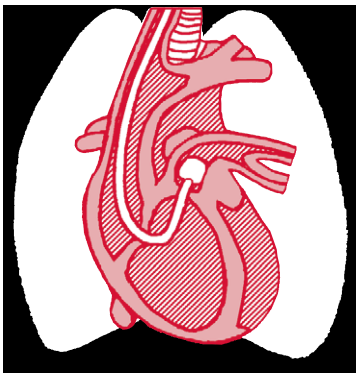

CASE CONFERENCE

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CASE 2—2006
Catastrophic Cardiovascular Collapse During Carotid Endarterectomy

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OPERATIVE CANDIDATES for vascular surgery have a high incidence of coronary artery disease (CAD), which is responsible for 50% of their perioperative mortality.[1,2] The authors present a patient scheduled for carotid endarterectomy (CEA) whose comprehensive preoperative cardiac evaluation showed him to be at low cardiac risk yet he suffered intraoperative catastrophic cardiovascular collapse. Appropriate preoperative evaluation of CEA patients, in whom CAD is prevalent,[3] is discussed with regard to the American Heart Association (AHA)/American College of Cardiology (ACC) perioperative cardiovascular evaluation guidelines for noncardiac surgery. In addition, the authors describe the intraoperative course of this patient, review the pathophysiology that is often seen in perioperative myocardial infarction, and present results from postoperative coronary arteriography.

CASE REPORT*

A 70-year-old, 80-kg, 176-cm man was found to have an asymptomatic right carotid bruit. Past medical history included elevated cholesterol, hypertension, smoking (<75 pack years, quit recently), chronic obstructive pulmonary disease, chronic stable angina, and peripheral vascular disease (PVD) (severe right calf pain with "vigorous walking"). Medications included benazepril (20 mg/d), verapamil (240 mg/d), pravastatin (40 mg/d), aspirin (325 mg/d), and hydroxyzine. Past surgical history was significant for an abdominal aortic aneurysm repair at age 50 and an open cholecystectomy at age 54.

A preoperative carotid duplex ultrasound showed 80% to 99% stenosis of the right internal carotid artery (ICA), 50% stenosis of the right external carotid artery (ECA), 50% to 79% stenosis of the left ICA, and 50% stenosis of the left ECA and right subclavian artery, with extensive, irregular heterogenous plaque at the bifurcation of the right ICA/ECA. A carotid angiogram confirmed these findings. Transthoracic echocardiographic examination showed normal left ventricular wall motion and function, 41% fractional area shortening, normal valves, and mild/moderate septal hypertrophy. Surgery was postponed after the patient suffered a mild stroke with transient aphasia and right-sided weakness during the carotid angiogram. The patient participated in stroke rehabilitation, stopped smoking, and 1 year later, CEA was rescheduled. A rest and stress myocardial perfusion study showed no stress-induced perfusion defects, a normal resting left ventricle, normal wall motion, and an ejection fraction of 75%. Repeat carotid duplex ultrasound examination was unchanged. An electrocardiogram (ECG) performed 2 months before surgery showed normal sinus rhythm at 61 beats/min (otherwise normal). A repeat ECG the week before surgery showed normal sinus rhythm (same rate), and new nonspecific ST-segment and T-wave changes in inferior leads when compared with earlier tracings.

On the morning of surgery, the patient took one half of his usual doses of verapamil and benazepril. His medications were unchanged from his initial evaluation except for the addition of a steroid-containing topical ointment for a persistent rash. He denied recent angina but reported that he had become increasingly sedentary since his stroke 14 months earlier. Intravenous access was obtained, the patient was premedicated with midazolam and metoclopramide, and was taken to the operating room, where routine monitors were placed. Heart rate was 68 to 70 beats/min, and noninvasive blood pressure was 104/42 mmHg. Two 10-μg doses of sufentanil were given during preoxygenation. General anesthesia was induced with lidocaine (70 mg), etomidate (26 mg), and vecuronium (10 mg). After induction, the blood pressure decreased to 84/30 mmHg, with a heart rate of 68 beats/min. Cricoid pressure was maintained throughout a straightforward direct laryngoscopy and atraumatic tracheal intubation. Blood pressure returned to 108/40 mmHg, and the heart rate decreased to 58 beats/min after laryngoscopy.

Blood pressure decreased slightly with the addition of isoflurane and additional sufentanil to a total of 40 μg. Ephedrine (5 mg) was given twice during the 20 minutes after induction and

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1053-0770/06/2002-0026$32.00/0
doi:10.1053/j.jvca.2005.12.009
Key words: carotid endarterectomy, ACC/AHA guidelines, preoperative evaluation, cardiovascular collapse, plaque instability

3 more times before skin incision 30 minutes later. After placement of a left radial arterial catheter, heart rate was 72 beats/min, arterial blood pressure was 102/50 mmHg, and the ECG was unchanged. Systolic blood pressure varied from 86 to 117 mmHg. One liter of crystalloid solution was infused over 30 minutes before skin incision, and the heart rate remained 55 to 65 beats/min despite five 5-mg doses of ephedrine.

End-tidal isoflurane concentration was increased from 0.7% to 1% before skin incision, which occurred 50 minutes after induction. Blood pressure increased from 92/34 to 150/60 mmHg, with an increase in heart rate from 56 to 78 beats/min. Five minutes later, the heart rate increased to 92 beats/min, and the blood pressure decreased to 98/56 mmHg. The ECG at this time displayed an abrupt ST-segment depression in leads II and V_5. As the blood pressure decreased, additional 5-mg doses of ephedrine, for mild indirect inotropic effect, and 100-μg doses of phenylephrine, for mild vasoconstriction, were given along with a fluid bolus for preload support. Phenylephrine was initially used because the severity of the cardiovascular collapse was not immediately apparent and was chosen to provide sufficient coronary perfusion pressure for myocardial function. After additional boluses of ephedrine, phenylephrine, and crystalloid, phenylephrine (50-100 μg/min) and nitroglycerin (60-100 μg/min) infusions were started for treatment of apparent myocardial ischemia, without immediate effect. Nitroglycerin, a nonspecific vasodilator, was added for coronary vasodilation because the immediate working hypothesis was myocardial ischemia and resulting ventricular dysfunction. Transesophageal echocardiography (TEE) was considered immediately but was not performed because of potential interference with the surgical field.

The surgeons were advised to terminate the procedure in the face of a suspected myocardial infarction. Dopamine was started at 5 μg/kg/min for inotropic support. Blood pressure continued to decrease, and over the next 15 minutes, the nitroglycerin infusion was stopped and the authors replaced the phenylephrine infusion with an epinephrine infusion (0.02 μg/kg/min), with the goal of supporting blood pressure and thereby coronary perfusion, and improving contractility. Dopamine, epinephrine, and then norepinephrine were added for contractility and afterload to preserve coronary perfusion. Blood pressure decreased from 80/42 to 60/40 mmHg, and the heart rate increased from 58 to 84 beats/min.

While the surgeons closed the incision, the epinephrine infusion was changed to a norepinephrine infusion at 0.05 μg/kg/min, again for coronary perfusion pressure. The choice of epinephrine versus norepinephrine is somewhat arbitrary and institution- or anesthesiologist-specific. This allowed the nitroglycerin infusion to be restarted, the heart rate increased to 110 beats/min, and the blood pressure slowly increased to 80/54 mmHg. Esmolol (10 mg) was given twice over 20 minutes to reduce the heart rate to around 90 beats/min. A longer acting beta-blocker was not considered in light of the preoperative bradycardia and tenuous blood pressure. The norepinephrine infusion was slowly increased to sustain the blood pressure around 100/60 mmHg. The surgical wound was closed 65 minutes after incision, and the low dose of the inhalation agent was discontinued. The patient was transported to the postanesthesia recovery room (PACU) monitored, sedated, and intubated, on 100% F_IO_2, with an initial blood pressure of 113/67 mmHg, heart rate of 107 beats/min, and infusions of nitroglycerin (0.3 μg/kg/min), norepinephrine (0.25 μg/kg/min), and dopamine (3 μg/kg/min). An ECG performed immediately on arrival to the PACU showed inferior subendocardial injury (Fig 1).

The patient's vital signs remained stable for approximately 15 minutes after arrival to the PACU. Laboratory results at this time included the following: hemoglobin 12.6 g/dL, hematocrit 38.2%, prothrombin time/partial thromboplastin time 1.12/26.1 sec, troponin-I $<$0.3 (normal 0-2.0), total creatine kinase 38 (normal 0-250), creatine kinase–MB 1.5 (normal $<$8.0 μg/L when total creatine kinase $<$250), and mild acidosis (pH 7.24). The patient then became hypotensive again, largely unresponsive to norepinephrine and dopamine infusions, and continued to display marked ST-segment depression in the inferior and lateral leads. A pulmonary artery catheter was inserted, as inotropic support was increased, and the patient was transferred emergently to the cardiac catheterization laboratory (approximately 80 minutes after admission to the PACU). Arterial systolic blood pressure was 82 mmHg, heart rate was 94 beats/min, and the patient remained intubated and largely unresponsive. An echocardiogram at this time showed normal valves, enlarged right atrium and right ventricle, no pericardial effusion, and severe left ventricular and right ventricular hypokinesis. An intra-aortic balloon pump was placed and cardiac catheterization was performed, which showed a severely calcified left coronary system, a subtotal left main coronary stenosis with a filling defect consistent with thrombus or plaque rupture (Fig 2), a significant long stenosis in the circumflex artery distal to the first marginal branch, and slow filling of the left anterior descending coronary artery. Angioplasty of the left main coronary artery was performed and a stent was placed, but despite continued resuscitation attempts, including atropine, epinephrine, amiodarone, intra-aortic balloon pump, and transvenous pacing, the patient could not be resuscitated and was pronounced dead approximately 60 minutes after arrival in the cardiac catheterization laboratory.

DISCUSSION

As clinical production and cost-effectiveness pressures increase, the difficulties in determining and ensuring an adequate and appropriate preoperative evaluation of patients at risk for CAD have increased dramatically. All preoperative tests engender expense and, often, at least some risk. Unfortunately, no specific preoperative tests for cardiac risk have been shown to be highly reliable in predicting patients who will have cardiac events in the perioperative period. Additionally, there are little data to support the hypothesis that specific cardiac interventions can decrease cardiac risk during surgery.

Perioperative myocardial infarction (MI) appears to be multifactorial, tending to cluster in a bimodal pattern and occurring either in the immediate postoperative period or several days postoperatively. This pattern is presumably caused by changing relative importance of different mechanisms. Platelet activation, vasospasm, increased catecholamines, and tachycardia have all been proposed as contributing factors in both acute and chronic events. Acute events, such as thrombosis or spasm in areas of mild-to-moderate stenosis, appear to be the cause of

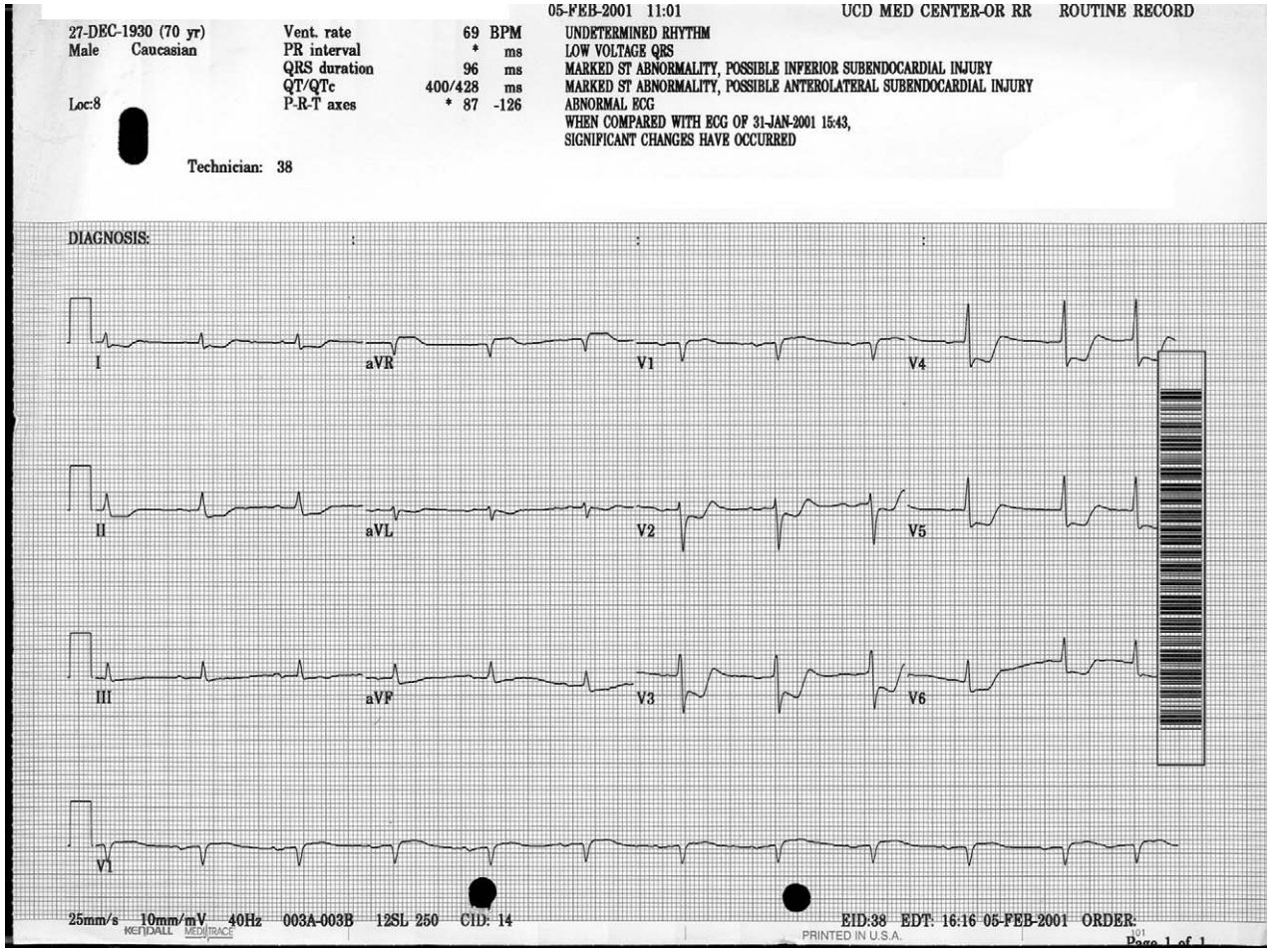

Fig 1. ECG immediately on arrival to PACU. Marked ST-segment depression noted in anterior, inferior, and lateral leads.

many perioperative MIs because post-MI coronary catheterization often reveals patent coronaries in the distribution of injury.[4,5] In approximately 50% of reported cases of fatal or nonfatal MI, there is no correlation with lesions in the referable distribution at autopsy or at angiography,[4] although left main disease is found more often in fatal MI.[6] Given the uncertainties in determining definitive mechanisms for perioperative MI, a balanced approach to preoperative cardiac risk assessment is indicated, including evaluation of clinical risk factors, extent of surgery planned, and costs and risks of the testing methods available.[7] The ACC and AHA have jointly published guidelines for this purpose based on consensus of an expert panel.[8] These guidelines were updated in 2002.[9]

The ACC/AHA guidelines discuss the impact of comorbid diseases, surgical risks, cardiac history, and the urgency of the procedure, in the context of the need and opportunity for preoperative cardiac evaluation. Surgical procedures of greatest risk include emergent major operations, particularly in the elderly; aortic and major thoracic, abdominal, or peripheral vascular surgery; and any prolonged procedure with large fluid shifts or blood loss. In contrast, CEA is considered to have an intermediate cardiac risk (<5%). Independent major clinical

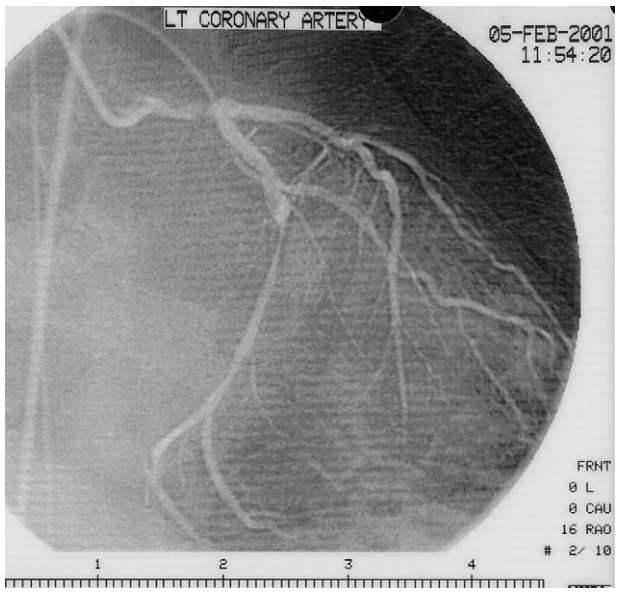

Fig 2. Cardiac catheterization findings. Significant occlusion of the left main coronary artery is shown before stent placement.

cardiac risk factors include acute coronary syndromes, decompensated heart failure, significant arrhythmias, and severe valvular disease. Heart-failure patients in particular have a much higher incidence of death within 30 days of noncardiac surgery than matched patients with CAD alone, whose death rate was similar to controls in a recent analysis of Medicare patients.[10] Although the guidelines state that "several large surveys have demonstrated that perioperative cardiac mortality is particularly concentrated among patients who undergo major thoracic, abdominal, or vascular surgery, especially when they are 70 years or older," CEA and advanced age were specifically excluded from high-risk categories. The guidelines also point out that ". . . patients who require vascular surgery appear to have increased risk for cardiac complications" because risk factors for PVD are similar to those for CAD.

According to the AHA/ACC guidelines, this patient had no major risk factors, and of the intermediate risk factors, only chronic mild angina (Canadian class I or II). Of minor risk factors, which do not independently increase cardiac risk, he had a low functional capacity with PVD, a history of a complication during cardiovascular evaluation (cerebrovascular accident during carotid angiography), and at least 1 abnormal ECG (left bundle branch block, strain pattern, possibly indicating left ventricular hypertrophy, and nonspecific ST-segment changes, noted previously). Comorbid diseases included smoking and chronic obstructive pulmonary disease. Notably, a footnote in the guidelines states that "severe angina (a major risk factor) may include 'stable angina in unusually sedentary patients'." Cardiac symptoms are also often masked because of the limitations of activity that result from PVD.

Using the "stepwise approach to perioperative cardiac assessment" found within the guidelines, the patient reported on here was a candidate for noninvasive cardiac testing.[7,9,11] The results of 2 separate myocardial perfusion studies some 18 months apart placed him into the "low-risk" category, meaning that no further testing was indicated, and therefore no coronary angiography was done. Although the report of distal aortic surgery 20 years before the CEA, a history of chronic PVD, and prior stable angina all increase the likelihood of extensive CAD; based on the noninvasive testing performed and the stability of the patient's symptoms, this patient was not at elevated risk for a coronary event according to the ACC/AHA guidelines. There was no contraindication to proceeding directly to the operative procedure. That he suffered a catastrophic cardiac complication during his surgery serves to emphasize that predictions of risk are only probability statements and not certainties. Despite the bad outcome in this specific case, invasive evaluation of all vascular surgery patients who present as this patient did is not indicated because the yield would not justify the potential morbidity of testing and cost. Based on autopsy and angiography studies,[4-6] it is also not certain that angiography would have shown a critical stenosis in this patient. A recent retrospective review[12] suggests that perioperative mortality is increased if vascular surgery is performed within 30 days of stent or coronary artery bypass graft (CABG) procedures, raising the specter of an increased risk of acute, presumably thrombotic events triggered by recent invasive improvements in coronary flow. In addition, McFalls et al[13] randomized more than 500 patients to either coronary artery revascularization or nonrevascularization before vascular surgery and found no significant improvement in long-term outcomes with revascularization. This, in part, contradicts the earlier, nonrandomized report of Rihal et al[14] that described benefit of coronary revascularization in vascular patients on mortality, without regard for the timing of revascularization. Angiography might have shown noncritical stenosis of the left main coronary artery that at the onset of surgery became unstable, resulting in near occlusion. The study by McFalls et al excluded patients with left main stenosis of greater than 50%.

The most recent ECG in this patient was 5 days before surgery and showed nonspecific ST-segment and T-wave changes. In the absence of new symptoms or new arrhythmias, nonspecific ECG findings in the context of low-risk preoperative stress evaluations did not change the anesthetic plan. The authors chose to place additional intravenous access and an arterial catheter but not a central venous catheter or pulmonary artery catheter. The ACC/AHA guidelines state that current evidence does not support the routine use of pulmonary artery catheters perioperatively, in agreement with the American Society of Anesthesiologists Practice Parameters.[15] This patient was considered class III in those practice parameters, undergoing a procedure with low risk of hemodynamic disturbance or massive fluid shifts. A pulmonary artery catheter might have provided additional information, but in the authors' estimation, aggressive symptomatic treatment was indicated immediately after the precipitous ST-segment depression occurred, and a pulmonary artery catheter would have changed neither a presumptive diagnosis nor immediate therapy.

Use of a TEE probe is awkward during a CEA procedure because of the surgical site. TEE is useful in detecting wall motion abnormalities, but it is also not obvious that this would have changed the interventions nor would it have led to any different or earlier therapeutic interventions. The severe stenosis of the left main coronary artery that was seen on postoperative cardiac catheterization was probably either because of plaque rupture and thrombus formation or preexisting severe stenosis that had been masked by inactivity. From the time of onset of marked ischemic changes on ECG until the incision was closed was about 35 minutes. After a brief period of stable vital signs while on inotropic support in the PACU, the patient again displayed marked cardiac instability and profound hypotension. He was transported to the cardiac catheterization laboratory within 80 minutes of arrival in the PACU. It is difficult to imagine a scenario that would have resulted in a different outcome or in the patient arriving for cardiac catheterization significantly sooner.

Despite the remarkable improvements in perioperative morbidity and mortality with the use of perioperative beta-blockers, it is clear that other factors continue to exert a significant role in perioperative cardiac events. Although clinicians are making progress in understanding the relationships among chronic stenosis, plaque stability and rupture, platelet activation, and perioperative stresses and events, definitive cause and effect remains elusive. Several authors[16-18] report that inflammatory markers are dramatically increased in coronary plaques that have ruptured. Indeed, plaque instability is more closely associated with perioperative cardiac morbidity than coronary artery stenosis alone.[19] Plaque instability and inflammatory re-

sponse may therefore be more important determinants of perioperative MI than critical stenosis.[16,20] For example, increased lipoprotein-associated phospholipase A2 co-localizes with inflammatory markers in sections of atherosclerotic plaque from sudden coronary death victims.[21,22] Similarly, thrombotically active (inflammatory) plaque in ipsilateral extracranial carotid arteries is also highly associated with the risk of transient ischemic attack or stroke.[23] The patient's genotype[24] and single nucleotide polymorphism (SNP) profile may also be a critical indicator of propensity to acutely thrombose a coronary vessel under the added stimulus of anesthetic and surgical "stress." Preoperative genetic testing may ultimately lead to patient-specific, or at least SNP-specific, therapeutic drug selection. Ultimately, to the perioperative beta-blocker, clinicians may eventually add a perioperative plaque stabilizer or perhaps a brief fibroblast-stimulating factor and a small interfering RNA to transiently suppress the inflammatory pathways that are contributory to the plaque instability and thrombus formation.

COMMENTARY 1†

One of the greatest clinical and public health achievements has been the decline in age-adjusted mortality from coronary heart disease and total cardiovascular disease.[25] These remarkable declines have accounted for substantial reductions in all-cause mortality. Pharmacologic primary and secondary prevention and surgical/interventional revascularization have contributed to these gains. Patients with congestive heart failure now live longer because of drug and device therapy. Despite these impressive advances, heart disease remains the leading cause of death in the United States, where it is a major cause of disability as well. As a consequence, patients live longer and present for surgery and anesthesia more often than in the past, despite severe comorbidities. Additionally, as interventions for carotid stenosis and other vascular conditions improve (and become less invasive), more patients with significant CAD will present for anesthetic management during revascularization procedures. These patients are at increased risk for perioperative cardiovascular complications.

In the case presented, the patient developed hemodynamic collapse during CEA, accompanied by ischemic ECG changes. In such a situation, the anesthesiologist will be challenged to balance myocardial perfusion against anesthetic requirements to blunt perioperative stress. A management plan to meet these challenges will include an anesthetic strategy that minimizes wide hemodynamic swings, early suspicion of ischemia as a cause of instability, and availability of resuscitation therapies that can increase coronary blood flow. In some cases, expeditious coronary intervention may also be indicated. The preceding case underscores the importance of these principles. This discussion will highlight various forms of intervention, realizing that the final outcome in this particular case was likely unavoidable.

This patient presented for CEA because of 80% to 99% stenosis of the right ICA. This lesion was originally asymptomatic, although the patient suffered a small stroke at the time of cerebral angiography. For this reason, many centers now usually use only noninvasive imaging studies such as Doppler ultrasonography or magnetic resonance angiography to define cerebrovascular anatomy. Available large studies suggest that these asymptomatic lesions may benefit from surgical intervention,[26] although benefits (and risks) are greater for surgical revascularization of patients with symptomatic carotid stenosis.[27] In recent years, carotid angioplasty and stenting (with devices that protect against distal embolization) have emerged as effective alternatives with potentially fewer cardiovascular complications.[28]

This patient suffered a devastating perioperative MI. Epidemiologically described as one type of complication of vascular surgery, perioperative MI is a heterogenous phenomenon with a mortality of at least 20%.[29] The presence of CAD is common to the majority of events, but pathogenesis varies. Most perioperative MIs occur in regions with diminished blood flow reserve, the result of inadequate oxygen supply in the face of heightened demand. Such events evolve in response to the hemodynamic demands of anesthesia and surgery. Less commonly, but possibly shown by this case, acute thrombosis may be superimposed over a coronary plaque and cause an infarction of downstream myocardium. Hemodynamic swings might stress sensitive plaques; additionally, catecholamines exert hemostatic changes that favor coagulation and decreased fibrinolysis. Diminished blood flow across stenoses, exacerbated by hypotension, favors stasis that might support thrombosis. The current conceptual understanding of perioperative MI is insufficient to accurately predict every patient and/or coronary territory in which an event will occur, but it does provide guidance as to risk and management.[19,30]

During CEA, maintaining adequate cerebral perfusion dominates intraoperative hemodynamic management, but the vigilant anesthesiologist must continually weigh ischemic risk to the myocardium. One important goal of management is to minimize hemodynamic perturbations during general anesthesia. Coronary stenoses complicate the circulatory goals of maintaining adequate end-organ perfusion in patients with cardiovascular disease. Hypotension, tachycardia, and hypertension correlate with cardiovascular morbidity and mortality.[31] Hypotension reduces flow across stenotic coronary arteries, leading to ischemia. Tachycardia increases myocardial oxygen consumption and decreases diastolic perfusion to the left ventricle. Hypertension increases left ventricular wall tension, increasing oxygen consumption. Ischemia increases wall tension and decreases cardiac output. The synergy of these phenomena may produce abrupt hemodynamic collapse. A carefully constructed anesthetic should balance anesthetic depth and stimulation to avoid hemodynamic swings.

As previously mentioned, advances in pharmacologic prophylaxis have improved survival in cardiovascular and cerebrovascular disease. However, chronic and perioperative patient medication regimens can adversely impact perioperative management. On the day of surgery, this patient took one half of his normal dose of angiotensin-converting enzyme inhibitor (ACEI). ACEIs are associated with hypotension after anesthetic induction[32] and may increase the risk of hemodynamic instability if given on the day of surgery. Despite this, patients who fail to resume chronic ACEI after noncardiac surgery may have

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greater numbers of postoperative cardiovascular complications.[33] Continuation of aspirin may be of benefit to prevent acute carotid thrombosis as well as to decrease the risk of acute coronary thrombosis but at the risk of increased surgical bleeding. Perioperative beta-blockade favorably alters the balance between myocardial oxygen supply and demand and may exert benefits independent of reduction in myocardial work.[34]

In the case of CEA, anesthesia may be provided with local infiltration, cervical plexus block, general anesthesia, or any combination of these. Although some authors have favored regional anesthesia for CEA,[35] a systematic analysis suggests that the literature published in this area is generally underpowered or not derived from randomized trials to an extent sufficient to allow evidence-based recommendations.[36] If general anesthesia is chosen and endotracheal intubation is performed, placing and removing the endotracheal tube are often the most stimulating phases of the anesthetic; otherwise, anesthetic requirements are generally low. Therefore, anesthetic induction is challenging because a depth of anesthesia sufficient to blunt hyperdynamic responses to intubation may soon thereafter lead to hypotension if the depth of anesthesia is not "lightened" once the trachea has been intubated. Hypotension after induction might precipitate myocardial or cerebrovascular ischemia in the high-risk patient. The authors induced this patient with a full induction dose of etomidate (0.32 mg/kg) and supplemental sufentanil (20 μg). Postintubation hypotension may have resulted from the residual effect of these intravenous agents. Etomidate is associated with less cardiovascular depression than other induction agents, but hypotension has been reported.[37] Maintenance with isoflurane and additional sufentanil may have contributed to a need for boluses of ephedrine after induction. In this patient, increased anesthesia depth and hypotension may have played a role in the evolution of ischemia. During CEA, a randomized trial has shown that elevating blood pressure with phenylephrine in patients receiving volatile anesthetics increases left ventricular wall stress and wall-motion abnormalities (which might indicate myocardial ischemia), more so than simply "lightening" the volatile anesthetic.[38] In the face of hypotension refractory to multiple ephedrine doses, earlier conversion to an alternative pressor, such as phenylephrine or vasopressin, might have been helpful. The latter is useful for combating hypotension in patients using ACEIs,[39] although it may carry the risk of coronary vasospasm[40] or mesenteric ischemia.[41] Physiologically, norepinephrine may have been a better option for treatment of hypotension associated with the use of volatile anesthetics because this drug better preserves left ventricular function in CAD patients than does phenylephrine.[42]

As hemodynamic instability became more apparent, myocardial ischemia/infarction emerged as the working diagnosis, especially in the absence of significant surgical blood loss. The appearance of ST-segment abnormalities strengthens the evidence for ischemia. The authors describe the changes as abrupt, although often the time of origin of ST-segment changes is difficult to ascertain without continuous archived ST-segment analysis.[43] At this point, TEE could have provided useful data to show wall-motion abnormalities, confirming the diagnosis of an acute infarction or severe ischemia. In this case, coronary intervention may have been considered earlier. Although technically more challenging, these commentators do not believe that CEA represents a contraindication to the placement of a TEE probe.[44] The anesthesia team appropriately focused on minimizing myocardial ischemia and attempted stabilization before eventual transfer for cardiac catheterization. Nitroglycerin and phenylephrine infusions, used together with the goal of increasing coronary perfusion, are described in earlier literature,[45] but the administration of a vasodilator can prove difficult in the setting of cardiogenic shock. Similarly, attempts at beta-blockade proved problematic in this patient. It is possible that earlier institution of intra-aortic balloon counterpulsation could have helped to unload the ischemic ventricle and improve coronary perfusion while waiting for surgical closure. The authors appropriately advised the surgeons to terminate the procedure to facilitate stabilization and coronary intervention. Decisions to stop or suspend a surgical procedure are complicated and require careful discussion between surgical and anesthetic teams. The surgeon must carefully weigh the urgency of the surgical procedure, the stage of the procedure, and ways to expedite further evaluation and therapy for ongoing ischemia. In this case, transfer to another service location for coronary angiography and intervention took highest priority.

Prompt cardiac catheterization for determination of coronary and valvular anatomy and possible percutaneous coronary intervention are important goals in this case. Cardiogenic shock has a mortality rate approaching 80%. Mortality is marginally improved with medical management (including intra-aortic balloon counterpulsation) but more significantly improved with early revascularization, surgical or percutaneous.[46] Once ischemia is recognized, all efforts should focus on rapid cardiac catheterization. It is not clear whether the CEA was completed, but surgical closure lasted 1 hour 5 minutes, expending valuable time for myocardial salvage. This patient was taken to the PACU, although direct transfer to the catheterization laboratory would have been preferable to save time. It is true, however, that this can be difficult to orchestrate.[47] Because the 12-lead ECG taken in the PACU was highly suggestive of ischemia in the face of hemodynamic instability, placement of a pulmonary artery catheter offered little additional information and potentially increased the delay to intervention. The patient was finally transferred to the catheterization laboratory 2 hours 25 minutes after surgical closure began.

Acute thrombosis of the left main coronary artery, as visualized in the catheterization laboratory, affirmed the diagnosis. Left main coronary artery lesions are classically treated by CABG surgery, although angioplasty and stenting are described.[48] Primary percutaneous intervention of left main disease is currently indicated only if emergent CABG is unavailable or if the patient is deemed inoperable. In the face of severe hemodynamic deterioration, the decision by the cardiologists involved to attempt to angioplasty the lesion made sense, and given the rapid clinical deterioration, it is unlikely that it would have been possible to surgically revascularize the patient before his demise.

In retrospect, it can be speculated whether the outcome would have been different had the patient received carotid artery stenting rather than traditional carotid artery CEA.[49] Left main coronary disease is more common in patients with severe carotid stenosis.[50] In this case, however, it is not surprising that

the preoperative stress test was negative; preoperative dobutamine stress echocardiography (DSE) does not reliably predict which segments of the heart may infarct after vascular surgery.[51] This study found that although most patients who suffered perioperative MI have a positive DSE, the area of infarct often extended far beyond what the DSE would have predicted. Alternatively, this patient may represent a case of "balanced ischemia," a situation in which there is significant 3-vessel disease (ie, no area of myocardium has normal perfusion), but the perfusion images seem normal. Nuclear stress tests detect perfusion defects relative to normally perfused segments. However, in these patients, there is no normal segment; all segments have similar perfusion and the images appear to be "normal." Were this the case, it might mean that the left main lesion was chronic rather than an acute event.

It can be suspected that the MI in this case arose because of acute coronary rupture and/or thrombosis in an atherosclerotic plaque that originally produced little to no luminal stenosis and not necessarily because of systemic hypotension. Many perioperative MIs likely result from prolonged elevations in myocardial oxygen demand that can be improved with hemodynamic management. However, in this case, the inability of hemodynamic manipulations to improve ischemia suggests a primary "supply" problem. It is hard to say from the single still angiographic image presented by the authors if this was a preexisting lesion or a new, acute thrombus. Acute thrombi do have a typical angiographic appearance; generally, a hazy filling defect (instead of luminal narrowing for chronic lesions). This is extremely difficult to discern on a still-frame picture. Acute lesions are usually "soft" and can be easily crossed with a wire via percutaneous intervention attempts.

The chronic and perioperative care of patients with known or suspected CAD have improved immensely in the past decades, but this case report emphasizes that vigilance is still required in the care of these complex and challenging situations.

COMMENTARY 2‡

These authors report on a case of catastrophic MI in a patient undergoing CEA. Unfortunately, the scenario described is all too familiar to practicing anesthesiologists: a stable patient undergoing a routine elective procedure suffers cardiovascular collapse and death despite appropriate preoperative cardiac evaluation and perioperative management. This, of course, begs the question, when everything is done right, why do things occasionally go wrong?

The ACC/AHA guidelines for perioperative cardiovascular evaluation for noncardiac surgery, originally released in 1996 and updated in 2002, provide a framework for the cardiac evaluation of patients presenting for noncardiac surgery based on a review of the literature and expert opinion. The guidelines consider both preexisting patient characteristics and risk of the proposed surgical procedure in assessing the extent of preoperative cardiac evaluation necessary.[52]

The guidelines stratify clinical predictors of increased perioperative cardiovascular risk into major, intermediate, and minor categories. Major risk factors include severe valvular disease, unstable coronary syndromes, significant arrhythmias, and decompensated congestive heart failure. Intermediate risk factors include mild angina, prior infarction, prior congestive heart failure, chronic renal insufficiency, and diabetes mellitus. All other clinical indicators are considered minor predictors of risk.[53]

In addition, the guidelines stratify the risk of the surgical procedure into high-, intermediate-, and low-risk categories based on the incidence of perioperative cardiac events. High-risk (greater than 5% incidence of cardiac event) procedures include emergent operations, major and peripheral vascular surgeries, and anticipated prolonged procedures with major fluid shifts and blood loss. Intermediate-risk procedures entail an incidence of a cardiac event between 1% and 5% and include CEA, thoracic, intra-abdominal, and orthopedic surgeries. Low-risk procedures carry a less than 1% risk of a cardiac event.

These factors, taken in conjunction with the patient's functional status, most recent cardiac evaluation, and history of revascularization, enable the clinician to determine the need for further noninvasive or invasive cardiac evaluation. Presumably, appropriate utilization of the guidelines and the preoperative cardiac workup influence clinical practice and thereby decrease the risk of a perioperative event.[54]

Do the guidelines actually decrease the risk of perioperative cardiac events? In a retrospective analysis of 468 consecutive patients who underwent abdominal aortic surgery before (control group) and after the implementation of the ACC/AHA guidelines at a single institution, Licker and colleagues[55] found that use of the guidelines was associated with increased myocardial scanning (44.3% *v* 20.6%), increased incidence of event-free surgery (from 91.3% to 98.2%), and a decreased incidence of cardiac complications (11.3%-4.5%). However, in a prospective randomized study of 99 patients with minor or intermediate risk factors undergoing peripheral vascular surgery, Falcone and colleagues[56] found that cardiac stress testing within the ACC/AHA guidelines framework did not further identify patients at increased risk for cardiac events.

The effectiveness of these guidelines in stratifying risk hinges on the utility of the invasive and noninvasive tests currently used to assess cardiac function and perfusion. To be clinically useful, noninvasive imaging tests must predict both perioperative events (positive predictive value) and the absence of these events (negative predictive value). Studies of myocardial perfusion imaging and dobutamine stress testing suggest that they are of little positive predictive value when compared with cardiac risk indices alone. Although the majority of studies show good negative predictive value for dobutamine stress testing, the evidence is mixed on the negative predictive value of myocardial perfusion imaging.[57] Clearly, a subset of patients at risk for perioperative cardiac events remains difficult to identify even with proper preoperative evaluation.

The pathophysiology of perioperative MI has been the focus of intense clinical research for the past decade. Two major paradigms of myocardial ischemia and injury exist, each with a unique pathophysiology and distinct clinical implications. Of particular interest to the anesthesiologist is the relationship between perioperative MI and the current understanding of MI in the nonsurgical patient.

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The pathophysiology of MI in the nonsurgical patient begins with the formation of an unstable plaque on a coronary vessel. Shear forces within the vessel lumen or inflammatory processes within the plaque lead to acute plaque rupture. The ruptured plaque induces local platelet aggregation, thrombin formation, which results in the development of thrombus within the coronary artery and, ultimately, myocardial ischemia and thrombosis.[4]

In contrast to the nonsurgical MI, "supply and demand" ischemia may play a more significant role in perioperative MI. In this model, the patient with a fixed high-grade coronary stenosis experiences a prolonged catecholamine surge in the perioperative period, leading to increased myocardial oxygen demand. In the face of the preexisting stenosis, this increased demand cannot be met with increased oxygen delivery, and myocardial ischemia and infarction ensue.

Current evidence suggests that both mechanisms are at play in the genesis of perioperative MI. Dawood and colleagues[6] found evidence of plaque rupture and acute coronary thrombosis on autopsy in 55% of subjects who suffered fatal perioperative MI. In addition, the severity and location of preexisting stenosis did not predict the resulting infarct territory. The inflammatory and prothrombotic stress responses induced by surgery, in addition to changes in intraluminal shear forces secondary to catecholamine surge, may considerably increase the risk of plaque rupture in the perioperative patient.

Preoperative testing and risk stratification are most useful in identifying patients at elevated risk for "supply and demand" ischemia. Once identified, the anesthetic management of these patients can be modified to reduce the incidence and duration of supply and demand mismatch. However, preoperative evaluation is clearly of little utility in identifying patients at risk for plaque rupture. In fact, those with mature, high-grade, stable stenosis may be at considerably less risk of rupture than those with low-grade but unstable lesions.[58]

Evidence continues to accrue that therapy directed at modulating risk of plaque rupture may be of tremendous benefit to patients undergoing surgery. In a case control study, Poldermans and colleagues[59] found that perioperative statin use resulted in a greater than 4-fold reduction in mortality risk, presumably because of plaque stabilization. Perioperative beta-blockade may decrease intraluminal shear forces and thereby prevent plaque rupture. The Coronary Artery Revascularization Prophylaxis trial that showed no benefit to coronary revascularization before elective major vascular surgery may represent an increased risk of plaque formation in the immediate post-revascularization period, obscuring the positive impact of revascularization on myocardial oxygen supply.[60,61]

Perioperative MI in the vascular surgery patient remains of major concern to the anesthesiologist, despite recent reductions in incidence and mortality. With the evolution of the understanding of the various pathways leading to MI, it has become clear that preoperative testing alone may be missing a significant population of patients at risk. However, as the ability to manipulate the surgical stress response and its effect on the coronary circulation develops, a future in which preoperative assessment in conjunction with pharmacologic intervention results in further dramatic reductions in cardiac morbidity and mortality may be just around the bend.

ACKNOWLEDGMENT

J.G.H. wishes to thank Ann Marie Tenuto for her valuable assistance in the preparation of this manuscript and Drs Neal Fleming and Lee Fleisher for their insightful comments.

The American College of Cardiology Web site is available at: http:/www.acc.org/clinical/guidelines/perio/dirIndex.htm. This document is available on the World Wide Web sites of the American College of Cardiology (www.acc.org) and the American Heart Association (www.americanheart.org). Single copies of this document (the complete Guidelines) as well as the Executive Summary that is published in the February 6, 2002 issue of the *Journal of the American College of Cardiology* and the March 5, 2002 issue of *Circulation* are available online or by calling 800-253-4636 (US only) or writing the American College of Cardiology, Educational Services, 9111 Old Georgetown Road, Bethesda, MD 20814-1699. To purchase additional reprints, please specify version (executive summary, 71-0220; full text, 71-0219): up to 999 copies, call 800-611-6083 (US only) or fax 413-665-2671; 1,000 or more copies, call 214-706-1466, fax 214-691-6342, or e-mail pubauth@heart.org. The Guideline Update was also published in *Anesthesia and Analgesia* (94:1052-1064, 2002).

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