Perioperative Myocardial Infarction in Patients Undergoing Noncardiac Surgery

TO THE EDITOR: I read the recent article by Devereaux and colleagues (1) regarding perioperative myocardial infarction (MI) with interest. Although the cohort data presented derive from a large prospective, randomized, controlled trial, the authors’ findings are consistent with and confirm those of prior studies regarding perioperative myocardial ischemia and infarction—namely, that perioperative MIs are common, often clinically silent, and associated with significant mortality (2, 3).

A notable finding is that increased preoperative or baseline heart rate was an independent risk factor for perioperative MI. Although the authors acknowledge this as a potentially modifiable risk factor, they refrain from commenting on their own prior findings that perioperative β-blockade reduced cardiovascular deaths. The authors also do not comment on the ensuing controversy regarding perioperative β-blockade prescribed in a goal-directed fashion, as opposed to the fixed doses used in the POISE (PeriOperative ISchemic Evaluation) study (4).

The authors’ call for randomized, controlled trials to investigate effective treatments for perioperative MI is appropriate. In the absence of such trials, however, their statement that “routine monitoring of cardiac biomarkers after surgery is essential” is premature and contrary to published American College of Cardiology/American Heart Association Perioperative Guidelines (5). The findings from the present study—that isolated biomarker elevation is more common than perioperative MI—should instead support the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery) developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, and Society for Vascular Surgery: J Am Coll Cardiol. 2007;50:e159-241. [PMID: 17950140]

Cardiac biomarker surveillance detects acute myocardial cell injury after it happens. Our efforts to decrease perioperative cardiac complications should be performed earlier to facilitate intervention before cell injury or death. Postoperative ST-segment depression has been shown to be a silent predecessor to clinical cardiac events (2, 3). Because ST-segment depression is present for 30 minutes before clinical events, early intervention based on ST-segment deviations holds greater potential to reduce perioperative cardiac morbidity and mortality than interventions instituted once damage has occurred. For these reasons, future randomized, controlled trials directed at interventions based on ST-segment deviations should be given higher priority than those using cardiac biomarker surveillance.

Darryl Potyk, MD
Internal Medicine Residency Spokane, University of Washington School of Medicine
Spokane, WA 99204

Potential Conflicts of Interest: None disclosed.

IN RESPONSE: Dr. Potyk states that we did not comment on the effects of perioperative β-blockade. On the basis of all the β-blocker trials in patients undergoing noncardiac surgery, there is strong evidence that β-blockade prevents perioperative MI. Contrary to Dr. Potyk’s statement, perioperative β-blockade probably increases the risk for death and almost certainly increases the risk for stroke (1, 2). Our interpretation of these data is that controlling the sympathetic system in the perioperative setting is beneficial, but we need to find a way to do it safely and practically.

Dr. Potyk believes that it is not necessary to monitor perioperative troponin levels in at-risk patients. We disagree for the following reasons. Our data suggest that 5.0% of at-risk patients will have an MI and that 65.3% of these events would have gone undetected without monitoring troponin levels. Patients who have had a perioperative MI without ischemic symptoms have a poor prognosis (a 12.5% mortality rate at 30 days). Although 8.3% of patients had isolated elevation of troponin levels, these elevations represent myocardial injury and carry a poor prognosis. The highest quartile of these elevations was associated with a substantial increase in 30-day mortality (adjusted odds ratio, 2.54 [95% CI, 1.65 to 3.90]).

We have also recently demonstrated that elevated troponin levels (adjusted odds ratio, 6.7 [CI, 4.1 to 10.9]) after surgery independently affect mortality until at least 12 months after surgery (3). Our data show that many patients with elevated troponin levels and perioperative MI leave the hospital without medications that decrease the risk for major cardiovascular events (for example, acetylsalicylic acid or statins).

Awareness of elevated troponin levels and perioperative MI is necessary for optimum informed decision making in the postoperative period. We agree that it is preferable to prevent a perioperative event than to need to treat it. Continued efforts at evaluating a wide range of strategies are needed.

References
Discordant Thymectomy in Identical Twins Concordant for Myasthenia Gravis

Background: Thymectomy is standard therapy for nonthymomatous myasthenia gravis despite the absence of randomized clinical trials (1). Myasthenia gravis is uncommonly reported in monozygous twins; disease concordance occurs in approximately one third of such identical twin pairs; and treatment for myasthenia gravis, when described, is usually concordant in identical twin pairs (2).

Objective: To report an 11-year clinical course of a pair of identical twins discordant for generalized acetylcholine receptor antibody–positive nonthymomatous myasthenia gravis with whom only 1 was treated with extended transsternal thymectomy.

Case Report: Twin A was a 19-year-old white woman who presented with an 8-week history of intermittent leg weakness, causing her to fall during activities, such as climbing stairs. On examination, she had moderately severe fatigable proximal muscle weakness and ptosis. Her weakness improved with intravenous edrophonium. Initial binding acetylcholine receptor antibody titer was 75.3 nmol/L (normal value, $<0.03$ nmol/L). Repeative 2-Hz nerve (median, ulnar, and facial) stimulation studies demonstrated up to a 12% decremental response. Chest computed tomography showed thymic tissue without thymoma. Twin A has not been treated with immunosuppressive therapy. Despite an invariably normal examination, her strength normalized approximately 1 month after thymectomy and has remained normal for 11 years. Binding acetylcholine receptor antibody titers have remained elevated to a similar degree. Twin A has not been treated with immunosuppressive therapy. Despite an invariably normal examination, the patient uses occasional low doses of pyridostigmine for subjective fatigue.

Five months after her twin sister had developed initial symptoms of myasthenia gravis, twin B developed ptosis, diplopia, and proximal muscle weakness associated with an upper respiratory infection. On examination, twin B had moderately severe fatigable proximal muscle weakness and ptosis. Her weakness improved with intravenous edrophonium. Initial binding acetylcholine receptor antibody titer was 75.3 nmol/L (normal value, $<0.03$ nmol/L). Repetitive 2-Hz nerve (median, ulnar, and facial) stimulation studies demonstrated up to a 12% decremental response. Chest computed tomography showed thymic tissue without thymoma. Twin B declined thymectomy and immunosuppressant therapy and continued to have bilateral ptosis and fatigable muscle weakness that was moderately severe and greater in the proximal muscles than the distal muscles; weakness has been responsive to pyridostigmine therapy. Binding acetylcholine receptor antibody titers have remained similarly elevated over the past 11 years.

Twins A and B had identical human leukocyte antigen typing (A1, A23, B8, B44, C4, DR13, DR17, DQ2, DQ6, DR52), suggesting that they are monozygous twins. Normal serum complement (C3 and C4) levels were reported in both twins. There was no other family history of autoimmune disease. Although acetylcholine receptor antibody titer levels do not correlate with disease severity, twin B had much higher levels at diagnosis (3). Twin A’s acetylcholine receptor antibody titer levels did not decrease after thymectomy, but her strength became normal.

Discussion: We report our clinical observation on thymectomy compared with the natural disease history in a single set of identical twins. Compared with untreated twin B, thymectomy in twin A was associated with sustained clinical remission, with no requirement to use immunosuppressive therapy to maintain it. Although most nonrandomized studies suggest that thymectomy is associated with improved outcomes in myasthenia gravis (4), demonstration of clinical efficacy must await the outcome of a prospective, randomized clinical trial (5). Because no immunosuppressive agent was given to twin B, our clinical observation could not be ethically replicated in randomized clinical trial (5).

Kevin R. Riggs, MD, MPH
Duke University School of Medicine
Durham, NC 27710-3182

Laurie Gutmann, MD
Jack E. Riggs, MD
West Virginia University School of Medicine
Morgantown, WV 26506-9180

Potential Conflicts of Interest: Dr. Gutmann: Grants/grants pending (money to institution): Allergan; Royalties: UpToDate; Travel/accommodations/Meeting expenses unrelated to activities listed: American Board of Psychology and Neurology.
Treatment of Chronic Hepatitis E in a Patient With HIV Infection

Background: Hepatitis E virus (HEV) infections in immunosuppressed patients can result in chronic hepatitis that rapidly progresses to cirrhosis (1, 2). When immunosuppressed transplant recipients are treated with pegylated α-interferon and ribavirin, HEV clears and liver histology improves (2). However, we are not aware of reports about how this therapy works in patients with HIV infection.

Objective: To describe the clinical and laboratory response to antiviral therapy for chronic HEV infection in a patient also infected with HIV.

Case Report: We studied a 48-year-old bisexual male with HIV-1 infection who was chronically infected with HEV genotype 3a and had several years of painful sensory neuropathy of uncertain cause in the lower limbs (3). He had malaise, persistently abnormal liver function tests, and active inflammation and cirrhosis on liver biopsy (Figure). Before beginning anti-HEV therapy, the patient had an undetectable HIV viral load and a CD4 cell count between 30 and 150 cells/mL for the previous 2 years while receiving combination antiretroviral therapy (abacavir–lamivudine once daily and lopinavir–ritonavir twice daily).

To control the patient’s HEV infection, we administered pegylated α-interferon: 135 µg/wk for 6 months, followed by 6 weeks of pegylated α-interferon with ribavirin, 1000 mg/d. We reduced the dose of ribavirin to 500 mg/d for an additional 6 weeks owing to marrow suppression. Shortly after therapy began, the patient’s malaise improved, and his liver function tests became normal. There was a gradual and sustained improvement in his neurologic symptoms. The HEV viral load in plasma and stool declined steadily during the 6-month course of interferon monotherapy, so that at the end of monotherapy, HEV viral load was undetectable in plasma but still detectable in stool at $2.2 \times 10^{04}$ GEq/mL. After ribavirin was added to therapy, viral load in the stool decreased rapidly. The HEV RNA levels eventually became undetectable and remained largely undetectable over the next 9 months. However, very low levels of HEV RNA (5 to 55 GEq/mL) were detected intermittently in both plasma and stool. A liver biopsy taken 3 months after therapy was completed showed reduced inflammation and fibrosis (Figure). The patient’s CD4 count improved from a pretreatment count of 94 cells/mL (7%) to 270 cells/mL (10%) 6 months after HEV clearance. We detected HEV RNA in cerebrospinal fluid before treatment and at completion of therapy, but not 3 months later.

Discussion: The data show that chronic HEV infection can be successfully treated with interferon and ribavirin therapy when the patient has HIV-1 co-infection, although our patient required a longer period of treatment to achieve viral clearance than has been reported in transplant patients. Clearance of HEV was associated with an improvement in the patient’s symptoms, normalization of liver function tests, reduction in inflammation and fibrosis on liver biopsy, and improvement in CD4 cell count. The data also suggest that HEV infection may be associated with peripheral neuropathy (4), which can respond to HEV treatment. In our patient, viral clearance of HEV from cerebrospinal fluid lagged behind viral clearance from serum and stool levels and improvement in neuropathy symptoms, perhaps because of viral “compartmentalization” in different tissue spaces (5).
Acknowledgment: The authors thank Nassim Kamar and Janice Main for their advice about the treatment given to this patient.

Potential Conflicts of Interest: None disclosed.

References