



Are the current perioperative risk management strategies for myocardial infarction flawed?

Coronary Assessment Before Noncardiac Surgery

Current Strategies Are Flawed

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The preoperative evaluation of patients scheduled for elective noncardiac surgery is a conspicuous component of the practice of cardiology and general internal medicine and has become a standard content area in general internal medicine training.¹ In particular, clinicians are expected to address coronary risk in such patients because the stress of surgery, induction of anesthesia, postoperative pain, and other complications may induce coronary ischemia through mismatch between coronary oxygen supply and demand or through rupture of vulnerable plaque.² Preoperative evaluation may involve estimation of the probability of perioperative cardiac events³ and application of algorithms that guide patients to stress testing or β -blocker therapy.^{4–6} Although these algorithms are informed by clinical research, their ultimate configuration is influenced substantially by expert opinion.

clinical references such as the *Washington Manual of Medical Therapeutics*⁸ and *UpToDate*.⁹ Because studies published during the past several years raised questions about recommendations that flowed from the 2002 algorithm, an updated ACC/AHA guideline was published in October 2007.⁶ In my view, the new guideline represents an improvement but still embodies ambiguity, fails to account fully for recent relevant medical literature, and remains problematic for clinicians.

In this article, I begin with a critique of the 2002 ACC/AHA guideline because it provides historical context for the recent revision. I will then review recently published data that render the guidelines problematic. Finally, I will offer a critique of the 2007 update.

Inherent Ambiguity in the 2002 Guideline

The 2002 version of the ACC/AHA guideline on perioperative evaluation made the following key point in the first paragraph of its executive summary: “Preoperative intervention is rarely necessary simply to lower the risk of surgery unless such intervention is indicated irrespective of the preoperative context.”⁴ Several paragraphs later, the following related comment appeared: “Coronary revascularization before noncardiac surgery to enable the patient to ‘get through’ the noncardiac procedure is appropriate only for a

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The most visible and widely cited guideline during the past decade, published initially in 1996 and updated in 2002 and 2006, is that of the American College of Cardiology (ACC) and the American Heart Association (AHA).^{4,5} The decision-making algorithm in the 2002 guideline exists as a pocket manual for easy reference⁷ and has been reprinted in popular

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small subset of patients at very high risk.”¹⁴ These statements imply that the mere fact of upcoming surgery is insufficient to warrant preoperative intervention; rather, the guideline invited physicians to ask the following question: “If this patient were here for a reason other than preoperative consultation, would I initiate an evaluation for coronary disease?”

The answer to this question is obvious if the patient’s history suggests symptomatic coronary ischemia that has not been addressed. However, when careful history taking excludes symptoms suggesting coronary disease, one is left with patients who are asymptomatic from the coronary perspective. For these patients, the language of the ACC/AHA statement logically collapses into the broader question of whether asymptomatic persons should undergo routine stress testing (possibly followed by revascularization if coronary disease is discovered), independent of a preoperative context. That question is addressed in other ACC/AHA guidelines that discuss stress testing in various subsets of asymptomatic persons, for example, those with multiple risk factors and sedentary persons who wish to start vigorous exercise.^{10,11} Recommendations in these guidelines are generally class II (“conflicting evidence and/or divergence of opinion”) and are based primarily on “expert opinion” (level C evidence) rather than empirical evidence; hence, they do not provide definitive guidance.

Although the narrative portion of the 2002 ACC/AHA guideline began on the cautionary note quoted above, the guideline’s 8-step algorithm guided considerable numbers of asymptomatic patients to noninvasive testing.¹² Specifically, the algorithm recommended noninvasive testing for 2 large subgroups of patients:

- Patients with “intermediate” predictors of increased perioperative risk (eg, diabetes or renal insufficiency), plus either poor functional capacity or high-risk upcoming surgery (eg, vascular surgery or an anticipated prolonged surgical procedure).
- Patients with “minor” predictors of perioperative risk (eg, advanced age, abnormal ECG), plus both poor functional capacity and high-risk upcoming surgery.

Clearly, many patients in these categories would not have undergone noninvasive testing outside of the preoperative context. Indeed, the very fact of the preoperative context was the decisive factor in the algorithm for many patients scheduled to undergo “high-risk surgery.” Hence, the guideline’s introductory statement (“is rarely necessary . . . unless such intervention is indicated irrespective of the preoperative context”) and the recommendations generated by the guideline’s algorithm were discordant.

New Evidence Relevant for Patients Undergoing Noncardiac Surgery

Several recently published studies bear directly on decisions to initiate noninvasive evaluations for coronary disease before noncardiac surgery, to perform revascularization before noncardiac surgery, and to provide perioperative β -blockade. Although

these studies do not resolve every question, clinicians who provide preoperative consultation should be familiar with them.

Noninvasive Testing

Over the years, studies have demonstrated that risk stratification through preoperative noninvasive testing (usually stress imaging) can refine estimates of perioperative risk for coronary events in some patient populations.¹³ Such information may be useful when clinicians counsel patients regarding the potential benefits and harms of the proposed noncardiac surgery. However, risk stratification does not necessarily improve perioperative outcomes unless it triggers interventions proven to reduce risk. Until recently, no prospective randomized trials addressed whether noninvasive testing before noncardiac surgery was associated with improved outcomes. Nonrandomized retrospective outcome studies have yielded contradictory results, suggesting benefit,¹⁴ no benefit,^{15–17} and even harm¹² from stress testing before noncardiac surgery. Selection bias, confounding, and disparate patient populations are likely responsible for the varied outcomes of these studies. The lack of evidence supporting preoperative noninvasive testing led Grayburn and Hillis¹⁸ to propose an algorithm in 2003 that essentially eliminated such testing. In early 2006, Auerbach and Goldman acknowledged that “whether judicious use of noninvasive tests improves outcomes remains unproved.”¹⁹

Finally, in 2006, researchers published the results of a multinational study (Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echo-II, or DECREASE-II) in which 770 “intermediate-risk” patients scheduled for vascular surgery were randomized to receive preoperative stress testing (dobutamine echocardiography or dobutamine or dipyridamole perfusion scintigraphy) or no testing.²⁰ On the basis of stress test results, a small number of patients were referred for coronary revascularization before the noncardiac surgery. At 30 days after the noncardiac surgery, the incidence of cardiac death or myocardial infarction was virtually the same in the no-testing and testing groups (1.8% versus 2.3%). Notably, all patients in this study received perioperative β -blockers. In a smaller randomized trial from the United States published in 2003, preoperative dobutamine stress echocardiography was not associated with improved outcomes in patients undergoing vascular surgery.²¹

Revascularization

A potential limitation of both retrospective and randomized studies of preoperative stress testing is that test results may not be applied consistently in subsequent decisions of whether to perform coronary revascularization. This limitation was obviated in the Coronary Artery Revascularization Prophylaxis (CARP) trial, published in 2004. The study included 510 patients who were scheduled for major vascular surgery and who had at least 1 major coronary artery with a stenosis $\geq 70\%$.²² Patients with left main coronary disease or left ventricular ejection fraction $< 20\%$ were excluded, but one third of patients had 3-vessel disease. Patients were



randomized to receive coronary revascularization (coronary artery bypass grafting [CABG] or percutaneous coronary intervention [PCI]) or no coronary revascularization before the noncardiac procedure. Neither 30-day nor 2-year outcomes were improved in the revascularization group compared with the no-revascularization group. Most patients in this trial received perioperative β -blockers.

Some critics have maintained that the CARP results cannot be generalized to the highest-risk patients.²³ The recently published DECREASE-V Pilot Study begins to fill this gap.²⁴ This randomized trial included 101 patients scheduled for major vascular surgery; all had at least 3 risk factors and extensive ischemia on noninvasive testing. Most patients had 3-vessel disease on angiography, and nearly half had ejection fractions $<35\%$. Patients were randomized to undergo coronary revascularization or no revascularization before the noncardiac surgery. At 1 month and at 1 year after the noncardiac surgery, there was no evidence of improved outcomes in the coronary revascularization group; for example, the 30-day incidence of death or myocardial infarction was 43% in the coronary revascularization group and 33% in the control group. Although the statistical power of this small study is limited, the high morbidity and mortality rates in the coronary revascularization group are noteworthy. Again, all patients received perioperative β -blockers.

Coronary stenting and antiplatelet therapy raise yet another concern. Two small case series published several years ago suggested a high mortality rate after noncardiac surgery (5% and 20% in the 2 studies, respectively) among patients who had received bare-metal coronary stents several weeks before the noncardiac surgery.^{25,26} More recently, data have indicated high rates of stent thrombosis among patients with drug-eluting stents who do not receive dual antiplatelet therapy (with aspirin and clopidogrel) for at least a year after placement of drug-eluting stents.^{27,28} Indeed, a recent advisory from several organizations (including the AHA and ACC) notes that noncardiac surgery may further increase the risk for stent thrombosis in patients who have discontinued dual antiplatelet therapy.²⁹ The implication is a possible delay in major elective noncardiac surgery until at least a year after placement of drug-eluting stents because many surgeons prefer to stop antiplatelet drugs before major surgery. Interestingly, in the aforementioned DECREASE-V study, dual antiplatelet therapy was continued through noncardiac surgery in patients who had received drug-eluting stents.²⁴ An unusually high prevalence of catastrophic outcomes after noncardiac surgery has not been reported among patients who have previously undergone CABG.

Finally, results from the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial, published in 2007, are relevant to this discussion.³⁰ In that study, patients with stable coronary disease, including many patients with 2-vessel and 3-vessel disease, received PCI plus optimal medical therapy or optimal medical therapy alone. Rates of mortality and myocardial infarction were

virtually identical in the 2 groups, mirroring results from previous smaller studies.³¹ If PCI is not superior to optimal medical therapy for patients with asymptomatic or stable coronary disease, an effort to find asymptomatic cases through preoperative stress testing can be questioned, particularly if patients' risk factors have been managed optimally.

Taken together, the stent controversy and the negative results of the revascularization trials must be factored into decisions about noninvasive testing before noncardiac surgery. Because a potential downstream consequence of stress testing is a recommendation for PCIs, a patient referred for preoperative stress testing before elective noncardiac surgery must be prepared to delay or postpone the noncardiac procedure. Postponement of elective surgery may be more acceptable for some procedures (eg, hip replacement) than for others (eg, cancer surgery or repair of a large abdominal aortic aneurysm).

Perioperative β -Blockade

Perioperative β -blockade became widely recommended largely because of 2 randomized trials, published in 1996 and 1999. In a US study, 200 patients scheduled for noncardiac surgery received perioperative atenolol or placebo; all patients had either known coronary disease or multiple risk factors.³² Although short-term postoperative outcomes were similar in the atenolol and placebo groups, significantly fewer cardiac events had occurred in the atenolol group during 1 year of follow-up (7 versus 22 events). In the other randomized trial (from Europe), 112 patients scheduled for major vascular surgery, all of whom had risk factors plus abnormal dobutamine echocardiography, received perioperative bisoprolol or placebo.³³ At 30 days, the bisoprolol group had experienced fewer cardiac deaths (2 versus 9) and fewer nonfatal myocardial infarctions (0 versus 9).

These impressive results resulted in widespread acceptance of perioperative β -blockade. Nevertheless, some authorities were troubled by uncritical acceptance of perioperative β -blockade in view of limitations in the relatively small body of evidence from clinical trials.^{34,35} These concerns were supported by the results of 2 additional randomized trials, both published in 2006 and larger than any previous trial. In a Danish trial (Diabetes Postoperative Mortality and Morbidity, or DIPOM), 921 diabetic patients undergoing various types of noncardiac surgery received metoprolol or placebo.³⁶ In a Canadian trial (Metoprolol after Vascular Surgery [MaVS]), 496 patients undergoing abdominal aortic or peripheral vascular surgery received metoprolol or placebo.³⁷ In both trials, no significant differences in cardiac outcomes were noted in the β -blocker and placebo groups. Possible reasons for the varied outcomes of the β -blocker trials include differences in patient populations, choice of β -blocker, and dosing strategies.

To address the deficiencies in the evidence regarding perioperative β -blockade, a much larger international randomized trial, the PeriOperative ISchemic Evaluation study (POISE), was conducted.^{38,39} It included more than 8000



patients with cardiac risk factors who were scheduled for noncardiac surgery. Patients received a protocol-specified regimen of either metoprolol or placebo, starting 2 to 4 hours before surgery and continuing for 30 days postoperatively. Although nonfatal myocardial infarction was lower in the metoprolol group than in the placebo group (3.6% versus 5.1%), the metoprolol group experienced a significantly higher incidence of stroke (1.0% versus 0.5%) and significantly higher total rate of death (3.1% versus 2.3%), which were possibly mediated by excessive hypotension and bradycardia with metoprolol.³⁹ The investigators were unable to identify subgroups that benefited from perioperative β -blockade. Patients already on β -blockers were excluded from this trial.

Given the results of the POISE trial, it is difficult to justify initiation of β -blockers immediately before noncardiac surgery. Certainly, patients already taking β -blockers for valid indications should continue them through the perioperative period. In 2006, the ACC and AHA focused on β -blocker therapy in an update of their 2002 guideline on perioperative cardiovascular evaluation.⁵ The update acknowledges limitations in the published evidence and appropriately makes cautious recommendations. For example, initiation of β -blockers several weeks before noncardiac surgery, with outpatient dose titration (as was done in the trial with the most striking benefit³³), is conceivably superior to starting immediately before surgery. Nevertheless, clinicians should be aware that data to support the initiation of β -blocker therapy perioperatively remain unconvincing, given the results of DIPOM, MaVS, and POISE (none of which were available when the 2006 ACC/AHA focused update was released).

The 2007 Revision of the Guideline

The revised ACC/AHA guideline, published in October 2007, acknowledges most of the recent studies summarized in this article.⁶ The guideline also includes a valuable discussion of the timing of noncardiac surgery and management of antiplatelet therapy in patients who have previously undergone PCI. Moreover, the 2007 algorithm appropriately identifies fewer candidates for noninvasive testing than did the 2002 version (Figure). The first 3 steps in the algorithm, which address emergency surgery, low-risk surgery, and treatment of “active cardiac conditions,” reflect common sense but are worth stating explicitly. In addition, the algorithm appropriately guides patients with no clinical risk factors on the Revised Cardiac Risk Index³ to proceed with surgery. However, for patients whose functional capacity is poor (ie, patients unable to perform physical activity requiring 4 metabolic equivalents) or “unknown” and who have at least 1 clinical risk factor, clinicians are instructed to “consider noninvasive testing if it will change management.” In my view, 2 aspects of this updated guideline remain problematic.

First, the use of functional capacity as the key decision point leading to potential candidates for noninvasive testing (step 4) has little support from empirical research. Patients

with poor or unknown functional capacity are a heterogeneous group encompassing patients impaired by diminished cardiopulmonary reserve, patients with mechanical limitations imposed by musculoskeletal or neurological disease, and patients who are sedentary for other reasons. To my knowledge, no prospective clinical trials have shown that systematic preoperative stress testing in this heterogeneous patient population results in interventions that improve perioperative outcomes. Interestingly, in the study referenced in the guideline’s discussion of functional capacity as an algorithmic decision point, functional capacity was not strongly correlated with extent of disease on coronary angiography.⁴⁰

Second, the ambiguity and circularity of the directive to “consider testing if it will change management” (end of step 5) recapitulates the ambiguity in the 2002 guideline, discussed previously in this article. On what grounds should clinicians decide whether testing “will change management”? Testing should change management only if we have reasonable evidence that a subset of test results should trigger interventions known to improve perioperative outcomes. However, on the basis of the literature reviewed above, no such evidence yet exists. Thus, for patients with risk factors and poor or unknown functional capacity, clinicians are ultimately left hanging: They are asked to make intuitive judgments (ie, “consider testing”) without reasonable guidance. This collapse of the lower half of the algorithm into clinical intuition raises questions about the need for the algorithm itself.

Anticipated Objections to This Analysis

Several objections to this analysis can be anticipated. First, one might argue that guidelines are only “rules of thumb” to be individualized and that clinicians should have considerable latitude in applying guidelines to specific cases. Although that perspective has merit, several factors, including fear of litigation and the increasing use of adherence to guidelines as a quality measure, may drive clinicians to do more rather than less testing under conditions of uncertainty.

Second, despite the lack of compelling evidence that noninvasive testing improves perioperative outcomes, one might claim that the perioperative context should be considered a special situation for which aggressive case finding is warranted, given the physiological stress associated with major surgery. But if that argument is valid, it is inconsistent with the guideline’s statement that preoperative intervention “is rarely necessary to simply lower the risk of surgery unless such intervention is indicated irrespective of the preoperative context.”⁶

Third, one might argue that clinicians should generally be ordering more stress tests for asymptomatic patients with risk factors (outside of the preoperative context) and that the preoperative context affords a convenient pretext to initiate interventions unrelated to the reason for the visit. But if guideline authors hold that view (for which there is little supporting evidence, especially after the COURAGE trial³⁰), it should be made explicit.

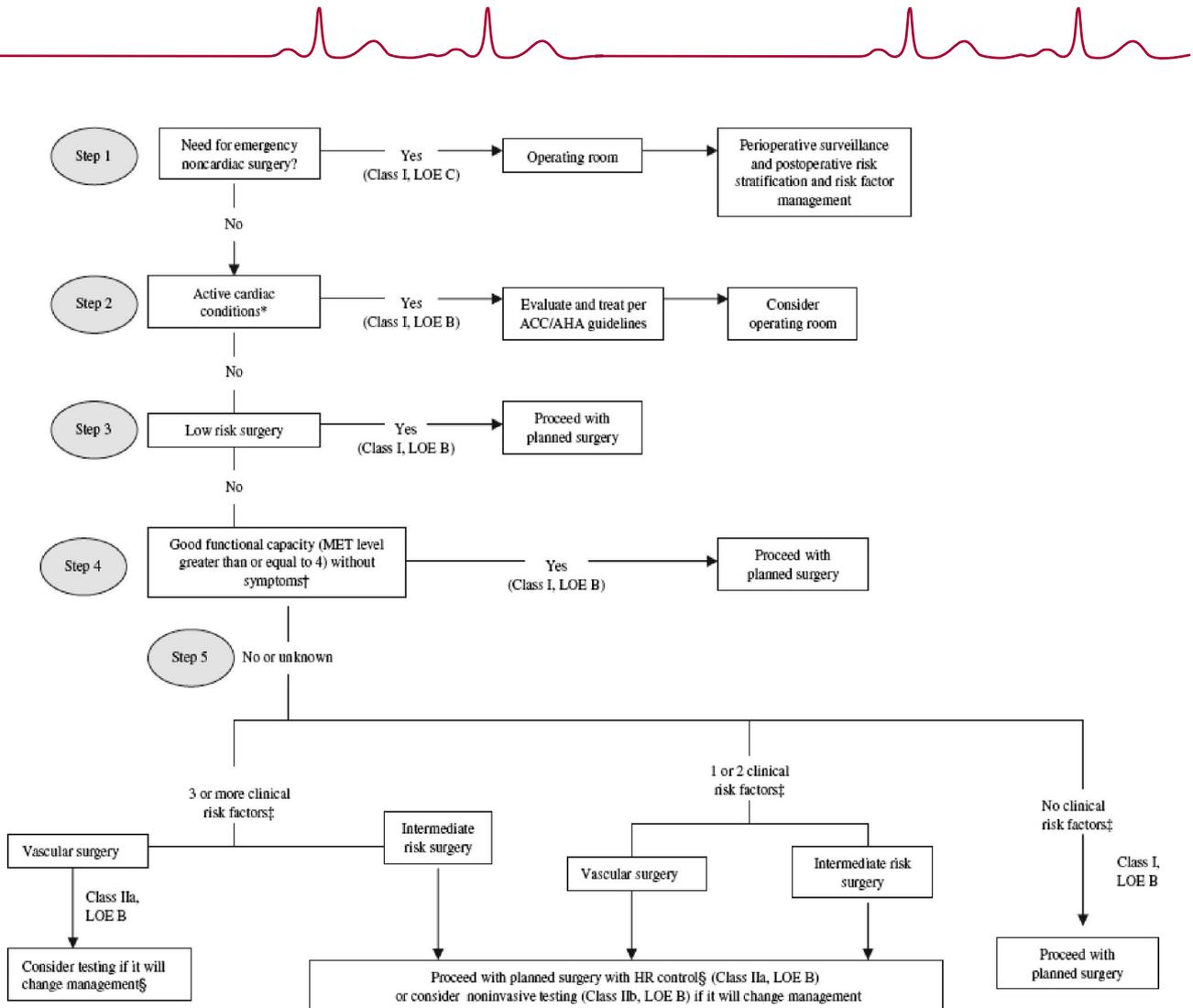


Figure. ACC/AHA algorithm for perioperative cardiac evaluation and care. HR indicates heart rate; LOE, level of evidence; and MET, metabolic equivalent. Reprinted from Fleisher et al. *Circulation*. 2007;116:1971–1996, with permission from Lippincott Williams and Wilkins. Copyright 2007, American Heart Association.

Fourth, one might claim that the purpose of preoperative exercise testing and imaging is not exclusively to select patients for revascularization but also to select patients for β -blockade or other medical interventions. However, indications for β -blockade remain muddled after the DIPOM, MaVS, and POISE trials,^{36–39} and it is unclear whether noninvasive testing would select appropriate candidates for β -blockade more accurately than clinical risk factors alone. Emerging evidence suggests that perioperative statin therapy may improve outcomes, perhaps through plaque-stabilizing effects, but large prospective trials are needed to confirm these findings.⁴¹

Finally, another potential role for preoperative risk stratification is to help patients balance the perioperative risks of elective noncardiac surgery against the perceived benefits of the procedure. However, simple application of the Revised Cardiac Risk Index³ may be sufficient for this purpose. Although noninvasive testing can add additional prognostic information for some subsets of patients,¹³ it is unclear whether such testing adds sufficient incremental information to justify its routine use in counseling patients about whether to proceed with (or avoid) the noncardiac surgery.

Conclusion

The ACC/AHA guideline on perioperative cardiovascular evaluation before noncardiac surgery is a well-intentioned document. Its narrative portion provides a comprehensive overview for those who perform perioperative consultation. However, the guideline is ultimately problematic. It presents the mixed message that preoperative coronary evaluation and revascularization should not be undertaken unless indicated apart from the preoperative context, yet it points some patients precisely in that direction. It acknowledges new evidence that raises questions about the benefits of noninvasive testing, coronary revascularization, and β -blocker therapy, yet its algorithm ends with an invitation to “consider” those options.

In my experience, clinicians performing preoperative cardiovascular consultation frequently feel pressured to “do something.” That pressure has multiple sources, including perceptions of the requesting surgeon’s expectations, perceptions that testing will reduce the probability of litigation, the authoritative appearance of algorithms published by respected organizations, and a

general medical ethos that favors action over inaction. Therefore, even if the subtext of a guideline allows for latitude and individualization rather than “lock-step” application, many clinicians are likely to follow algorithms literally and to routinely implement even weak recommendations.

Although subsets of patients who would benefit from an aggressive approach to preoperative stress testing, revascularization, and initiation of β -blockade may exist, the precise identity of those subsets remains elusive. In the meantime, the cornerstone of preoperative cardiovascular assessment should be a meticulous history and physical examination to ensure that active cardiac conditions have not been overlooked. Clinicians who decide to recommend preoperative stress testing for asymptomatic patients should closely monitor downstream actions that may occur after testing. Patients should be advised that evidence to support the benefit of such testing is limited, that a potential consequence of noninvasive testing is a recommendation for coronary revascularization (with possible morbidity from the invasive coronary procedure itself), and that potentially long delays in performing the originally intended surgery may result. Given the results of the POISE trial,³⁹ clinicians should be wary about initiating β -blockers immediately before surgery but should continue these drugs in patients who are already taking them.

Guideline development takes considerable time and effort, with inevitable delays between new research findings and publication of revisions. Nevertheless, guidelines should be modified as quickly as possible to incorporate new data from clinical trials. Future iterations of guidelines on perioperative assessment should be internally consistent, with reconciliation of general guiding principles, relevant research, and specific algorithmic recommendations.

Disclosures

None.

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Response to Brett

Gabriel Gregoratos, AB, MD

Dr Brett raises important issues regarding the utility and validity of the Perioperative Evaluation and Care Guidelines, with most of which I disagree. In addition to his list of “anticipated objections to this analysis,” I would submit the following: (1) The limitations and generalizability of the DECREASE-II, CARP, and DECREASE-V pilot studies are not adequately explored. (2) The statement “risk stratification does not necessarily improve perioperative outcomes unless it triggers interventions proven to reduce risk,” although true, does not take into account that high-risk results from noninvasive testing may trigger cancellation of an elective operation or substitution of a less risky procedure. (3) The applicability of the COURAGE trial to perioperative patients is highly questionable. (4) In dismissing functional capacity as an important decision point in the preoperative algorithm, 4 studies that form the basis of the guidelines position are ignored. (5) We agree that initiation of β -blockers immediately before noncardiac surgery is difficult to justify; however, the guidelines strongly suggest that β -blockers should be started days to weeks before elective surgery in selected patient groups. (6) The issue over which I disagree most strongly with Dr Brett is the manner in which these guidelines may be used. I submit that clinicians will use the guidelines as a “guide” and not as a “protocol.” There is ample documentation in these and other guidelines that the recommendations are to be interpreted and used in accordance with “particular patient circumstances” and that the treating physician has the ultimate responsibility to decide on a particular treatment mode. To state that “many clinicians are likely to follow algorithms literally and to routinely implement even weak recommendations” suggests that they lack the most important physician attribute: clinical judgment.