gold standards is that thermodilution has no better precision than the other methods surveyed during conditions of unstable hemodynamics. \cite{1,2} Furthermore, we welcome continued work by developers to improve the performance of new devices, and their subsequent independent testing in a variety of clinical scenarios.

Dr. Critchley's comments confirm that the ± 20% criterion for agreement with the true cardiac output is essentially an arbitrary one. Our data suggest the likely limits of agreement of each generic method with the true cardiac output are closer to ± 30%. We leave judgment of the acceptability of this for clinical decision-making to the interested clinician. However, the studies quoted above suggest it is likely that this is the real precision of thermodilution that we have been routinely working with for many years, while managing patients during cardiac surgery.

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**References**


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**Reduction of Postoperative Mortality: Pattern of Use of β-Blockade, Bias, or Both?**

*To the Editor:* Wallace *et al.* reported the effects of the implementation of a hospital protocol for the addition or continuation of perioperative β-blockade in almost 40,000 patients at risk for myocardial ischemia and operated on between 1996 and 2008.\cite{1} The addition of perioperative β-blockade in eligible patients was associated with a significant reduction in 30-day and 1-yr mortality. Continuation of existing β-blockade in these patients also was beneficial, whereas withdrawal was reported to be associated with increased mortality (almost 400% increased 30-day mortality and almost 200% increased 1-yr mortality). Wallace and coworkers should be commended for this important and large study, which seems to confirm existing evidence about the continuation and withdrawal of perioperative β-blockade using “real world” data.

However, as also acknowledged by the authors, confounding by indication and selection bias are likely to have influenced the results of this retrospective analysis considerably. Therefore, we have some important questions regarding this study.

First, the authors tried to adjust for these potential sources of bias by collecting confounders and performing a propensity analysis. However, the logistic regression model described in table 5 of the article seems to include only previous coronary artery disease and peripheral vascular disease and not age, sex, and other potential confounders mentioned in table 4 of the article. We would like to see a table with the β-blockade effect measures adjusted for all potential confounders, because it is unclear whether these have been taken into account in table 5. Moreover, the methods of the propensity analysis are poorly described, which makes it difficult to interpret the results of these analyses.

Second, figure 3 of the article shows a markedly decreased mortality rate over time, which hardly can be attributed solely to the β-blockade protocol. It may also reflect a change in other practice patterns over time. This problem with retrospective studies with long duration is also recognized in the accompanying editorial.\cite{2} In this case, clonidine was added to the protocol in 2004.\cite{1} Likely, however, other drugs, such as statins or aspirin, were continued or prescribed more often as well in more recent years. Furthermore, there may have been improvements in surgical care, such as an increase in minimally invasive surgery. Apparently, these variables were not available to adjust for as confounders. However, adding “time” to the multivariable analysis as a proxy for a change in these variables may partially adjust the β-blockade effect measures for this potential confounding and could at least have been conducted as a sensitivity analysis.

Finally, previous comparable studies showed that including nadir and postoperative hemoglobin both in regression analysis and propensity analysis significantly influenced the β-blockade effect measures.\cite{3,4} If available, including these hemoglobin values in the analyses may therefore reduce the remarkably strong reported association between β-blockade withdrawal and outcome (odds ratio, 3.9; 95% CI, 2.6–6.0).

In conclusion, we would like to see the results of a regression model that includes both the variable of interest (pattern of β-blockade use) as well as all potential confounders, including time and, if available, both nadir and postoperative hemoglobin values, in a proper and crystal-clear analysis.

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**References**

Perioperative β-Blockade Protocol Unproven

To the Editor:

I first became aware of the recent paper published in this journal not by my reading of ANESTHESIOLOGY, but through National Public Radio’s Web site and the American Society of Anesthesiologists E-Newsletter of October 6, 2010. The National Public Radio story began with the following sentence: “Patients at risk of a heart attack who are having surgery can cut their death risk 35% by simply taking a drug called a β-blocker.”*

I write from the perspective of an anesthesiologist in private practice. Over the past several years, the hospital with which I am affiliated has eagerly adopted protocols for perioperative care. All Surgical Care Improvement Project mandates have become required. Currently, reimbursement from our largest private payer is tied to the World Health Organization Surgical Safety Checklist—an instrument whose utility has been presented but has not been clearly validated for hospitals such as ours.1

Despite such pressures from administration, physicians must insist that mandated protocols dictating pathways of perioperative care require unequivocal evidence demonstrating overall benefit to patients.

The article published by Wallace in this journal’s October 2010 issue looks back at San Francisco Veterans Administration Medical Center patients who had inpatient or outpatient surgery from 1996 to 2008.2 During that time, a protocol for perioperative β-blockade was instituted at the San Francisco Veterans Administration Medical Center by Dr. Wallace, the author of the analysis. The protocol was not universally followed; it was voluntary. The protocol was based largely on evidence from a trial that had enrolled 200 patients, authored by Mangano, Layug, Wallace, and Tateo in 1996.3

The patients in the analysis were not studied based on their participation in the author’s protocol. They were studied in groups defined by their receipt of “at least one dose of B-blocker medication after surgery, either as an in-patient or out-patient.”

During the time of the analysis, 30-day mortality decreased, as did 1-yr mortality. Over the time of the analysis, the β-blocker use increased. Through regression and propensity analysis, the author concludes that the addition of a single dose of β-blocker during the perioperative period was independently associated with a reduction in 30-day and 1-yr mortality.

However, patients having vascular surgery did not share this benefit at the 1-yr mark, which stands in contrast to the results of a small prospective, randomized trial that showed remarkable benefit for vascular patients (odds ratio for cardiac death or nonfatal myocardial infarction over 22 months with β-blockade of 0.16 vs. placebo).4

During the period of the analysis, other investigators conducted three large prospective, randomized trials of perioperative β-blockade that enrolled a total of 9,768 patients. None of these three prospective, randomized, controlled trials found overall benefit (decreased mortality) of the investigated protocol.5–7

One statement in the Wallace article requires particular scrutiny. Wallace states in his conclusion that “appropriate use of the PCRRRT protocol is clearly associated with a reduction in 30-day and 1-yr mortality.” The analysis associates the addition of a single dose of any β-blocker with benefit, not the Perioperative Cardiac Risk Reduction Therapy protocol with benefit; this protocol was not an arm of this analysis.

Wallace’s analysis does deserve careful study; in particular, regarding the hazard of withdrawing β-blockers during the perioperative period. In addition, the article suggests that some β-blockers administered to patients at risk may be helpful, and that patients who should have been taking β-blockers for medical indications, outside of any perioperative considerations, may present for surgery.

However, it cannot be argued that this analysis provides evidence for benefit of a particular protocol for perioperative β-blockade, certainly not one eligible for mandated care.

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References