CLINICAL UPDATE

Update in Perioperative Medicine

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Medical complications are an important source of morbidity after surgery. Consulting internists often evaluate patients in the office and in the hospital setting to estimate risk of medical complications, to consider the potential role of testing to further stratify risk, and to propose strategies to reduce the risk of postoperative medical complications. The growth of inquiry in this field allows medical consultants to more confidently provide evidence-based advice in these areas. We present this update in perioperative medicine to summarize recent key advances in this field. In this paper, we summarize selected articles chosen for presentation at the 29th annual session of the Society of General Internal Medicine.

We used a systematic search strategy to survey the relevant literature for the period January 1, 2005 through May 1, 2006. 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*, and *surgery*. We added the following text words: intraoperative OR perioperative OR postoperative AND venous thromboembolism (VTE) OR complication OR event. As our audience is general internists, we excluded studies of transplantation surgery, cardiac surgery, and pediatric surgery. We discuss here important studies that change the way we practice perioperative medicine and divide the articles into 5 categories: perioperative cardiac care, preoperative pulmonary evaluation and risk reduction strategies, VTE prophylaxis, bariatric surgery, and postoperative delirium.

PERIOPERATIVE CARDIAC CARE

Validation of the Revised Cardiac Risk Index (RCRI) in a Large Administrative Database

Boersma E, Kertai MD, Schouten O, et al. Perioperative cardiovascular mortality in noncardiac surgery: validation of the Lee cardiac risk index. *Am J Med.* 2005;118:1134–41.

This paper derives from the presentation: Update in Perioperative Medicine at the 29th annual session of SGIM, April 2006.

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The Lee revised cardiac risk index (RCRI) was developed from a prospective study of 4,315 patients aged >50 years undergoing noncardiac, non-neurologic surgery with an expected length of stay ≥ 2 days.¹ Six factors (high-risk surgery, ischemic heart disease, heart failure, cerebrovascular disease, renal insufficiency, and insulin requiring diabetes mellitus) were found to predict the risk of major cardiac complications (myocardial infarction, pulmonary edema, cardiac arrest, and cardiac death). This study aimed to validate the RCRI in predicting perioperative cardiovascular death.

The authors retrospectively analyzed an administrative database from the Netherlands of 108,593 noncardiac surgical procedures performed from 1991 to 2000 to estimate the Lee index for each patient. The primary endpoint was cardiovascular death including stroke until hospital discharge or 30 days after surgery, whichever day came first. They also used univariable logistic regression analysis to evaluate the relation of an adapted Lee index with additional variables from their database. Subsequent multivariable analyses were done to evaluate whether age and more detailed information on the type of surgery (low, low-intermediate, high-intermediate, and high-risk) could improve the predictive power of the adapted Lee index.

A total of 1,877 patients (1.7%) died perioperatively of which 543 (0.5%) were classified as cardiovascular death. The cardiovascular death rates were 0.3%, 0.7%, 1.7%, and 3.6% for Lee class 1 through class 4, respectively. Corresponding odds ratios (ORs) were 1, 2.0, 5.1, and 11.0. The authors determined the C statistic, which correlates outcomes with model rank order: 1.0 indicates perfect performance and 0.5 indicates no correlation. The C statistic for predicting cardiovascular mortality was 0.63 with the Lee index but increased to 0.79 by including type of surgery and to 0.85 with the further addition of age. The authors concluded that the Lee RCRI predicted cardiovascular mortality but could be improved by the addition of age and a more detailed classification of type of surgery. Important study limitations were the use of an administrative database to identify patient-related cardiac risk factors and the use of cardiovascular death as the study endpoint, which failed to include clinically relevant cardiac complications such as myocardial infarction and pulmonary edema.

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This study validates the utility of the Lee RCRI in predicting risk and suggests value in a more detailed risk stratification that also incorporates type of surgery.

Balloon Angioplasty (BA) is a Safe Strategy when Considering Coronary Revascularization Before Noncardiac Surgery

Brilakis ES, Orford JL, Fasseas P, et al. Outcome of patients undergoing balloon angioplasty in the two months prior to noncardiac surgery. *Am J Cardiol.* 2005;96:512–4.

A potential outcome of preoperative risk stratification is to identify patients who may benefit from coronary revascularization; however, this strategy may not decrease perioperative risk. In fact, several studies have reported that percutaneous coronary intervention (PCI) and stent placement before noncardiac surgery may carry a high risk of perioperative death or myocardial infarction.^{2,3} This is particularly true if surgery is required within the first 2 months after PCI and antiplatelet therapy is stopped prematurely. This study examined the frequency of cardiac events in patients undergoing BA shortly before noncardiac surgery.

Using a Mayo Clinic database, the authors retrospectively analyzed outcomes of 345 patients who underwent 416 noncardiac procedures within 60 days of BA from 1988 to 2001. Five patients underwent BA followed by noncardiac surgery twice. Patients undergoing minor procedures were excluded.

One patient died (0.3%) and 2 patients had a nonfatal myocardial infarction (0.6%) after surgery. All 3 patients were among the 188 patients who underwent surgery within 2 weeks of BA. Repeat target vessel revascularization within 2 months was required in 10 patients (2.9%), 3 of 188 patients (1.6%) within the first 2 weeks after BA and 7 of 138 (5.1%) undergoing surgery 3 to 7 weeks after BA. No events occurred in the 24 patients when surgery followed BA after 7 weeks. The authors concluded that for patients who require PCI preoperatively, BA appears to be safe, including for patients in whom noncardiac surgery is necessary early after PCI.

BA should be considered as an alternative to stenting in patients who require noncardiac surgery with 4 to 8 weeks of PCI. The optimal time for surgery in this setting appears to be approximately 2 weeks after BA compared with 4 to 6 weeks after bare metal stent placement (and probably at least 6 months after a drug-eluting stent). At present, however, no

studies have proven that any form of PCI reduces postoperative cardiac complications when compared with standard medical therapy.

Systematic Review: Perioperative β -Blockers Marginally Reduce Cardiac Risk and Increase Risk of Bradycardia and Hypotension

Devereaux PJ, Beattie WS, Choi PT, et al. How strong is the evidence for the use of perioperative beta-blockers in noncardiac surgery? Systematic review and meta-analysis of randomized controlled trials. *BMJ.* 2005;331:313–21.

Several quality and safety organizations have advocated the use of prophylactic perioperative β -blockers to decrease cardiovascular events after noncardiac surgery.⁴ These recommendations, however, are based on a small number of randomized controlled trials with relatively small patient sample sizes.^{5,6} More recent studies and unpublished results (e.g., DIPOM, MaVS) have not shown a consistent beneficial effect.^{7,8} Using a systematic review and meta-analysis to summarize the growing literature, the authors sought to determine the effect of perioperative β -blocker treatment among patients undergoing noncardiac surgery.

The authors used a systematic search strategy to identify 22 eligible randomized controlled trials ($n=2,437$) that reported perioperative outcomes within 30 days of noncardiac surgery. Perioperative β -blockers did not significantly reduce any individual outcome but significantly increased bradycardia and hypotension requiring treatment (Table 1). The only statistically significant benefit was a nominal reduction in the composite outcome of cardiovascular mortality, nonfatal myocardial infarction, and nonfatal cardiac arrest. The 2 largest studies contributed disproportionately to the pooled risk reduction estimates. The number of patients in the meta-analysis was likely inadequate to reliably determine a beneficial treatment effect.

Perioperative β -blockers may reduce the risk of major perioperative cardiovascular events but increase the risk of bradycardia and hypotension requiring treatment in patients undergoing noncardiac surgery. The evidence to support their use is mixed and inconclusive, and additional studies are needed to inform clinical decision making, especially in low risk patients. Physicians should therefore be cautious in their use of perioperative β -blockers to prevent adverse cardiac events. The updated American College of Cardiology/Ameri-

Table 1. Effect of Perioperative β -Blockers Within 30 Days After Noncardiac Surgery

Principal Outcomes	# of Trials (n)	Event Rate		Risk Reduction (95% CI)	NNT (CI)
		β -Blocker (%)	Control (%)		
Total mortality	4 (907)	9/453 (2.0%)	19/454 (4.2%)	0.56 (0.14 to 2.31)	NS
Cardiovascular mortality	4 (907)	5/453 (1.1%)	13/454 (2.9%)	0.40 (0.14 to 1.15)	NS
Nonfatal myocardial infarction	6 (853)	21/441 (4.8%)	37/412 (9.0%)	0.38 (0.11 to 1.29)	NS
Nonfatal cardiac arrest	2 (299)	2/148 (1.4%)	5/151 (3.3%)	0.50 (0.11 to 2.29)	NS
Major cardiovascular events	8 (1152)	28/589 (4.8%)	55/563 (9.8%)	0.44 (0.2 to 0.97) (99%CI: 0.16 to 1.24)	
Complications				Risk Increase (95% CI)	NNH (CI)
Congestive heart failure	5 (861)	23/427 (5.4%)	15/434 (3.5%)	1.54 (0.83 to 2.87)	NS
Nonfatal stroke	1 (200)	4/99 (4.0%)	1/101 (1.0%)	4.08 (0.46 to 35.9)	NS
Hypotension requiring treatment	10 (1712)	216/986 (22%)	147/726 (20%)	1.27 (1.04 to 1.56)	19 (9 to 24)
Bradycardia requiring treatment	9 (1196)	87/621 (14%)	31/575 (5.4%)	2.27 (1.53 to 3.36)	15 (8 to 35)
Bronchospasm	11 (1761)	29/986 (2.9%)	25/775 (3.2)	0.91 (0.55 to 1.50)	

CI, confidence interval; NNT, number needed to treat; NS, nonsignificant; NNH, number needed to harm.

can Heart Association (ACC/AHA) guidelines state that β -blockers (1) should be continued in patients currently taking them and started before surgery for patients undergoing vascular surgery who have ischemia on a stress test; (2) are “probably recommended” for patients with coronary artery disease or who have a high risk for cardiac events who are undergoing vascular or intermediate-to-high risk surgery; (3) “may be used” in other patients undergoing vascular surgery and in patients with intermediate cardiac risk undergoing intermediate-to-high risk surgery.⁹ The data were insufficient to make a recommendation for low risk surgeries. Clear evidence supporting the use of perioperative β -blockers in noncardiac surgery awaits results of further large-scale trials including the POISE and DECREASE IV trials. Pending these results, we tend to agree with the updated ACC/AHA guidelines outlined above.

Perioperative β -Blocker Use Associated with Benefit Only Among High-Risk Patients According to the RCRI Classification

Lindenauer PK, Pekow P, Wang K, et al. Perioperative β -blocker therapy and mortality after major noncardiac surgery. *N Engl J Med*. 2005;353:349–61.

Despite limited evidence, the current standard of practice is to use prophylactic β -blockade in selected patients to reduce morbidity and mortality after noncardiac surgery. This study assessed the association of perioperative β -blocker use with in-hospital mortality.

The authors used a database of 782,969 patients to perform a retrospective cohort study of patients undergoing major noncardiac surgery at 329 U.S. hospitals. Using a propensity score to adjust for β -blocker use, they matched 119,632 patients receiving β -blockers during the first 2 days of admission with 216,290 control patients who were not taking β -blockers. Multivariable logistic modeling was used to compare in-hospital mortality between the 2 groups.

Eighty-five percent of all patients had no contraindications to β -blockers but only 18% of these patients received β -blockers during the first 2 hospital days. Although there was no overall benefit associated with β -blocker use, the relationship between perioperative β -blockers and risk of in-hospital death varied directly with cardiac risk according to the RCRI score (Table 2). In low risk patients with an RCRI score of 0 to 1, there was no benefit and possible harm associated with β -blocker use. Among patients at higher risk (RCRI ≥ 3), β -blockers were associated with a reduced risk of death. The mortality benefit increased with increasing baseline risk. Important limitations included the observational, nonrandom-

ized nature of the study, the possibility of other confounders not accounted for by propensity matching, and the lack of knowledge regarding the indication for β -blocker use (e.g., prophylaxis, continuation of usual therapy, treatment of a postoperative complication).

This large observational study supports the routine use of perioperative β -blockers only in high-risk patients (RCRI ≥ 3), and suggests harm in low risk patients (RCRI 0 to 1). Clinicians should individualize their use in patients with 2 RCRI factors based on the specific factors and type of surgery. These findings are similar to those of the recommendations by the updated ACC/AHA guideline discussed above.

Narrative Review: Perioperative Statin Therapy Reduces Postoperative Cardiac Complications

Biccard BM, Sear JW, Foëx P. Statin therapy: a potentially useful perioperative intervention in patients with cardiovascular disease. *Anaesthesia* 2005;60:1106–14.

In addition to their well established role in reducing cardiovascular events among selected patients with elevated serum cholesterol, acute administration of statins improve outcomes among patients with acute coronary syndromes.^{10,11} In the past 5 years, investigators have begun to ask the question of whether perioperative statin use may similarly reduce cardiovascular events after major noncardiac surgery. In this paper, Biccard and colleagues reviewed the English language literature from 1994 through April 2005 to identify randomized trials and systematic reviews of statin administration following acute coronary syndromes and in the perioperative period. For the purposes of our question of interest, we restrict our discussion to the retrieved data on perioperative statin use.

The authors identified 10 studies that contained relevant data; 8 studies were of noncardiac surgery (7 studies of vascular surgery, one of major noncardiac surgery). Only 1 study was a randomized trial ($n=100$) and 1 was a prospective study ($n=981$); the remaining studies were retrospective analyses. The timing of statin administration varied among the eligible studies.

In a case control study of patients undergoing major vascular surgery, the adjusted OR for perioperative mortality associated with statin use was 0.22 (95% confidence interval [CI] 0.10 to 0.47). In a retrospective study of patients undergoing vascular surgery who had ischemia on dipyridamole-thallium testing, the OR for mortality for statin use was 0.49 (95% CI 0.25 to 0.96); this was not significant after multivariate analysis. Five studies reported number needed to treat (NNT) to reduce mortality; these results ranged from NNT 3 to 103. The remaining retrospective study reported a NNT of 15 to prevent all cardiac complications. The single randomized controlled trial was of atorvastatin 20 mg daily or placebo for a mean of 30 days before and 15 days after vascular surgery. The NNT to prevent a combined cardiac endpoint was 5.6; there was no difference in mortality between the 2 groups. In the single study that stratified results by RCRI score (a measure of prior probability of postoperative cardiac events), the NNT ranged from 186 (RCRI score 0) to 20 (RCRI score ≥ 4).

The available evidence is primarily based on retrospective data but suggests a potentially compelling benefit from the use of perioperative statins.

Table 2. Adjusted Odds Ratio for In-Hospital Death Associated with β -Blocker Therapy

RCRI Score	Entire Study Cohort OR (95% CI)	Propensity-Matched Cohort OR (95% CI)
0	1.36 (1.27 to 1.45)	1.43 (1.29 to 1.58)
1	1.09 (1.01 to 1.19)	1.13 (0.99 to 1.30)
2	0.88 (0.80 to 0.98)	0.90 (0.75 to 1.08)
3	0.71 (0.63 to 0.80)	0.71 (0.56 to 0.91)
≥ 4	0.58 (0.50 to 0.67)	0.57 (0.42 to 0.96)

RCRI, revised cardiac risk index; OR, odds ratio, CI, confidence interval.

PREOPERATIVE PULMONARY EVALUATION AND RISK REDUCTION STRATEGIES

A Systematic Review and Guideline for Risk Factors, Laboratory Testing, and Risk Reduction Strategies for Postoperative Pulmonary Complications

Smetana GW, Lawrence VA, Cornell JE. Preoperative pulmonary risk stratification for noncardiothoracic surgery: systematic review for the American College of Physicians. *Ann Intern Med.* 2006;144:581–95.

Lawrence VA, Cornell JE, Smetana GW. Strategies to reduce postoperative pulmonary complications after noncardiothoracic surgery: systematic review for the American College of Physicians. *Ann Intern Med.* 2006;144:596–608.

Gaseem A, Snow V, Fitterman N, et al., for the Clinical Efficacy Assessment Subcommittee of the American College of Physicians. 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;144:575–80.

Pulmonary complications are as common and morbid as cardiac complications after surgery.¹² While guidelines for perioperative cardiac care have been available for the past decade, no similar guideline has assisted clinicians when faced with a patient who may be at risk for postoperative pulmonary complications. This series of articles provides a systematic review of preoperative pulmonary risk stratification, strategies to reduce risk, and an accompanying guideline from the American College of Physicians (ACP). These papers represent the first systematic review of the entire field. The authors reviewed the literature dating to 1980, used a rigorous systematic search strategy, and excluded studies that used administrative data only, those that evaluated physiologic outcomes only, and those that had no explicit definition for postoperative pulmonary complications. Among 15,736 articles reviewed by title and abstract, 85 eligible studies provided univariate analysis, 29 studies provide adjusted data using multivariable analysis, 20 studies were randomized controlled trials, and 11 eligible studies were systematic reviews.

The authors estimated the magnitude of risk of individual risk factors by use of pooled and trim-and-fill meta-analytic methods for studies that used multivariable analysis, and provided summary strength of the evidence for each factor using a modified version of the U.S. Preventive Services Task Force (USPSTF) criteria. Table 3 provides the strength of recommendation and estimated ORs for patient- and procedure-related risk factors and laboratory tests. Important patient-related observations include the significance of age even after adjustment for comorbidities more common with advanced age, the value of the American Society of Anesthesiologists (ASA) classification to stratify risk, and the lack of effect of asthma or obesity on pulmonary complication rates. High-risk surgical site was the single strongest predictor. Among laboratory tests, low serum albumin level was the most important predictor. In the accompanying guideline, the ACP recommended against routine use of preoperative spirometry or chest radiography to estimate risk.

The literature regarding risk reduction strategies varied substantially in quality. The only intervention to earn an “A”

Table 3. Summary Strength of the Evidence for the Association of Patient, Procedure, and Laboratory Factors with Postoperative Pulmonary Complications

Factor	Strength of Recommendation*	Odds Ratio
Potential patient-related risk factor		
Advanced age	A	2.09 to 3.04
ASA class ≥ 2	A	2.55 to 4.87
CHF	A	2.93
Functionally dependent	A	1.65 to 2.51
COPD	A	1.79
Weight loss	B	1.62
Impaired sensorium	B	1.39
Cigarette use	B	1.26
Alcohol use	B	1.21
Abnormal chest examination	B	NA
Diabetes	C	
Obesity	D	
Asthma	D	
Obstructive sleep apnea	I	
Corticosteroid use	I	
HIV infection	I	
Arrhythmia	I	
Poor exercise capacity	I	
Potential procedure-related risk factor		
Aortic aneurysm repair	A	6.90
Thoracic surgery	A	4.24
Abdominal surgery	A	3.01
Upper abdominal surgery	A	2.91
Neurosurgery	A	2.53
Prolonged surgery	A	2.26
Head and neck surgery	A	2.21
Emergency surgery	A	2.21
Vascular surgery	A	2.10
General anesthesia	A	1.83
Perioperative transfusion	B	1.47
Hip surgery	D	
Gynecologic or urologic surgery	D	
Esophageal surgery	I	
Laboratory tests		
Albumin level < 35 g/L	A	2.53
Chest radiography	B	4.81
BUN level > 7.5 mmol/L (> 21 mg/dL)	B	NA
Spirometry	I	

*Recommendations: A=good evidence to support the particular risk factor or laboratory predictor; B=at least fair evidence to support the particular risk factor or laboratory predictor; C=at least fair evidence to suggest that the particular factor is not a risk factor or that the laboratory test does not predict risk; D=good evidence to suggest that the particular factor is not a risk factor or that the laboratory test does not predict risk; I=insufficient evidence to determine whether the factor increases risk or whether the laboratory test predicts risk, and evidence is lacking, is of poor quality, or is conflicting.

Adapted with permission from **Smetana GW, Lawrence VA, Cornell JE.** Preoperative pulmonary risk stratification for noncardiothoracic surgery: systematic review for the American College of Physicians. *Ann Intern Med.* 2006;144:581–95.

ASA, American Society of Anesthesiologists; BUN, blood urea nitrogen; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; NA, not available.

level of evidence was postoperative lung expansion maneuvers (deep breathing exercises or incentive spirometry). Fair evidence supported the use of selective (rather than routine) nasogastric tube placement after abdominal surgery, short acting neuromuscular blockers, and laparoscopic (vs open) surgery. The evidence was insufficient for smoking cessation, intraoperative neuraxial blockade, postoperative epidural

analgesia, and immunonutrition. The authors concluded that routine total parenteral or enteral nutrition and right heart catheterization do not reduce risk.

These papers summarize the existing state of the science and provide an evidence based approach to confidently estimate pulmonary risk and to employ strategies to reduce the risk of pulmonary complications after surgery.

A Systematic Review of the Value of Preoperative Chest Radiographs Confirms a Low Yield for Younger Patients and for Older Patients without Risk Factors

Joo HS, Wong J, Naik VN, Savoldelli GL. The value of screening preoperative chest x-rays: a systematic review. *Can J Anesth* 2005;52:568–74.

Many customarily obtained preoperative tests have little impact on perioperative management and do not accurately identify high-risk patients. In many institutions, clinicians obtain routine preoperative chest radiographs to stratify risk or to serve as a baseline in the event of a need for a postoperative study. The value of this approach remains debated. In this review, Joo et al. systematically reviewed the literature from 1996 through April 2004 regarding preoperative chest radiographs and included studies of adult noncardiothoracic surgery in developed countries. The authors identified 14 eligible studies and sought to determine the impact of preoperative chest radiographs on preoperative investigation or management, anesthetic management, surgical management, and perioperative complication rates.

All studies were uncontrolled and nonrandomized. Six studies were fair quality; the remainder were of poor quality. The yield of abnormalities for patients with no risk factors ranged from 0.4% to 34%; that for patients with risk factors from 21% to 61%. Among the 2 studies that reported comparison with previous test results, 56% to 64% of abnormal findings were previously known. Diagnostic yield was low for patients <50 years of age and ranged from 3% to 16%. The most commonly reported abnormal findings were cardiomegaly and chronic obstructive pulmonary disease (COPD).

Most abnormal results did not lead to a change in management. Further investigation resulted from 3% to 47% of patients with abnormal radiographs. However, only 10% of these investigations led to a change in management. In a single large study, only 0.5% of patients had a change in anesthetic management due to the finding of an abnormal chest radiograph.¹³ Changes in surgical management due to abnormal chest radiographs occurred in 1% to 4% of patients. Only 2 eligible studies reported pulmonary complication results stratified based on a normal or abnormal preoperative chest radiograph and neither study found a difference in complication rates. Joo et al. conclude that there is fair evidence that clinicians should not obtain routine studies for patients <70 years of age and insufficient evidence to support routine use for patients older than 70 years of age. They recommend preoperative chest radiographs for patients >70 years old with risk factors.

The results of this systematic review are similar to previous reports. For example, in a 2003 review ($n=20,518$), 21.2% of all preoperative chest radiographs were abnormal but only 3.0% influenced management.¹⁴ In the previously mentioned

systematic review for the ACP guideline development, only 2 studies used adjusted data to estimate pulmonary risk and both studies reported abnormal preoperative chest radiograph to be an independent predictor. The findings of Joo et al. are similar to the conclusions of the ACP guideline but differ by the age threshold above which chest radiographs may have value for patients with risk factors (the ACP guideline used age 50 years). Both reports conclude that clinicians can predict most chest radiograph abnormalities based on clinical findings and its value as a routine test is limited.

No Paradoxical Increase in Pulmonary Complications After Thoracotomy Among Smokers Who Have Recently Quit Smoking

Barrera R, Shi W, Amar D, et al. Smoking and timing of cessation. Impact on pulmonary complications after thoracotomy. *Chest* 2005;127:1977.

A counterintuitive finding has appeared in the medical literature regarding the impact of cigarette use on postoperative pulmonary complications. This is the observation that recent quitters may have a higher incidence of complications than current smokers. In this prospective study of 300 patients, Barrera et al. aimed to determine if similar findings would result from a cohort of patients undergoing thoracotomy. Eligible patients were >18 years old undergoing thoracotomy for primary or secondary lung tumors. Exclusion criteria were patients undergoing a second procedure on the same admission or concomitant rib, chest wall, diaphragmatic, pericardial, or pleural resections. Physicians were blinded to self reported smoking status. Smoking status was defined as non smokers, past quitters (quit >2 months before surgery), recent quitters (quit >1 week and ≤ 2 months before surgery), and ongoing smokers (smoked in the week before surgery). The authors provided explicit definitions for the outcome measures of respiratory failure, pneumonia, atelectasis, pulmonary embolism, and supplemental oxygen use at hospital discharge.

Recent quitters were a mean of 4 years younger than past quitters ($P=.004$). The overall pulmonary complication rate was 17%. Complication rates were: non smokers (8%), past quitters (19%), recent quitters (23%), and ongoing smokers (23%). These differences were not statistically significant ($P=.14$). In a subgroup analysis, no significant differences existed between recent quitters and past quitters in the rates of any of the component outcomes or length of stay. In a multivariable analysis, only pack-years and diffusing capacity for carbon monoxide (DLCO) were significant predictors.

These findings differ from those of previous studies. Among a cohort of 200 patients undergoing coronary artery bypass grafting, Warner et al.¹⁵ reported pulmonary complication rates of 57.1% among recent quitters (defined as 2 months) versus 14.5% among past quitters. Bluman et al.¹⁶ made a similar observation among patients undergoing elective noncardiac surgery. Possible mechanisms for this counterintuitive finding are an increase in sputum production among recent quitters and selection bias in that sicker patients may correctly identify themselves at risk and be more likely to attempt to reduce smoking before elective surgery. Why might the current study produce different results? The authors included 2 unconventional outcomes for pulmonary

complications (pulmonary embolus (PE) and oxygen requirement) but this inclusion does not appear to have influenced the primary results. It is possible that timing of cessation may impact complication rates differently for patients undergoing thoracotomy than for other high-risk surgeries. However, the single previous study of timing of cessation among patients undergoing pulmonary surgery showed a trend towards higher complication among recent quitters than among current smokers.¹⁷ The current study provides some comfort for physicians who must counsel patients before semiurgent surgery. However, the preponderance of the literature still suggests that physicians should advise a full 2 months of smoking cessation before elective surgery. Further research should be sufficiently powered to confidently distinguish modest differences between patient subgroups based on timing of cessation.

Selective Nasogastric Tube Placement After Abdominal Surgery May Reduce Postoperative Pulmonary Complications

Nelson R, Tse B, Edwards S. Systematic review of prophylactic nasogastric decompression after abdominal surgery. *Br J Surg.* 2005;92:673–80.

The presence of a nasogastric tube after abdominal surgery could conceivably increase the risk of aspiration and postoperative pneumonia or other pulmonary complications. Selective nasogastric tube use refers to its use for symptoms such as nausea or vomiting, or abdominal distension, rather than routine use. In an earlier systematic review published in 1995, pneumonia (RR 0.49, $P < .0001$) and atelectasis (RR 0.46, $P = .001$) were each less common among patients who received a nasogastric tube selectively rather than routinely.¹⁸ Nelson et al. set out to update the previous analysis to determine if these findings still held true.

The authors used a systematic search strategy and included randomized controlled trials of adults undergoing all types of abdominal surgery other than laparoscopic procedures. Twenty-seven eligible studies included patients undergoing colorectal surgery (7 studies), gastroduodenal surgery (7 studies), biliary surgery (2 studies), gynecologic surgery (2 studies), vascular surgery (1 study), trauma surgery (1 study), and all abdominal surgeries (7 studies). The pulmonary complication endpoint was a combination of pneumonia and atelectasis rates. The authors calculated meta-analytic relative risk estimates and used random effects models when heterogeneity existed. The relative risk for pulmonary complications for routine nasogastric tube use was 1.35 (95% CI 0.98 to 1.86). Return of bowel function occurred significantly earlier among patients who received selective nasogastric tubes. There were no significant differences for rates of wound infection, ventral hernia, or anastomotic leak.

The 1995 review included non randomized trials and case control studies which may have overestimated the magnitude of the reduction in pulmonary complication rates associated with selective nasogastric tube use. The current review identifies a trend towards higher pulmonary complication rates and no benefit in surgical outcomes among patients who received a routine nasogastric tube. Pending further study, medical consultants can recommend selective nasogastric tube use as a potential strategy to reduce pulmonary complication rates.

VTE PROPHYLAXIS

Fondaparinux Is Similar to Dalteparin in Preventing VTE After High-Risk Abdominal Surgery

Agnelli G, Bergqvist D, Cohen AT, Gallus AS, Gent M. Randomized clinical trial of postoperative fondaparinux versus perioperative dalteparin for prevention of venous thromboembolism in high-risk abdominal surgery. *Br J Surg.* 2005;92(10):1212–20.

The incidence of deep vein thrombosis (DVT) in patients undergoing abdominal surgery is approximately 25% in the absence of thromboprophylaxis.¹⁹ Low dose unfractionated heparin (UFH) every 8 hours or low-molecular-weight heparins (LMWHs) once daily are recommended for high-risk patients by the American College of Chest Physicians (ACCP). In a meta-analysis, LMWH was associated with a 29% relative risk reduction in clinically overt VTE compared with UFH.²⁰

Fondaparinux is a new synthetic selective and specific inhibitor of Factor Xa that has shown efficacy compared with enoxaparin in major orthopedic surgery trials.²¹ This multicenter, international, double-blind and double-dummy randomized clinical trial (PEGASUS) was designed to determine whether fondaparinux is more effective and safer than LMWHs in high-risk abdominal surgery. Eligible patients were aged >60 years undergoing abdominal surgery lasting >45 minutes under general anesthesia or patients aged >40 years with at least 1 of the following: obesity, prior VTE, heart failure (New York heart association grade III or IV), COPD, inflammatory bowel disease, or cancer surgery.

Fondaparinux 2.5 mg subcutaneous (SC) was started 6 hours postoperatively compared with dalteparin 2,500 IU SC given 2 hours before and then 12 hours after the preoperative dose followed by 5,000 IU per day SC. The primary efficacy outcome measure was asymptomatic DVT and symptomatic DVT and PE. All patients underwent a screening venography by postoperative day #10. Patients with signs and symptoms of DVT were evaluated with ultrasonography and later confirmed with venography. Patients with symptoms of PE received a helical computed tomography, ventilation perfusion scan, or pulmonary angiography. The primary safety outcome measure was major bleeding defined as fatal bleeding, bleeding that was retroperitoneal, intracranial, intraspinal, or involved with any other critical organ, bleeding leading to reoperation or intervention and a bleeding index of ≥ 2 .

Among 2,048 eligible patients, the VTE rate was 4.6% for fondaparinux compared with 6.1% for dalteparin, a relative risk reduction of 24.6% (95% CI -9 to 47.9), which met the predetermined criterion for noninferiority of fondaparinux. Major bleeding occurred in 3.4% of patients given fondaparinux and 2.4% of those given dalteparin ($P = .122$). In a subgroup analysis, fondaparinux was more effective than dalteparin for patients that underwent cancer surgery and those with median surgery time of >2.5 hours.

This was a large study that utilized a central adjudication committee to monitor events and used high-quality venography with a high-evaluability rate. Fondaparinux was at least as effective as perioperative dalteparin. There was no difference in major bleeding between the 2 agents. The pharmaceutical sponsor of fondaparinux funded and oversaw

the study. Fondaparinux is now FDA approved and is an alternative anticoagulant for VTE prophylaxis in high-risk abdominal surgery.

VTE Is Common After Cancer Surgery and Often Occurs Late

Agnelli G, Bolis G, Capussotti L, et al. A clinical outcome-based prospective study on venous thromboembolism after cancer surgery: the @RISTOS project. *Ann Surg*. 2006;243(1):89–95.

The risk of DVT is 2-fold higher and that of fatal PE 3-fold higher in patients undergoing cancer surgery than in those undergoing noncancer surgeries.^{19,22} Over the years, an increase in VTE prophylaxis, advances in technology, improvement in surgical technology, and shorter hospital stays may all lead to changes in the epidemiology of VTE in cancer surgery patients.

The investigators prospectively enrolled consecutive patients at 31 Italian centers undergoing abdominal, thoracic, gynecologic, and urologic surgery for cancer. The primary outcome measures were clinically overt DVT, PE, and death due to PE at day 35 after cancer surgery or more if hospital stay was longer than 35 days. A secondary aim was to identify potential risk factors for VTE. All clinically suspected venous thromboembolic events were reviewed and adjudicated by an external committee of 3 clinicians.

Twelve hundred and thirty-eight patients (52.2%) underwent general surgery (49.1% abdominal and 3.1% thoracic surgery), and 450 (18.9%) and 685 (28.8%) patients had gynecologic and urologic surgery, respectively. Fifty patients (2.1%) developed VTE or died while another 42 possibly had VTE but this was not confirmed. Death was attributed to VTE in 19 cases (0.82%). The incidence of VTE was 2.8% in general surgery, 2.0% in gynecologic surgery, and 0.87% in urologic surgery. In multivariate logistic regression analysis, 5 risk factors were identified: age above 60 years (2.63, 95% CI 1.21 to 5.71), previous VTE (5.98, 2.13 to 16.80), advanced cancer (2.68, 1.37 to 5.24), anesthesia lasting more than 2 hours (4.50, 1.06 to 19.04), and bed rest longer than 3 days (4.37, 2.45 to 7.78). Forty percent of VTEs occurred more than 21 days after surgery (Fig. 1). A study limitation was lack of standardization of the prophylactic regimen.

FIGURE 1. Venous thromboembolic events stratified by post-operative day. Reprinted with permission from Agnelli G, Bolis G, Capussotti L, et al. *Ann Surg* 2006;243:89–95.

The high incidence of symptomatic VTE despite prophylaxis suggests a need for a more aggressive approach in patients with cancer and risk factors. Forty percent of events occurred more than 21 days after surgery and half occurred in the absence of prophylaxis. The high proportion of late events supports the ACCP recommendation to use extended prophylaxis for up to 4 weeks in patients with abdominal and pelvic surgery for cancer and suggests we also use this practice for thoracic and urologic cancer surgery patients.

BARIATRIC SURGERY

Older Age, Male Gender, Congestive Heart Failure, Renal Failure, and Medicaid as Primary Insurance Each Predict In-Hospital Mortality After Bariatric Surgery

Poulose BK, Griffin MR, Moore DE, et al. Risk factors for post-operative mortality in bariatric surgery. *J Surg Res*. 2005;127:1–7.

As worldwide rates of morbid obesity continue to increase, there has been a tremendous increase in bariatric surgery. As many bariatric patients have multiple comorbidities and risk factors for postoperative complications, clinicians need parameters to identify which patients are at higher risk of death in the perioperative period.

In this study, authors used the 2001 Nationwide Inpatient Sample (NIS) to evaluate 54,878 bariatric surgical patients ≥ 18 years old. The NIS represents a sample of 20% of all U.S. nonfederal hospitalizations. Assuming postoperative mortality after Roux-en-y gastric bypass to be in the range of 0.5% to 1.5%, the investigators estimated a need for at least 1,500 patients in each comparison group to detect a mortality difference of 1% with enough statistical power. The authors used a multivariate logistic regression model to evaluate 30 comorbid conditions, gender, insurance, age, and the need for reoperation.

The overall in-hospital mortality was 0.4% with a mean length of stay of 3.9 days. The mean length of stay for patients who died was 17.6 days. In a univariate analysis, Medicaid patients (OR 2.8 [95% CI 0.9 to 8.5]) and Medicare patients (OR 4.6 [95% CI 2.5 to 8.7]) both had a higher mortality. Medicare status was not a significant factor after multivariable adjustment. In a multivariable analysis, male gender was a risk factor for postoperative death; the adjusted OR was 2.1 (CI 1.1 to 4.3). Increasing age also proved to be risk factor; the adjusted ORs for ages 40 to 49 and 50 to 59 were 2.6 (CI 1.1 to 6.5) and 4.3 (CI 1.7 to 11), respectively. Of the medical comorbidities studied, only congestive heart failure and renal failure were statistically significant predictors. The adjusted ORs for mortality were 14.9 (CI 4.6 to 48.5) and 13.1 (CI 3.1 to 55.4), respectively.

As the authors identified risk factors through use of a preexisting database, no information was available for certain patient characteristics that may have influenced mortality (for example race and BMI). Despite this limitation, this study provides guidance for patient selection before potential bariatric surgery. Future research should include prospective determination of risk factors and blinded outcome ascertainment.

POSTOPERATIVE DELIRIUM

Prophylactic Haloperidol Reduces Duration of Postoperative Delirium and Length of Stay for Elderly Patients at Risk for Delirium

Kalisvaart KJ, de Jonghe JFM, Bogaards MJ, et al. Haloperidol prophylaxis for elderly hip-surgery patients at risk for delirium: a randomized placebo-controlled study. *J Am Geriatr Soc.* 2005;53:1658–66.

In elderly hip fracture patients, delirium is a serious postoperative complication. It occurs in 5% to 45% of patients undergoing hip surgery and is associated with increased length of stay, high rates of institutionalization after discharge, and increased morbidity and mortality. Predisposing factors include cognitive impairment, sensory impairment, severity of illness, and dehydration. Although a variety of nonpharmacologic interventions reduce the risk of delirium, one meta-analysis reported that absolute risk reduction for these interventions was only 13%.²³ The authors of this paper studied haloperidol in a randomized placebo controlled trial to evaluate its effectiveness as a prophylactic measure in susceptible elders. Delirium is associated with cholinergic deficiency due to decreased levels of acetylcholine. The authors hypothesized that as haloperidol-induced dopamine D2 receptor blockade is associated with enhanced acetylcholine release, haloperidol may indirectly cause a reduction in delirium.

Kalisvaart et al. enrolled 430 consecutive hip surgery patients age ≥ 70 with an intermediate or high risk of delirium based on previously validated risk predictors of visual impairments, severity of illness, Mini Mental Status Exam, and volume depletion. Patients received haloperidol (0.5 mg tid) or placebo on admission through postoperative day 3. The primary outcome was postoperative delirium; secondary outcomes were severity of delirium, duration of delirium, and length of stay.

The incidences of postoperative delirium in the haloperidol and placebo groups were not statistically different at 15.1% and 16.6%, respectively. However, the duration of delirium in the haloperidol group was 6.4 days shorter than the placebo group (95% CI 4.0 to 8.0). The mean length of stay was 5.5 days shorter in the haloperidol group compared with the placebo group (95% CI 1.4 to 2.3). The study had several limitations. First, it was underpowered given the low delirium rates. This may have been due to the inclusion of more patients with intermediate rather than high-risk factors. Finally, the treatment group received a lower dose of haloperidol than is often used in clinical practice, which may have biased the results in favor of no effect.

Despite these limitations, clinicians may consider use of prophylactic haloperidol or similar medications when evaluating patients at high risk for delirium in the perioperative period.

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