Update in Perioperative Medicine 2011

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J Gen Intern Med 26(11):1358-63

DOI: 10.1007/s11606-011-1839-x

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INTRODUCTION

The field of perioperative medicine continues to mature as evidenced by the growing number of high-quality articles published each year. This is encouraging given the increasingly complex patient population that routinely undergoes major surgery. Furthermore, as surgeons have become more subspecialized, there is increased reliance on the generalist to perform consultative medicine for the preoperative patient, as well as co-manage patients throughout the hospitalization.

METHODS

This article is a summary of the Update in Perioperative Medicine session presented at the 34th Annual Meeting of the Society of General Internal Medicine (SGIM). From May 2010 to April 2011, the perioperative and consultative medicine interest group gathered articles that contributed to the field of perioperative medicine and impacted daily practice for clinicians who provide care for the surgical patient. The interest group discussed these articles and ranked them in order of clinical relevance, then categorized them into the following: consultative medicine, perioperative cardiac medicine, perioperative pulmonary medicine, perioperative medication management, and venous thromboembolism.

RESULTS/CONCLUSIONS

Consultative Medicine

Outcomes and Processes of Care Related to Preoperative Medical Consultation. Wijeyesundera DN, Austin PC, Beattie WS, et al. *Arch Intern Med* 2010;170:1365-1374. Surgeons request

preoperative medical consultations for various reasons to improve management and outcomes; however, the impact of these consults is unclear. This population-based cohort study sought to determine whether preoperative medical consultation was associated with reduced mortality or length of stay after major elective noncardiac surgery.

The Ontario Health Insurance Plan (OHIP) claims-based definition of preoperative consultation includes those performed by an internist, cardiologist, endocrinologist, or geriatrician within 4 months before surgery. Of 269,866 patients in the cohort, 38.8% had consultations. An analysis of a propensity score-matched cohort of 191,852 patients found that consultation was associated with an increased 30-day mortality (RR 1.16; 95% CI 1.07–1.25; NNH 516), 1-year mortality (1.08; 95% CI 1.04–1.12; NNH 227), and mean hospital stay (9.07 vs 8.39 days; difference 0.67 days; 95% CI 0.59–0.76; $p < 0.001$). These findings were consistent across various subgroups and persisted for sensitivity analyses that adjusted for potential confounders. Preoperative consultation was also associated with changes in care that included increases in preoperative testing, beta-blockers or statin use, cardiac interventions, and postoperative use of mechanical ventilation and monitored beds.

Patients referred for consultation had more comorbid illnesses and were at increased risk for adverse outcomes. Limitations of this observational study, which could negate the small increase in mortality, include unmatched cases, the potential for residual confounding, the exclusion of cancelled surgeries, differences between consultants (generalist vs specialist), and duration of postoperative follow-up.

Implications for Clinical Practice. Other smaller single-center studies have shown that preoperative medical consultation shortly before surgery is associated with increased length of hospital stay and cost with no difference in process of care (beta-blocker use).¹ Previous studies of outpatient consultation have demonstrated a reduction in last minute surgical delays but no effect on hospital stay or postoperative complication rates.² Compliance with consultants' recommendations and the degree of perioperative comanagement may vary considerably. Due to the previously noted limitations, it is unlikely that preoperative consultations actually increase mortality, although more selective consultation may be warranted. The practice of obtaining preoperative consultations, particularly for patients felt to be at increased risk, should not change until multicenter studies employing rigorous qualitative and quantitative research methods better define mechanisms by which consultation

Received June 13, 2011

Revised August 3, 2011

Accepted August 9, 2011

Published online August 31, 2011

influences outcome and identify which interventions improve outcomes.

Perioperative Cardiac Medicine

Characteristics and Short-Term Prognosis of Perioperative Myocardial Infarction in Patients Undergoing Noncardiac Surgery. Devereaux PJ, Xavier D, Pogue J, et al. *Ann Intern Med* 2011;154:523-528. More than 200 million patients worldwide undergo major noncardiac surgical procedures each year.³ Previous studies have estimated that approximately 1–5% of these patients will have a major cardiovascular complication within 30 days after surgery such as cardiovascular death, nonfatal myocardial infarction (MI), or stroke.⁴ Little is known about the characteristics and short-term prognosis of perioperative MI in patients having noncardiac surgery. In this report, the investigators of the POISE (PeriOperative ISchemic Evaluation) trial studied the prevalence and features of perioperative MI. POISE was a randomized controlled trial of perioperative beta-blockers that was conducted at 190 centers in 23 countries and included 8,351 patients.⁴

Four cardiac biomarker or enzyme assays were measured within 3 days of surgery. The definition of perioperative MI included either autopsy findings of acute MI or an elevated level of a cardiac biomarker or enzyme, and at least 1 of the following defining features: ischemic symptoms, new pathologic Q waves, ischemic changes on electrocardiography, coronary artery intervention, or cardiac imaging evidence of MI. A month after random assignment in the POISE trial, a total of 415 patients (5.0%) had a perioperative MI. Most MIs (74.1%) occurred within 48 h of surgery; 65.3% of patients did not experience ischemic symptoms. The 30-day mortality rate was 11.6% among patients who had a perioperative MI and 2.2% among those who did not ($P < 0.001$). Among patients with a perioperative MI, mortality rates were elevated and did not differ for those with and without ischemic symptoms (9.7% vs 12.5%, respectively). Independent predictors of perioperative MI included a 10-beats/min increase in baseline heart rate (OR 1.29; 95% CI 1.13–1.50) and serious bleeding (OR 3.62; 95% CI 2.07–6.36). Emergency or urgent surgery was also associated with perioperative MI (OR 2.94; 95% CI 1.65–5.26). The authors concluded that clinicians should routinely measure postoperative troponin levels for high-risk patients to detect asymptomatic MIs, as the outcomes are similar to those of symptomatic MIs.

Implications for Clinical Practice. Most patients who sustain a perioperative MI do not experience ischemic symptoms. Both asymptomatic and symptomatic perioperative MI confers increased rates of 30-day mortality. Therefore, routine monitoring of cardiac biomarkers in high-risk patients is essential after surgery. The highest risk for death after perioperative MI was in the first 48 h; this was true regardless of whether the patient experiences ischemic symptoms. Whether intervention to treat asymptomatic MIs after surgery improves outcomes is unknown based on the study results. Randomized, controlled trials to establish effective treatments for perioperative MI are urgently needed. Until such trials are conducted, beneficial interventions for secondary cardiac prevention (such as statins, beta blockers, and angiotensin-converting enzyme inhibitors) seem reasonable.

Prognostic Implications of Asymptomatic Left Ventricular Dysfunction in Patients Undergoing Vascular Surgery. Flu WJ, van Kruijk JP, Hoeks SE, et al. *Anesthesiology* 2010;112:1316-1324. Although symptomatic heart failure is a well-established perioperative cardiovascular (CV) risk factor, it is unknown what affect asymptomatic left ventricular (LV) dysfunction has on perioperative outcomes. Flu et al. performed a prospective cohort study performing preoperative echocardiography on 1,005 consecutive patients undergoing elective vascular surgery at a single center in The Netherlands. Systolic dysfunction was defined as an ejection fraction of less than 50%, both with and without accompanying diastolic dysfunction. The study endpoints were 30-day cardiovascular events (defined as myocardial ischemia, infarction, and mortality) and long-term cardiovascular mortality. The authors performed a multivariate regression analysis to evaluate the relation between LV function and the study endpoints.

LV dysfunction was present in half of all patients; 80% of these patients were asymptomatic. The 30-day CV event rate was highest in patients with symptomatic heart failure (49%), followed by those with asymptomatic systolic LV dysfunction (23%), asymptomatic diastolic LV dysfunction (18%), and normal LV function (10%). These differences were statistically significant; a similar trend existed for long-term CV mortality (Fig. 1). Adjusting for medication use (such as beta-blockers and statins) did not change the prognostic value of LV dysfunction.

Implications for Clinical Practice. The widely adopted Revised Cardiac Risk Index (RCRI) includes stable congestive heart failure as an independent clinical predictor of perioperative CV risk.⁵ This study suggests that detecting *preclinical* LV dysfunction may also be of value in vascular surgery patients. The presence of asymptomatic LV dysfunction may alter perioperative management (i.e., optimization of cardiac medications, judicious fluid management, and intensive postoperative surveillance) and influence operative decisions such as favoring an endovascular approach over an open procedure when possible.

Although this study adds important information to the perioperative literature, it is too early to recommend routine preoperative echocardiography for high-risk patients. A study by Xu-Cai et al. demonstrated that patients with clinically stable heart failure did not have increased mortality rates in association with elective major noncardiac surgery.⁶ Furthermore, the recently published guidelines on appropriate use criteria for echocardiography state it is “inappropriate” to assess ventricular function in patients without signs or symptoms of CV disease in the preoperative setting.⁷

Perioperative Pulmonary Medicine

Perioperative Mortality in Patients with Pulmonary Hypertension Undergoing Major Joint Replacement. Memtsoudis SG, Ma Y, Chiu YL, et al. *Anesth Analg* 2010;111:1110-1116. The impact of pulmonary hypertension on perioperative outcomes is not well established. In this study, the authors used the National Inpatient Sample (NIS), from a 20% stratified sample of US hospitals, to identify all patients with pulmonary hypertension

Figure 1. Left ventricle function and postoperative outcomes.

undergoing knee (TKA) or hip (THA) replacement surgery from 1998–2006. Subjects were eligible if they had ICD-9 codes for primary total hip or knee arthroplasty, and also a code for primary pulmonary hypertension or chronic pulmonary heart disease. The primary outcome measure was mortality; secondary outcomes were pulmonary embolus (PE), deep venous thrombosis (DVT), and adult respiratory distress syndrome (ARDS). The authors identified a sample without pulmonary hypertension that was matched for age, Deyo comorbidity index, gender, race, hospital size and location, teaching hospital status, and admission type. A multivariable regression analysis was performed to adjust for potential confounding factors.

The authors identified 3,302 patients with pulmonary hypertension for whom they could identify a matched sample (THA=1,245, THR=2,057). Patients were well matched according to the above demographic variables. For patients undergoing THA, the unadjusted odds ratio for mortality was 3.72 (95% CI 2.13–6.39, rate 2.41% vs 0.65%) for patients with pulmonary hypertension. The corresponding result for TKA was OR 4.55 (95% CI 0.91 2.16–9.39, rates 0.91% vs 0.2%). Adjusted odds ratios were similar. Adjusted odds ratios for ARDS, PE, and DVT were 4.86 (95% CI 3.60–6.57), 4.63 (95% CI 3.32–6.45), and 2.35 (95% CI 1.92–2.88), respectively, for THA. Results were similar for patients undergoing TKA. Independent predictors of mortality were pulmonary hypertension, advanced age, male gender, Deyo comorbidity index, and emergency surgery. Mortality rates were approximately three times higher for patients with primary pulmonary hypertension than for those with secondary pulmonary hypertension.

Implications for Clinical Practice. This is by far the largest study of the importance of pulmonary hypertension as a risk factor for perioperative morbidity and mortality. Three previous studies^{8–10} contained a total of 236 patients. Mortality rates among patients with pulmonary hypertension undergoing noncardiac surgery in these reports ranged from 7% to 10%. Important limitations of the study include the use of ICD-9 coding to identify cases (which may fail to capture all cases), the potential for disease misclassification, and lack of data on disease severity. Strengths of the study are the large number of subjects and the use of mortality as an outcome. It is unknown if clinically unapparent pulmonary hypertension carries the same risk or if we should screen for pulmonary hypertension in patients with risk factors for the disease before surgery. Finally, this study does not establish which interventions, if any, reduce this risk. Based on this study, clinicians should consider pulmonary hypertension, both primary and secondary, as an important patient-related predictor for mortality and venous thromboembolic complications.

Prediction of Postoperative Pulmonary Complications in a Population-Based Surgical Cohort. Canet J, Gallart L, Gomar C, et al. *Anesthesiology* 2010;113:1338–1550. Few large prospective studies exist that examine potential risk factors for postoperative pulmonary complications (PPC). In this study, Canet and colleagues prospectively evaluated a random sample of 2,464 patients undergoing non-obstetric inpatient surgery in 59 hospitals in Spain (to create a risk prediction model for PPC). Before surgery, anesthesiologists administered a standardized questionnaire to collect information on demographic characteristics and potential

risk factors. The authors used an explicit set of definitions for PPC that included respiratory infection, respiratory failure, pleural effusion, atelectasis, pneumothorax, bronchospasm, and aspiration pneumonia. Thirty-three variables were entered into a multivariable analysis.

A total of 242 pulmonary complications occurred in 123 patients (5.0% of all subjects). Respiratory failure was the most common complication (2.6%). Length of stay was substantially longer among patients who developed a PPC than among those who did not (12 vs 3 days). Ninety-day mortality was also significantly greater (24.4% vs 1.2%, $p < 0.001$). Independent predictors of PPC after adjustment were advanced age, preoperative hypoxemia, recent respiratory infection, anemia, high-risk surgical site, prolonged surgery, and emergency surgery. The authors constructed a weighted multifactorial index (Table 1) that performed well; the area under the receiver operating characteristic curve was 0.90 for the development subsample and 0.88 for the validation cohort. PPC rates in the validation sample were 1.6%, 13.3%, and 42.1% for low, intermediate, and high-risk scores.

Implications for Clinical Practice. This is the largest prospective study of PPC risk factors that used a structured instrument to capture potential factors in a uniform fashion. This study reconfirms factors identified in the 2006 American College of Physicians guideline including advanced age, high-risk surgical site, prolonged surgery, and emergency surgery.¹¹ Novel factors are preoperative oxygen desaturation, preoperative anemia, and recent respiratory infection. When compared to the most robust existing multifactorial risk index for respiratory failure, from the NSQIP database,¹² overall PPC rates are higher in each group largely because of the inclusion of minor complications of minimal clinical significance (for example, new wheezing treated with bronchodilators). The

index is, however, much simpler to use and has only 7 factors rather than 28 factors. The study reconfirms the morbidity and high mortality of PPC. While it may overestimate the risk of serious PPC, this study is an important advance in our ability to stratify PPC risk before surgery. It is an appropriate tool to guide decision-making and informed consent discussions with patients.

Perioperative Medication Management

Timing of Pre-Operative Beta-Blocker Treatment in Vascular Surgery Patients. Flu W, van Kujik J, Chonchol M, et al. *J Am Coll Cardiol* 2010;56:1922-9. Studies of prophylactic perioperative beta-blockers have yielded mixed results. The reported benefit has varied because of factors including the specific agent, dosing schedule, timing of initiation, patient population, and surgical procedure. In this retrospective, observational study, Flu and colleagues evaluated the timing of beta-blocker initiation in 940 patients undergoing vascular surgery. Exclusions included emergency surgery, preoperative bradycardia (<50 beats/min), and participation in previous beta-blocker trials. The primary outcomes were 30-day cardiovascular events (composite of myocardial ischemia or infarction, stroke, and mortality) and long-term mortality.

Investigators stratified patients into three groups based on the duration of preoperative beta-blocker use: <1, >1 to 4, and >4 weeks before surgery. Bisoprolol was used in 70% of the patients. Median baseline heart rates (74, 70, and 66 beats/min, respectively) were lower in patients whose treatment was initiated >1 week before surgery ($p < 0.001$), but hsCRP was not significantly different. Treatment for >1–4 and >4 weeks before surgery was associated with a lower incidence of 30-day cardiac events (OR 0.46; 95% CI 0.27–0.76 and OR 0.46; 95% CI 0.29–0.79, respectively) and long-term mortality (HR 0.52; 95% CI 0.21–0.67 and HR 0.50; 95% CI 0.25–0.71) when compared to treatment initiated <1 week preoperatively (Table 2) for both high-risk and intermediate risk procedures.

Implications for Clinical Practice. This study demonstrated improved postoperative outcomes for patients who received beta-blockers for at least 1 week before surgery, presumably

Table 1. Seven Independent Predictors of Postoperative Pulmonary Complications and Associated Weighted Risk Score

	Adjusted OR (95% CI) n=1,624	Risk score
Age, years		
• ≤50	1	
• 51–80	1.4 (0.6–3.3)	3
• >80	5.1 (1.9–13.3)	16
Preoperative SpO ₂ , %		
• ≥96	1	
• 91–95	2.2 (1.2–4.2)	8
• ≤90	10.7 (4.1–28.1)	24
Respiratory infection in the last month	5.5 (2.6–11.5)	17
Preoperative anemia (≤10 g/dl)	3.0 (1.4–6.5)	11
Surgical incision		
• Peripheral	1	
• Upper abdominal	4.4 (2.3–8.5)	15
• Intrathoracic	11.4 (4.9–26.0)	24
Duration of surgery, h		
• ≤2	1	
• >2 to 3	4.9 (2.4–10.1)	16
• >3	9.7 (4.7–19.9)	23
Emergency procedure	2.2 (1.0–4.5)	8

CI=confidence interval; OR=odds ratio; PPC=postoperative pulmonary complications; SpO₂=oxyhemoglobin saturation by pulse oximetry breathing air in supine position

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Table 2. Timing of β-Blocker Initiation Before Surgery and Postoperative Outcome

Postoperative outcome	0–1 weeks (n=158)	>1–4 weeks (n=393)	>4 weeks (n=389)	p value (0–1 week vs combined >1–4 and >4 weeks)
30-day outcome	n (%)			
Troponin-T release	40 (25)	54 (14)	56 (14)	0.032
Mortality	6 (4)	8 (2)	11 (3)	0.495
Stroke	3 (1.9)	2 (0.5)	2 (0.5)	0.021
Cardiovascular events	42 (27)	58 (15)	62 (16)	<0.001
Long-term outcome				
Mortality	30 (19)	55 (14)	57 (15)	0.039

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related to better heart rate control. The increased incidence of perioperative stroke among patients who received beta blockers for <1 week before surgery is similar to the findings of the POISE trial, in which stroke rates were increased when beta blockers were started on the day of surgery.⁴ In all previous clinical trials that failed to show a benefit, beta-blockers were also started <1 week before surgery; this may account for the conflicting results. These findings support the European Society of Cardiology guidelines,¹³ which recommend initiation of beta-blocker treatment between 1 week and 30 days before surgery, and the American College of Cardiology guidelines,¹⁴ which suggest starting beta-blockers days to weeks before elective surgery.

Risk of Intraoperative Hypotension with Loop Diuretics: A Randomized Controlled Trial. Khan NA, Campbell NR, Frost SD et al. *Am J Med* 2010;123:1059.e1-1059.e8. The data on preoperative medication management are limited. Medications that affect blood pressure, such as diuretics, are of particular concern, yet wide variation of practice exists on the management of these agents prior to surgery. In a double-blind, randomized, placebo controlled trial, Khan et al. compared the effects of continuing or withholding furosemide on the day of noncardiac elective surgery on intraoperative hypotension among chronic users of furosemide. Secondary outcomes included the risk of congestive heart failure (CHF), a composite cardiovascular (CV) event, and change in renal function and electrolytes.

Of the 212 patients enrolled, 193 underwent surgery. The mean age was 67 years, and two thirds of the patients were female. The most common indications for furosemide were hypertension and edema; only 19% of patients received this medication for congestive heart failure. Intraoperative hypotension (defined as systolic blood pressure <90 mmHg or mean arterial pressure <35% from baselines, or use of a vasopressor agent) occurred in 49% in the furosemide group as compared to 52% in the placebo group [relative risk 0.95 (95% CI 0.72–1.24) $p=0.78$]. In addition, no significant differences were present for CV events, CHF, electrolytes, and renal function.

Implications for Clinical Practice. To our knowledge, this is the first randomized controlled trial to evaluate the safety of continuing a medication on the morning of surgery. It appears the feared risk of loop diuretics causing intraoperative hypotension is theoretical as no significant difference in blood pressure occurred. This trial consisted of a patient population undergoing a wide variety of surgeries and different anesthetic techniques. Although this study was adequately powered to detect significant differences in intraoperative blood pressure, the secondary endpoints should be interpreted with caution as it was underpowered to evaluate differences for these outcomes. Given these findings, physicians may choose to either hold or continue furosemide on the day of surgery without fear of causing an appreciable effect on intraoperative hemodynamics.

Venous Thromboembolism

Preoperative Placement of Inferior Vena Cava Filters and Outcomes After Gastric Bypass Surgery. Birkmeyer NJ, Share D, Baser O, et al. *Ann Surg* 2010;252:313-318. Approximately 200,000 patients undergo bariatric surgery in the US each

year. These bariatric surgery patients are at high risk for postoperative venous thromboembolism (VTE), with pulmonary embolism being the second leading cause of perioperative death after anastomotic leak.¹⁵ Whether VTE prophylaxis in bariatric surgery should include preoperative inferior vena cava (IVC) filters is controversial.

In this study, investigators used a large, prospective, externally audited clinical registry involving 20 Michigan hospitals to evaluate variability in the use and outcomes of IVC filters in gastric bypass surgery patients. They identified 6,376 patients undergoing gastric bypass surgery between 2006 and 2008. They then assessed relationships between IVC filter placement and complications within 30 days of surgery using propensity scores and fixed effects logistic regression to control for potential selection bias. A total of 542 gastric bypass patients (8.5%) underwent preoperative IVC filter placement, most of whom (65%) had no history of VTE. The use of IVC filters varied widely across hospitals (range, 0%–34%). Patients who received an IVC filter had similar rates of postoperative VTE (OR 1.28; 95% CI 0.51–3.21), serious complications (OR 1.40; 95% CI 0.91–2.16), and **death/permanent disability (OR 2.49; 95% CI 0.99–6.26)**. More than half (57%) of the IVC filter patients who experienced death/permanent disability had a fatal pulmonary embolism or complications directly related to the IVC filter itself, including thrombosis of the vena cava or filter migration. The authors concluded that prophylactic IVC filters for gastric bypass surgery do not reduce the risk of pulmonary embolism and may lead to additional complications.

The most important limitation of this study is potential selection bias. Although the authors used propensity score methods to minimize the risk of confounding, unknown variables (i.e., the presence of a thrombophilia) are not accounted for. Other limitations include a lack of statistical power to demonstrate significant harm associated with IVC filter use, no reported data on the type of IVC filters used, and the absence of long-term follow-up, which may underestimate the potential harm of IVC filters over time.

Implications for Clinical Practice. Routine use of prophylactic IVC filters for before gastric bypass surgery provides no clinical benefit and confers increased rates of major complications. Furthermore, among patients who receive prophylactic IVC filters, half of all cases of death or permanent disability were directly related to the device itself. Aside from their potential risks, IVC filters increase the cost of care. The authors concluded that excess costs attributable to preoperative IVC filter placement in bariatric surgery patients may total 250 million dollars in the US annually. Pending further study, clinicians should not recommend routine use of IVC filters before bariatric surgery.

Conflict on interest: Paul J. Grant and Steven L. Cohn - None Disclosed. Amir K. Jaffer consultant for Sanofi-Aventis, Ortho-McNeil, Canyon Pharmaceuticals, Daiichi Sankyo, and Otsuka Pharmaceuticals. Gerald W. Smetana Stock ownership/options in Anvita Health.

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