β -Blockers: Beyond binary

Dawn S. Hui, MD, and Richard Lee, MD, MBA

From the Center for Comprehensive Cardiovascular Care, St Louis University, St Louis, Mo.

Disclosures: Authors have nothing to disclose with regard to commercial support.

Received for publication Aug 31, 2017; accepted for publication Sept 1, 2017; available ahead of print Sept 28, 2017.

Address for reprints: Richard Lee, MD, MBA, Center for Comprehensive Cardiovascular Care, St Louis University, 3635 Vista Ave, DT 13F, St Louis, MO 63110 (E-mail: rick.lee@health.slu.edu).

J Thorac Cardiovasc Surg 2018;155:630-1

0022-5223/\$36.00

Copyright © 2017 Published by Elsevier Inc. on behalf of The American Association for Thoracic Surgery

<https://doi.org/10.1016/j.jtcvs.2017.09.003>

Richard Lee, MD, MBA, and Dawn S. Hui, MD

Central Message

This meta-analysis suggests that preoperative β -blocker use is a limited quality indicator but does not definitively show lack of benefit. Future studies should include dosing initiation and adequacy.

See Article page 620.

Wang and colleagues¹ present the first meta-analysis of short-term clinical outcomes of preoperative β -blocker use in isolated coronary artery bypass grafting (CABG). Some comments on the history of this quality metric and the details of the studies in the meta-analysis may provide context with which to judge the findings.

The 2011 American College of Cardiology Foundation/American Heart Association guidelines address 4 aspects of perioperative β -blocker use: preoperative administration, postoperative/discharge continuation, route of administration, and subgroup benefit (Table 1). The strength of the recommendation is Class I for reduction of atrial fibrillation and Class IIa for reduction in ischemia and mortality.² Although the evidence for atrial fibrillation reduction includes randomized controlled trials, the studies cited for mortality benefit consist of 3 observational studies from the 1990s: A Society of Thoracic Surgeons (STS) National Adult Cardiac Surgery Database (NCD) study³ and 2 single-institution observational studies.^{4,5} These latter 2 analyzed combinations of perioperative medications, which was an exclusion criteria in the present meta-analysis.

Comparatively, the meta-analysis by Wang and colleagues¹ improves on the quantity of evidence, encompassing 1.23 million patients from 6 studies, of which 3 were national database studies (Table 2). Nearly 90% of the patients were derived from only 2 studies: the STS/NCD study that showed a small mortality benefit (risk-adjusted odds ratio [OR], 0.94; 95% confidence interval [CI], 0.91-0.97 and propensity-matched OR, 0.97; 95% CI, 0.93-1.00),³ and Brinkman and colleagues'

TABLE 1. 2011 American College of Cardiology Foundation/American Heart Association guidelines on perioperative β -blocker use for coronary artery bypass grafting²

Class	Level of evidence
Class I	
β -Blockers should be administered for at least 24 h before coronary artery bypass grafting to all patients without contraindications to reduce the incidence or clinical sequelae of postoperative atrial fibrillation	B
β -blockers should be reinstituted as soon as possible after coronary artery bypass grafting in all patients without contraindications to reduce the incidence or clinical sequelae of atrial fibrillation	B
β -blockers should be prescribed to all coronary artery bypass grafting patients without contraindications at the time of hospital discharge	C
Class IIa	
Preoperative use of β -blockers in patients without contraindications, particularly in those with an left ventricular ejection fraction > 30%, can be effective in reducing the risk of in-hospital mortality	B
β -blockers can be effective in reducing the incidence of perioperative myocardial ischemia	B
Intravenous administration of β -blockers in clinically stable patients unable to take oral medications is reasonable in the early postoperative period	B
Class IIb	
The effectiveness of preoperative β -blockers in reducing in-hospital mortality rate in patients with left ventricular ejection fraction < 30% is uncertain	B

TABLE 2. Studies in the meta-analysis

Author, year	Period	n	Source	% Taking β -blocker
Ferguson, 2002 ²	1996-1999	629,877	Society of Thoracic Surgeons National Adult Cardiac Surgery Database	60
Brinkman, 2014 ⁶	2008-2012	506,110	Society of Thoracic Surgeons	83
LaPar, 2013 ⁷	2001-2011	43,747	Virginia Cardiac Surgery Quality Initiative	80.2
Kohsaka, 2016 ⁸	2008-2011	34,980	Japanese Cardiovascular Surgery Database	30
Brinkman, 2011 ⁹	2000-2008	12,855	North Texas regional database	62
Srinivasan, 2003 ¹⁰	1997-2002	4381	Cardiothoracic Center Liverpool	65

STS/NCD study from the 2000s that showed no mortality benefit (OR, 0.96; 95% CI, 0.87-1.06; $P = .38$).⁶ As a side note, the study by LaPar and colleagues⁷ derived its cohort from the Virginia Cardiac Surgery Quality Initiative, which would likely have partially overlapped with the study by Brinkman and colleagues,⁶ thus double-counting a subset of patients. More importantly, the 2 national STS/NCD studies analyzed patients from disparate time periods separated by more than a decade. The older study reported 30-day mortality rates of 2.8% to 3.4%, whereas the more contemporary study reported rates of 1.12% to 1.17%. It is possible that contemporary CABG outcomes have improved such that mortality is an insensitive outcome by which to measure the effects of β -blockade. As for study design, Ferguson and colleagues³ found that recent myocardial infarction was among the strongest predictors of preoperative β -blocker use, whereas the study by Brinkman and colleagues⁶ excluded patients with myocardial infarction within 21 days (as well as high-risk presenting symptoms), potentially removing from the pool of analysis patients who might most derive mortality benefit.

Whether one believes preoperative β -blocker use should be a quality metric depends on several things: whether there is a clinical benefit to β -blockade, and whether current definitions and documentation of preoperative β -blocker use reflect appropriate dosing practices. The quantity of patients in this meta-analysis does not make up for limitations inherent to the registry data upon which it is based. Deficiencies include lack of granularity as to the dosage, type, preoperative duration, and postoperative continuation of β -blockade. The 2 observational studies cited in the 2011 guidelines^{4,5} showing mortality benefit specified “regular daily use” as the qualifying criteria for preoperative β -blockade, a metric that the STS database does not capture. β -Blocker use does not necessarily equate to β -blockade. Although the American College of Cardiology Foundation/American Hospital Association guidelines specify β -blockade administration “for at least 24 hours” preoperatively, the STS definition of

preoperative β -blockade is “within 24 hours preceding surgery.”

The study by Wang and colleagues¹ does not speak to whether there is a benefit of preoperative β -blockade. Rather, it highlights its limitation as a quality indicator according to current documentation practices and the restrictions of studying its benefits through large database studies. Although the authors call for randomized controlled trials as the next step, this alone may not be sufficient. Future studies should include details such as therapeutic effect, timing of administration, and subgroup analysis.

References

1. Wang L, Wang H, Hou X. Short-term effects of preoperative beta-blocker use for isolated coronary artery bypass grafting: a systematic review and meta-analysis. *J Thorac Cardiovasc Surg.* 2018;155:620-9.e1.
2. Hillis LD, Smith PK, Anderson JL, Bittl JA, Bridges CR, Byrne JG, et al. 2011 ACCF/AHA guideline for coronary artery bypass graft surgery: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Thorac Cardiovasc Surg.* 2012;143:4-34.
3. Ferguson TB Jr, Coombs LP, Peterson ED. Preoperative beta-blocker use and mortality and morbidity following CABG surgery in North America. *JAMA.* 2002;287:2221-7.
4. ten Broecke PW, De Hert SG, Mertens E, Adriaensen HF. Effect of preoperative beta-blockade on perioperative mortality in coronary surgery. *Br J Anaesth.* 2003;90:27-31.
5. Weightman WM, Gibbs NM, Sheminant MR, Whitford EG, Mahon BD, Newman MA. Drug therapy before coronary artery surgery: nitrates are independent predictors of mortality and beta-adrenergic blockers predict survival. *Anesth Analg.* 1999;88:286-91.
6. Brinkman WT, Herbert MA, O'Brien S, Filardo G, Prince S, Dewey T, et al. Preoperative beta-blocker use in coronary artery bypass grafting surgery: National database analysis. *JAMA Intern Med.* 2014;174:1320-7.
7. LaPar DJ, Crosby IK, Kron IL, Kern JA, Fonner E Jr, Rich JB, et al. Preoperative beta-blocker use should not be a quality metric for coronary artery bypass grafting. *Ann Thorac Surg.* 2013;96:1539-44.
8. Kohsaka S, Miyata H, Motomura N, Imanaka K, Fukuda K, Kyo S, et al. Effects of preoperative beta-blocker use on clinical outcomes after coronary artery bypass grafting: a report from the Japanese Cardiovascular Surgery Database. *Anesthesiology.* 2016;124:45-55.
9. Brinkman WT, Herbert MA, Prince SL, Magee MJ, Dewey TM, Smith RL, et al. Preoperative beta-blocker usage: is it really worthy of being a quality indicator. *Ann Thorac Surg.* 2011;92:788-95.
10. Srinivasan AK, Shackcloth MJ, Grayson AD, Fabri BM. Preoperative beta-blocker therapy in coronary artery bypass surgery: a propensity score analysis of outcomes. *Interact Cardiovasc Thorac Surg.* 2003;2:495-500.