



Why you shouldn't start beta-blockers before surgery

A new meta-analysis finds that initiating beta-blockers before surgery increases patients' risk of death.

PRACTICE CHANGER

Do not routinely initiate beta-blockers in patients undergoing intermediate- or high-risk noncardiac surgery. Beta-blockers appear to increase the 30-day risk of all-cause mortality.¹

STRENGTH OF RECOMMENDATION

A: Based on meta-analysis of 9 randomized controlled trials (RCTs).

Bouri S, Shun-Shin MJ, Cole GD, et al. Meta-analysis of secure randomised controlled trials of β -blockade to prevent perioperative death in non-cardiac surgery. *Heart*. 2014;100:456-464.

ILLUSTRATIVE CASE

A 67-year-old woman with diabetes, hypertension, and hyperlipidemia comes to your office for an evaluation before undergoing a total hip arthroplasty. She is not taking a beta-blocker. Should you prescribe one?

Current guidelines from the American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) recommend starting beta-blockers to prevent cardiac events in patients about to undergo intermediate- or high-risk surgery or vascular surgery who have a history of inducible ischemia, coronary artery disease (CAD), or at least one risk factor for CAD.² However, the majority of the evidence for these guidelines, which were published in 2009 and are in the process of being updated, came from the DECREASE (Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography) trials, which have been discredited due to serious methodologi-

cal flaws, including falsified descriptions of how outcomes were determined and fictitious databases.³ A new meta-analysis by Bouri et al¹ that excluded the DECREASE trials found that although preoperative beta-blockers reduce the rate of certain nonfatal outcomes, they increase the risk of death and stroke.

STUDY SUMMARY

Multiple RCTs find preop beta-blockers do more harm, than good

Bouri et al¹ conducted a meta-analysis of published RCTs evaluating preoperative beta-blockers vs placebo for patients undergoing noncardiac surgery. Of the 11 studies that met eligibility criteria, 2 were the discredited DECREASE trials. Thus, Bouri et al¹ analyzed 9 high-quality RCTs that included 10,529 patients.

Most studies included patients undergoing vascular surgery. Some studies also included intra-abdominal, intrathoracic, neurosurgical, orthopedic, urologic, and gynecologic surgeries. Beta-blockers were started no more than a day before surgery and were discontinued at hospital discharge or up to 30 days postop. Metoprolol was used in 5 trials, bisoprolol in one trial, atenolol in 2 trials, and propranolol in one trial. The primary endpoint was all-cause mortality within 30 days.

A total of 5264 patients were randomized to beta-blockers and 5265 to placebo. There were 162 deaths in the beta-blocker group and 129 deaths in the placebo group. Patients who received beta-blockers had a 27% increased

Anne Mounsey, MD;
Jodi M. Roque, MD;
Mari Egan, MD
Department of Family Medicine, University of North Carolina Chapel Hill (Drs. Mounsey and Roque); Department of Family Medicine, The University of Chicago (Dr. Egan)

PURLs EDITOR

James J. Stevermer, MD, MSPH
Department of Family and Community Medicine, University of Missouri-Columbia

➤ While beta-blockers protect against nonfatal MIs, they increase the risk of nonfatal strokes and death.

risk of all-cause mortality (risk ratio [RR]=1.27; 95% confidence interval [CI], 1.01-1.60; $P=.04$). The number needed to harm was 160.

Six of the studies also evaluated rates of nonfatal myocardial infarction (MI), nonfatal stroke, and hypotension. Beta-blockers lowered the risk of nonfatal MI (RR=.73; 95% CI, .61-.88; $P=.001$), but increased the risk of nonfatal stroke (RR=1.73; 95% CI, 1.00-2.99; $P=.05$) and hypotension (RR=1.51; 95% CI, 1.37-1.67; $P=.00001$).

This meta-analysis was dominated by the 2008 Peri-Operative ISchemic Evaluation (POISE) trial, an RCT that compared placebo to extended-release metoprolol, 100 mg 2 to 4 hours before surgery followed by 200 mg/d for 30 days, in 8351 patients with, or at risk for, atherosclerotic disease.⁴ While beta-blockers reduced the risk of MI and atrial fibrillation, they increased the risk of mortality and stroke, likely due to drug-induced hypotension. The slightly larger-than-typical doses of beta-blockers used in the POISE study may have contributed to the excess mortality.

WHAT'S NEW

Avoiding beta-blockers in surgery patients will prevent deaths

Bouri et al¹ found that while beta-blockers protect against nonfatal MIs, they increase the risk for nonfatal strokes and death. This new meta-analysis challenges the ACCF/AHA recommendations by suggesting that abandoning the use of beta-blockers for preoperative patients who aren't already taking them will prevent a substantial number of perioperative deaths. Bouri et al¹ estimate that in the United Kingdom, where 47,286 deaths occur annually within 30 days of intermediate or high-risk

procedures, the number of iatrogenic deaths would drop by approximately 10,000 if beta-blockers were not used.¹

CAVEATS

Don't stop beta-blockers in patients who already take them

This meta-analysis did not evaluate outcomes in patients who were already taking beta-blockers. Patients who are already on beta-blockers should continue to take them in the perioperative period, which is in line with current ACCF/AHA guidelines.

CHALLENGES TO IMPLEMENTATION

Some physician may be reluctant to disregard published guidelines

Some physicians may not be comfortable ignoring the current ACCF/AHA guidelines that make a Class IIa recommendation (it is reasonable to administer this treatment) for the use of preoperative beta-blockade for patients at risk of cardiovascular events who were not previously taking a beta-blocker. This updated meta-analysis excludes the discredited DECREASE trials and challenges us to act against these current guidelines while we wait for updated recommendations. **JFP**

ACKNOWLEDGEMENT

The PURLs Surveillance System was supported in part by Grant Number UL1RR024999 from the National Center For Research Resources, a Clinical Translational Science Award to the University of Chicago. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center For Research Resources or the National Institutes of Health.

Copyright © 2014. The Family Physicians Inquiries Network. All rights reserved.

References

1. Bouri S, Shun-Shin MJ, Cole GD, et al. Meta-analysis of secure randomised controlled trials of β -blockade to prevent perioperative death in non-cardiac surgery. *Heart*. 2014;100:456-464.
2. American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines; American Society of Echocardiography; American Society of Nuclear Cardiology; Heart Rhythm Society; Society for Cardiovascular Anesthesiologists; Society for Cardiovascular Angiography and Interventions; Society for Vascular Medicine; Society for Vascular Surgery; Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery. *J Am Coll Cardiol*. 2009;54:e13-e118.
3. Erasmus Medical Center Follow-up Investigation Committee. Report on the 2012 follow-up investigation of possible breaches of academic integrity. CardioBrief Web site. Available at: <http://cardiobrief.files.wordpress.com/2012/10/integrity-report-2012-10-english-translation.pdf>. Published September 30, 2012. Accessed March 31, 2014.
4. POISE Study Group; Devereaux PJ; Yang H; Yusuf S; et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet*. 2008;371:1839-1847.