UPDATE

Perioperative Medicine Update

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KEY WORDS: preoperative evaluation; postoperative care; thromboembolism and consultation.

J Gen Intern Med 24(7):863–71
DOI: 10.1007/s11606-009-0965-1

Evidence-based preoperative risk stratification and implementation of therapies to decrease morbidity and mortality are the focus of the preoperative evaluation that internists often perform in the office or the hospital setting. In this paper, we summarize some recent key advances in the field of perioperative medicine. We used a systematic search strategy to survey the relevant literature for the period January 1, 2007 through April 1, 2008. We performed a MEDLINE search using the medical subject heading (MeSH) terms intraoperative complications, postoperative complications, preoperative care, intraoperative care, perioperative care, postoperative care, intraoperative period, preoperative period, acute renal failure, cirrhosis, venous thromboembolism, and surgery. We added the following text words: intraoperative OR perioperative OR postoperative AND/OR complication OR event. As our target audience is general internists, we excluded studies of transplantation surgery, cardiac surgery, and pediatric surgery. We discuss studies that the four authors agreed had the most important practice implications for perioperative medicine. We have divided the articles into four sections: perioperative cardiac care, perioperative anticoagulant therapy, prevention of postoperative respiratory failure, and predicting postoperative risk of morbidity and mortality.

This paper derives from the presentation Update in Perioperative Medicine at the 31st annual session of SGIM, May 2008.
Received July 26, 2008
Revised November 19, 2008
Accepted March 17, 2009
Published online April 9, 2009

PERIOPERATIVE CARDIAC CARE

Updated American College of Cardiology/ American Heart Association (ACC/AHA) Guidelines Simplify Cardiac Risk Stratification for Non-Cardiac Surgery

Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 Guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: Executive summary. J Am Coll Cardiol 2007;50:1707–1732. PMID: 17950159.

The 2007 ACC/AHA guidelines updated those published in 2002 and provide an evidence-based framework for evaluation and management of patients undergoing noncardiac surgery. Results of literature searches from 2002–2007 were used for this update, and the writing committee made recommendations based on class (I, II, III) and level of evidence (A, B, C) (Table 1). The overriding theme of the guidelines was that cardiac interventions (e.g., revascularization) are rarely necessary solely to get the patient through non-cardiac surgery.

The three principal elements of the updated guidelines are clinical risk predictors, surgery specific risk, and self-reported exercise capacity. The authors changed the terminology for the clinical risk predictors: the 2002 "major clinical predictors" are now "active cardiac conditions," the former "intermediate" predictors are now "clinical risk factors," and "minor" predictors have been deleted (with cerebrovascular disease moved to clinical risk factors). Surgery-specific risk was divided into major vascular surgery, intermediate risk operations (intrathoracic, intraperitoneal, orthopedic surgery, carotid endarterectomy, and the newly added endovascular aortic aneurysm repair by stent or coil), and low risk procedures. The definition of adequate exercise capacity (4 METS) is unchanged.

The guideline authors simplified the new algorithm (see Fig. 1) and incorporated the revised cardiac risk factors (RCRI) in the last step. The emphasis was to minimize noninvasive testing (NIT) unless the results would change management. New information on revascularization, stents and antiplatelet therapy, beta-blockers, and statins were added to the guidelines, and there is an expanded discussion of noninvasive testing and perioperative surveillance for myocardial infarction.

Implications for Clinical Practice. These updated evidence-based guidelines, presented in a new, simplified algorithm, should result in fewer unnecessary preoperative noninvasive tests.

Table 1. ACA/ACH Recommendation Classifications and Levels of Evidence

Classification of recommendations	Definition
Class I	Benefit>>risk
Class IIa	Benefit>>risk; additional studies with focused objectives needed
Class IIB	Benefit>risk; additional studies with broad objectives needed;
Class III	Risk>benefit; no additional studies needed

Levels of evidence	
Level A	Multiple (3–5) population risk strata evaluated; general consistency of direction and magnitude of effect
Level B	Limited (2–3) population risk strata evaluated
Level C	Very limited (1–2) population risk strata evaluated

Perioperative Beta-Blockers in High Doses Increase Mortality

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 randomized controlled trial. Lancet 2008; 371:1839–47. PMID: 18479744.

Trials of beta-blockers in non-cardiac surgery have reported conflicting results regarding effects on perioperative ischemia, myocardial infarction (MI), and death. Small studies by Mangano[1] and Poldermans (DECREASE)[2] suggested a benefit, but larger studies (MAVS,[3] DIPOM,[4] and POBBLE[5]) found no difference in outcome. Despite these findings, various regulatory agencies and organizations, including the American College of Cardiology guidelines,[6] recommend perioperative beta-blockers.

In the POISE trial, investigators randomly assigned 8,351 patients aged 45 or older undergoing noncardiac surgery with an expected hospital length of stay of at least 2 days who had atherosclerotic disease or risk factors to receive extended-release metoprolol (n=4,174) or placebo (n=4,177). A 100-mg metoprolol dose was given 2 to 4 h preoperatively followed by a second 100-mg dose within 6 h after surgery. A 200-mg dose was given 12-h after the first postoperative dose and continued as a daily dose for 30 days. The drug was temporarily withheld for a heart rate <45 beats per minute or a systolic blood pressure <100 mmHg and then restarted at 100 mg daily. Cardiac enzymes and electrocardiograms (ECG) were obtained during the first 2 to 3 days following surgery with another ECG at 30 days.

The primary endpoint was a composite of cardiovascular death, non-fatal MI, and non-fatal cardiac arrest. Other endpoints included non-fatal stroke, total mortality, postoperative atrial fibrillation, and need for revascularization. Safety measures included significant bradycardia or hypotension. Statistical analysis was by intention-to-treat and used Cox proportional hazard models.

Fewer patients in the metoprolol group than in the placebo group reached the primary endpoint [244 (5.8%) vs 290 (6.9%); HR 0.84, 95% confidence interval (CI) 0.70–0.99, p=0.40]. This was driven primarily by a reduction in non-fatal MI in the metoprolol group [176 (4.2%) vs 239 (5.7%)] as there was no difference in cardiac death. However, the metoprolol group had more deaths [129 (3.1%) vs 97 (2.3%), HR 1.33, 95% CI 1.03–1.74, p=0.0317], and strokes [41 (1.0%) vs 19 (0.5%), HR 2.17, 95% CI 1.26–3.74, p=0.0053] than the placebo group. Also, clinically significant hypotension and bradycardia occurred more frequently in patients receiving metoprolol (15% vs 9.7%, HR 1.55, 95% CI 1.38–1.74 and 6.6% vs 2.4%, HR 2.74, 95% CI 2.19–3.43, respectively), with both p values <0.001. Study outcomes are shown in Table 2.

The authors proposed that the increased death rate was potentially due to clinically significant hypotension, bradycardia, and stroke. Sepsis was the only cause of death significantly more common in the metoprolol group. Hypotension might predispose patients to developing nosocomial infections, and beta blockers could mask the tachycardia associated with infection and delay diagnosis. Additionally, the compensatory increase in cardiac output needed by septic patients would be blunted by beta-blockade.

This was the largest study of perioperative beta-blockers and demonstrated that extended-release metoprolol reduced the risk of MI, but at the expense of increased stroke and overall mortality. Although these results are valid and potentially generalizable, many physicians are unwilling to use this dose of metoprolol. The editorialists[7] noted that beta-blocker naïve patients receiving a relatively high dose started immediately before surgery were more likely to become hypotensive, which partly explained the excess adverse events. However, it is unknown whether starting a lower dose more in advance of surgery would have improved outcomes. They also stressed the importance of appropriately evaluating and treating the underlying cause of postoperative tachycardia rather than having protocols that would mandate an additional or increased dose of beta-blockers.

Implications for Clinical Practice. Although patients currently on beta-blockers should continue them in the perioperative period, it is unclear which, if any, beta-blocker naïve subgroups would benefit from prophylactic beta-blockers. POISE should lead physicians and regulatory agencies to re-evaluate recommendations and guidelines for prophylactic perioperative beta-blockers.

Preoperative Revascularization Fails to Show Benefit Even in High Risk Patients Undergoing Vascular Surgery

Poldermans D, Schouten O, Vidakovic R, et al for the DECREASE Study Group. A clinical randomized trial to evaluate the safety of a noninvasive approach in high-risk patients undergoing major vascular surgery. J Am Coll Cardiol 2007; 49:1763–1769. PMID: 17466225.

The purpose of the preoperative cardiac evaluation is to assess risk and decide which patients would benefit from further diagnostic testing or interventions in an attempt to lower that risk. If revascularization did not improve outcome, then there would be little reason to subject patients to these tests or interventions.

An observational study[2] found that perioperative beta-blockers improved outcomes in higher risk groups, including those with abnormal dobutamine stress echocardiograms (DSE) with one to four abnormal segments. However, perio-

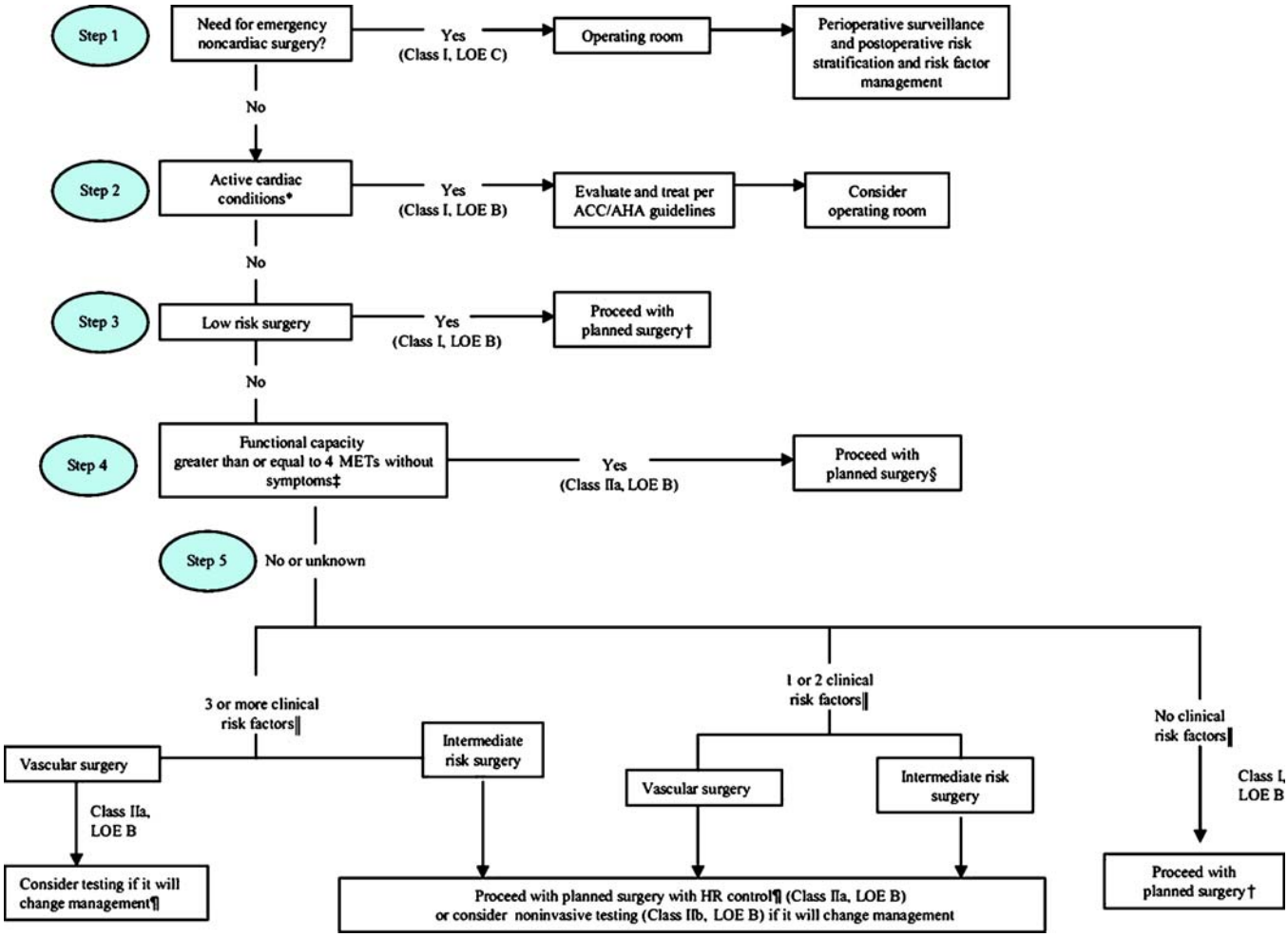

Figure 1. Cardiac evaluation and care algorithm for non-cardiac surgery. Reproduced with permission (pending). Active cardiac conditions: unstable coronary syndromes, decompensated heart failure, significant arrhythmias, and severe valvular disease. Clinical risk factors: history of heart disease, history of compensated or prior heart failure, history of cerebrovascular disease, diabetes mellitus, and renal insufficiency.

perative beta-blockers showed no benefit for patients with more severe ischemia (five or more abnormal segments); these patients might be potential candidates for preoperative revascularization. Conversely, the Coronary Artery Revascularization Prophylaxis (CARP) trial[8] failed to show that revascularization reduced perioperative myocardial infarction (MI), cardiac death at 30 days, or long-term mortality (average 2.7 years) in patients with stable cardiac disease who were undergoing elective vascular surgery. If a benefit exists, it would most likely occur in the highest risk patients with extensive coronary artery disease; these patients formed the basis of the DECREASE-V Pilot Study.

The investigators screened 1,880 patients scheduled for major vascular surgery, and those with ≥3 risk factors (n=430) underwent DSE or stress nuclear imaging. The 101 patients with extensive stress-induced ischemia (≥5 segments or ≥3 walls) were randomly assigned to revascularization (n=49) or no revascularization (n=52). All patients received perioperative beta-blockers (target heart rate of 60–65 beats per minute) and antiplatelet therapy. The primary endpoint was the composite

Table 2. Select Endpoints and Safety Measures from the POISE Study

Outcome	Metoprolol (n=4,174)	Placebo (n=4,177)	Hazard ratio (CI)	P value
CV death, MI, cardiac arrest	244 (5.8%)	290 (6.9%)	0.84 (0.70–0.99)	0.0399
CV death	75 (1.8%)	58 (1.4%)	1.30 (0.92–1.83)	0.1368
Nonfatal MI	176 (4.2%)	239 (5.7%)	0.73 (0.60–0.89)	0.0017
Nonfatal stroke	41 (1.0%)	19 (0.5%)	2.17 (1.26–3.74)	0.0053
Total mortality	129 (3.1%)	97 (2.3%)	1.33 (1.03–1.74)	0.0317
Clinically significant hypotension	625 (15.0%	404 (9.7%)	1.55 (1.38–1.74)	<0.0001
Clinically significant bradycardia	277 (6.6%)	101 (2.4%)	2.74 (2.19–3.43)	<0.0001

Abbreviations: CV = cardiovascular, MI = myocardial infarction

of all-cause death or MI at 30 days; the secondary endpoint was the same composite at 1 year follow-up.

Coronary angiography revealed two-vessel, three-vessel, and left-main disease in 25%, 67%, and 8% of patients, respectively. Seventeen patients underwent coronary bypass surgery (CABG) with one sustaining an MI and not having vascular surgery; two others died before vascular surgery from a ruptured aneurysm. PCI was performed in 32 patients—drug-eluting stents (DES) were placed in 30 and a bare-metal stent (BMS) in 2—with incomplete revascularization occurring in 7 of these patients. The median duration from revascularization to operation was 30 days. Aspirin and clopidogrel were continued during surgery in all PCI patients with no significant difference in perioperative transfusion rates.

The 30-day composite event rate was 42.9% in the revascularization group vs. 32.7% in the control group [HR 1.4 (95% CI 0.73–2.8); p=0.30]. The event rate by 1 year was 49.0% vs. 44.2%, respectively [HR 1.2 (95% CI 0.68–2.3); p=0.48].

Although underpowered, the DECREASE-V Pilot Study showed that preoperative revascularization failed to improve outcome even in a high-risk group of patients. The authors estimated that a study with over 300 patients in each arm would be necessary to demonstrate a 20% benefit from prophylactic revascularization. The optimal preoperative evaluation and management of very high risk vascular surgery patients therefore remain unclear. The lack of benefit with revascularization may suggest that mechanisms other than blood-flow limiting coronary lesions (e.g., unstable coronary plaques) may be more important in perioperative MI. Furthermore, the need to delay vascular surgery after revascularization, especially in patients with an aortic aneurysm, may result in rupture; therefore, revascularization may best improve long-term outcome in these patients if done postoperatively.

Implications for Clinical Practice. Preoperative/prophylactic revascularization, even in high-risk patients undergoing high-risk vascular surgery, cannot be recommended at this time.

Higher Statin Dose and Lower Preoperative LDL Predict Lower Cardiovascular Complication Rates after Major Vascular Surgery

Feringa HH, Schouten O, Karagiannis SE, et al. Intensity of statin therapy in relation to myocardial ischemia, troponin T release, and clinical cardiac outcome in patients undergoing major vascular surgery. J Am Coll Cardiol 2007; 50:1649–1656.

A growing body of data, mostly from observational studies, suggests a potential beneficial effect of perioperative statins to reduce cardiac complication rates. However, the potential for residual confounding in these studies leaves this question unresolved.[9] In this observational study, the authors sought to prospectively assess the relationship between statin dose and cardiac outcomes in patients undergoing major vascular surgery.

The study cohort was comprised of 359 patients undergoing aortic aneurysm, peripheral artery bypass, and carotid surgery. Exclusions were patients with a recent myocardial infarction (<6 months), pacemaker, left ventricular hypertrophy, bundle branch block, or atrial fibrillation. All patients had a preoperative dobutamine stress echocardiogram, and those with a positive study were referred for further cardiac evaluation.

The authors performed a multivariate analysis to evaluate the relationship between statin dose and LDL cholesterol values and outcomes. Covariates included in the model were age, gender, coronary artery disease by history or stress testing, history of congestive heart failure, cerebrovascular disease, diabetes, renal failure, hypertension, type of surgery, medications (beta-blockers, aspirin, ACE inhibitors, calcium channel blockers), and the propensity score for receiving a statin. Outcomes were troponin T release (measured at 1, 3, and 7 days after surgery, at discharge, and when indicated by clinical status), perioperative ischemia (measured by continuous 12-lead electrocardiography from 1 day before surgery to up to 2 days after surgery), and major cardiac events (cardiac death and nonfatal Q-wave infarction) within 30 days after surgery (early) and during outpatient follow-up (late = mean 2.3 years). Outpatient data were available for all patients; no patient was lost to follow-up.

Higher statin dose, even after multivariable adjustment for confounders including baseline cholesterol values, was associated with lower rates of myocardial ischemia and troponin T release. Myocardial ischemia was twice as common among patients receiving 50% or less of the maximal recommended statin dose than among those receiving more than 50% of the recommended dose; unadjusted ischemia rates were 20% and 11%, respectively (p<0.001). After multivariable adjustment, each 10% increase of maximal recommended therapeutic statin dose was associated with an odds ratio of 0.85 (95% CI 0.76–0.93) for perioperative ischemia. Findings were similar after adjusting for baseline LDL cholesterol values (OR 0.88, 95% CI 0.80–0.96). A similar relationship existed between LDL cholesterol values and both myocardial ischemia and troponin T release. For example, unadjusted myocardial ischemia rates for patients with a baseline LDL cholesterol value of <80 mg/dl and for those with LDL values of >154 mg/dl were 12% and 46%, respectively (p<0.001). After multivariable adjustment, each 10-mg/dl decrease in LDL cholesterol level was associated with an odds ratio of 0.87 (95% CI 0.81–0.91) for ischemia.

Statin dose was also associated with early and late cardiovascular complications. For example, the adjusted odds ratio for cardiac death or Q-wave myocardial infarction for each 10% increase of maximally recommended statin dose was 0.66 (95% CI 0.42–0.98) for early complications and 0.80 (95% CI 0.67–0.94) for late complications.

This study is the first to suggest a dose-response relationship between statin dose and both proxy and clinical cardiac outcomes after major vascular surgery. This relationship adds strength to the argument that there is a causal relationship between statin use and reduced perioperative cardiac morbidity. If the relationship was due to unmeasured confounders, a dose response relationship would be unlikely. However, this is an observational study, and caution is necessary when applying these findings to clinical practice. A large-scale randomized controlled trial of perioperative statin use would help to resolve this controversy. Unanswered questions about perioperative statins include drug choice, dose, time of initiation, and duration of therapy.

Implications for Clinical Practice. This report adds support to the recent ACC/AHA task force recommendations[6] that statin use is reasonable (class IIa) for patients undergoing vascular surgery and can be considered (class IIb) for patients

undergoing intermediate risk surgery with at least one risk factor.

PERIOPERATIVE ANTICOAGULANT THERAPY

Risk of Bleeding with Perioperative Bridging Therapy is High

Garcia DA, Regan S, Henault L et al. Risk of thromboembolism with short-term interruption of warfarin therapy. Arch Intern Med 2008; 168(1):63–69. PMID: 18195197.

The management of patients on warfarin who need a surgery or a procedure is uncertain because few studies have addressed thromboembolism risk when warfarin is stopped for the procedure. This was a prospective observational study of 1,293 warfarin interruptions in 1,024 individuals and was done at 101 primarily community-based physician office practices between April 2000 and March 2002. The aim of the study was to assess the frequency of thromboembolism (TE) and bleeding within 30 days of warfarin interruption. The mean age (SD) of the patients was 71.9 (10.6) years, and 42.8% were female. The most common indications for anticoagulant therapy were atrial fibrillation (n=550), venous thromboembolism (n=144), and mechanical heart valves (n=132). Approximately, 108 (8.4%) were bridged with heparin, which was almost exclusively low-molecular weight heparin (LMWH). The most common procedures were colonoscopy, oral surgery, and ophthalmic surgery. Seven patients [0.7%; 95% confidence interval (CI), 0.3%–1.4%] experienced postprocedure TE within 30 days. None of the seven patients who experienced TE received periprocedural bridging therapy. Six patients (0.6%; 95% CI, 0.2%–1.3%) experienced major bleeding, whereas an additional 17 patients (1.7%; 95% CI, 1.0%–2.6%) experienced a clinically significant, non-major bleeding episode. Of the 23 patients who had bleeding episodes, 14 received periprocedural heparin or low-molecular-weight heparin. Although the duration of warfarin therapy interruption was variable, it was 5 or fewer days for more than 80% of patients. The authors concluded that for many patients undergoing a minor procedure, periprocedural interruption is associated with low risk of TE. These data are not applicable to patients requiring hospitalization for major surgery. In addition, given the limited number of thromboembolic events, the risk of perioperative thromboembolism may be underestimated. On the other hand, the risk of major bleeding in patients undergoing minor procedures was substantial.

Implications for Clinical Practice. The risks of bleeding and thromboembolism depend upon patient-specific, procedure-specific, and physician-specific factors. This study emphasizes that clinicians should weigh the patient's estimated risk of bleeding with bridging therapy against the low risk of TE.

An Oral Direct Thrombin Inhibitor Shows Promise

Eriksson BI, Dahl, OE, Rosencher N et al. Dabigatran etexilate versus enoxparin for prevention of venous thromboembolism after total hip replacement: a randomized, double-blind, non-inferiority trial. Lancet 2007; 370:949–956. PMID: 17869635.

As total hip arthroplasty (THA) is associated with a high risk of VTE that persists after discharge, existing guidelines recommend extended prophylaxis.[10] Currently, only warfarin and parenteral anticoagulants are approved for use for this indication. Dabigatran is one of several new anticoagulants that are being tested in clinical trials against the parenteral LMWHs. The aim of this trial was to assess the safety and efficacy of the oral direct thrombin inhibitor dabigatran for the prevention of VTE after hip surgery in a non-inferiority study design. This randomized, double-blind study was conducted at 115 centers across the world. Investigators randomly assigned 3,494 patients undergoing THA to dabigatran 220 mg orally once daily (n=1157), dabigatran 150 mg (n=1,174) orally once daily starting with a half-dose 1–4 h after surgery or subcutaneous enoxaparin 40 mg once daily starting the evening before surgery. Main outcome measures were efficacy (total VTE and death), major bleeding, and clinically relevant bleeding. The median treatment duration was 33 days. Overall, 880 patients in the dabigatran 220 mg group, 874 in the dabigatran 150 mg group, and 897 in the enoxaparin group were available for the primary efficacy outcome analysis; the main reason for exclusion in all three groups was the lack of adequate venographic data. The primary efficacy outcome (VTE and death) occurred in 60 (6.7%) of 897 individuals in the enoxaparin group, 53 (6.0%) of 880 patients in the dabigatran 220 mg group (absolute difference −0.7%, 95% CI −2.9 to 1.6%), and 75 (8.6%) of 874 people in the 150 mg group (1.9%, 95% CI −0.6 to 4.4%). Both doses were thus non-inferior to enoxaparin. There was no significant difference in major bleeding rates with either dose of dabigatran compared with enoxaparin (p=0.44 for 220 mg, p=0.60 for 150 mg). The frequency of increases in liver enzyme concentrations and of acute coronary events during the study did not differ significantly between the groups. The authors concluded that oral dabigatran was as effective and safe as enoxaparin for VTE prevention after total hip arthroplasty. The trial used robust randomization, double-dummy blinding, central outcome-adjudication with imaging, and prespecified statistical analyses, and was reported according to CONSORT criteria. About 24% of their population did not have data for primary outcomes, and this could have impacted the results, but the authors and the accompanying editorial think otherwise because over-enrollment may have mitigated the risks of missing data.

Impact on Clinical Practice. These results and those from a large phase III clinical trial program with dabigtran shows promise and will help define the future of this drug (which is not yet approved either in the US or Europe) for VTE prevention after joint replacement.

PREVENTION OF POSTOPERATIVE RESPIRATORY FAILURE

Systematic Review: Thoracic Epidural Analgesia Reduces Postoperative Cardiac and Pulmonary Complication Rates after High Risk Surgery

Liu SS and Wu CL. Effect of postoperative analgesia on major postoperative complications: a systematic update of the evidence. Anesth Analg 2007; 104:689–702. PMID: 17312231.

Postoperative pain may decrease lung volumes and increase pulmonary complication rates due to splinting and inability to take deep breaths, particularly after thoracic, aortic, and upper abdominal surgeries. The impact of pain on other postoperative medical complications is less well established. This paper updates a previously published review of pulmonary complications[11] and aims to determine the impact of differing types of postoperative analgesia on a broader range of major medical complications.

The authors performed a MEDLINE and Cochrane database search from 1996–2006 and included previous meta-analyses and new data reported since earlier meta-analyses. They excluded studies with fewer than 200 subjects. Eligible studies included 18 meta-analyses, 10 systematic reviews, 8 additional randomized trials, and 2 observational database studies.

The authors found that epidural analgesia may have an impact on perioperative mortality, but the data are mixed. The largest meta-analysis to date reported a reduction in mortality, but also included patients receiving epidural or spinal anesthesia. Subsequent trials reported that epidural analgesia does not reduce the risk of cardiovascular complications after general surgery, but does reduce the risk after major vascular surgery. Abundant good quality data indicate that postoperative epidural analgesia reduces postoperative pulmonary complication rates. The evidence is strongest for coronary bypass and aortic surgery with risk reductions ranging from 29% to 64%. There was minimal evidence on whether epidural analgesia affected rates of thromboembolic complications, wound infection, postoperative delirium, or chronic postoperative pain. Intravenous patient-controlled analgesia did not influence rates of perioperative morbidity or mortality. Strengths of this study include the systematic search strategy; a weakness was the lack of explicit assessment of the rigor and quality of the retrieved articles.

Implications for Clinical Practice. Thoracic epidural analgesia is recommended for patients undergoing major vascular surgery and coronary artery bypass surgery and should be considered for high-risk patients undergoing abdominal surgery.

PREDICTING POSTOPERATIVE RISK OF MORBIDITY AND MORTALITY AFTER NON-CARDIAC SURGERY

Updated Multifactorial Risk Index Predicts Risk of Postoperative Respiratory Failure

Johnson RG, Arozullah AM, Neumayer L, et al. Multivariable predictors of postoperative respiratory failure after general and vascular surgery: results from the patient safety in surgery study. J Am Coll Surg 2007;204:1188–1198. PMID: 17544077.

Clinicians have used multifactorial risk indices to predict the risk of postoperative cardiac complications for over 3 decades.[12] Similar risk indices to predict postoperative pulmonary complications have slowly gained acceptance since the first published reports dating to 2000 and 2001.[13,14] In this study, Johnson and colleagues updated a previously published multifactorial risk index to predict postoperative respiratory failure[13] by including more recent data and data from non-Veterans Administration (VA) hospitals.

The authors used the methodology of the National Surgical Quality Improvement Program (NSQIP) and the Patient Safety in Surgery Study (PSS) to collect data from 128 VA and 14 private sector academic hospitals for the period of 2002 to 2004. Data were available for 45 potential risk factors among patients undergoing major general or vascular procedures. Respiratory failure was defined as mechanical ventilation for more than 48 h or unplanned reintubation. The authors used a logistic regression analysis to identify factors that independently predicted respiratory failure rates and developed a weighted scoring system based on the strength of each factor in the multivariable analysis.

The overall respiratory failure rate among 180,359 patients was 3.0%. The 30-day mortality was 26.5% for patients who developed respiratory failure, but only 1.4% in those who did not ($p<0.0001$). This highlights the high morbidity of postoperative pulmonary complications. Twenty-eight variables were independently associated with respiratory failure (Table 3). The strongest predictors were ASA class >2, work relative value units (RVU) as a proxy for surgical complexity, respiratory surgery, head and neck surgery, emergency surgery, and age >65. Point scores accurately predicted respiratory failure rates. Rates in the validation cohort for low-risk (<8 points), medium-risk (8–12 points), and high-risk (>12 points) patients were 0.08%, 0.84%, and 6.75%, respectively. P values for model goodness-of-fit chi-squared tests for the derivation and validation cohorts were 0.0046 and 0.0001, respectively.

This updated index accurately identifies patients at high risk for the development of respiratory failure in both VA and non-veteran populations. The risk index is complicated and will be most helpful as a tool in future research rather than for day-to-day clinical practice. Consistent with previous studies, most factors are not modifiable. Risk factors were similar to those of the recently published ACP guideline[15] with several exceptions. New risk factors were high work RVU, preoperative sepsis, ascites, and hypernatremia. Functional dependence, low serum albumin, and congestive heart failure conferred lower risk than that estimated by the ACP guideline.

Strengths of this study were the large sample size, use of explicit outcome definitions, and the multivariable analysis. A weakness was lumping together patients undergoing a variety of general and vascular surgeries because data regarding surgery-specific risk factors were unavailable. In addition, the risk index is complicated and will be most helpful as a tool in future research rather than for day-to-day clinical practice. Consistent with previous studies, most factors are not modifiable.

Implications for Clinical Practice. This paper provides information for clinicians assessing the risk for postoperative pulmonary complications. The study will improve the quality of future intervention studies by providing a tool to accurately estimate baseline risk and to characterize important confounders.

A Risk Score Can Predict Acute Renal Failure After Non-Cardiac Surgery

Kheterpal S, Tremper KK, Englesbe MJ et al. Predictors of postoperative acute renal failure after noncardiac surgery in patients with previously normal renal function. Anesthesiology 2007; 107:892–902. PMID: 18043057.

Table 3. Independent Predictors of Postoperative Respiratory Failure after Major General or Vascular Surgery

Risk factor	Odds ratio (95% CI)	Score
ASA class (3 vs. 1–2)	2.88 (2.46–3.36)	+3
ASA class (4–5 vs. 1–2)	4.90 (4.11–5.85)	+5
Emergency (yes vs. no)	2.42 (2.17–2.69)	+2
Work RVU (10–17 vs. <10)	2.30 (1.94–2.73)	+2
Work RVU (>17 vs. <10)	4.45 (3.72–5.31)	+4
Preoperative albumin (≤3.5 vs. >3.5)	1.49 (1.34–1.64)	+1
Integumentary vs. hernia*	1.14 (0.87–1.51)	+1
Respiratory and hemic vs. hernia*	3.12 (2.18–4.47)	+3
Heart vs. hernia*	2.31 (1.67–3.20)	+2
Aneurysm vs. hernia*	1.55 (1.20–2.00)	+2
Mouth, palate vs. hernia*	6.64 (4.78–9.21)	+7
Stomach, intestines vs. hernia*	2.13 (1.66–2.73)	+2
Endocrine vs. hernia*	1.54 (0.99–2.38)	+2
Preoperative sepsis (yes vs. no)	2.00 (1.71–2.34)	+2
Preoperative creatinine ≥1.5 vs. <1.5	1.65 (1.49–1.83)	+2
History of severe COPD (yes vs. no)	1.52 (1.36–1.69)	+2
Ascites (yes vs. no)	1.85 (1.50–2.28)	+2
Dyspnea (yes vs. no)	1.32 (1.19–1.46)	+1
Impaired sensorium (yes vs. no)	1.50 (1.22–1.84)	+1
Preoperative bilirubin >1.0 vs. ≤1.0	1.21 (1.08–1.35)	+1
>2 (vs. ≤ 2) alcoholic drinks/day in 2 weeks before admission	1.30 (1.14–1.49)	+1
Bleeding disorders	1.25 (1.07–1.46)	+1
Age (40–65 years vs. <40 years)	1.70 (0.86–3.37)	+2
Age (>65 years vs. <40 years)	2.06 (1.54–2.77)	+2
Preoperative white blood count (<2.5 vs. 2.5–10)	1.48 (0.89–2.47)	+1
Preoperative white blood count (>10 vs. 2.5–10)	1.20 (1.09–1.33)	+1
Preoperative serum sodium >145 vs. ≤145	1.56 (1.21–2.03)	+2
Weight loss >10% (yes vs. no)	1.26 (1.10–1.44)	+1
Preoperative acute renal failure (yes vs. no)	1.51 (1.17–1.94)	+2
Gender (male vs. female)	1.19 (1.06–1.35)	+1
Congestive heart failure <30 days before operation (yes vs. no)	1.30 (1.09–1.55)	+1
Current smoker (yes vs. no)	1.15 (1.05–1.26)	+1
Preoperative platelet count ≤150 vs. >150	1.21 (1.06–1.38)	+1
CVA/stroke with neurologic deficit (yes vs. no)	1.27 (1.10–1.47)	+1
Wound class (clean/contaminated vs. clean)	1.16 (1.02–1.30)	+1
Wound class (contaminated vs. clean)	1.36 (1.15–1.61)	+1
Wound class (infected vs. clean)	1.25 (1.04–1.50)	+1
Preoperative SGOT >40 vs. ≤40	1.16 (1.04–1.30)	+1
Preoperative hematocrit ≤38 vs. >38	1.11 (1.01–1.23)	+1
CVA/stroke without neurologic deficit (yes vs. no)	1.23 (1.02–1.45)	+1

Surgery type defined according to current procedural terminology (CPT) code definitions
Adapted with permission from: J Am Coll Surg 2007;204:1188–1198

Previous literature regarding postoperative acute renal failure (ARF) has primarily focused on cardiac surgery patients. Risk factors identified in these patients include age, hypertension, preoperative renal insufficiency, peripheral vascular disease, low ejection fraction, COPD, emergent and high-risk surgeries.[16,17] Factors unique to cardiac surgery, including aortic cross-clamping and cardiopulmonary bypass, may affect postoperative renal function. This large prospective observational study identified risk factors for postoperative renal failure in 15,102 noncardiac surgery patients. Patients with normal preoperative renal function, defined as a creatinine clearance greater than 80 ml/min, were eligible. Exclusion criteria included preoperative intravenous contrast, suprarenal aortic cross clamping, ureteral manipulation, urologic and transplant surgeries. The primary outcome measure was acute renal failure (ARF) (defined as a creatinine clearance of 50 ml/min or less); mortality was a secondary outcome. A multivariable analysis identified independent predictors of ARF.

Independent preoperative predictors of postoperative ARF included age >58 (HR 4.2, 95% CI 2.9–6.0), liver disease (HR 2.4, 95% CI 1.4–4.3), body mass index >32 (HR 1.9, 95% CI 1.3–2.7), peripheral vascular disease (HR 4.2, 95% CI 2.5–7.1), COPD (HR 3.0, 95% CI 1.9–5.0), emergent surgery (HR 1.9, 95% CI 1.2–3.0), and high-risk surgery (HR 2.9, 95% CI 2.0–4.3). The frequency of postoperative ARF increased with the number of preoperative predictors [0 risk factors 0.3%, 1 risk 0.5% (HR 2.0, 95% CI 1.1–3.6), 2 risks 1.3% (HR 4.7, 95% CI 2.6–8.5), 3 risks 4.3% (HR 16.0, 95% CI 8.9–28.8)]. Significant

Table 4. MELD Score and Postoperative Mortality

Mortality, rounded to nearest %						
MELD score	7 days	30 days	90 days	1 year	5 years	10 years
0–7	2	6	10	19	51	73
8–11	3	10	18	29	59	78
12–15	8	25	32	45	70	87
16–20	15	44	56	71	94	94
21–25	23	54	67	85	92	100
>25	30	90	90	100	100	100

intraoperative predictors included vasopressor use (2.2% among patients without renal failure and 16% among patients with renal failure) and total vasopressor dose (2% without ARF, 5.3% with ARF), as well as diuretic administration (5.8% without ARF, 16% with ARF; $p<0.05$). Postoperative ARF was significantly associated with mortality at 30 days, 60 days, and 1 year (HR 6.5, 95% CI 2.7–15; HR 3.8, 95% CI 1.9–7.6 and HR 2.6, 95% CI 1.5–4.4, respectively).

The incidence of postoperative ARF in noncardiac surgical patients was 0.8%. Certain risk factors were the same as those in the cardiac surgical population, including high-risk and emergent surgeries, COPD, advanced age, and peripheral vascular disease. Risk factors unique to noncardiac surgical patients included liver disease and elevated body mass index. Although intraoperative vasopressor use was associated with ARF, it is unclear if this was a direct effect of vasopressors or underlying hypotension.

Limitations of this study include the exclusion of over 6,000 patients with no preoperative creatinine measurements. These patients may not have had creatinine levels measured because they were considered at low risk to develop ARF. Excluding these patients could have resulted in a falsely high estimated risk of postoperative ARF. Additionally, some studied co-morbidities were not well defined.

Implications for Clinical Practice. Although many risk factors identified in this study are not modifiable, identifying patients at high risk for postoperative ARF is particularly useful when counseling patients considering elective procedures.

Model of End-Stage Liver Disease (MELD) Scores Predict Postoperative Mortality in Cirrhotics

Teh SH, Nagorney DM, Stevens SR, et al. Risk factors for mortality after surgery in patients with cirrhosis. *Gastroenterology* 2007;132:1261–1269. PMID: 17408652.

Cirrhosis is a significant risk for perioperative mortality; the Child-Turcotte-Pugh scores and the presence of other co-morbidities each predict risk.[19] Previous studies have demonstrated that Child's class is significantly related to postoperative mortality. The subjective components and non-continuous variables of the Child's classification make this a difficult model to use for estimating perioperative risk in patients with cirrhosis, unlike the MELD (Model of End-stage Liver Disease) scoring system. This retrospective chart review study of 772 patients undergoing major digestive, orthopedic, and cardiac surgeries determined the relationship between preoperative MELD scores and postoperative mortality in patients with cirrhosis (Table 4). The authors found that MELD score, American Society of Anesthesia (ASA) class, and age greater than 70 were significant predictors of mortality throughout the follow-up period. Postoperative mortality did not significantly differ for the two study periods of 1980–1990 and 1994–2004. During the first 7 postoperative days, ASA class was the strongest predictor of mortality. Beyond 7 days, MELD score was the best predictor of mortality. Mortality from 1–10 years was relatively constant, suggesting mortality was due primarily to the underlying medical condition rather than perioperative complications. Between 30 and 90 days postoperatively, a single point increase in the MELD score conferred an average 14% increased mortality. ASA class increase from III to IV was equal to 5.5 additional MELD points when predicting mortality. Age over 70 was equal to 3 additional MELD points. MELD scores allow an estimate of postoperative mortality; age and ASA class are used as modifiers. Mortality did not differ between the two time periods, demonstrating that postoperative mortality in cirrhotic patients has not improved over 25 years. Limitations of this study include its retrospective design and the possibility of a selection bias for patients with lower severity of illness. Additionally, this model predicts perioperative mortality, not morbidity.

Implications for Clinical Practice. The study provides an objective scoring system for predicting postoperative mortality in cirrhotic patients that can guide preoperative decision making.

Acknowledgements: *Dr. Smetana has received honoraria from Harvard Medical International/Novartis Pharma Schweiz (course director) and is a consultant for Safe Med. Dr. Cohn is on the speakers bureau of Sanofi-Aventis and Pfizer and has stock ownership in Astra-Zeneca, Glaxo, Merck, and Pfizer. Dr. Jaffer has been a consultant for Astra-Zeneca and Sanofi-Aventis in the past 3 years, has received honoraria, and is on the speakers bureau of Sanofi-Aventis, and has received grant and research support from Astra-Zeneca in the past 3 years. He also serves as a board member for both the Anticoagulation Forum and for the Society of Perioperative Assessment and Quality Improvement (SPAQI). Dr. Slawski has no conflicts in the past 3 years to declare.*

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REFERENCES

1. **Mangano DT, Layug EL, Wallace A, Tateo I.** Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery. Multicenter Study of Perioperative Ischemia Research Group. N Engl J Med. 1996;335(23):1713–20.
2. **Boersma E, Poldermans D, Bax JJ, et al.** Predictors of cardiac events after major vascular surgery: Role of clinical characteristics, dobutamine echocardiography, and beta-blocker therapy. JAMA. 2001;285(14): 1865–73.
3. **Yang H, Raymer K, Butler R, Parlow J, Roberts R.** The effects of perioperative beta-blockade: results of the Metoprolol after Vascular Surgery (MaVS) study, a randomized controlled trial. Am Heart J. 2006;152(5):983–90.
4. **Juul AB, Wetterslev J, Kofoed-Enevoldsen A, Callesen T, Jensen G, Gluud C.** The Diabetic Postoperative Mortality and Morbidity (DIPOM) trial: rationale and design of a multicenter, randomized, placebo-controlled, clinical trial of metoprolol for patients with diabetes mellitus who are undergoing major noncardiac surgery. Am Heart J. 2004;147 (4):677–83.
5. **Brady AR, Gibbs JS, Greenhalgh RM, Powell JT, Sydes MR.** Perioperative beta-blockade (POBBLE) for patients undergoing infrarenal vascular surgery: results of a randomized double-blind controlled trial. J Vasc Surg. 2005;41(4):602–609.
6. **Fleisher LA, Beckman JA, Brown KA, et al.** ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery): developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for

Vascular Medicine and Biology, and Society for Vascular Surgery. Circulation. 2007;116(17):e418–499.
7. **Fleisher LA, Poldermans D.** Perioperative beta blockade: where do we go from here? Lancet. 2008;371(9627):1813–14.
8. **McFalls EO, Ward HB, Moritz TE, et al.** Coronary-artery revascularization before elective major vascular surgery. N Engl J Med. 2004;351 (27):2795–804.
9. **Kapoor AS, Kanji H, Buckingham J, Devereaux PJ, McAlister FA.** Strength of evidence for perioperative use of statins to reduce cardiovascular risk: systematic review of controlled studies. BMJ. 2006;333 (7579):1149.
10. **Geerts WH, Pineo GF, Heit JA, et al.** Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest. 2004;126(3 Suppl):338S–400S.
11. **Ballantyne JC, Carr DB, deFerranti S, et al.** The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analyses of randomized, controlled trials. Anesth Analg. 1998;86 (3):598–612.
12. **Goldman L, Caldera DL, Nussbaum SR, et al.** Multifactorial index of cardiac risk in noncardiac surgical procedures. N Engl J Med. 1977;297 (16):845–50.
13. **Arozullah AM, Daley J, Henderson WG, Khuri SF.** Multifactorial risk index for predicting postoperative respiratory failure in men after major noncardiac surgery. The National Veterans Administration Surgical Quality Improvement Program. Ann Surg. 2000;232(2):242–53.
14. **Arozullah AM, Khuri SF, Henderson WG, Daley J.** Development and validation of a multifactorial risk index for predicting postoperative pneumonia after major noncardiac surgery. Ann Intern Med. 2001;135(10):847–57.
15. **Qaseem A, Snow V, Fitterman N, et al.** Risk assessment for and strategies to reduce perioperative pulmonary complications for patients undergoing noncardiothoracic surgery: a guideline from the American College of Physicians. Ann Intern Med. 2006;144(8):575–80.
16. **Chertow GM, Lazarus JM, Christiansen CL, et al.** Preoperative renal risk stratification. Circulation. 1997;95(4):878–84.
17. **Wijeysundera DN, Karkouti K, Beattie WS, Rao V, Ivanov J.** Improving the identification of patients at risk of postoperative renal failure after cardiac surgery. Anesthesiology. 2006;104(1):65–72.
18. **Hanning CD.** Postoperative cognitive dysfunction. Br J Anaesth. 2005;95(1):82–7.
19. **Teh SH, Nagorney DM, Stevens SR, et al.** Risk factors for mortality after surgery in patients with cirrhosis. Gastroenterology. 2007;132 (4):1261–69.