30
Prior CABG	5.4	8.9	12.1	0.15
Family history	8.1	7.1	4.8	0.56
Increased cholesterol	12.2	18.7	18.6	0.41
Cigarettes	38.7	40.4	43.2	0.73
Laboratory analysis				
Blood urea nitrogen (BUN) (mg/dl)	25 ± 22	25 ± 16	27 ± 27	0.67
Creatinine (mg/dl)	1.6 ± 2.7	1.7 ± 2.0	1.6 ± 1.5	0.75
Hematocrit (%)	38 ± 6	37 ± 6	37 ± 6	0.64
Prior surgery				
Carotids	5.3	8.8	5.8	0.48
Peripheral vascular	37.5	34.6	26.2	0.17
Aortic aneurysm	0.8	4.9	2.2	0.11
Preoperative medications				
Beta blocker	19.6	17.7	22.2	0.63
Calcium channel blocker	24.6	25.0	22.2	0.83
Digoxin	17.4	24.3	24.2	0.28
Nitrates	15.2	13.4	20.1	0.27
Diuretic	32.6	39.0	39.6	0.41

CHF = congestive heart failure; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty; CABG = coronary artery bypass graft.

All data are represented as percentages except for age, BUN, creatinine, and hematocrit. There were no significant differences between the three groups by three-way ANOVA F test or chi-square, or between any individual anesthetic by *t* tests and Fisher's exact test. *P* values reference chi-square tests for categorical data, ANOVA F test for continuous data.

(9.4% *vs.* 1.6%) than for those patients who had a successful regional or general anesthetic. There was a trend for an increased myocardial infarction and congestive heart failure rate in those in the inadequate regional anesthesia group, but this trend was not significant (table 4).

Among all patients who received epidural anesthesia, there were no significant differences for any postoperative outcomes between those patients who received epidural morphine (40%) *versus* parenteral opioids (60%) for postoperative pain control in the postanesthesia care unit. Postoperative myocardial infarction rates in the epidural group were 4.9% *versus* 7.3% for those patients who received epidural morphine *versus* parenteral opioids, respectively. The death rate was 4.9% in those patients who received epidural morphine *versus* 1.8% for those patients in the epidural group who received parenteral opioids. None of the patients in the epidural group, however, appeared to have died as a direct result of a myocardial infarction. The causes of death were determined by the surgical team and based on the clinical findings at the time of the patient's death. No autopsies were performed on these patients.

Analysis of Outcomes by Type of Anesthesia Received

A separate analysis according to the type of anesthesia received was performed on the 315 patients who fulfilled treatment protocol (inadequate regional anesthetics were excluded; fig. 1). Therefore, 108 patients who were included in the intention to treat group were excluded from the type of anesthesia received group (66 patients did not have femoral to distal vascular surgery, 10 did not receive a pulmonary artery catheter, and 32 had inadequate regional anesthesia). Nine patients in the epidural group were converted to spinal anesthesia after inadvertent dural puncture. All outcome results were similar to those reported in the in-

Table 2. Outcomes by Intention to Treat

Outcome	General (n = 138)	Spinal (n = 136)	Epidural (n = 149)	*P*
Postoperative events				
Cardiac event or death*	23 (16.7)	29 (21.3)	23 (15.4)	0.40
Myocardial infarction	5 (3.6)	7 (5.2)	7 (4.7)	0.82
Angina	10 (7.3)	14 (10.3)	10 (6.7)	0.49
Congestive heart failure	12 (8.7)	14 (10.3)	13 (8.7)	0.87
Death	4 (2.9)	4 (2.9)	5 (3.4)	0.97
Secondary outcomes				
Operating room time (min)	307 ± 89	305 ± 84	297 ± 87	0.36
Maximum pulmonary artery diastolic pressure (mmHg)	18 ± 5	15 ± 7†	15 ± 6†	<0.0005
Maximum central venous pressure (mmHg)	11 ± 4	9 ± 5†	9 ± 4†	<0.0005
Operative fluids (L)	2.2 ± 1.1	1.8 ± 0.8†	2.1 ± 1.3	0.05
Recovery room days	0.5 ± 0.6	0.5 ± 0.5	0.6 ± 0.7	0.056
Intensive care unit days	1.2 ± 2.8	1.4 ± 2.6	1.7 ± 3.4	0.10
Hospital days	18 ± 14	17 ± 15	18 ± 18	0.92

Percentages are given in parentheses. Recovery room, intensive care, and hospital days were compared using Kruskal–Wallis nonparametric ANOVA. The only outcomes with significant outcomes across groups by ANOVA were the maximum pulmonary and central venous pressures and the operative fluids. Significance tests indicated by the symbols compare the specific regional anesthetic to general.

* Includes patients who have any of the following events: myocardial infarction, angina, congestive heart failure, or death.

† Significant at $P < 0.001$.

tention to treat analysis. Table 5 compares outcomes by type of anesthesia received. There were no significant differences among the three anesthesia groups in the incidence of adverse cardiac events or death. There were no significant differences in the incidence of single cardiac events among the three anesthesia groups. Operating room time, time spent in a monitored care unit, and hospital length of stay did not vary significantly among anesthesia groups. Similar to results reported in the intention to treat analysis, the maximum

Table 3. Absolute Difference in Risk, General *Versus* Spinal, General *Versus* Epidural, and General *Versus* All Regional Anesthesia by Intention to Treat and Anesthesia Received

	General *Vs.* Spinal		General *Vs.* Epidural		General *Vs.* All Regional	
Outcome	Risk Difference (%)	95% Confidence Limits	Risk Difference (%)	95% Confidence Limits	Risk Difference (%)	95% Confidence Limits
By intention to treat						
Postoperative events						
Cardiac event or death	−4.7	−13.9, 4.6	1.2	−7.3, 9.7	−1.6	−9.2, 6.1
Myocardial infarction	−1.5	−6.4, 3.3	−1.1	−5.7, 3.5	−1.3	−5.3, 2.7
Angina	−3.0	−9.7, 3.6	0.5	−5.4, 6.4	1.2	−6.6, 4.2
Congestive heart failure	−1.6	−8.5, 5.3	−0.03	−6.6, 6.5	−0.8	−6.6, 5.0
Death	−0.04	−4.0, 3.9	−.05	−4.5, 3.6	−0.3	−3.7, 3.2
By anesthesia received						
Postoperative events						
Cardiac event or death	−3.4	−12.9, 6.1	−4.3	−14.2, 5.6	−3.8	−12.0, 4.3
Myocardial infarction	−0.2	−5.1, 4.8	−2.7	−8.6, 3.3	−1.3	−5.9, 3.2
Angina	−0.3	−6.8, 6.2	−4.1	−11.7, 3.4	−2.1	−8.0, 3.8
Congestive heart failure	−2.2	−9.5, 5.1	−1.2	−8.5, 6.1	−1.7	−7.9, 4.4
Death	2.7	−0.3, 5.6	−0.4	−8.5, 4.1	−1.2	−2.2, 4.6

None of the risk differences is significant. Negative numbers indicate less risk for general anesthesia.

Table 4. Outcomes of Inadequate Regional Anesthetics

	Inadequate Regional Anesthesia (n = 32)	General (n = 112)	Regional (n = 203)	*P*
Postoperative outcomes				
Cardiac event or death*	8 (25.0)	15 (13.4)	35 (17.2)	0.29
Myocardial infarction	2 (6.3)	4 (3.6)	10 (4.9)	0.77
Angina	3 (9.4)	7 (6.3)	17 (8.4)	0.75
Congestive heart failure	5 (15.6)	8 (7.1)	18 (8.9)	0.33
Death	3 (9.4)	3 (2.7)	3 (1.5)†	0.03

Percentages are given in parentheses. Statistics based on individual pairwise comparisons between the failed regionals and successful regional or general anesthetic.

* Includes patients who have any of the following events: myocardial infarction, angina, congestive heart failure, or death.

† Significant at $P < 0.05$ by chi-square or Fischers' exact test where appropriate.

pulmonary artery diastolic pressures and maximum central venous pressures were significantly lower in the spinal and epidural groups when compared to the general anesthesia group. The spinal group also received less operative fluid than the general anesthesia group.

Absolute risk differences observed in our data between general and all regional anesthetics are presented in table 3. Similar to the intention to treat analysis, there was also a trend for general anesthesia to be superior to regional anesthesia. However, if differences existed, they are likely to be small and on the order of 1–4%.

Discussion

This study is the largest prospective randomized trial to date designed to evaluate the effects of regional anesthesia techniques (spinal or epidural) *versus* general anesthesia on perioperative cardiac morbidity and

Table 5. Outcomes by Type of Anesthetic Received

Outcome	General (n = 112)	Spinal (n = 107)	Epidural (n = 96)	All Regional (n = 203)
Postoperative events				
Cardiac event or death*	15 (13.4)	18 (16.8)	17 (17.7)	35 (17.2)
Myocardial infarction	4 (3.6)	4 (3.7)	6 (6.3)	10 (4.9)
Angina	7 (6.3)	7 (6.5)	10 (10.4)	17 (8.3)
Congestive heart failure	8 (7.1)	10 (9.4)	8 (8.3)	18 (8.9)
Death	3 (2.7)	0 (0.0)	3 (3.1)	3 (1.5)
Secondary outcomes				
Operating room time (min)	317 ± 88	299 ± 77	308 ± 83	303 ± 80
Maximum diastolic pulmonary artery pressure (mmHg)	18 ± 6	15 ± 7†	15 ± 6†	15 ± 7
Maximum central venous pressure (mmHg)	12 ± 5	9 ± 4†	8 ± 5†	9 ± 5
Operative fluids (L)	2.3 ± 1.1	1.8 ± 0.8†	2.1 ± 1.4	1.9 ± 1.1
Recovery room days	0.5 ± 0.6	0.6 ± 0.6	0.6 ± 0.6	0.6 ± 0.6
Intensive care unit days	1.4 ± 3.0	1.3 ± 2.0	1.9 ± 3.4	1.6 ± 2.7
Hospital days	17.9 ± 14.3	17.2 ± 14.8	19.0 ± 17.4	18.0 ± 16.1

None of the postoperative events was significantly different across groups by ANOVA, or to individual pairwise comparisons between the specific regional anesthetic and general. The only secondary outcomes with significant outcomes across groups by ANOVA were the maximum pulmonary and central venous pressures and the operative fluids. Significance tests indicated by the symbols compare the specific regional anesthetic to general. Because it is a post hoc grouping analysis, significance tests are not reported between general and all regional (spinal + epidural). Percentages are given in parentheses.

* Includes patients who have any of the following events: myocardial infarction, angina, congestive heart failure, or death.

† Significant at $P < 0.001$.

overall mortality in patients undergoing peripheral vascular surgery. Furthermore, this is the only study to compare cardiac outcome after general anesthesia with that of both spinal and epidural in any patient population. Our results suggest that the type of anesthesia given for peripheral vascular surgery does not significantly affect cardiac morbidity or mortality, overall mortality, or hospital length of stay. Although the 95% confidence limits do not allow for precise measurement, the absolute risk of most of the individual cardiac events implies a trend for greater risk in regional as compared to general anesthesia. If differences exist, their magnitude is on the order of 1–4% depending on the subset analyzed. These conclusions remain valid regardless whether the data are analyzed by intention to treat or by type of anesthesia received.

Four previous studies specifically examined whether regional anesthesia alone is superior to general anesthesia in reducing the incidence of perioperative complications in patients undergoing peripheral vascular surgery.[13,16–18] Cook *et al.* prospectively randomized 100 patients to either general or spinal anesthesia for peripheral vascular surgery and found no difference in rate of perioperative myocardial infarction.[16] Neither a precise definition of myocardial infarction nor a description of the screening methods for diagnosis was delineated in this study. Rivers *et al.*, in a prospective nonrandomized evaluation of 213 patients undergoing peripheral vascular surgery, compared epidural and general anesthesia and found no significant difference.[17] Damask *et al.* reported similar results but studied only 19 patients.[13] Christopherson *et al.* prospectively randomized 100 patients to general or epidural anesthesia and found no difference in cardiac morbidity and mortality.[18] The cumulative results of these studies are consistent with our findings that the incidence of cardiovascular morbidity and mortality is similar regardless whether the patient receives a general, spinal, or epidural anesthetic.

The diagnosis of perioperative myocardial infarction by CK-MB fraction analysis in surgical patients is controversial. For example, in the context of a small myocardial infarction associated with limb ischemia, the creatine phosphokinase could be increased, but the CK-MB fraction may be less than 5%. The myocardial infarction would go undiagnosed. Conversely, it is known that the CK-MB isoform may be released from damaged skeletal muscle, and under these circumstances, it is possible that the prevalence of myocardial infarction could be overestimated.[20] The overall incidence of myocardial infarction using CK-MB fraction analysis in this study (4.5%) is at the lower end of the range (4–15%) reported in other similar studies.[4,16–18,21,22] These findings are remarkable given the large incidence of diabetes, hypertension, and cardiac disease in our patient population. Perioperative cardiac morbidity and mortality have been shown to be greater in patients who are male, diabetic, and hypertensive and have a history of coronary artery disease.[9,23–25] These are the clinical characteristics present in the majority of our patient population. Several of the following factors may account for the low event rate in this study.

All patients in our study were monitored with radial and pulmonary artery catheters for the first 48 h to continuously assess and treat hemodynamic changes during the perioperative period. The use of both pulmonary artery catheter monitoring and prophylactic nitroglycerin, however, remains controversial. Some investigators suggest that pulmonary artery catheter monitoring is a relatively insensitive monitor for detecting myocardial ischemia, probably is overutilized, and may not significantly affect cardiac outcome.[26–28] In contrast, Rao *et al.* found that the incidence of reinfarction in high-risk patients undergoing noncardiac surgery could be reduced by aggressive hemodynamic monitoring in the perioperative period.[29] Berlauk *et al.* demonstrated that use of pulmonary artery catheters to optimize hemodynamic variables before surgery according to a defined treatment algorithm improved cardiac outcomes in patients undergoing peripheral vascular surgery.[30] In our study, no treatment algorithms or protocols were used to clinically manage patients, and invasive monitoring techniques were not randomized. Pulmonary artery catheters were not used to improve the patients' hemodynamic status preoperatively but were used to improve the patients' hemodynamic status intraoperatively and for the first 48 h after surgery. The sympathetic blockade and resulting venodilation presumably caused by the spinal and epidural anesthesia may account for the lower pulmonary artery and central venous pressures found in the regional anesthesia groups. These lower filling pressures, however, did not result in a smaller incidence of clinical heart failure in the regional anesthesia group.

Use of intravenous nitroglycerin in the majority of our study patients may have contributed to the low cardiac event rate. Coriat *et al.* found that intravenous nitroglycerin of at least 1.0 $\mu g \cdot kg^{-1} \cdot min^{-1}$ was effective in reducing episodes of ischemia in high-risk patients undergoing cardiac surgery.[31] In contrast, other

investigators found that intravenous nitroglycerin was not effective in reducing myocardial ischemia in patients with either known or suspected coronary artery disease.[32,33] Because pulmonary artery catheter monitoring and use of intravenous nitroglycerin were not randomly assigned in our study, no firm conclusions can be made regarding the possible impact of these treatment modalities on reducing the myocardial event rate.

The characteristics of the myocardial infarctions that occurred in the randomly assigned patient population were similar to those reported in other studies. For example, all of the myocardial infarctions detected occurred within 4 days of surgery (average 1.5 days), and the majority of these were silent.[8,34,35] Moreover, patients who suffered a previous myocardial infarction were at greatest risk for reinfarction.[21,24,36] The reinfarction rate for patients who had a prior myocardial infarction in our study was 6%, which is consistent with the reinfarction rates of 5–8% reported in other studies.[21,24,35,36] Interestingly, only 3 of the 19 patients (16%) who suffered a myocardial infarction in the intention to treat population died. In each case, the cause of death was attributed to the myocardial infarction, based on both the clinical evidence and assessment of the surgical team caring for the patient. This finding is in contrast with other studies that report that the risk of dying after a perioperative myocardial infarction can range from 32% to 70%.[21,24,29,35] The smaller incidence of death after a myocardial infarction in our study may be attributed to the fact that all of the patients were in a monitored care setting for the first 48 h postoperatively thus enabling earlier medical intervention and management.

Another interesting finding was that the death rate associated with an inadequate regional anesthetic that necessitated conversion to a general anesthetic was significantly higher (9.4% *vs.* 1.6%) when compared to patients who had a successful regional or general anesthetic (table 4). The inadequate regional anesthesia group also demonstrated a trend toward increased cardiac morbidity. The inadequate regional anesthetic rate in our study was 11% and consistent with rates reported at other teaching hospitals.[37,38] The trend toward increased cardiac morbidity in this group may be an important finding or may represent a statistical anomaly because of the small number of patients (32) in the inadequate regional anesthesia group. However, patients with inadequate regional anesthetics are not often included in other studies, and this specific subgroup warrants further investigation.

This study has several limitations. Uniform clinical protocols were not used to manage perioperative hemodynamic changes or to control postoperative pain. Therefore, anesthetic management of patients may have differed among anesthesia groups. There were, for instance, relatively minor yet significant differences between the regional and general anesthesia groups in the maximum pulmonary artery and central venous pressures and intraoperative fluid therapy. The use of intravenous nitroglycerin also varied but not significantly among the three anesthesia groups. Interestingly, the lack of specific treatment protocols may be viewed as one of the strengths of this study. Despite the inherent differences in management style among anesthesiologists, there was no clinically significant difference in cardiac morbidity or mortality or overall mortality between general and regional anesthesia. These findings, therefore, may be more generalizable than if the management of patients were governed by tightly controlled treatment protocols.

Several studies suggest that postoperative pain management using epidural infusion techniques may provide superior postoperative analgesia when compared to on-demand opioids and, therefore, decrease the incidence of postoperative cardiac events.[11,12] Management techniques to control pain were not randomly assigned in our study. However, because all of the patients remained in a monitored care setting for the first 48 h, the patients' postoperative pain control needs could be addressed promptly. In the epidural group, 40% of the patients received epidural morphine for postoperative pain control for the first 24 h, and the remaining patients received parenteral opioids. No significant difference in cardiac morbidity or mortality was found between the two epidural subgroups. These results are consistent with Christopherson *et al.*, who found no significant benefit to epidural analgesia when compared to intravenous patient-controlled opioid analgesia in managing pain during the first 24 h after lower extremity peripheral vascular surgery.[18] The lack of any significant benefit of epidural analgesia in our study may be due to the fact that patients undergoing lower extremity peripheral vascular surgery do not experience the same intensity of postoperative pain as patients undergoing orthopedic or other major intraabdominal procedures.[39] Moreover, diabetics over time often develop sensorimotor peripheral neuropathies, which may minimize their analgesic requirements.

Another study limitation is the lack of a uniform preoperative cardiac evaluation of patients. Although the baseline demographics suggest that the randomly assigned groups have similar risk factors for coronary artery disease, the screening of patients using noninvasive myocardial perfusion imaging techniques may have provided more objective criteria for evaluating cardiac risk among the anesthesia groups. Studies such as dipyridamole thallium scintigraphy are not routinely performed on patients undergoing vascular surgery at the New England Deaconess Hospital because they have not been shown to be predictive of cardiac morbidity or mortality in our patient population.[10] Other investigators have questioned the predictive potential of dipyridamole thallium scintigraphy as a preoperative screening test.[40,41]

Although we were unable to demonstrate any significant differences in cardiac outcome between general and regional anesthesia, the possibility exists that in a larger trial, these differences may have become significant. A larger trial, by necessity, would need to enroll thousands of patients and would likely have to be multiinstitutional in design. Even if differences in cardiac outcome between general and regional anesthesia could be demonstrated in a larger clinical trial, our data suggest they are likely to be small and, therefore, have little impact on the current practice of anesthesia. In conclusion, this study suggests that the choice of anesthesia does not significantly influence cardiac morbidity and overall mortality in patients undergoing peripheral vascular surgery.

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