Update in Perioperative Medicine

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Medical consultation for patients preparing for surgery is an important activity for internists. Many clinicians may, however, feel unprepared for this role because the science and clinical recommendations do not follow intuitively from the day-to-day care of medical patients in the office or the hospital. Over the past 3 decades, this field has evolved from one of clinical experience and anecdote to a more evidence-based discipline. We present this first Update in Perioperative Medicine to review recent key articles and advances in this field.

We polled colleagues and used a systematic search strategy to identify articles of particular relevance for the medical care of patients before surgery. We searched MEDLINE for the period from 1 January 2001 through 30 August 2003. Medical Subject Heading terms included *intraoperative complications, postoperative complications, preoperative care, intraoperative care, perioperative care, postoperative care, intraoperative period,* and *preoperative period*; we also included the following text words in the title or abstract: *intraoperative* OR *postoperative* OR *perioperative* AND *complication* OR *event*. We excluded articles related to transplantation, cardiac, and pediatric surgery. We ran this search monthly during the eligible period and selected studies that were methodologically sound, were of interest to practicing internists, addressed common and morbid postoperative outcomes, and could potentially change the approach to diagnosis, risk stratification, or prevention of postoperative medical complications. Each author independently generated a list of articles for potential inclusion; we determined the final list by consensus.

We consider here 5 broad topic areas: cardiac risk stratification and risk reduction strategies, preoperative pulmonary evaluation, venous thromboembolism prophylaxis, diabetes mellitus, and postoperative delirium.

Cardiac Risk Stratification and Risk Reduction Strategies

β-Blockers Reduce Perioperative Cardiac Morbidity and Mortality

Auerbach AD, Goldman L. β-Blockers and reduction of cardiac events in noncardiac surgery: scientific review. JAMA. 2002;287: 1435-44. [PMID: 11903031]

The literature on perioperative β-blocker therapy has evolved from small observational studies to hypothesis-testing randomized clinical trials and now a systematic review of trial evidence. The authors searched MEDLINE for reports published since 1980 and reviewed the reference lists of relevant articles and guidelines to identify randomized clinical trials of β-blockers and perioperative myocardial ischemia or infarction and mortality.

Five trials, reported in 6 publications, met inclusion criteria. Regimens varied in the following ways: 1) the use of intravenous and oral drugs; 2) start times (several weeks before surgery or immediately before surgery); 3) postoperative stop times (immediately, 48 hours, until hospital discharge or 7 days, and 30 days); 4) target heart rates (55 to 65 beats/min, 50 to 80 beats/min, <80 beats/min, "20% below the ischemic threshold" but ≥60 beats/min); and 5) outcome measures (2 studies included myocardial ischemia and 3 reported myocardial infarction, pulmonary edema, cardiac death, or all-cause mortality).

β-Blockers significantly reduced the incidence of ischemia in 3 studies and cardiac death in 2 studies. In one study reporting no benefit for postoperative ischemia and myocardial infarction, trends favored β-blockers for both outcomes. Numbers needed to treat for benefit ranged from 2.5 to 8.3. The primary adverse effect was bradycardia. In the largest study ($n = 200$), third-degree heart block, hypotension, congestive heart failure, and bronchospasm did not increase with an atenolol dose titrated to a heart rate of 55 to 65 beats/min.

We agree with the authors of this meta-analysis; in our practices we routinely recommend, in the absence of contraindication, perioperative β-blocker therapy for patients with at least 1 major or 2 minor risk factors for postoperative cardiac complications. Major criteria include high-risk surgical site (intraperitoneal, intrathoracic, suprainguinal vascular), ischemic heart disease, symptomatic cerebrovascular disease, diabetes mellitus requiring insulin therapy, and a creatinine level greater than 177 μmol/L (>2.0 mg/dL). Minor criteria include age 65 years or older, hypertension, current smoker, serum cholesterol level of 6.2 mmol/L or greater (≥240 mg/dL), and diabetes mellitus not requiring insulin therapy.

One remaining area of uncertainty is timing and duration (current evidence suggests at least 1 week after surgery) of β-blocker therapy. Another unresolved question concerns the pros and cons of empirical therapy versus additional risk stratification by noninvasive testing or cardiac catheterization.

Managing Preoperative Cardiac Risk: Balancing Noninvasive Testing and Empirical β-Blocker Therapy

Boersma E, Poldermans D, Bax JJ, et al. Predictors of cardiac events after major vascular surgery: role of clinical characteristics, dobu-

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For author affiliations, see end of text.

tamine echocardiography, and β-blocker therapy. JAMA. 2001;285: 1865-73. [PMID: 11308400]

The growing evidence on use of perioperative β-blocker therapy raises another question: When does empirical therapy render preoperative noninvasive testing unnecessary? In a retrospective "patchwork" analysis, investigators examined the relationship between clinical factors, dobutamine stress echocardiography, and cardiac outcome in a cohort of patients undergoing major vascular surgery. Of 1351 patients, 1091 (81%) underwent dobutamine stress echocardiography. Most of these patients ($n = 846$) had this test because of the presence of at least one major cardiac risk factor; the remainder had the test at the discretion of their referring physician. Three hundred sixty patients (27%) received perioperative β-blocker therapy; 301 were already receiving long-term β-blocker therapy, and 59 began receiving this therapy within the context of a randomized trial (1).

Because 84% of patients were already receiving long-term β-blocker therapy for hypertension, arrhythmia, or coronary disease, those receiving perioperative treatment had a higher baseline risk profile. Nevertheless, patients receiving β-blockers had a significantly lower risk for cardiac death or myocardial infarction (unadjusted overall odds ratio, 0.1 [95% CI, 0.1 to 0.3]). In a multivariable model of clinical and dobutamine stress echocardiography variables, the following were independently associated with outcome: age 70 years or older, congestive heart failure, previous cerebrovascular accident, abnormal findings on dobutamine stress echocardiography at rest and with stress, and perioperative β-blocker therapy.

The investigators concluded that patients with a revised cardiac risk index score (2) less than 3 have a cardiac risk less than 2% as long as they received perioperative β-blocker therapy. Dobutamine stress echocardiography results were unhelpful and did not modify this low risk. This test did provide useful information for patients with a risk score of 3 or greater; those with negative results who received β-blockers had a low risk (0.4% to 1.2%). Patients with a risk score of 3 or greater and an abnormal result on dobutamine stress echocardiography had a high risk for cardiac events. In this selected subset, even patients who received perioperative β-blocker therapy had high risk.

This report suggests that empirical β-blocker therapy in low-risk patients may obviate the need for preoperative noninvasive testing and that higher-risk patients with a negative result on a pharmacologic stress test can proceed to surgery with perioperative β-blockers. Patients with at least 5 abnormal segments on dobutamine stress echocardiography did not benefit from β-blockers and may need cardiac catheterization and revascularization; however, the value of this strategy remains unproven.

Clonidine May Reduce Perioperative Cardiac Morbidity and Mortality

Nishina K, Mikawa K, Uesugi T, et al. Efficacy of clonidine for prevention of perioperative myocardial ischemia: a critical appraisal and meta-analysis of the literature. Anesthesiology. 2002;96:323-9. [PMID: 11818763]

Not everyone with increased perioperative cardiac risk can tolerate β-antagonists. Clonidine, a centrally acting α_2-agonist, may ultimately prove to be an effective alternative. Perioperatively, it is used as a sedative, anxiolytic, and analgesic and reduces hypertension, tachycardia, and norepinephrine release associated with surgical stress. This systematic review, using standard methods, assessed its effect on cardiac morbidity and mortality.

Five studies (306 patients) of coronary artery bypass grafting (CABG) and 2 studies (358 patients) of noncardiac operations met inclusion criteria. Clonidine was given only short-term perioperatively. In the larger study of noncardiac operations ($n = 297$), a single oral dose of 2 μg/kg of body weight was given 90 minutes before surgery; in the smaller study ($n = 61$), transdermal clonidine, 0.2 mg/d, was given the night before, and oral clonidine (0.3 mg) was given 1 to 1.5 hours before surgery. The clonidine dosage used in the studies of patients undergoing CABG was 3 to 5 μg/kg per hour intravenously in 2 studies and 5 μg/kg per hour orally once or twice in the remaining 3 studies. The postoperative observation interval varied from the operative period to 48 hours or hospital discharge.

Pooled odds ratios and 95% CIs for clonidine and the surrogate end point of myocardial ischemia were 0.53 (CI, 0.29 to 0.93) and 0.47 (CI, 0.29 to 0.77) for studies of CABG and noncardiac surgery, respectively. Clinically significant complications of myocardial infarction and death were uncommon, but trends favored clonidine. Rates for clonidine versus control groups were 4.4% versus 7.5% for myocardial infarction and 0.7% versus 1.7% for death. In the largest study of CABG ($n = 150$), clonidine was associated with significantly higher odds of bradycardia and hypotension. These findings were similar to those of a recent meta-analysis of randomized, controlled trials of α_2-agonists (including clonidine, dexmedetomidine, and mivazerol) that reported a relative risk for death of 0.64 (CI, 0.42 to 0.99) for α_2-agonist administration (3).

This systematic review has important limitations: Sample sizes were small, myocardial infarction and death were rare, the brief period of postoperative observation may have underestimated complication rates, and a surrogate marker (myocardial ischemia) was the primary outcome measurement. The review includes studies of patients undergoing both cardiac and noncardiac surgery; substantial differences exist between these 2 populations. However, the review is a provocative springboard; internists providing perioperative care should be aware that larger,

well-done trials are needed to assess the use of clonidine as a strategy to reduce perioperative cardiac risk.

A Perioperative Cardiac Risk Guideline Confirms Earlier Risk Stratification and Management Recommendations

Eagle KA, Berger PB, Calkins H, et al. ACC/AHA guideline update for perioperative cardiovascular evaluation for noncardiac surgery—executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1996 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). J Am Coll Cardiol. 2002;39:542-53. [PMID: 11823097]

This guideline updates the 1996 practice guideline for perioperative cardiac risk management in light of more than 400 studies published since its original publication. Unchanged from the earlier version, the guideline recommends consideration, in sequence, of 3 major factors: 1) clinical predictors, 2) functional capacity, and 3) surgery-specific risk. Examples of major clinical predictors are unstable coronary syndromes, decompensated heart failure, significant arrhythmias, and severe valvular disease. Intermediate predictors include mild angina (Canadian class I or II), previous myocardial infarction, compensated or previous heart failure, diabetes mellitus (especially type 1), and renal insufficiency.

The authors define poor functional capacity as the inability to perform activities that require at least 4 metabolic equivalents; such activities include climbing a flight of stairs, walking up a hill, or walking on level ground at 6.4 km/h (4 miles/h). High-risk surgeries include emergency major surgery, major vascular surgery, and anticipated prolonged surgeries associated with large fluid shifts or blood loss. Intermediate-risk surgeries are carotid endarterectomy, head and neck surgery, abdominal and chest surgery, orthopedic surgery, and prostate surgery. An algorithm that incorporates these factors guides clinicians to recommendations to proceed directly to surgery, obtain noninvasive testing, consider coronary angiography, or consider cancellation or delay of surgery and risk factor modification.

After incorporating recent evidence, the new guideline confirms the value of the earlier version. Important clinical risk predictors remain unchanged except for the addition of renal insufficiency as an intermediate-level predictor. Included are the results of validation studies that confirm that risk stratification according to the American College of Cardiology/American Heart Association algorithm leads to a low rate of cardiac events. The authors acknowledge the value of self-reported exercise capacity to stratify cardiac risk and provide recommendations for specific noninvasive testing methods and interventions.

The new guideline also confirms that preoperative revascularization is rarely necessary solely to reduce risks associated with noncardiac surgery unless an independent indication exists to reduce long-term cardiovascular mortality. New evidence supports delaying noncardiac surgery for at least 1 week after angioplasty and 2 to 4 weeks after coronary stenting. The guideline also summarizes advances in perioperative prophylactic medical therapies, with the strongest evidence indicating that β-blockers reduce perioperative ischemia and possibly infarction and death in high-risk patients.

Coronary Angioplasty and CABG Equally Reduce Cardiac Risk in Subsequent Noncardiac Surgery

Hassan SA, Hlatky MA, Boothroyd DB, et al. Outcomes of noncardiac surgery after coronary bypass surgery or coronary angioplasty in the Bypass Angioplasty Revascularization Investigation (BARI). Am J Med. 2001;110:260-6. [PMID: 11239843]

Preoperative cardiac evaluation aims to estimate risk, to identify patients who will benefit from additional testing, and to identify high-risk patients for whom additional medical therapy or coronary revascularization may prevent postoperative cardiac complications. No randomized studies have examined preoperative coronary revascularization to prevent postoperative cardiac complications, but retrospective studies have suggested a modest cardiac risk reduction for subsequent noncardiac surgery. This prospective study compared the effect of CABG to percutaneous coronary angioplasty in patients with multivessel disease who were randomly assigned to one strategy or the other and who subsequently underwent noncardiac surgery.

Among 934 participants in the Bypass Angioplasty Revascularization Investigation (BARI) trial, 501 subsequently underwent 1049 noncardiac procedures during a mean follow-up of 7.8 years at a median of 29 months after the most recent revascularization. The incidence of perioperative cardiac events was 1.4% (11 deaths, 4 myocardial infarctions) and was higher after high-risk procedures than low-risk ones (2.3% vs. 1.0%). Event rates for the CABG and angioplasty groups were 1.3% and 1.6%, respectively ($P > 0.2$). A second intervention occurred in 96 patients before noncardiac surgery (9% of the CABG group and 29% of the angioplasty group). In a multivariate analysis, age was the most important predictor of cardiac events (odds ratio, 1.3/y), followed by years since last revascularization (odds ratio, 1.3/y). Cardiac event rates were 0.8% if revascularization occurred less than 4 years previously versus 3.6% if it occurred 4 or more years previously. Similar trends occurred in Coronary Artery Surgery Study (CASS) patients (1.7% cardiac event rate 2 to 4 years after CABG and 3.6% after 6 years) (4) and in a recent study of vascular surgery patients that defined events broadly (7.5% cardiac event rate if revascularization occurred <5 years previously vs. 16.7% for ≥ 5 years previously) (5).

This study demonstrated that successful coronary revascularization with angioplasty or CABG resulted in sim-

ilarly low event rates of postoperative myocardial infarction or death after subsequent noncardiac surgery for approximately 4 years. After 4 to 5 years, risk of noncardiac surgery increases again, but the relative benefits of empirical perioperative β-antagonist therapy or additional testing are unclear. This report provides no evidence on the relative risk reduction of coronary revascularization compared with a conservative strategy of perioperative β-blocker use.

Pulmonary Artery Catheters Do Not Reduce Mortality among High-Risk Surgical Patients

Sandham JD, Hull RD, Brant RF, et al. A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients. N Engl J Med. 2003;348:5-14. [PMID: 12510037]

The value of pulmonary artery catheters in high-risk surgical patients is controversial. Previous literature has consisted of uncontrolled reports and small randomized trials that have commonly shown no benefit or even harm. In a widely cited cohort study, a 3-fold increase in major postoperative cardiac events existed among patients who received a pulmonary artery catheter to guide perioperative management (6).

In this trial, Sandham and colleagues randomly assigned 1994 patients undergoing urgent or elective major noncardiac surgery to either standard care or hemodynamic manipulation directed by pulmonary artery catheter. Patients were categorized as high risk if they were 60 years of age or older and were in American Society of Anesthesiologists (ASA) class III or IV. The authors provided physiologic goals for patients who were assigned to receive a pulmonary artery catheter. As a result, more patients in the catheter group than in the control group received inotropic agents, vasodilators, antihypertensive medication, packed red cells, and colloid. In-hospital mortality was 7.8% for the pulmonary-catheter group and 7.7% for the control group ($P > 0.2$). Study groups did not significantly differ for any secondary outcome: 6- and 12-month mortality and in-hospital morbidity (myocardial infarction, congestive heart failure, supraventricular tachycardia, ventricular tachycardia, pulmonary embolism, renal or hepatic insufficiency, catheter-related complications, wound infection, and pneumonia). In contrast to earlier studies that may have insufficiently controlled for confounding comorbid conditions, this trial found neither benefit nor harm with pulmonary artery catheters.

This first large randomized, controlled trial establishes that pulmonary catheter use does not decrease perioperative morbidity or mortality and should no longer be recommended as a risk reduction strategy in high-risk surgical patients.

Statin Therapy Reduces Perioperative Mortality in Patients Undergoing Vascular Surgery in a Case–Control Study

Poldermans D, Bax JJ, Kertai MD, et al. Statins are associated with a reduced incidence of perioperative mortality in patients undergoing major noncardiac vascular surgery. Circulation. 2003;107:1848-51. [PMID: 12695283]

Statin therapy reduces serum low-density lipoprotein cholesterol levels and systemic inflammation as measured by C-reactive protein levels. In the Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL) study, early use of statins in patients with acute coronary syndromes significantly reduced the risk for major cardiovascular end points by 16%; most of this difference was due to lower rates of recurrent ischemia requiring hospitalization (7). No randomized, controlled trials have studied statin therapy as a potential strategy to reduce postoperative cardiac complications.

In this study, Poldermans and colleagues used a case–control design to estimate the effect of current statin use on perioperative cardiac complications in patients undergoing major noncardiac vascular surgery. From among 2816 sequential patients, the authors identified 160 case-patients (5.8%) who died of any cause in the perioperative period while in the hospital. Two control patients were identified for each case-patient: the patient whose surgery immediately preceded the case surgery and a patient whose surgery followed the case. Case-patients and controls were matched only by type of surgery. Baseline characteristics did not statistically differ for sex, history of hypertension, elevated cholesterol level, or diabetes mellitus. Significantly more case-patients had a history of myocardial infarction, angina, congestive heart failure, and stroke. The authors performed a multivariable logistic regression analysis and adjusted for age, sex, history of cardiovascular disease or cerebrovascular disease, and cardiovascular therapy.

Eight percent of case-patients were taking statin therapy at the time of surgery compared with 25% of control patients ($P < 0.001$). This difference existed despite the higher prevalence of known cardiovascular disease among the case-patients. For example, the incidence of previous myocardial infarction was 53% among case-patients who died in the perioperative period. The risk for perioperative death was significantly lower in statin users than in nonusers; the adjusted odds ratio was 0.22 (CI, 0.10 to 0.47). After adjustment for confounders, no significant interaction existed between aspirin or β-blocker use and statin use.

This study is subject to the limitations of the case–control design. Unmeasured factors may have accounted for some of the observed mortality reduction among statin users. In addition, the methods of the multivariate modeling were not described in detail. However, a clinically significant reduction in mortality occurred even after adjustment for known cardiovascular disease and the use of other

cardiovascular medications, including β-blockers. This report suggests that statin therapy may reduce mortality in the perioperative period, but the limitations of the study design prevent firm conclusions. A definitive randomized, controlled trial is necessary to determine whether clinicians should recommend routine statin therapy for all patients at risk for postoperative cardiac complications.

Recent Coronary Stenting Increases the Risk for Postoperative Cardiac Complications

Wilson SH, Fasseas P, Orford JL, et al. Clinical outcome of patients undergoing non-cardiac surgery in the two months following coronary stenting. J Am Coll Cardiol. 2003;42:234-40. [PMID: 12875757]

While the value of coronary revascularization to reduce the risk for cardiac complications is modest and has not been tested by randomized, controlled trials, clinicians occasionally consider this strategy for high-risk patients who have few other opportunities for risk reduction interventions. In the modern era, a coronary stent is often placed as a component of percutaneous coronary interventions. In the only previous report of noncardiac surgery after coronary stenting, patients whose stent was placed before the noncardiac surgery had a high risk for both bleeding complications and cardiac complications (8). In that report, 7 myocardial infarctions, 8 deaths, and 11 major bleeding episodes occurred among 40 patients who underwent coronary stenting within 6 weeks of noncardiac surgery; the greatest risk was for surgery within 2 weeks after coronary stent placement.

Wilson and colleagues retrospectively studied a larger group of patients whose coronary stent preceded noncardiac surgery. The authors identified 207 patients who, over a 10-year period, underwent noncardiac surgery in the 2 months after successful coronary stent placement. Eight patients (3.9%) sustained a major postoperative cardiac complication; 6 (3.0%) of these patients died. All of the cardiac complications and deaths occurred among patients whose surgery took place within 6 weeks after coronary stenting.

The proportion of patients receiving aspirin, ticlopidine, clopidogrel, β-blockers, angiotensin-converting enzyme inhibitors, and calcium-channel blockers after stent placement was similar in patients who did and those who did not develop a postoperative cardiac complication. Patients received ticlopidine or clopidogrel for 2 to 4 weeks after stent placement. Only 2 patients had excessive surgical bleeding, although this determination was based solely on chart review. One patient was receiving aspirin and ticlopidine, and the other was receiving aspirin alone. Treating physicians attributed no major clinical adverse outcomes to excessive bleeding.

This study confirms the previously demonstrated association between recent coronary stenting and an increased risk for postoperative cardiac complications and death. The absolute risks for cardiac complications and bleeding were both lower than previously estimated. On the basis of these observations, clinicians should delay elective noncardiac surgery until at least 6 weeks after coronary stent placement.

Preoperative Pulmonary Evaluation

A Preoperative Smoking Cessation Intervention Decreases Perioperative Morbidity among Patients Undergoing Hip or Knee Replacement

Moller AM, Villebro N, Pedersen T, et al. Effect of preoperative smoking intervention on postoperative complications: a randomised clinical trial. Lancet. 2002;359:114-7. [PMID: 11809253]

Current cigarette smoking is an important risk factor for postoperative pulmonary complications. Previous research has shown it increases the risk for pulmonary complications by up to 4-fold, even among patients without chronic obstructive pulmonary disease. In this study, Moller and colleagues randomly assigned 108 patients scheduled for elective knee or hip replacement to a smoking intervention group or control group. All patients were daily smokers. Mean age was 65 years, and patients were relatively healthy; 95% were in ASA class I or II.

The intervention began 6 to 8 weeks before surgery and continued until 10 days after surgery. Intervention patients met weekly with a study nurse and received advice about smoking cessation, benefits and side effects, managing withdrawal symptoms, and a personalized nicotine substitution schedule. The primary study end points were postoperative complications within 4 weeks of surgery.

Of the 60 patients in the intervention group, 36 stopped smoking and 14 reduced smoking before surgery. Overall complication rates were 18% and 52% in the intervention and control groups, respectively. Most of this difference was due to a large difference in wound complication rates (5% vs. 31%, respectively). Only wound complications and urinary tract infection rates were significantly different between the 2 groups. The only pulmonary complication studied was postoperative ventilatory support in the intensive care unit; this occurred in only 1 patient in each group. In the intervention group, there were trends toward shorter average length of stay (11 days vs. 13 days; $P > 0.2$) and fewer cardiac complications (0% vs. 10%; $P = 0.08$).

This is the first randomized, controlled trial of a preoperative smoking cessation intervention. Although it may be difficult to implement such a program in a practice setting, we believe this report is an important step toward understanding the value and timing of advice for preoper-

ative smoking cessation. Two factors limited the ability of this study to demonstrate a reduction in pulmonary complications. First, hip and knee replacement are procedures intrinsically at low risk for pulmonary complications. Second, previous research has shown an unexpected but consistent finding of paradoxically increased pulmonary complications among smokers who quit or reduce their cigarette use in the 1 to 2 months before surgery (9, 10). A recent randomized, controlled trial of 60 patients undergoing colorectal surgery likewise found no reduction in the low rates of postoperative pulmonary complications among patients randomly assigned to a 2- to 3-week preoperative smoking cessation intervention (11). Future trials of preoperative smoking cessation will need to study longer periods of abstinence and high-risk surgery.

A Multifactorial Risk Index Predicts Postoperative Pneumonia

Arozullah AM, Khuri SF, Henderson WG, et al., for the National Veterans Administration Surgical Quality Improvement Program. Development and validation of a multifactorial risk index for predicting postoperative pneumonia after major noncardiac surgery. Ann Intern Med. 2001;135:847-57. [PMID: 11712875]

In contrast to validated and widely used cardiac risk indices, progress in the development of risk indices for postoperative pulmonary complications has been slower. In this report, Arozullah and colleagues used a large database of veterans undergoing noncardiac surgery to develop a risk index to predict postoperative pneumonia. This study is a companion to the same authors' earlier report on a multifactorial index to predict postoperative respiratory failure in the same cohort (12).

The authors studied both derivation and validation cohorts that included 316 071 predominantly male (95%) and older (mean age, 61.3 years) patients. In the derivation cohort, 1.5% of patients developed postoperative pneumonia. The authors used logistic regression to develop a multifactorial risk index (**Tables 1** and **2**) and assigned patients to risk classes as follows: class 1 (0 to 15 points), class 2 (16 to 25 points), class 3 (26 to 40 points), class 4 (41 to 55 points), and class 5 (>55 points). Postoperative pneumonia rates in the derivation cohort were 0.24%, 1.19%, 4.0%, 9.4%, and 15.8%, respectively. Pneumonia rates and index performance were similar in the validation cohort.

This index advances the field of preoperative pulmonary risk assessment and provides a valuable tool for clinicians. As was seen in previous smaller studies, type of surgery dominates the analysis, although less so than in the authors' parallel report of risk for postoperative respiratory failure. The 2 indices have most variables in common. Unfortunately, most risk factors in both are not modifiable, unless a lower-risk alternate procedure is feasible for a particular patient. Age is a stronger risk factor than suggested by earlier literature or the respiratory failure index. New observations from this index are the importance of functional status, weight loss, impaired sensorium, a history of stroke, and mild renal insufficiency. We encourage readers to adopt this index as part of the approach to preoperative risk stratification.

Table 1. **Multifactorial Risk Index for Predicting Postoperative Pneumonia***

Preoperative Risk Factor	Odds Ratio in Derivation Cohort (95% CI)	Point Value
Type of surgery		
Abdominal aortic aneurysm repair	4.29 (3.34–5.50)	15
Thoracic surgery	3.92 (3.36–4.57)	14
Upper abdominal surgery	2.68 (2.38–3.03)	10
Neck surgery	2.30 (1.73–3.05)	8
Neurosurgery	2.14 (1.66–2.75)	8
Vascular surgery	1.29 (1.10–1.52)	3
Age		
≥80 y	5.63 (4.62–6.84)	17
70–79 y	3.58 (2.97–4.33)	13
60–69 y	2.38 (1.98–2.87)	9
50–59 y	1.49 (1.23–1.81)	4
Functional status		
Totally dependent	2.83 (2.33–3.43)	10
Partially dependent	1.83 (1.63–2.06)	6
Weight loss > 10% in past 6 months	1.92 (1.68–2.18)	7
History of chronic obstructive pulmonary disease	1.72 (1.55–1.91)	5
General anesthesia	1.56 (1.36–1.80)	4
Impaired sensorium	1.51 (1.36–1.80)	4
History of cerebrovascular accident	1.47 (1.26–1.82)	4
Blood urea nitrogen level		
<2.86 mmol/L (<8 mg/dL)	1.47 (1.26–1.72)	4
7.85–10.7 mmol/L (22–30 mg/dL)	1.24 (1.11–1.39)	2
≥10.7 mmol/L (≥30 mg/dL)	1.41 (1.22–1.64)	3
Transfusion > 4 units	1.35 (1.07–1.72)	3
Emergency surgery	1.33 (1.16–1.54)	3
Steroid use for chronic condition	1.33 (1.12–1.58)	3
Current smoker within 1 year	1.28 (1.17–1.42)	3
Alcohol intake > 2 drinks/d in past 2 weeks	1.24 (1.08–1.42)	2

* Reprinted with permission from Arozullah et al. Ann Intern Med. 2001;135:847–57.

Table 2. **Risk Classes in the Postoperative Pneumonia Multifactorial Risk Index**

Risk Class	Total Points, *n*	Rate of Postoperative Pneumonia in Derivation Cohort, %
1	0–15	0.24
2	16–25	1.19
3	26–40	4.0
4	41–55	9.4
5	>55	15.8

* Adapted with permission from Arozullah et al. Ann Intern Med. 2001;135:847–57.

Symptom-Limited Stair Climbing Predicts Postoperative Complications

Girish M, Trayner E, Dammann O, et al. Symptom-limited stair climbing as a predictor of postoperative cardiopulmonary complications after high-risk surgery. Chest. 2001;120:1147-51. [PMID: 11591552]

Physicians have long recognized the importance of fitness and stamina as predictors of surgical risk. In an earlier era, physicians commonly walked patients up stairs as a simple tool to gauge how well they would tolerate surgery. A recent study reported that patient self-report of exercise capacity in a preoperative medical evaluation clinic predicted cardiac and total serious complications (13).

In this study, Girish and colleagues prospectively evaluated 83 patients undergoing high-risk surgeries, including thoracotomy, sternotomy, and upper abdominal laparotomy. Before surgery, patients were asked to climb a hospital stairway as far as possible at their own pace using the railing only for balance. The primary outcome was cardiopulmonary complications within 30 days after surgery.

Pulmonary complications were nearly 3 times as common as cardiac complications (30% vs. 11%, respectively). The number of stairs climbed was the strongest predictor of complications and proved more useful than age, preexisting pulmonary disease, weight, or spirometric values. No patient who could climb 7 flights of stairs had a postoperative complication, whereas 8 of 9 patients unable to climb even 1 flight of stairs had a complication. Defining 4 flights of stairs as good exercise capacity resulted in a sensitivity of 71% and a specificity of 77%. Stair climbing did not predict perioperative mortality.

This study adds to a growing body of literature that shows self-reported or directly observed exercise capacity stratifies risk for major postoperative cardiopulmonary complications. In addition to the use of clinical criteria and multifactorial risk indices, clinicians may incorporate this simple technique into their office evaluation of patients before surgery.

Risk Factors for Postoperative Pulmonary Complications Emerge from a Prospective Study of Clinical and Laboratory Variables

McAlister FA, Khan NA, Straus SE, et al. Accuracy of the preoperative assessment in predicting pulmonary risk after nonthoracic surgery. Am J Respir Crit Care Med. 2003;167:741-4. [PMID: 12598217]

Many studies of risk factors for postoperative pulmonary complications have been limited by lack of explicit definitions for postoperative pulmonary complications, lack of blinded outcome ascertainment, and inclusion of complications of minimal clinical significance. Established risk factors from previous reports have included current cigarette use; ASA class greater than II; age older than 70 years; chronic obstructive pulmonary disease; upper abdominal surgery, thoracic surgery, neck surgery, aortic surgery, and neurosurgery; prolonged surgery; general anesthesia; intraoperative pancuronium; emergency surgery; and an albumin level less than 3 g/dL (12, 14).

In this study, McAlister and colleagues recruited 272 consecutive patients referred for medical evaluation before nonthoracic surgery. The authors excluded patients who were mechanically ventilated at the time of preoperative assessment and those with sleep apnea, neuromuscular disease, and medical problems that prevented them from participating in the data collection (for example, cognitive impairment). Outcome ascertainment was blinded to preoperative factors; investigators used explicit criteria for postoperative pulmonary complications.

The overall pulmonary complication rate was 8% (22 patients). Among clinical factors in a bivariate analysis, significant predictors of postoperative pulmonary complications included age 65 years or older, 40 or more pack-year cigarette history, chronic obstructive pulmonary disease, exercise capacity of 2 blocks or fewer or 1 flight of stairs, surgery duration of 2.5 hours or more, maximal laryngeal height of 4 cm or less (distance between the top of the thyroid cartilage and the suprasternal notch at the end of expiration), body mass index of 30 kg/m^2 or greater, positive result on a cough test (patient takes a deep inspiration and coughs once; a positive result is recurrent coughing), positive result on a wheeze test (patient takes 5 deep breaths; a positive result is audible wheezing by auscultation), and forced expiratory time of 9 seconds or less. Several spirometric and arterial blood gas results were also associated with pulmonary complication rates, but the evaluating physicians obtained these tests at their discretion and may have oversampled patients at high risk for complications.

In a multiple regression model, 3 clinical factors best predicted the risk for pulmonary complications: age 65 years or older (odds ratio, 1.8; $P = 0.02$), 40 or more pack-year cigarette history (odds ratio, 1.9; $P = 0.02$), and maximal laryngeal height of 4 cm or less (odds ratio, 2.0; $P = 0.007$). Current cigarette smoking has been a consistent risk factor in previous studies, whereas the impact of age has been controversial. The finding that maximum laryngeal height predicts risk is a new observation. The authors evaluated this examination finding because of the previous observation that it predicts obstructive airways disease (15). This study provides a simple tool based on the history and physical examination to identify patients with an increased risk for postoperative pulmonary complications.

Venous Thromboembolism Prophylaxis

Fondaparinux Is Similar to Enoxaparin in Preventing Postoperative Venous Thromboembolism

Turpie AG, Bauer KA, Eriksson BI, et al. Fondaparinux vs enoxaparin for the prevention of venous thromboembolism in major orthopedic surgery: a meta-analysis of 4 randomized double-blind studies. Arch Intern Med. 2002;162:1833-40. [PMID: 12196081]

Despite the use of appropriate thromboprophylaxis, venous thromboembolism (VTE) remains a frequent and morbid complication among patients undergoing major orthopedic surgery. Fondaparinux is a new synthetic pentasaccharide that specifically inhibits factor Xa and subsequent thrombin generation. It has a half-life of 15 hours and is renally excreted. Turpie and colleagues conducted a meta-analysis of 4 multicenter, randomized, double-blind trials of patients undergoing elective hip replacement, major knee surgery, or hip fracture surgery that compared the efficacy and safety of fondaparinux (2.5 mg subcutaneously once daily starting 6 hours after surgery) with those of enoxaparin (either 30 mg subcutaneous twice daily starting 12 to 24 hours after surgery or 40 mg once daily starting 12 hours before surgery and then 12 to 24 hours after surgery). The dosing schedules were those recommended by the manufacturers. The primary end points were 1) VTE up to day 11 detected by venography, 2) documented symptomatic deep venous thrombosis (DVT) or pulmonary embolus, and 3) major bleeding. The 4 lead authors of each of the included studies were also the authors of this meta-analysis. The pharmaceutical manufacturer of fondaparinux sponsored each of the 4 included studies; a majority of the members of the steering committee that designed each study, interpreted the data, and wrote the articles were representatives of the pharmaceutical sponsor.

The incidence of venographically confirmed VTE was lower with fondaparinux than with enoxaparin (6.8% vs. 13.7%; common odds reduction, 55.2% [CI, 45.8% to 63.1%]); significant differences existed for patients having hip replacement, hip fracture, and major knee surgery. However, the low rates of symptomatic VTE (0.6% vs. 0.4%, respectively) and fatal pulmonary embolism (0.3% in each group) did not differ between the 2 treatment groups. Major bleeding events were more common in the fondaparinux group (2.7% vs. 1.7%; $P = 0.008$), but these did not lead to a higher likelihood of reoperation, surgical site complications, fatal bleeding, or length of stay.

A decrease in asymptomatic (but not symptomatic or fatal) VTE in fondaparinux-treated patients was offset by an increase in major bleeding episodes when the drug was used according to the dosing schedule recommended by the manufacturers. Since fondaparinux is more costly than enoxaparin, future studies should consider its cost-effectiveness. In this review, fondaparinux proved to be an effective agent to reduce VTE rates in patients undergoing major orthopedic surgery and represents a comparable alternative agent for VTE prophylaxis in addition to currently accepted standard therapies of low-molecular-weight heparin and warfarin.

Four to 6 Weeks of Postoperative VTE Prophylaxis Reduces the Incidence of Symptomatic Thrombotic Events to a Greater Degree Than Traditional Short-Duration Prophylaxis after Hip or Knee Replacement

Eikelboom JW, Quinlan DJ, Douketis JD. Extended-duration prophylaxis against venous thromboembolism after total hip or knee replacement: a meta-analysis of the randomised trials. Lancet. 2001; 358:9-15. [PMID: 11454370]

Patients are often not fully ambulatory for several weeks after major orthopedic surgery and remain at increased risk for VTE during this time. The role of extended-duration prophylaxis after major orthopedic surgery is unclear. This meta-analysis examined 9 trials of extended-duration prophylaxis with heparin (8 trials of low-molecular-weight heparin, 1 trial of unfractionated heparin) compared with traditional prophylaxis ending at hospital discharge. Perioperative prophylactic regimens and VTE screening methods varied, but in all cases prophylaxis was given for 4 to 6 weeks.

Extended-duration prophylaxis significantly reduced the incidence of symptomatic VTE (1.3% vs. 3.3%) and asymptomatic venographic DVT (9.6% vs. 19.6%) (**Table 3**). This risk reduction was greater with total hip replacement (1.4% vs. 4.3%; odds ratio, 0.33; number needed to treat for benefit, 34) than with total knee replacement (1.0% vs. 1.4%; odds ratio, 0.74; number needed to treat for benefit, 250). Extended-duration prophylaxis increased minor (3.7% vs. 2.5%) but not major bleeding.

Considerations for extended prophylaxis include the clinical importance of asymptomatic DVT and risk for bleeding. In this meta-analysis, prophylaxis reduced the incidence of both asymptomatic DVT and symptomatic VTE. Asymptomatic DVT may, therefore, be a reasonable surrogate marker for symptomatic VTE. The risk for major bleeding was low, but some orthopedic surgeons may still be concerned about excess minor bleeding if it involves the surgical incision.

This review confirms that extended-duration prophylaxis with low-molecular-weight heparin or unfractionated heparin significantly reduces the risk for both symptomatic and asymptomatic VTE in patients undergoing total hip or knee replacement. Another recent report confirmed the value of 4 weeks of enoxaparin prophylaxis after high-risk surgery for abdominal or pel-

Table 3. **Incidence of Thromboembolic and Bleeding Complications among Patients Receiving Extended-Duration Postoperative Prophylaxis versus Controls**

Outcome (Out of Hospital)	Heparin Group, *n/n (%)*	Control Group, *n/n (%)*	Odds Ratio (95% CI)	Number Needed To Treat for Benefit (Harm)
Symptomatic venous thromboembolism	25/1964 (1.3)	58/1744 (3.3)	0.38 (0.24–0.61)	50
Asymptomatic deep venous thrombosis by venography	101/1047 (9.6)	167/854 (19.6)	0.48 (0.36–0.63)	10
Minor bleeding	77/2073 (3.7)	46/1834 (2.5)	1.56 (1.08–2.26)	(83)
Major bleeding	2/2114 (0.1)	5/1872 (0.3)	0.62 (0.22–1.75)	–
Death	3/2132 (0.1)	5/1888 (0.3)	0.68 (0.25–1.88)	–

vic cancer (incidence of DVT was 4.8% in the extended-duration prophylaxis group compared with 12% in the placebo group) (16). Clinicians should strongly consider extended-duration thromboprophylaxis for patients undergoing high-risk orthopedic surgery and abdominal cancer surgery; we follow this approach for our own patients.

Diabetes Mellitus

Intensive Insulin Therapy Reduces Mortality and Morbidity in Critically Ill, Primarily Postoperative, Patients

van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in the critically ill patients. N Engl J Med. 2001;345:1359-67. [PMID: 11794168]

Critically ill patients, including those without previous diabetes, commonly have insulin-resistant hyperglycemia. A recent randomized trial showed that tight glucose control in diabetic patients with acute myocardial infarction improved outcomes (17). In this study, van den Berghe and colleagues tested tight glucose control in primarily postoperative patients.

All mechanically ventilated patients admitted to a surgical intensive care unit (SICU) were eligible; 1548 were randomly assigned to intensive insulin (infusion for glucose level >6.10 mmol/L [>110 mg/dL] and then maintenance to a range of 4.44 to 6.10 mmol/L [80 to 110 mg/dL]) or conventional insulin (infusion for glucose level >11.93 mmol/L [>215 mg/dL] and then maintenance to a range of 9.99 to 11.10 mmol/L [180 to 200 mg/dL]). All patients received parenteral or enteral feeding according to a standardized protocol.

Most patients (63%) had cardiac operations; the remainder had neurologic disease, brain surgery, thoracic operations, respiratory insufficiency, abdominal operations, peritonitis, vascular surgery, transplantation, multiple trauma, and severe burns. The tight-control group required insulin significantly more often (99% vs. 39%), higher insulin dosages (median, 71 IU/d vs. 33 IU/d), and longer duration of insulin therapy (100% of SICU stay vs. 67%) ($P < 0.001$ for all comparisons). The tight-control group had significantly lower SICU mortality (4.6% vs. 8%; $P < 0.04$) and overall inpatient mortality (7% vs. 11%; $P = 0.01$).

By multivariate analysis, independent predictors of death were Acute Physiology and Chronic Health Evaluation II score, older age, admission for an indication other than cardiac surgery, tertiary referral, and conventional insulin therapy. Statistically significant effects of intensive insulin extended to an array of secondary outcome measures: duration of SICU stay and ventilatory support for patients in the SICU longer than 5 days, peak bilirubin level greater than 34.2 μmol/L (>2 mg/dL), septicemia in the SICU, antibiotic treatment for longer than 10 days, and critical illness polyneuropathy ($P < 0.007$ for all comparisons).

This trial expands the growing indications for intensive insulin treatment in different critical care sittings to include postoperative SICU care. The extent to which tight control is beneficial in other postoperative settings remains unclear.

Postoperative Delirium

A Multicomponent Targeted Medical Intervention Reduces Postoperative Delirium in Elderly Persons Undergoing Hip Fracture Repair

Marcantonio ER, Flacker JM, Wright RJ, et al. Reducing delirium after hip fracture: a randomized trial. J Am Geriatr Soc. 2001;49:516-22. [PMID: 11380742]

Hip fractures are common (>250 000 Americans per year) and expensive (direct costs >$10 billion annually). The high frequency of postoperative delirium (35% to 65%) and independent association with poorer functional recovery suggest the potential value of strategies to reduce postoperative delirium. A previous study confirmed the value of a multifactorial intervention in medical patients (18). To assess an intervention to prevent postoperative delirium, Marcantonio and colleagues randomly assigned patients 65 years of age or older who were admitted for hip fracture repair and did not have metastatic cancer or life

expectancy less than 6 months to geriatrics consultation ($n = 62$) or usual care ($n = 64$). For intervention patients, a geriatrician made specific recommendations regarding oxygenation, fluids, electrolytes, pain, unnecessary medications, bowel and bladder function, nutrition, early mobilization, prevention and management of major postoperative medical complications, orientation cues, and treatment of agitated delirium. Recommendations were limited to 5 for the first visit and 3 for follow-up visits. Orthopedic surgeons managed usual care patients with ad hoc medical or geriatrics consultation.

Patients were well matched at baseline except for a nonsignificant trend toward more prefracture dementia and impaired functional status in patients receiving usual care. The mean age (±SD) was 79 ± 8 years; most patients were white (90%) and female (78%).

The average number of recommendations was 9.5 per patient, and the average adherence rate by the orthopedics team was 77% (range, 32% to 100%). Delirium and serious delirium were significantly less frequent in the intervention group (delirium: 32% vs. 50%, $P = 0.04$; serious delirium: 12% vs. 29%, $P = 0.02$). The groups did not differ for the secondary outcome measures of length of stay and discharge site (for example, nursing home or rehabilitation hospital). The intervention was most effective in patients without prefracture cognitive or functional impairment. The primary study limitations were lack of data on consultants' recommendations in the usual care group and failure of randomization to equalize groups for prefracture cognitive and functional status at baseline.

Congruent with the trial in hospitalized medical patients, a structured preventive approach reduces the incidence and severity of postoperative delirium.

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