ONLINE EXCLUSIVE

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.

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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 ß-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 methodological flaws, including falsified descriptions of how outcomes were determined and fictitious databases.[3] A new meta-analysis by Bouri et al[1] 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 al[1] 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 al[1] 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

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.

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

WHAT'S NEW

Avoiding beta-blockers in surgery patients will prevent deaths

Bouri et al[1] 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 al[1] 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

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