

Perioperative Use of β -Blocker Therapy in Patients Undergoing Noncardiac Surgery

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An estimated 30% of the approximately 27 million patients who undergo surgery annually in the United States have coronary artery disease (CAD). The presence of CAD results in a marked increase in postoperative cardiac morbidity and mortality. Between 8% and 15% of patients with CAD experience a postoperative myocardial ischemic event such as infarction, unstable angina, or cardiac death. The cost of in-hospital and long-term care for these patients is approximately \$20 billion annually.¹⁻³ In addition, patients who experience perioperative ischemia have a ninefold increase in the risk of developing a serious adverse cardiac outcome during hospitalization and a more than twofold increase in the risk of premature death over the first 6 months after surgery.³ Patients who develop postoperative myocardial infarction in the hospital have a 28-fold increase in the rate of subsequent cardiac complications within 6 months, a 15-fold increase within 1 year, and a 14-fold increase within 2 years.⁴ Given these outcomes, it is important to use cardioprotective strategies in surgical patients with or at risk for CAD to minimize serious perioperative cardiac complications and death.

Use of β -adrenergic blockers has been shown in randomized trials to reduce perioperative cardiac complications and improve survival.^{5,6} Administration of perioperative β -blockers controls adverse hemodynamic variables and successfully decreases the incidence of ischemic events. β -Blockade is the only pharmacologic means of reducing perioperative cardiac mortality and morbidity, both short- and long-term, in patients with CAD.^{6,7} In addition, β -blocker therapy is effective in preventing postoperative atrial fibrillation in patients undergoing cardiac surgery.⁸⁻¹⁰ Atrial fibrillation is the most common postoperative cardiac complication of surgery, with an incidence of 2% to 4% in elderly patients undergoing noncardiac surgery¹¹ and 10% to 40% in patients undergoing cardiothoracic surgery.¹²⁻¹⁴ Postoperative atrial fibrillation is associated with increased length of stay,^{11,15} utilization of resources,¹⁴ and hospital costs; the estimated annual

expenditure in the United States exceeds \$1 billion.¹⁶

Despite overwhelming evidence supporting the use of β -blockade in patients undergoing surgery, this therapy is underutilized as a cardioprotective strategy in current clinical practice. It is estimated that only approximately 50% of patients who would benefit from perioperative β -blockers actually receive them.¹⁷⁻¹⁹ The reason for underutilization is not clear but may include lack of familiarity with the data; failure to identify patients at risk; lack of specific information about the type, dose, titration, and duration of β -blockade; and physicians' understandable concerns about the use of β -blockers in certain patient groups.

This article offers practical guidance to physicians on the use of perioperative β -blockers. It provides a concise discussion of indications and contraindications for perioperative β -blockers and reviews the approach to agent selection, dosing, and titration using a series of questions and answers that mimic the thought process of a clinician performing a preoperative medical evaluation. This is not intended to be a comprehensive review but rather a distillation of the literature to highlight practical information. The reader is referred to several excellent articles for a more comprehensive review of the literature.^{5,6,20-23}

INDICATIONS

- **Which patients should receive β -blockers preoperatively?**

A number of studies have demonstrated the benefit of β -blockers in patients with known CAD or at high risk for CAD who undergo cardiac or noncardiac surgery.^{24,25} The magnitude of benefit is greatest in patients with established CAD (high-risk patients) undergoing high-risk surgeries (eg, cardiac or vascular

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Table 1. Selection of Patients for Perioperative β -Blocker Therapy**Patients undergoing surgery who meet any of the following 5 criteria should receive β -blockers:**

1. Known history of CAD:
 - Previous myocardial infarction or cardiac bypass surgery
 - Typical or atypical angina in past or current medical history
 - Symptomatic arrhythmias
 - Positive findings on stress test
2. Two or more risk factors for CAD:
 - Age > 65 years
 - Uncontrolled systemic hypertension
 - Current smoker
 - Diabetes mellitus not requiring insulin
 - Serum cholesterol concentration > 240 mg/dL
 - Abnormal electrocardiogram
3. Diabetes mellitus requiring insulin
4. Cerebrovascular disease
5. Renal insufficiency (creatinine, ≥ 2 mg/dL)

CAD = coronary artery disease.

surgery). In a randomized, multicenter trial, Poldermans et al assessed the effect of perioperative β -blockers in patients undergoing vascular surgery who were identified as high risk based on clinical factors and positive dobutamine echocardiography.⁵ Patients who received β -blockers had a reduced incidence of cardiac death (3.4% versus 17%; $P = 0.02$) and nonfatal myocardial infarction (0% versus 17%; $P < 0.001$). Mangano et al⁶ and Wallace et al²² studied patients undergoing a variety of noncardiac procedures, including intraperitoneal, intrathoracic, and suprainguinal vascular surgeries, and found reductions in all-cause mortality at 2 years (9% versus 21%; $P = 0.02$), cardiac death at 2 years (4% versus 12%; $P = 0.03$), and postoperative ischemia (24% versus 39%; $P = 0.03$).

Based on these and other data, the American College of Cardiology/American Heart Association (ACC/AHA) developed recommendations for perioperative β -blocker use in various clinical situations.²⁶ These recommendations are categorized as class I (conclusive evidence) or class II (strong evidence) depending on the strength of the supporting evidence. According to these recommendations, perioperative β -blockers should be used in patients who require β -blockers to control symptoms (angina, arrhythmia, hypertension) (class I), in patients undergoing vascular surgery whose preoperative testing results are positive for ischemia (class I), and in patients with CAD or major risk factors for CAD (class II). **Table 1**

summarizes clinical situations where β -blocker use is recommended at class I or II strength of supporting evidence guidelines.²⁶

AGENT SELECTION, DOSING, AND TITRATION**• How does one determine which agent to use?**

A proposed mechanism of the cardioprotective effect of β -blockers is abrogation of the surgical stress response. The benefits conferred by β -blockers in the perioperative period are likely to be a class effect rather than specific to a particular agent.^{5,6,20–22,27–31} Most studies of β -blockers have used selective β_1 inhibitors. Although atenolol is the most frequently studied agent, bisoprolol, metoprolol, esmolol, labetalol, oxprenolol, and propranolol have also been studied and found to be effective.^{5,28,29,32,33} As a practical matter, the preferred agent is the one that the physician is most familiar with or the one that the patient is already receiving without adverse effects. However, for patients already on a β -blocker before surgery, the dose may need to be adjusted to achieve the recommended target heart rate.

• What is the recommended starting dose and target heart rate?

Tachycardia in the perioperative period is associated with high risk of ischemia and adverse cardiac events, while a heart rate of less than 60 bpm is cardioprotective. Two large randomized studies used atenolol or bisoprolol titrated to achieve a target heart rate less than 60 bpm and found significant cardioprotection.^{5,6} A number of other studies have shown that an average heart rate less than 70 bpm is protective.^{20,21} Given these findings, physicians should start with a low dose and titrate to achieve a heart rate of 70 bpm or less. Common regimens include atenolol 50 to 100 mg (or bisoprolol 5–10 mg) orally once a day and atenolol or metoprolol 5 to 10 mg intravenously in patients who cannot take medications by mouth or before induction of anesthesia. Clear communication and appropriate nursing orders to withhold medications for severe bradycardia (heart rate, < 55 bpm) and/or hypotension (systolic blood pressure, < 100 mm Hg) are critical to avoid complications. The same dose should be continued while the patient is in the hospital.

• When should β -blockers be started and for how long should they be continued?

The cardioprotective effect of β -blockers is related to their sympatholytic effect before induction of anesthesia. Thus, oral β -blockade should be initiated at least 24 to 48 hours prior to surgery to allow sufficient time to

achieve the target heart rate and should be maintained in the immediate perioperative period. The amount of time required to achieve the target heart rate varies depending on agent, route, and patient-related factors. Intravenous β -blocker agents may be preferred for urgent or emergent situations.

There is no clear guidance from the literature regarding the duration for which β -blockade should be maintained. The risk of perioperative cardiac events is highest in the first 48 hours after surgery, and β -blockers should be maintained at least for this critical period. Interestingly, even a short period of β -blocker use (for 7 days postoperatively) seems to confer improved survival for up to 2 years.⁶ There is emerging evidence that a longer period (30 days) of β -blocker therapy is associated with additional benefit on cardiac mortality for up to 3 years in certain patient populations.⁷

CONTRAINDICATIONS

• Which patients should not receive β -blockers?

The potential benefits of β -blockers have to be balanced against the risks of such therapy. For most patients, the benefits will outweigh the risks, and more widespread perioperative use of β -blockers is likely to save lives and health care cost. β -Blockers should not be used in certain patients, such as those with high-grade cardiac conduction defects, severe bradyarrhythmias, and decompensated heart failure (**Table 2**). Appropriate caution should be exercised in patients with compensated heart failure, chronic obstructive pulmonary disease, and reactive airway disease. However, most patients with these conditions can safely receive β -blockers and should not be denied the benefits of this treatment.^{34,35}

CONCLUSION

Perioperative use of β -blockers for the prevention of surgical cardiovascular morbidity and mortality is based on physiologic principles and is supported by currently available evidence. The cardioprotective benefit of β -blockers seems to be a class effect rather than being confined to a specific β -adrenergic blocking agent. More widespread and generous use of this cardioprotective strategy in the perioperative period can be expected to improve patient outcomes. **HP**

Test your knowledge and comprehension of this article with Review Questions on page 43.

Table 2. Absolute and Relative Contraindications for Perioperative β -Blocker Therapy

β -Blockers should not be given to patients with any of the following:

- Bradyarrhythmia at baseline, heart rate < 50 bpm
- Second-degree or third-degree heart block
- Oral steroid-dependent or oxygen-dependent COPD
- History of intubations secondary to exacerbation of COPD in last 6 months
- Decompensated congestive heart failure
- Allergy to β -blockers

β -Blockers should be used with caution in patients with:

- Reactive airway disease (use low dose if indicated)
- Moderate COPD

COPD = chronic obstructive pulmonary disease.

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