Defining higher-risk surgery

Gareth L. Ackland[a] and Mark Edwards[b]

[a]Department of Medicine, Wolfson Institute for Biomedical Research and [b]Centre for Anaesthesia, Critical Care and Pain Medicine, University College London Hospitals, University College London, London, UK

Correspondence to Gareth L. Ackland, PhD, FRCA, Department of Medicine, Wolfson Institute for Biomedical Research, Cruciform Building (Wing 3.2), University College London, London WC1E 6BT, UK
E-mail: g.ackland@ucl.ac.uk

Current Opinion in Critical Care 2010, 16:339–346

Purpose of review
Defining the contemporary high-risk noncardiac surgical population using objective clinical outcomes data is paramount for the rational allocation of healthcare resources, truly informed patient consent and improving patient-centered outcomes.

Recent findings
Data from independent healthcare systems have identified that the development, and consequences, of postoperative morbidity extend beyond the immediate postoperative hospital period and confer substantially increased risk of death. Cardiac insufficiency, rather than the relatively heavily explored paradigm of perioperative cardiac ischemia, is emerging as the dominant factor associated with excess risk of prolonged postoperative morbidity. The development of prospective, validated, time-sensitive morbidity data collection tools has also helped define patients at higher risk of noncardiac morbidities and short-term perioperative outcomes.

Summary
Higher risk surgical patients present an increasingly major challenge for healthcare resource utilization. Detailed outcome studies using validated morbidity tools are urgently required to establish the extent to which postoperative morbidity may be predicted. Robust identification of patients at the highest risk of perioperative morbidity may permit further clinic-to-bench translational understanding of the pathophysiologic mechanisms underlying postoperative organ dysfunction. Defining the high-risk surgical patient population is as critically important for global public health planning as it is for the perioperative team.

Keywords
anesthesia, complications, morbidity, perioperative, postoperative

Curr Opin Crit Care 16:339–346

1070-5295

Introduction

Different, largely cultural viewpoints define the high-risk surgical patient. Defining precise, individualized perioperative risk is partly contingent on consensus among several stakeholders in the perioperative process [1]. This presents a critical obstacle in defining relative risk (RR). Although patient-centered outcomes may hinge upon the ability to return to work or the legacy of disability, the perioperative team may view relatively short-term, healthcare cost-insensitive measures as critical to gauging risk. Nevertheless – and now beyond question – postoperative morbidity and mortality in an ageing population undergoing increasingly complex surgery presents an immense, expanding healthcare challenge. Previous projections for cardiovascular complications alone associated with noncardiac surgery [2] have been underestimated [3,4•]. Here, we consider recent data that redefine the high-risk surgical population, based upon pivotal studies exploring the impact of postoperative complications on short-term and longer term mortality. Several factors that hamper a clearer characterization of the higher risk surgical population will be considered.

Postoperative mortality is a major source of hospital death

Typical contemporary mortality rates for various major surgical procedures [5,6] are similar to community-acquired pneumonia [7] and even worse than acute coronary syndromes [8,9], both common, arguably higher profile hospital-treated disorders. A prospective 13-year observational study of the Whitehall II cohort [10••] of 6478 British civil servants aged 35–55 years examined the link between diagnoses associated with medical absence from work and long-term all-cause mortality. Physician-certified sickness absence attributable to undergoing a surgical operation was associated with a more than two-fold increased risk of mortality. Apart from circulatory disease, surgery was associated with the highest risk of later death compared with psychiatric, infectious and respiratory disease. Moreover, mortality was not associated with increased sickness absences occurring shortly before death.

High-risk as defined by mortality in the noncardiac surgical population is brought into further sharp focus by comparison to cardiac surgery. Internationally, mortality following noncardiac surgery frequently exceeds that of coronary artery bypass grafting [11–13]. The majority of adverse noncardiac surgical outcomes are sustained by a large minority of patients [6]. In surgical procedures known to have a mortality of greater than 5% in the UK, elderly patients (mean age 75 years) and emergency procedures account for over 80% of deaths but less than 15% of total procedures [6]. However, focussing on mortality alone underestimates substantially the magnitude of the high-risk surgical population. This renders many preoperative risk assessments associated with mortality/morbidity, including American Society of Anesthesiologists grade [14] and Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity (POSSUM) [15], to be limited, subjective and lacking sensitivity/specificity for the identification of individual patients at risk of postoperative complications.

High-risk should be defined by the incidence of postoperative morbidity

Recent data focussing on perioperative morbidity – a relatively new, critical and welcome addition to this literature – have helped redefine the high-risk population (Table 1 [16–23,24•,25–29]).

The American College of Surgeons Department of Veterans Affairs National Surgical Quality Improvement Project (NSQIP) has been pivotal in furthering the definition of the high-risk noncardiac surgical patient [30], although the definitions of preoperative risk factors are nonscaled and discrete, which may limit more sensitive definitions of the higher risk population. The impact of postoperative morbidity as defined by NSQIP on 30-day and longer term mortality was analyzed in 105 951 Veterans Administration patients followed up for an average of 8 years [25]. Complications of any type occurred in approximately 15% of patients. This proportion of patients is strikingly similar to that reported across a range of international studies in the UK [10••], Australia [31] and USA [22,23,32], including another prospective NSQIP study [24•] in which approximately 17% of 84 730 general and vascular surgical patients sustained major postoperative complications. Further evidence for the extent of postoperative morbidity, as defined by unplanned rehospitalization, is provided by the Medicare Provider Analysis and Review [33•] of 11 855 702 Medicare beneficiaries. Again, over 15% of Medicare patients undergoing a surgical procedure were rehospitalized within 30 days, ranging from 15% (major orthopedic and gastrointestinal surgery) to 25% (vascular) of patients. Within 90 days, more than 27% of surgical patients had been rehospitalized, a further 3% had died during this period. Among patients who were rehospitalized within 30 days after a surgical discharge, more than 70% were rehospitalized for a medical condition. Cardiovascular, pulmonary, gastrointestinal, infectious and nutritional morbidities chiefly characterized these unplanned rehospitalizations. These data are important, as they permit more meaningful international comparisons, which are usually predicated on short-term, in-hospital outcomes.

The persistent increased risk of developing postoperative morbidity beyond the hospital period is reinforced by compelling data derived from the prospective Million Women Study [34••] of 947 454 middle-aged women. The postoperative risk of venous thromboembolism peaked about 3 weeks after surgery, but persisted up to 12 weeks postoperatively, with thromboembolism occurring in approximately 2% of all women who underwent surgery. Although inpatient, joint replacement and cancer surgery were associated with greater risk than day case procedures, venous thromboembolism remained a significant threat even after ambulatory surgery. Incidence rates for venous thromboembolism in the first 6 postoperative weeks were over 100 times the rates without surgery, and 7–12 weeks after inpatient surgery rates remained almost 20 times higher than without surgery.

Thus, more than 15% of inpatient surgical patients sustain postoperative morbidity; more than 50% of complications are classified as serious. The development of any postoperative complication within 30 days of surgery was the most important predictor of 30-day mortality (Table 2) and the third most important predictor of long-term mortality, following age and nutritional status [25]. The presence of any specific complication (except superficial wound infection) reduced median life expectancy from 18.4 to 9.6 years. Postoperative complications appeared to be independent of preoperative risk factors. Whether competing-risk analyses [35] would alter the interpretation of many of these findings remains unclear.

Smaller scale studies demonstrate similar short-term and longer term associations. Postoperative complications [as defined by International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) codes] following hepatectomy or esophagectomy resulted in approximately nine-fold increased RR for in-hospital mortality (13.4%) and prolonged hospital stay [26]. The occurrence of a defined postoperative complication or requirement for postoperative critical care has also been associated with a marked increase in hospital admissions per patient-year after the index episode of critical illness [36,37] and reduced 5–10-year disease-free and overall

Table 1 Variety of methods used to describe postoperative morbidity in recent cohort studies

Reference	Original or review	Descriptors of morbidity	Source of morbidity information	Surgical population	Number of patients	Overall morbidity described	Severity of complications described?	Time points described?	Duration of follow-up	Mortality?
Strasberg *et al.* [16,17]	Review	T92 and variants (Sloane–Kettering Memorial, Clavien-Dindo)	Various	Various: 75% general, 16% urology, 7% gynecology and 2% others	44 600 (129 studies; median 152, range 10–2775)	Varies with study; 8792 complications described in entire group	Yes	No	Variable	Included as part of severity score, rates vary between studies
Bennett-Guerrero *et al.* [18]	Original	POMS morbidity domains	Prospective, blinded data collection	Various major elective noncardiac surgery	438	26% of all patients on POD 8	No	Yes, days 5, 8 and 15	15 days	1.6%
Grocott *et al.* [19]	Original	POMS morbidity domains	Prospective data collection	Various major elective noncardiac surgery	439	31% of all patients on POD 8	No	Yes, days 3, 5, 8 and 15	Morbidity: 15 days, hospital discharge. Mortality	1.4%
Ackland *et al.* [20]	Original	POMS morbidity domains	Prospective data collection	Elective lower limb arthroplasty	129	9% of all patients on POD 8	No	Yes, days 5 and 8	Morbidity: 15 days. Mortality: hospital admission	0%
McNicol *et al.* [21]	Original	11 predefined major complication diagnoses	Prospective data collection	Various major elective noncardiac surgery	1102	20%	All classified as major	No	Duration of hospital mortality	6% 30-day mortality
Liu and Leung [22]	Original	Predefined complications	Retrospective data collection	Noncardiac surgery in patients >80 years	367	25%	No	No	In hospital mortality	4.5%
Turrentine *et al.* [23]	Original	NSQIP-defined complications	Retrospective analysis of prospectively collected data	Single-center general, thoracic and vascular elective and emergency surgery	1628	28% (50% >80 years)	No	No	30 day hospital mortality	5%
Ghaferi *et al.* [24•]	Original	Specific NSQIP-defined complications	Retrospective analysis of prospectively collected clinical database (NSQIP)	Major general and vascular surgery with mortality >1%	84 730	24–28% all complications, 15–18% major complications	Certain complication excluded from analysis of 'major' complications	No	30 days	3.5–6.9% at 30 days across hospital mortality quintiles
Khuri *et al.* [25]	Original	Specific NSQIP-defined complications	Retrospective analysis of prospectively collected clinical database (NSQIP)	8 major general, vascular and orthopedic procedures	105 951	18% of all patients with any 30-day complication	No	No	Morbidity, 30 days; mortality, up to 8 years via BIRLS database	3% at 30 days, 36% within the study follow-up
Dimick *et al.* [26]	Original	12 specified ICD-9-CM-coded complications	Retrospective analysis of prospectively collected clinical database (Maryland hospital discharge database)	Esophagectomy and hepatectomy	935	38.4%	No	No	Hospital admission	6.1%
Dimick *et al.* [27]	Original	ICD-9-CM codes	Retrospective analysis of US Nationwide Inpatient Sample administrative database	Esophagectomy, pancreatectomy, AAA repair	17 878	30–51% esophagectomy, 6–12% pancreatectomy, 9–18% AAA	No	No	Hospital admission	2.5–19% depending on operation and occurrence of a complication
Ghaferi *et al.* [28]	Original	Eight specified ICD-9-CM-coded complications	Retrospective using Medicare claims database (MEDPAR)	Pancreatectomy, esophagectomy, AAA, CABG, aortic valve or mitral valve replacement	269 911	33–36%	No	No	Hospital admission	3–8% at 30 days across hospital mortality quintiles
Bailey *et al.* [29]	Original	Predefined NSQIP complications	Prospectively collected clinical database (NSQIP)	Esophagectomy	1777	50%	No	No	30 day	10%

AAA, abdominal aortic aneurysm; BIRLS, Beneficiary Identification and Records Locator Subsystem; CABG, coronary artery bypass grafting; ICD-9-CM, International Classification of Disease, Ninth Revision, Clinical Modification; MEDPAR, Medicare Provider Analysis and Review; NSQIP, National Surgical Quality Improvement Project; POD, postoperative day; POMS, Postoperative Morbidity Survey.

Table 2 The relative importance of preoperative, intraoperative and postoperative variables for 30-day and long-term mortality

Rank	30-day mortality	Long-term survival
1	Any complication	Age
2	ASA class	Albumin (g/dl)
3	Emergency surgery	Any complication
4	Albumin (g/dl)	ASA class
5	RBC units intraoperatively	BUN >40 mg/dl
6	Age	History of COPD
7	Sodium <135 nmol/l	Smoking
8	Disseminated cancer	Diabetes
9	BUN >40 mg/dl	Functional status
10	SGOT >40 IU/ml	Disseminated cancer

ASA, American Society of Anesthesiologists; BUN, body urea nitrogen; COPD, chronic obstructive pulmonary disease; RBC, red blood cell; SGOT, serum glutamic oxaloacetic transaminase. Data from Khuri *et al.* [25].

survival following surgery for malignancy [29,38–45]. Thus, similar to other hospital-treated diseases (e.g. community-acquired pneumonia), many patients may leave hospital with ongoing subclinical inflammation, which is associated with an increased risk of death despite apparent clinical recovery [46•].

Short-term postoperative mortality does not necessarily reflect the incidence of morbidity

Several flaws have emerged in defining high-risk patients through mortality, as highlighted by short-term outcome studies and the impact of process on determining short, and possibly, longer term outcomes. Although postoperative complications may be related significantly with patient factors rather than to quality of care, these associations are not consistent [14]. Despite a two-fold variation in mortality rates between hospitals, ICD-9-CM-defined complication rates, including major complications, were similar across all hospitals (25–35% patients) [24•,28]. The apparent contradictory finding of similar morbidity yet widely varying in-hospital mortality is explained by increasingly compelling data demonstrating the importance of effective management of complications [24•] or 'failure to rescue' an increasingly important factor in determining outcome in critically ill patients [28,47,48]. The frequency of having any complication also partly varies in relation to hospital [27] and surgical [49] volume. These controversial data [50] are significant confounding factors in defining the high-risk patient on the basis of morbidity/mortality data and reinforce the need for the collection of hospital-specific morbidity data. The complete perioperative package of resources, including surgical, anesthesia and nursing [51] expertise and accessibility to high-quality, well resourced postoperative critical care [47,52–54], are all likely to contribute to lower frequency of complications. However, NSQIP analyses suggest that surgical volume should not be substituted for prospectively monitored, risk-adjusted outcomes as a comparative measure of the quality of surgical care or as a definition of risk [55].

Emergence of cardiac insufficiency rather than cardiac ischemia as a marker of high risk

Most of the focus on defining perioperative high risk has previously centered on cardiac ischemic events and mortality attributed to coronary artery disease [56]. These data are biased heavily by patients undergoing vascular surgical procedures [56–58]. The PostOperative ISchemic Evaluation (POISE) trial [59], in which over 40% of 8351 patients underwent vascular surgical procedures, revealed a baseline perioperative myocardial infarction (MI) rate of 5.7%. Although further morbidity data are awaited from the POISE trial, by comparison to other studies, cardiac ischemic morbidity (typically <10%) is greatly outweighed by noncardiac morbidities in the nonvascular surgical population [18–20]. Interestingly, in the modern era of advanced cardiologic diagnosis and intervention for acute MI, the cause of in-hospital death has shifted from cardiovascular to noncardiovascular [60]. Indeed, several contemporary studies in the nonvascular, noncardiac surgical population demonstrate a significant disconnect between the high rates of cardiac ischemic morbidity seen in the vascular surgical population and far lower rates in other surgical subspecialties [61]. An important shift in emphasis has recently targeted cardiac insufficiency, the prevalence of which continues to rise. Two separate retrospective analyses [3,4•] of more than 200 000 patients revealed that US Medicare patients of at least 65 years of age undergoing major noncardiac procedures with preoperative heart failure were around twice as likely to die following nonvascular operations and sustain more (undefined) complications leading to readmission, even compared with patients with established coronary artery disease. These data are consistent with objective preoperative measures of cardiopulmonary insufficiency elicited by cardiopulmonary exercise testing [62,63] and various other assessments of exercise tolerance [64,65] that demonstrate a strong association with increased perioperative morbidity/mortality. If future studies demonstrate an excess association with noncardiac postoperative morbidity, then the implications for redefining the high-risk population are considerable.

Importance of nutritional and renal insufficiency as preoperative risk factors

In addition to preexisting cardiac morbidity, studies in specific surgical subspecialties have identified several preoperative risk factors linked to outcome, although the vast majority have focused predominantly on in-hospital mortality. Serum albumin concentration is a strong predictor of outcome [66,67], whereas chronic renal insufficiency [68–70] is recurrently associated with perioperative cardiovascular mortality and death predominantly in vascular surgical patients, although associations with other morbidities are underexplored. Mild degrees of preoperative anemia or polycythemia are associated with an increased risk of 30-day postoperative mortality and cardiac events in older patients, mostly in men undergoing major noncardiac surgery [71,72]. Surgical complexity [73,74] and the extremes of older age [21–23,31,32] are also linked to poorer outcomes.

The use of novel biomarkers may enhance definition of the high-risk surgical population

Identifying biological variables perioperatively that are associated with robustly defined postoperative outcomes should aid more precise risk stratification, chiefly because they are simple to measure in statistically valid numbers of surgical patients. Elevated postoperative troponin levels are associated with increased risk-adjusted long-term all-cause mortality after major vascular surgery [75–77]. These data echo similar identification of higher risk patients in other medical populations [78]. Caution over this approach is warranted, as various novel plasma biomarkers do not seem to offer any predictive value over traditional risk factors in the general population for cardiovascular morbidity/mortality [79,80]. Given that very few studies have been conducted into how various perioperative assessments, risk scores or both relate to postoperative morbidity, head-to-head comparisons between such tools and novel biomarkers are clearly disappointingly scarce. The benefit of a range of biomarkers may, however, become apparent in the perioperative period simply because several logistic factors conspire to present particular challenges for adequate risk assessment. A lack of timely, objective preoperative assessment [81] or cardiology consultation [82] is common and impairs clear delineation of the epidemiology of the higher risk patient, particularly for emergent surgery. Consistent with recent data on cardiac failure conferring increased risk in noncardiac surgery, meta-analyses [83–85] reveal that raised preoperative brain natriuretic peptide (BNP) is associated with increased cardiac morbidity and mortality after major surgery. The ongoing prospective Vascular Events In Noncardiac Surgery Patients Cohort Evaluation (VISION) study [86] exploring the predictive role of BNP in redefining the high-risk surgical population will likely provide a major advance.

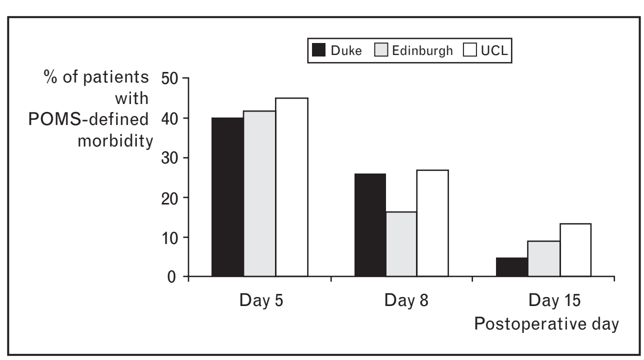
Limitations of retrospective data extraction and nonstandardized definitions of morbidity

The lack of robustly defined postoperative morbidity outcomes [16] along with inconsistency in the quality of reporting over time and between institutions [87] hampers further refinement of the definition of the high-risk surgical population. The critical importance of prospectively acquired, objective, validated, time-sensitive data is reinforced by the poor sensitivity in describing morbidity provided by administrative databases utilizing hospital coding of postoperative complications [88,89]. Electronic patient records could enhance quality data acquisition and identify patients at higher risk of postoperative complications [90]. Although length of hospital stay serves as a useful indicator of outcome, this may be flawed [91].

Timing and severity of postoperative morbidity may refine the definition of higher risk

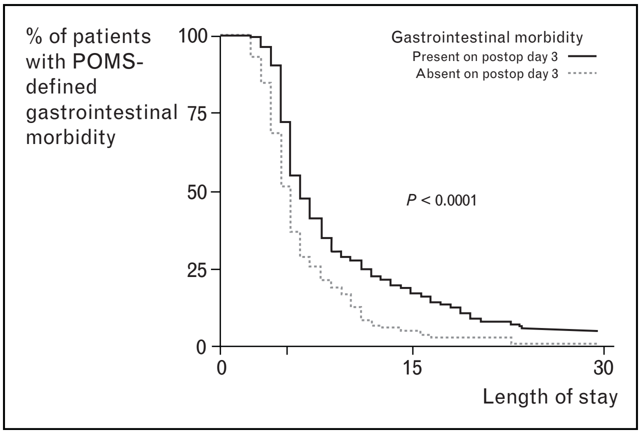
In addition to the type of complication, the severity, timing and patterns of postoperative morbidity are likely to help identify subsets of high-risk patients, although these data are lacking. Over 250 publications, and The Safe Surgery Saves Life Study Group, have employed the Clavien/T92 system [16], or variants thereof [17], as one of the standard composite endpoints in evaluating and improving the safety of surgery. This grading system ranks morbidity by severity based on the therapy (and success thereof) used to treat postoperative complications, the further refinement of which may enhance the definition of higher risk (Table 1). The influence of apparently minor, though common, morbidities on outcome may also be underestimated. Time-sensitive, prospective data collection of short-term postoperative morbidity using the Postoperative Morbidity Survey (POMS) [18,19] has demonstrated that specific patterns of morbidity tend to recur similarly (Fig. 1) across operations and healthcare systems [18–20]. Of these morbidities, gastrointestinal dysfunction – defined by either an inability to tolerate an enteral diet by mouth or feeding tube, nausea, vomiting or abdominal distension – occurs commonly and irrespective of the type of surgery or pain

Figure 1 Postoperative Morbidity Survey-defined morbidity is similar across different healthcare systems (USA vs. UK), hospitals (Duke University Medical Center, Edinburgh Royal Infirmary, University College London Hospitals) and (qualitatively) many types of operation



POMS, Postoperative Morbidity Survey. (■) Duke, (□) Edinburgh and (□) University College London.

Figure 2 Early gastrointestinal morbidity as defined by Post-operative Morbidity Survey – defined by either an inability to tolerate an enteral diet by mouth or feeding tube, nausea, vomiting or abdominal distension – typically occurs in around 30% of patients undergoing nongastrointestinal surgery



Early gastrointestinal morbidity is associated with around more than 4-day delayed hospital discharge. Adapted from data from [20].

medication. Consistent with the hypothesis that gastrointestinal hypoperfusion is a unifying cause of postoperative morbidity [92], gastrointestinal dysfunction is associated with the development of further postoperative complications and prolonged length of stay (Fig. 2) [18]. The concept of a failure to return to normal function – such as ongoing, evolving or both postoperative dysmobility – also needs to be taken into account to define higher risk. The potential importance of physical deconditioning as a consequence of postoperative morbidity is exemplified by substantial data showing that reduced walking speed is associated strongly with subsequent excess cardiovascular mortality [93]. Valid and reliable instruments for assessing health-related quality of life are widely available [94].

Conclusion

The higher risk surgical population remains poorly defined, largely due to the variable outcome measures employed. Critically, our understanding of what constitutes high risk has been transformed by recent data exposing the significant ongoing burden of postoperative morbidity beyond the perioperative period. Lack of data on the trajectory, interrelationships and attendant pathophysiologic processes underlying various postoperative morbidities limits further understanding and translation into predicting short-term and longer term impact. High-quality databases collecting validated, patient-centered outcome data are required urgently to fully define the high-risk surgical population. User-friendly clinical risk scores, perhaps in combination with novel biomarkers, may help define individualized risk more precisely, particularly if longer term morbidity and mortality outcomes are considered. Defining the high-risk surgical patient population is just as critically important for global, public health planning as it is for the perioperative team.

Acknowledgements

This work was supported by an Academy Medical Sciences/Health Foundation Clinician Scientist Award (to G.L.A.) and The Centre for Anaesthesia, Pain Management and Critical Care, University College London grant (to M.E.). This work was undertaken at University College London Hospital/University College London which received a proportion of funding from the UK Department of Health's National Institute for Health Research Biomedical Research Centre funding scheme.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:
- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 395).

1 Boyd O, Jackson N. How is risk defined in high-risk surgical patient management? Crit Care 2005; 9:390–396.

2 Mangano DT. Perioperative medicine: NHLBI working group deliberations and recommendations. J Cardiothorac Vasc Anesth 2004; 18:1–6.

3 Hernandez AF, Whellan DJ, Stroud S, *et al.* Outcomes in heart failure patients after major noncardiac surgery. J Am Coll Cardiol 2004; 44:1446–1453.

4 • Hammill BG, Curtis LH, nett-Guerrero E, *et al.* Impact of heart failure on patients undergoing major noncardiac surgery. Anesthesiology 2008; 108:559–567.

A large retrospective study demonstrating the stronger association of overt cardiac failure rather than coronary artery disease with perioperative adverse outcomes.

5 Birkmeyer JD, Siewers AE, Finlayson EV, *et al.* Hospital volume and surgical mortality in the United States. N Engl J Med 2002; 346:1128–1137.

6 Pearse RM, Harrison DA, James P, *et al.* Identification and characterisation of the high-risk surgical population in the United Kingdom. Crit Care 2006; 10:R81.

7 Kellum JA, Kong L, Fink MP, *et al.* Understanding the inflammatory cytokine response in pneumonia and sepsis: results of the Genetic and Inflammatory Markers of Sepsis (GenIMS) Study. Arch Intern Med 2007; 167:1655–1663.

8 Goodman SG, Huang W, Yan AT, *et al.* The expanded Global Registry of Acute Coronary Events: baseline characteristics, management practices, and hospital outcomes of patients with acute coronary syndromes. Am Heart J 2009; 158:193–201.

9 Fox KA, Steg PG, Eagle KA, *et al.* Decline in rates of death and heart failure in acute coronary syndromes, 1999–2006. JAMA 2007; 297:1892–1900.

10 •• Head J, Ferrie JE, Alexanderson K, *et al.* Diagnosis-specific sickness absence as a predictor of mortality: the Whitehall II prospective cohort study. BMJ 2008; 337:a1469.

A prospective, detailed long-term follow-up study highlighting underappreciated impact of surgical-related deaths, second only to mortality following primary cardiovascular events (MI and stroke).

11 Pagano D, Freemantle N, Bridgewater B, *et al.* Social deprivation and prognostic benefits of cardiac surgery: observational study of 44 902 patients from five hospitals over 10 years. BMJ 2009; 338:b902.

12 Likosky DS, Dacey LJ, Baribeau YR, *et al.* Long-term survival of the very elderly undergoing coronary artery bypass grafting. Ann Thorac Surg 2008; 85:1233–1237.

13 O'Rourke DJ, Malenka DJ, Olmstead EM, *et al.* Improved in-hospital mortality in women undergoing coronary artery bypass grafting. Northern New England Cardiovascular Disease Study Group. Ann Thorac Surg 2001; 71:507–511.

14 Wolters U, Wolf T, Stutzer H, Schroder T. ASA classification and perioperative variables as predictors of postoperative outcome. Br J Anaesth 1996; 77:217–222.

15 Copeland GP, Jones D, Walters M. POSSUM: a scoring system for surgical audit. Br J Surg 1991; 78:355–360.

16 Clavien PA, Strasberg SM. Severity grading of surgical complications. Ann Surg 2009; 250:197–198.

17 Strasberg SM, Linehan DC, Hawkins WG. The accordion severity grading system of surgical complications. Ann Surg 2009; 250:177–186.

18 Bennett-Guerrero E, Welsby I, Dunn TJ, *et al.* The use of a postoperative morbidity survey to evaluate patients with prolonged hospitalization after routine, moderate-risk, elective surgery. Anesth Analg 1999; 89:514–519.

19 Grocott MP, Browne JP, Van der MJ, *et al.* The Postoperative Morbidity Survey was validated and used to describe morbidity after major surgery. J Clin Epidemiol 2007; 60:919–928.

20 Ackland GL, Scollay JM, Parks RW, *et al.* Preoperative high sensitivity C-reactive protein and postoperative outcome in patients undergoing elective orthopaedic surgery. Anaesthesia 2007; 62:888–894.

21 McNicol L, Story DA, Leslie K, *et al.* Postoperative complications and mortality in older patients having noncardiac surgery at three Melbourne teaching hospitals. Med J Aust 2007; 186:447–452.

22 Liu LL, Leung JM. Predicting adverse postoperative outcomes in patients aged 80 years or older. J Am Geriatr Soc 2000; 48:405–412.

23 Turrentine FE, Wang H, Simpson VB, Jones RS. Surgical risk factors, morbidity, and mortality in elderly patients. J Am Coll Surg 2006; 203:865–877.

24 • Ghaferi AA, Birkmeyer JD, Dimick JB. Variation in hospital mortality associated with inpatient surgery. N Engl J Med 2009; 361:1368–1375.
Demonstration of importance of process and system impacting on the interpretation of surgical morbidity.

25 Khuri SF, Henderson WG, DePalma RG, *et al.* Determinants of long-term survival after major surgery and the adverse effect of postoperative complications. Ann Surg 2005; 242:326–341.

26 Dimick JB, Pronovost PJ, Cowan JA, Lipsett PA. Complications and costs after high-risk surgery: where should we focus quality improvement initiatives? J Am Coll Surg 2003; 196:671–678.

27 Dimick JB, Pronovost PJ, Cowan JA Jr, *et al.* Variation in postoperative complication rates after high-risk surgery in the United States. Surgery 2003; 134:534–540.

28 Ghaferi AA, Birkmeyer JD, Dimick JB. Complications, failure to rescue, and mortality with major inpatient surgery in medicare patients. Ann Surg 2009; 250:1029–1034.

29 Bailey SH, Bull DA, Harpole DH, *et al.* Outcomes after esophagectomy: a ten-year prospective cohort. Ann Thorac Surg 2003; 75:217–222.

30 American College of Surgeon's National Surgical Quality Improvement Project; 2010.

31 Story DA, Fink M, Leslie K, *et al.* Perioperative mortality risk score using pre and postoperative risk factors in older patients. Anaesth Intensive Care 2009; 37:392–398.

32 Hamel MB, Henderson WG, Khuri SF, Daley J. Surgical outcomes for patients aged 80 and older: morbidity and mortality from major noncardiac surgery. J Am Geriatr Soc 2005; 53:424–429.

33 • Jencks SF, Williams MV, Coleman EA. Rehospitalizations among patients in the Medicare fee-for-service program. N Engl J Med 2009; 360:1418–1428.
This study highlights the extent of prolonged postoperative morbidity as defined by rehospitalizations, most of which were for medical complications.

34 •• Sweetland S, Green J, Liu B, *et al.* Duration and magnitude of the postoperative risk of venous thromboembolism in middle aged women: prospective cohort study. BMJ 2009; 339:b4583.
Compelling data consistent with the concept that the hyperinflammatory, procoagulant state induced by surgical tissue trauma has a profound impact well beyond the perioperative period, even for apparently minor interventions.

35 Satagopan JM, Ben-Porat L, Berwick M, *et al.* A note on competing risks in survival data analysis. Br J Cancer 2004; 91:1229–1235.

36 Williams TA, Ho KM, Dobb GJ, *et al.* Effect of length of stay in intensive care unit on hospital and long-term mortality of critically ill adult patients. Br J Anaesth 2010; 104:459–464.

37 Williams TA, Dobb GJ, Finn JC, *et al.* Determinants of long-term survival after intensive care. Crit Care Med 2008; 36:1523–1530.

38 Farid SG, Aldouri A, Morris-Stiff G, *et al.* Correlation between postoperative infective complications and long-term outcomes after hepatic resection for colorectal liver metastasis. Ann Surg 2010; 251:91–100.

39 Law WL, Choi HK, Lee YM, Ho JW. The impact of postoperative complications on long-term outcomes following curative resection for colorectal cancer. Ann Surg Oncol 2007; 14:2559–2566.

40 Laurent C, Sa CA, Couderc P, *et al.* Influence of postoperative morbidity on long-term survival following liver resection for colorectal metastases. Br J Surg 2003; 90:1131–1136.

41 Ito H, Are C, Gonen M, *et al.* Effect of postoperative morbidity on long-term survival after hepatic resection for metastatic colorectal cancer. Ann Surg 2008; 247:994–1002.

42 Schiesser M, Chen JW, Maddern GJ, *et al.* Perioperative morbidity affects long-term survival in patients following liver resection for colorectal metastases. J Gastrointest Surg 2008; 12:1054–1060.

43 Chok KS, Ng KK, Poon RT, *et al.* Impact of postoperative complications on long-term outcome of curative resection for hepatocellular carcinoma. Br J Surg 2009; 96:81–87.

44 Rizk NP, Bach PB, Schrag D, *et al.* The impact of complications on outcomes after resection for esophageal and gastroesophageal junction carcinoma. J Am Coll Surg 2004; 198:42–50.

45 Molina de Melo G, Ribeiro KC, Kowalski LP, Deheinzelin D. Risk factors for postoperative complications in oral cancer and their prognostic implications. Arch Otolaryngol Head Neck Surg 2001; 127:828–833.

46 • Yende S, D'Angelo G, Kellum JA, *et al.* Inflammatory markers at hospital discharge predict subsequent mortality after pneumonia and sepsis. Am J Respir Crit Care Med 2008; 177:1242–1247.
A proof-of-principle observational study showing that persistent, subclinical inflammation is associated with higher mortality.

47 Goldhill DR. Preventing surgical deaths: critical care and intensive care outreach services in the postoperative period. Br J Anaesth 2005; 95:88–94.

48 Silber JH, Williams SV, Krakauer H, Schwartz JS. Hospital and patient characteristics associated with death after surgery. A study of adverse occurrence and failure to rescue. Med Care 1992; 30:615–629.

49 Birkmeyer JD, Stukel TA, Siewers AE, *et al.* Surgeon volume and operative mortality in the United States. N Engl J Med 2003; 349:2117–2127.

50 Khuri SF, Daley J, Henderson W, *et al.* Relation of surgical volume to outcome in eight common operations: results from the VA National Surgical Quality Improvement Program. Ann Surg 1999; 230:414–429.

51 Amaravadi RK, Dimick JB, Pronovost PJ, Lipsett PA. ICU nurse-to-patient ratio is associated with complications and resource use after esophagectomy. Intensive Care Med 2000; 26:1857–1862.

52 Bennett-Guerrero E, Hyam JA, Shaefi S, *et al.* Comparison of P-POSSUM risk-adjusted mortality rates after surgery between patients in the USA and the UK. Br J Surg 2003; 90:1593–1598.

53 Jhanji S, Thomas B, Ely A. Mortality and utilisation of critical care resources amongst high-risk surgical patients in a large NHS trust. Anaesthesia 2008; 63:695–700.

54 Dimick JB, Pronovost PJ, Heitmiller RF, Lipsett PA. Intensive care unit physician staffing is associated with decreased length of stay, hospital cost, and complications after esophageal resection. Crit Care Med 2001; 29:753–758.

55 Khuri SF, Henderson WG. The case against volume as a measure of quality of surgical care. World J Surg 2005; 29:1222–1229.

56 Poldermans D, Hoeks SE, Feringa HH. Preoperative risk assessment and risk reduction before surgery. J Am Coll Cardiol 2008; 51:1913–1924.

57 Poldermans D, Bax JJ, Boersma E, *et al.* Guidelines for preoperative cardiac risk assessment and perioperative cardiac management in noncardiac surgery: the Task Force for Preoperative Cardiac Risk Assessment and Perioperative Cardiac Management in Noncardiac Surgery of the European Society of Cardiology (ESC) and endorsed by the European Society of Anaesthesiology (ESA). Eur Heart J (in press).

58 Fleisher LA, Beckman JA, Brown KA, *et al.* ACC/AHA 2007 Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery: Executive Summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery) Developed in Collaboration With the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, and Society for Vascular Surgery. J Am Coll Cardiol 2007; 50:1707–1732.

59 Devereaux PJ, Yang H, Yusuf S, *et al.* Effects of extended-release metoprolol succinate in patients undergoing noncardiac surgery (POISE trial): a randomised controlled trial. Lancet 2008; 371:1839–1847.

60 Roger VL, Weston SA, Gerber Y, *et al.* Trends in incidence, severity, and outcome of hospitalized myocardial infarction. Circulation 2010; 121:863–869.

61 Pearse RM, Dawson D, Fawcett J, *et al.* The incidence of myocardial injury following postoperative Goal Directed Therapy. BMC Cardiovasc Disord 2007; 7:10.

62 Older P, Hall A, Hader R. Cardiopulmonary exercise testing as a screening test for perioperative management of major surgery in the elderly. Chest 1999; 116:355–362.

63 Snowden CP, Prentis JM, Anderson HL, *et al.* Submaximal cardiopulmonary exercise testing predicts complications and hospital length of stay in patients undergoing major elective surgery. Ann Surg 2010; 251:535–541.

64 Reilly DF, McNeely MJ, Doerner D, *et al.* Self-reported exercise tolerance and the risk of serious perioperative complications. Arch Intern Med 1999; 159:2185–2192.

65 Biccard BM. Relationship between the inability to climb two flights of stairs and outcome after major noncardiac surgery: implications for the preoperative assessment of functional capacity. Anaesthesia 2005; 60:588–593.

66 Gibbs J, Cull W, Henderson W, *et al.* Preoperative serum albumin level as a predictor of operative mortality and morbidity: results from the National VA Surgical Risk Study. Arch Surg 1999; 134:36–42.

67 Longo WE, Virgo KS, Johnson FE, *et al.* Risk factors for morbidity and mortality after colectomy for colon cancer. Dis Colon Rectum 2000; 43:83–91.

68 O'Brien MM, Gonzales R, Shroyer AL, *et al.* Modest serum creatinine elevation affects adverse outcome after general surgery. Kidney Int 2002; 62:585–592.

69 Mathew A, Devereaux PJ, O'Hare A, *et al.* Chronic kidney disease and postoperative mortality: a systematic review and meta-analysis. Kidney Int 2008; 73:1069–1081.

70 Seliger SL, Zhan M, Hsu VD, *et al.* Chronic kidney disease adversely influences patient safety. J Am Soc Nephrol 2008; 19:2414–2419.

71 Wu WC, Schifftner TL, Henderson WG, *et al.* Preoperative hematocrit levels and postoperative outcomes in older patients undergoing noncardiac surgery. JAMA 2007; 297:2481–2488.

72 Hogue CW Jr, Goodnough LT, Monk TG. Perioperative myocardial ischemic episodes are related to hematocrit level in patients undergoing radical prostatectomy. Transfusion 1998; 38:924–931.

73 Aust JB, Henderson W, Khuri S, Page CP. The impact of operative complexity on patient risk factors. Ann Surg 2005; 241:1024–1027.

74 Davenport DL, Henderson WG, Khuri SF, Mentzer RM Jr. Preoperative risk factors and surgical complexity are more predictive of costs than post-operative complications: a case study using the National Surgical Quality Improvement Program (NSQIP) database. Ann Surg 2005; 242:463–468.

75 Landesberg G, Shatz V, Akopnik I, *et al.* Association of cardiac troponin, CK-MB, and postoperative myocardial ischemia with long-term survival after major vascular surgery. J Am Coll Cardiol 2003; 42:1547–1554.

76 Kertai MD, Boersma E, Klein J, *et al.* Long-term prognostic value of asymptomatic cardiac troponin T elevations in patients after major vascular surgery. Eur J Vasc Endovasc Surg 2004; 28:59–66.

77 Winkel TA, Schouten O, van Kuijk JP, *et al.* Perioperative asymptomatic cardiac damage after endovascular abdominal aneurysm repair is associated with poor long-term outcome. J Vasc Surg 2009; 50:749–754.

78 Hsieh BP, Rogers AM, Na B, *et al.* Prevalence and prognostic significance of incidental cardiac troponin T elevation in ambulatory patients with stable coronary artery disease: data from the Heart and Soul study. Am Heart J 2009; 158:673–679.

79 Kaptoge S, Di AE, Lowe G, *et al.* C-reactive protein concentration and risk of coronary heart disease, stroke, and mortality: an individual participant meta-analysis. Lancet 2010; 375:132–140.

80 Tzoulaki I, Liberopoulos G, Ioannidis JP. Assessment of claims of improved prediction beyond the Framingham risk score. JAMA 2009; 302:2345–2352.

81 Older P, Hall A. Clinical review: how to identify high-risk surgical patients. Crit Care 2004; 8:369–372.

82 Dudley JC, Brandenburg JA, Hartley LH, *et al.* Last-minute preoperative cardiology consultations: epidemiology and impact. Am Heart J 1996; 131:245–249.

83 Ryding AD, Kumar S, Worthington AM, Burgess D. Prognostic value of brain natriuretic peptide in noncardiac surgery: a meta-analysis. Anesthesiology 2009; 111:311–319.

84 Cuthbertson BH, Amiri AR, Croal BL, *et al.* Utility of B-type natriuretic peptide in predicting perioperative cardiac events in patients undergoing major noncardiac surgery. Br J Anaesth 2007; 99:170–176.

85 Feringa HH, Schouten O, Dunkelgrun M, *et al.* Plasma N-terminal pro-B-type natriuretic peptide as long-term prognostic marker after major vascular surgery. Heart 2007; 93:226–231.

86 Vascular Events In Noncardiac Surgery Patients Cohort Evaluation Study (VISION); 2010.

87 Bruce J, Russell EM, Mollison J, Krukowski ZH. The measurement and monitoring of surgical adverse events. Health Technol Assess 2001; 5:1–194.

88 Romano PS, Chan BK, Schembri ME, Rainwater JA. Can administrative data be used to compare postoperative complication rates across hospitals? Med Care 2002; 40:856–867.

89 Romano PS, Schembri ME, Rainwater JA. Can administrative data be used to ascertain clinically significant postoperative complications? Am J Med Qual 2002; 17:145–154.

90 Vigoda MM, Rodriguez LI, Wu E, *et al.* The use of an anesthesia information system to identify and trend gender disparities in outpatient medical management of patients with coronary artery disease. Anesth Analg 2008; 107:185–192.

91 Alijani A, Hanna GB, Ziyaie D, *et al.* Instrument for objective assessment of appropriateness of surgical bed occupancy: validation study. BMJ 2003; 326:1243–1244.

92 Mythen MG. Postoperative gastrointestinal tract dysfunction. Anesth Analg 2005; 100:196–204.

93 Dumurgier J, Elbaz A, Ducimetiere P, *et al.* Slow walking speed and cardiovascular death in well functioning older adults: prospective cohort study. BMJ 2009; 339:b4460.

94 Ruta D, Garratt A, Abdalla M, *et al.* The SF 36 health survey questionnaire. A valid measure of health status. BMJ 1993; 307:448–449.