Perioperative cardiac risk reduction:

Doing it right

ANDREW D. AUERBACH, MD, MPH

Various interventions to reduce the risk of cardiac complications during surgery have been proposed. This article evaluates the evidence for these preventive approaches, examines methods of incorporating new and conflicting evidence into a coherent clinical approach, and reviews systems for successfully implementing evidence-based interventions in the hospital.

APPROACHES FOR PREVENTING CARDIAC COMPLICATIONS

With revascularization reserved as a preventive measure for those patients at extremely high risk of cardiac complications, other less invasive preventive approaches should be considered.

Maintenance of normothermia

One preventive approach is maintenance of normal body temperature. In a randomized, controlled clinical study of 300 patients with or at high risk for coronary disease who underwent major abdominal or vascular surgery, supplemental warming care was associated with a significant ($P = .02$) reduction in perioperative morbid cardiac events compared with routine thermal care.[1] The risk of supplemental warming is low and the potential reward is high; in addition to the reduction in cardiac complications, patients randomized to normothermia in this study had a lower rate of surgical-site infections, less nausea, and better pain control.

Calcium channel blocker therapy

A recent meta-analysis[2] demonstrated a significant reduction in adverse coronary endpoints with the use of calcium channel blockers, compared with placebo, as preventive therapy in patients undergoing various types of surgery. This reduction in the risk of events, however, was driven entirely by a significant reduction in the incidences of ischemia and supraventricular tachycardia, with no effect of calcium channel blockers on perioperative myocardial infarction (MI) or death. The largest reductions in risk with calcium channel blockers occurred in patients undergoing thoracic surgery. In most of the studies in which a favorable effect of calcium channel blockers was observed, patients were on concomitant beta-blockade that was not adequately controlled for, which obscures interpretation of the meta-analysis. For these reasons, calcium channel blockers should not be considered first-line therapy as a preventive strategy.

Perioperative adrenergic modulation: Clonidine and other alpha-2 agonists

Adrenergic modulation includes not only beta-blockers but clonidine and other alpha-2 agonists. A trend toward a reduction in mortality was observed in recipients of alpha-2 agonists (most often clonidine) in a meta-analysis of 23 trials that included 3,395 surgical patients.[3] In patients undergoing vascular surgery, who represent a higher-risk group in which a positive effect is more likely to be uncovered, these agents were associated with significant reductions in the risk of mortality ($P = .02$) and MI ($P = .02$) relative to placebo.

Clonidine is a hospital-only drug; it has no first-line indications in long-term patient care, which is a deterrent to its use since transition to therapy outside the hospital is difficult. Transdermal delivery is an advantage to the use of clonidine in the surgical setting. The patch can be applied in the preanesthesia holding area and then removed when the patient is discharged.

Perioperative adrenergic modulation: Beta-blockers

As in the ambulatory setting, beta-blockers reduce ischemia, prevent MI, and reduce mortality from

From the Department of Medicine, University of California, San Francisco, CA.

Address: Andrew D. Auerbach, MD, MPH, Department of Medicine Hospitalist Group, University of California, San Francisco, Box 0131, San Francisco, CA 94143; ada@medicine.ucsf.edu.

Disclosure: Dr. Auerbach reported that he has no financial relationships that pose a potential conflict of interest with this article.

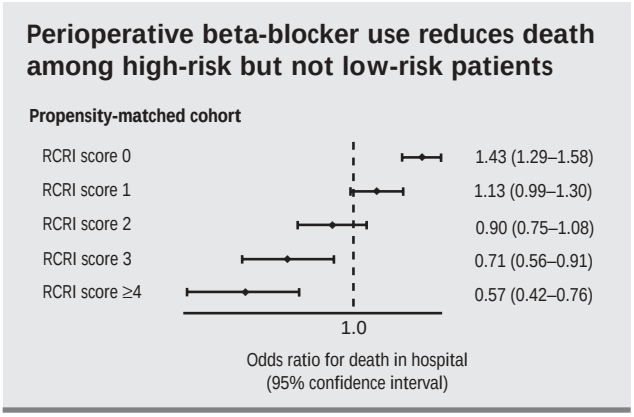

FIGURE 1. Adjusted odds ratio for in-hospital death associated with perioperative beta-blocker therapy in a review of patients undergoing major noncardiac surgery, according to patients' Revised Cardiac Risk Index (RCRI) score (the lower the score, the lower the cardiac risk).[13] Adapted, with permission, from Lindenauer PK, et al, N Engl J Med 2005; 353:346–361. Copyright © 2005 Massachusetts Medical Society. All rights reserved.

coronary artery disease (CAD) in the surgical setting.

In 2001, the Agency for Healthcare Research and Quality (AHRQ) ranked perioperative beta-blocker use for reduction of morbidity and mortality second only to venous thromboembolism prophylaxis in a ranking of patient safety practices according to the strength of supportive evidence.[4] Of note, perioperative beta-blocker use was rated higher than other well-established practices in surgical medicine, including antibiotic prophylaxis. This ranking of perioperative beta-blockers was based on four studies published from 1996 to 2001[5–8] showing that perioperative beta-blockade reduced the risks of death and MI. With beta-blocker prophylaxis, Mangano et al[5] found a 50% reduction ($P < .005$) in mortality at 2 years, Poldermans et al[6] reported a 90% reduction ($P < .001$) in cardiac death/MI at 28 days, Urban et al[7] found a 67% reduction in the risk of postoperative MI that did not reach statistical significance, and Boersma et al[8] reported a 70% reduction in the adjusted relative risk of MI.

Recent caveats. Since this AHRQ report, two randomized controlled trials in vascular surgery patients found metoprolol to have no effect on the incidence of major cardiac events.[9,10] Moreover, a meta-analysis of seven randomized controlled trials of beta-blockers in patients undergoing noncardiac surgery showed encouraging but not statistically significant beneficial effects on 30-day adverse outcomes.[11] As a result, the authors of the meta-analysis urged cautious interpretation of American College of Cardiology/American Heart Association guidelines[12] recommending perioperative beta-blocker treatment for varying groups of patients undergoing noncardiac surgery.

Greater benefit in high-risk patients. In 2005, a retrospective review of more than 600,000 patients undergoing major noncardiac surgery revealed that perioperative beta-blockers reduced the risk of in-hospital death among high-risk but not low-risk patients (Figure 1).[13] Among the patients with a Revised Cardiac Risk Index (RCRI) of 3, which indicates high-risk status, the risk of in-hospital death was reduced by 29% with beta-blockers compared with placebo. Among patients with an RCRI of 4 or greater, this risk was reduced by 43% with perioperative beta-blockade. This finding offers a potential explanation for the concentration of benefit of perioperative beta-blockers in patients undergoing vascular surgery, which is a higher-risk surgery.

A higher threshold for beta-blocker use? Most patients who are strong candidates for perioperative beta-blockers have indications for long-term beta-blocker therapy. The likelihood of an unexpected side effect from perioperative beta-blocker use is unclear, potentially reducing these agents' benefit-to-risk ratio in lower-risk patients. Because of the limited randomized data with beta-blockers in the surgical setting, as well as the reliance on observational data in making recommendations for their use, some have proposed raising the threshold for starting beta-blockers in surgical patients.

Statins

Observational data show a favorable effect of statin use on perioperative mortality, substantially paralleling statins' efficacy in the treatment of acute coronary syndromes. Statin therapy to reduce perioperative risk is intuitive, since most patients at risk for postoperative MI have long-term indications for statins.

Observational studies. Poldermans et al[14] found a 78% reduction in the adjusted risk of perioperative mortality among vascular surgery patients taking statins compared with those not taking statins. In an analysis of more than 600,000 patients undergoing noncardiac surgery,[15] statins reduced the risk of in-hospital death by 29%; the number needed to treat to prevent one death ranged from 30 in high-risk patients (RCRI ≥ 2) to 186 in low-risk patients. Kertai et al[16] found a 60% reduction in all-cause mortality and a 70% reduction in cardiovascular mortality with statin use, independent of beta-blocker use, over a follow-up of almost 5 years in a retrospective review of 530 patients undergoing surgery for abdominal aortic aneurysm. When modeling the effects of

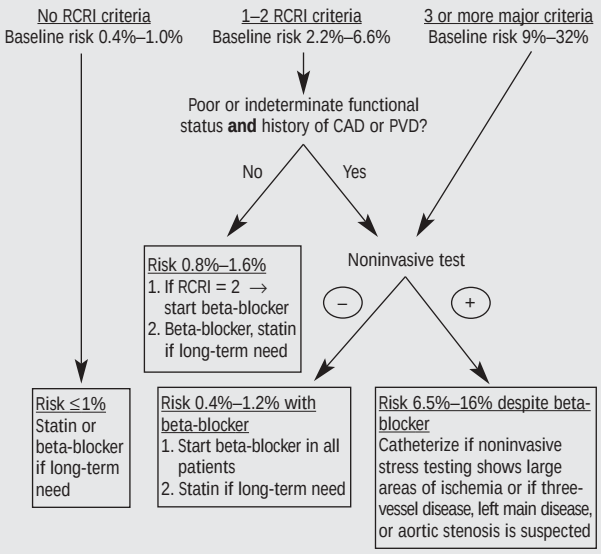

FIGURE 2. Algorithm for selection of patients for cardioprotective drug therapy and further testing before major noncardiac surgery. Adapted from reference 18.

different therapies, a synergism between statins and beta-blockers was suggested.[16]

Randomized trials. The one published randomized trial to date was a small study (N = 100) in which atorvastatin or placebo was started 1 month before vascular surgery.[17] Atorvastatin was associated with a 70% reduction in the combined endpoint of death from cardiac causes, nonfatal MI, unstable angina, and ischemic stroke. Liver function test abnormalities were more frequent in the atorvastatin group, but no patient had to discontinue therapy.

FORMULATING AN APPROACH TO CARDIAC RISK ASSESSMENT

Initial evaluation

In assessing the risk of cardiac complications, the initial evaluation should focus on finding new or unstable CAD, heart failure, or aortic stenosis.

During the evaluation, collect elements of the RCRI (see next section) and conduct a detailed review of symptoms. Listen for rales and bruits. Identify patients with unexplained or unstable symptoms and those who have a history of CAD or peripheral vascular disease plus poor or no exercise tolerance; in these patients, a preoperative electrocardiogram (ECG) is reasonable, to check for cardiac ischemia. Be aware that patients may report having angina or claudication in the past, but not recently, because they are no longer able to exercise or walk because of degenerative diseases.

If surgery is to be performed on an emergency basis, explain the risks and benefits of the surgery to the patient, surgeon, and family, and start cardioprotective agents (ie, beta-blockers) when able. Close postoperative monitoring (ie, telemetry, serial troponin measurements, and ECGs) is warranted following emergency surgery. The need for the intensive care unit should be decided on a case-by-case basis. Invasive intraoperative monitoring using right heart catheterization should be considered in selected patients, such as those with congestive heart failure or aortic stenosis.

TABLE 1
Revised Cardiac Risk Index (RCRI) criteria

History of coronary artery disease
History of transient ischemic attack or cerebrovascular accident
Creatinine >2 mg/dL
Diabetes mellitus
High-risk surgery (chest, abdominal, or pelvic vascular)

Use RCRI criteria to determine baseline risk

Use of the RCRI criteria to determine baseline risk is advised for selecting patients for further testing and/or beta-blockade before major noncardiac surgery (Figure 2).[18] Under the RCRI criteria, one point is awarded for each of the five criteria listed in Table 1; a risk class is then assigned based on the number of criteria present.

In the absence of RCRI criteria, which translates to an extremely low baseline risk of cardiac complications, beta-blockers or statins can be started if a long-term indication already exists for these agents. Because the presence of CAD is an indication for beta-blockade, patients whose lone risk criterion is CAD should be started on beta-blockers. Otherwise, secondary prevention should be practiced for a patient with an RCRI of 1.[18]

With an RCRI of 1 or 2, which corresponds to a baseline risk of 2.2% to 6.6%, noninvasive testing is recommended for patients with a history of CAD or peripheral vascular disease who have poor or indeterminate functional status. In patients with an RCRI of 1 or 2, a history of CAD or peripheral vascular disease, and normal exercise tolerance, beta-blockers should always be initiated, and statins can be started if needed long-term.[18]

Consider catheterization if large areas of ischemia are detected on noninvasive testing or if the patient has a high probability of three-vessel disease, left main disease, or aortic stenosis. Patients with three or more RCRI criteria have a 9% to 32% baseline risk of cardiac complications, and a noninvasive stress test is helpful to further stratify risk.[18]

IMPLEMENTING THE PRACTICE EFFECTIVELY

Know your systems

Understanding the systems in place at your institution is imperative for effective implementation of perioperative protective therapy. You should know the following:

- Which surgeons, anesthesiologists, and internists will be involved
- The final common pathway to the operating room
- How discharge medications are coordinated
- Who is available to screen patients, titrate drug dosages, and ensure continuity of medications.

Look at the preoperative clinic, preoperative holding area, operating room, and rehabilitation clinic/skilled nursing facility as opportunities to enter patients into the treatment algorithm. These are all potential places to start and titrate the dosage of beta-blockers, if deemed appropriate, and ensure that they are continued for the optimal duration of 30 days.

When to start therapy, and with which agent?

Starting beta-blocker therapy early, before admission, is optimal. The ideal time to start is when the patient is first referred for surgery, although a beta-blocker can still be initiated until the day of surgery—in the preanesthesia holding area, if necessary. The key to beta-blocker therapy is to start it soon enough to be able to titrate the dosage to reduce the heart rate to 55 to 65 beats per minute. In every clinical trial in which beta-blockers were shown to reduce cardiac complications in surgical patients, dosages had been titrated so that patients' heart rates were 55 to 65 beats per minute at the time of surgery.

With respect to the choice of beta-blocker, nonselective beta-blockers have the potential to induce bronchospasm and are associated with a greater likelihood of hypotension compared with selective beta-blockers, but agents within the class of beta-1-selective drugs (ie, atenolol, metoprolol) are roughly equivalent.

If a patient meets the criteria for beta-blockade but is receiving a calcium channel blocker, ask the patient's primary care physician to stop the calcium channel blocker for the surgery and switch to a beta-blocker.

Overcoming barriers

Effective implementation of protective agents is fraught with barriers. No one may want to take the responsibility for initiating protective agents, believing that someone else should do it. Objections may also take the form of "I have too many other things to think about." Strategies to overcome these objections should aim to put the task into the hands of someone who cares, make it so easy that there is no reason to object, and combine or simplify other tasks while adding the new one. For example, my institution recently rolled out a combined order set that encompasses deep vein thrombosis prevention, surgical infection prophylaxis, and perioperative beta-blocker use all in a single order, for use in all patients.

Consistent reinforcement through education is also crucial.

Finally, skeptics may claim not to believe the data. If this is the case, the contents of this review may appease them.

MOTIVATING YOUR HOSPITAL

A number of incentives can be used to motivate your hospital to adopt safety practices to prevent perioperative and postoperative cardiac complications. Not the least among these is the fact that operative mortality is reported publicly. Furthermore, perioperative beta-blocker use is a focus of national health care quality-improvement organizations such as the Surgical Care Improvement Project, the Leapfrog Group, and the National Quality Forum, and safety practices that are assessed by these groups are likely to be used as standards of care when hospital safety is graded by *Consumer Reports* and *U.S. News & World Report*.

Don't underestimate the challenge

Nevertheless, be aware that instituting patient safety practices is never easy. The difficulty is exemplified by two recent studies showing low utilization of perioperative beta-blockers.[19,20] One study found that 67% of ideal candidates for beta-blockade who underwent noncardiac surgery in one large US hospital did not receive perioperative beta-blockers.[19] The authors concluded that 62 to 89 lives could potentially be saved at their institution each year through full use of beta-blockade for eligible surgical patients. Even in Canada, where the efficacy of beta-blockers in the surgical setting is accepted almost universally by anesthesiologists, less than 10% of hospitals have a formal protocol in place for perioperative beta-blocker use, and less than 57% of surveyed anesthesiologists prescribed them regularly for this purpose.[20]

UCSF PERIOPERATIVE BETA-BLOCKER PROTOCOL

At my institution, the University of California, San Francisco, screening candidates for beta-blockade is conducted in the preoperative clinic for more than 95% of elective surgical cases. The eligibility criteria for beta-blockade are based on the algorithm mentioned previously (Figure 2). In eligible patients, oral metoprolol is started the day of screening or, in patients who are already receiving a beta-blocker, the dosage is titrated as needed. Postoperative dose titration is performed by physicians on the basis of the patient's heart rate. Metoprolol, 10 mg intravenously every 4 to 6 hours, is delivered in the telemetry unit in patients on NPO orders.

We have carry-through orders for discharge medications, in which beta-blockers are to be continued to day 7 or discharge, whichever is later, and continued indefinitely in patients with long-term indications for their use.

CONCLUSIONS

The preoperative evaluation represents a chance to screen patients for unstable symptoms that would require intervention even in the absence of surgery. It also represents an opportunity to initiate secondary prevention with beta-blockers and statins in appropriate patients.

Data to date indicate that perioperative adrenergic blockade appears to be effective in reducing morbidity and mortality in high-risk patients, but further data from randomized trials are needed to establish this definitively. The patients most likely to benefit from this therapy are those at the greatest cardiac risk (RCRI ≥ 2). Current evidence on statins in the perioperative setting is not robust enough to support their use in patients without a long-term indication for statin therapy.

The ingredients for an effective institutional approach to perioperative cardiac risk reduction are thorough knowledge of the key clinical players, identification of the final common pathway to the operating room, a coordinated "closing of the loop" at discharge, and a simple and well-integrated system for ordering perioperative protective therapy.

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