OVERVIEW

Perioperative morbidity and mortality is a function of both patient and surgery-specific risk factors. It is imperative to have accurate risk estimation models that allow for shared decision making regarding preoperative risk modification, choice of surgical technique, and resource utilization. The American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) Surgical Risk Calculator was developed based on data from 1,414,006 patients encompassing 1,557 unique CPT codes (1). The model performs well for estimating mortality/morbidity and as both a universal and procedure-specific risk calculator. The ACS NSQIP Surgical Risk Calculator is available as a web-based, easy to navigate application which further improves its utility in the preoperative evaluation of the surgical patient (2).

This chapter will guide the practitioner on the preoperative evaluation of the high-risk patient presenting for surgery with particular emphasis on the cardiac, pulmonary, renal, and neurologic system.

CARDIOVASCULAR

Noncardiac Surgery

Of the approximately 44 million patients undergoing noncardiac surgery in the United States yearly, 30% either have or are at risk for coronary artery disease (CAD). The presence of CAD increases the incidence of perioperative myocardial ischemia, with a 2.8-fold increase in adverse postoperative cardiac events (3). In an attempt to provide current evidence-based recommendations to manage the cardiac patient presenting for noncardiac surgery, the American College of Cardiology/American Heart Association (ACC/AHA) Task Force on Practice Guidelines convened a panel of experts and published a guideline on the perioperative cardiovascular evaluation and management for noncardiac surgery (4); this was revised in 2014. The important aspects of the guideline are to identify high-risk patients, appropriately stratify them according to their risk category, and perform preoperative testing in a rational and cost-effective manner. The guideline emphasizes that no test should be performed unless it is likely to influence patient treatment.

The ACC/AHA approach to cardiac assessment for CAD is a seven-step algorithm that incorporates clinical predictors based on the patient's history and physical examination, surgery-specific risk, and functional capacity (5). Use of the algorithm must occur within the context of the patient's values and preferences to ensure shared decision making. In the event of emergency surgery, risk assessment should occur, and the patient should be taken to surgery (step 1) with further evaluation, if indicated, performed postoperatively.

The presence of heart failure (HF), significant valvular heart disease, or cardiac dysrhythmias may necessitate further evaluation and management prior to elective or urgent surgery. Among HF patients, those with left ventricular ejection fraction (LVEF) less than 30% have significantly worse survival than those with preserved LVEF; however, HF patients with preserved LVEF still have higher mortality rates than patients without HF. Left-sided stenotic valvular lesions also increase cardiac risk, and patients may require surgical or transcatheter valve replacement or percutaneous balloon dilation prior to noncardiac surgery. It should be noted that while percutaneous aortic valve balloon dilation can be performed safely, mortality and recurrence of stenosis remain high within 6 months of the procedure.

In the absence of an emergent procedure, the decision making proceeds to step 2 of the ACC/AHA algorithm with determination of the presence of an acute coronary syndrome (ACS). The management of these patients should be according to existing guidelines for unstable angina/non–ST-elevation myocardial infarction and ST-elevation myocardial infarction (6,7) and is discussed further in Chapter 94.

In the absence of an ACS, the perioperative risk of major adverse cardiac events (MACE) should be estimated in step 3 by integrating the clinical and surgical risks. Both Goldman et al. (8) and Lee et al. (9) devised cardiac risk indices that have been in use for many years. More recently, Gupta et al. (10) analyzed the 2007 NSQIP database, which included over 200,000 patients from multiple centers, to determine significant risk factors for perioperative myocardial infarction or cardiac arrest (MICA) up to 30 days after surgery. Multivariate analysis demonstrated the following variables to be associated with greater risk: American Society of Anesthesiologist (ASA) physical status (Table 53.1), dependent functional status, increasing age, elevated creatinine (>1.5 mg/dL), and type of surgery. With regard to type of surgery, aortic and...
peripheral vascular surgeries are generally associated with the highest risk. With the advent of less invasive endovascular approaches, however, this risk is mitigated. Thus, with continually evolving surgical techniques, it has become challenging to assign surgery-specific risk.

The NSQIP risk model (10) had excellent discrimination, or the ability to discern between those who developed MICA and those who did not, with a C-statistic (area under the receiver operating characteristic curve) of 0.88. When the 2008 NSQIP database was assessed, the risk model continued to perform well, with a C-statistic of 0.87. This was compared to the Revised Cardiac Risk Index, developed by Lee et al. (9), which had a C-statistic of 0.75.

Vascular surgery patients represent a unique cohort, as the incidence of CAD in this population group is disproportionately higher than in the general population. Given the deficiencies of the prior cardiac risk indices in patients undergoing major vascular surgery, Gupta et al. (10) applied their risk model to this patient population and found more modest discrimination, with a C-statistic of 0.75. Two risk calculators, the NSQIP MICA and NSQIP Surgical Risk Calculator (2,10), were subsequently developed as additional tools for the surgical decision-making process and can be accessed online. Although the former only estimates the risk of MICA, the latter includes a wider range of potential complications.

Patients at low risk for MACE (<1%) based on the combined clinical and surgical risk may proceed to surgery without further testing (step 4 of the ACC/AHA guideline), whereas patients with elevated risk for MACE (at least 1%) should have an assessment of functional status (step 5). This is most commonly estimated by activities of daily living and functional capacity, which is expressed in metabolic equivalents (METs). One MET is 3.5 mL/kg/min of O2 consumption in a 70-kg, 40-year-old man at rest. Increasing levels of activity correlate with increasing METs, with activities of daily living or walking at 2 to 3 mph on level ground requiring between 1 and 3 METs and strenuous sports requiring greater than 10 METs. Climbing a flight of stairs or walking uphill is associated with greater than 4 METs. The need for assistance with activities of daily living and inability to perform at least 4 METs are associated with increased perioperative morbidity and mortality (4,11). Therefore, patients with functional capacity of at least 4 METs do not require further testing before surgery.

For those patients with poor (<4 METs) or unknown functional capacity, it should be determined if further testing to delineate cardiac ischemic burden will influence perioperative care (i.e., alter the decision to perform the planned surgery or undergo coronary revascularization if indicated following testing) (step 6). If so, it would be reasonable to order stress testing. If not, it would be appropriate to either proceed to surgery or explore alternate approaches, such as less invasive therapies or palliation (step 7).

Delineation of the ischemic burden can be broadly achieved by two methods. The first method involves coronary vasodilatation and induction of a “steal” phenomenon by pharmacologic agents, followed by a nuclear imaging technique to determine the degree of myocardial ischemia. The second method involves increasing myocardial oxygen demand and evaluating electrocardiographic or echocardiographic data for evidence of ischemia. Myocardial oxygen demand can be increased either by exercise stress testing or pharmacologically with dobutamine or atropine.

Once the degree of myocardial ischemia is quantified, patients can undergo either preoperative medical optimization or revascularization by percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG). The ACC/AHA guideline emphasizes that patients should only undergo revascularization if otherwise indicated by existing clinical practice guidelines for PCI (12) and CABG (13) and not prior to noncardiac surgery solely to decrease perioperative cardiac events. In the Coronary Artery Revascularization Prophylaxis (CARP) trial (14), patients scheduled for elective vascular surgery who had CAD diagnosed by coronary angiography were randomized to revascularization (CABG or PCI) or no revascularization; there was no difference in 30-day and long-term mortality, MI, or stroke.

For patients in whom PCI is indicated, the process involves balloon angioplasty, which is usually followed by placement of either a bare-metal stent (BMS) or a drug-eluting stent (DES); stents reduce both the acute risk of major complications and long-term restenosis rate. Following placement of a stent, patients require antiplatelet therapy to prevent instant thrombosis. Dual antiplatelet therapy (DAPT) is maintained for 1 to 12 months, depending on whether a BMS or DES is placed, respectively. The presence of antiplatelet therapy adds a new dimension of complexity to the patient presenting for noncardiac surgery following PCI. The risk–benefit ratio of preventing thrombosis of the stent versus the risk of catastrophic perioperative bleeding must be carefully weighed. Kaluza et al. (15) reported 7 myocardial infarctions, 11 major bleeding episodes, and 8 deaths in 40 consecutive patients presenting for noncardiac surgery following placement of a stent. All deaths and MIs, as well as 8 of the 11 bleeding episodes, occurred within 2 weeks of coronary stent placement. Wilson et al. (16) reported a 4% incidence of death, MI, or stent thrombosis among 207 patients at the Mayo Clinic; they documented no adverse events in the 39 patients undergoing surgery 7 weeks after stent placement. It appears from these two important studies that the greatest risk of adverse cardiovascular events and bleeding complications occur within 2 weeks of stent placement. According to the ACC/AHA guideline (4), elective surgery should be delayed for at least 14 days after balloon angioplasty and 30 days after BMS implantation to allow for endothelialization of the stent. For patients with a DES, elective noncardiac surgery should ideally be delayed 365 days following DES implantation. Recent data, however, suggest that elective noncardiac surgery may be considered after 180 days following DES implantation (17,18).
**Perioperative β-Blockade Therapy**

Of the pharmacologic agents that have been used during the perioperative period, β-blockade therapy remains the most studied. β-Blockers have several salutary effects that decrease the risk for cardiovascular morbidity and mortality in a selected cohort of patients. β-Blockers help to correct the imbalance between myocardial oxygen demand and supply. They have additional plaque-stabilizing, antiarrhythmic, anti-inflammatory, and altered gene expression effects (19). Much work has been done to assess their impact on perioperative outcomes; however, this has been accompanied by significant controversy. In particular, the Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group (DECREASE)-1 (20) and DECREASE-IV randomized controlled trials and other work by Poldermans have been scrutinized due to concerns for scientific misconduct. Moreover, while the PeriOperative Ischemic Evaluation (POISE)-1 (21) trial included over 8,000 patients, it has been criticized for its β-blocker dosing and timing strategy.

To address these concerns and assess the influence of these trials on overall conclusions, in 2014 the ACC/AHA Task Force on Practice Guidelines published a systematic review evaluating perioperative β-blockade in noncardiac surgery (22). This analysis reviewed 17 studies, with all but one being randomized controlled trials. It was determined that perioperative β-blockade led to a decrease in 30-day or in-hospital nonfatal MI, with a relative risk (RR) of 0.68 compared to control. Excluding the DECREASE trials had minimal effect on the RR. However, β-blockade was associated with a greater risk of nonfatal stroke (RR 1.79); this association remained on exclusion of the DECREASE trials (RR 1.86). Conversely, while the DECREASE trials demonstrated a trend toward reduced all-cause mortality, the remaining studies showed a statistically significant increase in all-cause mortality (RR 1.30). Moreover, β-blockade increased the risk of hypotension and bradycardia. Notably, despite concerns with the POISE-1 trial’s protocol of starting high-dose extended-release metoprolol merely hours prior to surgery, the POISE-1 findings were overall in agreement with the remaining non-DECREASE trials. Thus, with important questions regarding the safety of longer duration perioperative β-blockade looming after exclusion of the DECREASE trials, the only class I recommendation from the ACC/AHA guideline is to continue β-blockade in patients taking these drugs chronically (4). The guideline recommends against starting β-blockade on the day of surgery.

**Cardiac Surgery**

Perioperative and long-term risk evaluation in cardiac surgery is complicated by several factors, including procedural and patient factors as well as data collection. Cardiovascular surgery, with its many confounding variables, requires large patient numbers for studies to be statistically relevant. Appropriate and meaningful data collection has previously been hampered by the reluctance to publish data on high-risk subgroups and the inclusion of data from low-output centers that were not part of a larger data collection network. However, this collection effort has improved, with the Society of Thoracic Surgeons (STS) National Adult Cardiac Surgery Database (NCD) now representing approximately 90% of cardiac surgery providers in the United States (23).

Examining multiple databases, such as the NCD, and large case series, identifies risk factors for cardiac surgery. Unfortunately, many of the assessments of statistical risk are based on odds ratios. In addition, multiple risk factors frequently coexist, making risk profiling for the individual patient difficult. Although patients are presenting cumulatively with more risk factors, the impact of the individual risk factor appears to be decreasing. Data accrued suggest a steady improvement in cardiac surgical outcomes (24). This improvement is attributed to better surgical technique, perioperative care, and patient selection.

**Preoperative Evaluation**

Cardiac risk profiling begins with a thorough clinical evaluation and a review of the completed special investigations. Additional investigations will be guided by the presence and severity of other organ dysfunction. Cardiac risk evaluation can be performed by risk assessment tools, which are based on large databases, such as the European System for Cardiac Operative Risk Evaluation (EuroSCORE) and the STS NCD (23–26). The value of these databases is that standardized definitions are used to classify patients. The risk assessment tools have two important objectives:

1. Identifying independent risk factors for morbidity and mortality in valvular, coronary, and thoracic aortic surgery.

2. Risk prediction modeling through multivariate logistic regression analysis with goals to assess individual patient risk, compare and audit individual units, and appropriately allocate resources.

Statistical analysis techniques have been used to generate scoring systems. The Parsonnet score, developed in the late 1980s, predicts risk for CABG and valvular surgery based on an additive score of weighted risk factors (27). In 1999, Nashef et al. (24) published an additive-weighted scoring system called EuroSCORE based on and validated using the EuroSCORE database; a logistic model was added in 2003 (28). Given the tendency of EuroSCORE to overestimate perioperative mortality (29), EuroSCORE II was developed in 2012 and is based on a cohort of 22,381 patients (25). In modern practice, EuroSCORE II and the STS risk models (21,24) are commonly used for risk assessment.

Important differences exist between EuroSCORE II and the STS risk models. Although EuroSCORE II only assesses mortality risk, the STS risk models additionally include the following outcomes: permanent stroke, renal failure, prolonged ventilation, deep sternal wound infection, reoperation, prolonged postoperative length of stay, and short postoperative length of stay. Moreover, the STS risk models allow the user to specify the particular surgery being performed (e.g., CABG or combined CABG and aortic valve replacement); EuroSCORE II simply assigns isolated CABG a baseline risk and adds “weight” for non-CABG or combined procedures. On the other hand, unlike the STS risk models, EuroSCORE II provides support for thoracic aortic procedures.

Both systems are well calibrated and provide good discrimination for perioperative mortality. When applied to a validation data set of 5,553 patients, EuroSCORE II predicted in-hospital mortality to be 3.95%, while actual mortality was marginally greater at 4.18% (25). The C-statistic was 0.81, demonstrating good discrimination; however, this was not significantly different
from the original EuroSCORE. The STS risk models for CABG, isolated valve, and valve plus CABG surgeries had C-statistics for in-hospital or 30-day mortality of 0.81, 0.80, and 0.75, respectively, when applied to the validation sample (23,26). The performance of the STS risk models varied with regard to the aforementioned morbidity outcomes, but the C-statistics were overall less robust (0.62 to 0.79) than those for mortality.

The strongest risk factors for mortality identified by EuroSCORE II were symptomatic status (i.e., New York Heart Association class IV), prior cardiac surgery, current antibiotic treatment for endocarditis, critical illness preoperatively, decreased LVEF (<31%), emergent or salvage surgery (requiring cardiopulmonary resuscitation prior to anesthetic induction), two or more major cardiac procedures, thoracic aortic surgery, and renal dysfunction. Interestingly, patients on chronic dialysis had lower risk than patients with severe renal dysfunction—creatinine clearance below 50 mL/min—but not yet requiring dialysis.

The important risk factors in the STS risk models were generally consistent with those found in EuroSCORE II, though some definitions were slightly different. Variables with the highest odds ratios for mortality included age of at least 70 years, renal dysfunction—with preoperative dialysis having the greatest risk—severe chronic lung disease, preoperative shock, myocardial infarction within 6 hours, prior cardiac surgery, an emergent or salvage operation, and active infectious endocarditis.

Scoring systems have a role in predicting both perioperative and long-term mortality and intensive care unit (ICU) resource use (30–32). Furthermore, they provide a framework to direct clinical examination and special investigations, thereby facilitating the process of identifying and modifying preoperative risk. These scoring systems can better identify patients with a prohibitive perioperative risk. The EuroSCORE II and STS risk models have been adapted for easy use by clinicians at the bedside and are available online (33,34).

There has been an improvement in the ability to identify and categorize the high-risk patient presenting for cardiac surgery. As more data are accrued, risk profiling is becoming more accurate. This will allow for cost-effective implementation of promising preoperative interventions in the appropriate patient.

PULMONARY SYSTEM

The incidence of postoperative pulmonary complications (PPC) is 5% to 20% for noncardiothoracic surgery (35). The economic burden of perioperative pulmonary complications is significantly higher compared to cardiovascular complications: respiratory (median and IQR): $62,704 ($27,959–135,463) versus cardiovascular: $8,496 ($8,262–56,857) (36). Preoperative identification of the high-risk pulmonary cohort can aid with risk stratification and modification prior to surgery. Currently there exists no standard definition for PPC, which makes risk modeling more variable. Despite the lack of a standard definition, several well-validated studies have been performed that can aid the clinician.

In a systematic review, Smetana et al. (37) identified several important preoperative risk factors associated with PPC after noncardiothoracic surgery. Patient-related factors supported with good evidence include advanced age, ASA Class II, HF, functional dependency, and chronic obstructive pulmonary disease (COPD). Procedure-related factors include vascular, abdominal, thoracic, neurologic, and emergency surgery. Subsequently in a prospective, multicenter observational study, Canet et al. (35) identified low preoperative arterial oxygen saturation, acute respiratory infection during the previous month, preoperative anemia and surgical duration of at least 2 hours as additional risk factors associated with PPC. Finally, Gupta et al. (10), based on a large cohort from the NSQIP database, developed a postoperative respiratory failure risk calculator to facilitate surgical decision making, which can be accessed online (2).

For lung cancer surgery, the STS Database Risk Models developed by Kozower et al. (38) identified pneumonectomy, bilobectomy, ASA rating, Zubrod performance status, renal dysfunction, induction chemoradiation therapy, steroids, age, urgent procedures, male gender, forced expiratory volume 1 (FEV1), and body mass index as risk factors for developing postoperative major morbidity and mortality.

Pulmonary Evaluation

The evaluation of the high-risk pulmonary patient begins with a thorough history and physical examination, which guides further special investigations. Laboratory investigations with good predictive value for PPC include blood urea nitrogen (BUN) greater than 7.5 mMol/L (21 mg/dL), creatinine level greater than 133 μmol/L (1.5 mg/dL) and preoperative anemia (26,35,39,40). In addition, serum albumin below 3.0 g/dL correlates with an increased 30-day perioperative morbidity and mortality (41).

The utility and cost effectiveness of routine preoperative chest radiography has been extensively debated. An abnormal chest radiograph does predict postoperative complications; however, only 4.9% of radiographs in patients younger than 50 years of age will be abnormal. Among routine preoperative chest radiographs ordered, only 0.1% to 3% will alter management (37,42). A focused history and physical examination should identify the patient who is likely to have an abnormal preoperative chest radiograph; this is supported by practice guideline issued by the American College of Physicians suggesting that (37):

1. Only patients with known cardiopulmonary disease should have a routine preoperative chest radiograph.
2. Patients older than 50 years undergoing procedures with high pulmonary risk should have a preoperative chest radiograph. These procedures include aortic surgery (thoracic or abdominal), neurosurgery, abdominal surgery, and prolonged surgery.

The factors listed above for both noncardiothoracic and cardiothoracic surgery can assist the perioperative physician in identifying the high-risk cohort and tailor their management to mitigate postoperative complications.

Pulmonary Function Testing

The three most commonly performed pulmonary function tests include spirometry, measurement of lung diffusing capacity, and measurement of lung volumes. Spirometry and measurement of lung diffusing capacity (DLCO) remain the most commonly utilized pulmonary function tests. For lung resection surgery spirometry, lung diffusing
capacity and cardiopulmonary exercise testing form the cornerstone of the evaluation process prior to surgery (43,44). The perioperative risk of morbidity and mortality and eligibility for surgery is directly related to this three-legged physiologic testing algorithm. Based on the guidelines from the American College of Chest Physicians, the preoperative workup for lung resection surgery begins with an estimation of the postoperative FEV₁ (PPO FEV₁) and DLCO (PPO DLCO) (45). Although threshold limits are used to stratify risk, mitigating factors need to be considered in the decision-making process. Although pulmonary function tests are integral to this workup, concomitant cardiac evaluation using the thoracic-revised cardiac risk index is also recommended; this is based on the high prevalence of cardiac disease in this cohort of patients.

When the PPO FEV₁ and PPO DLCO are greater than 60%, with a negative cardiac evaluation, the patient is considered to be low risk. For PPO FEV₁ and PPO DLCO between 30% and 60%, a stair climb or shuttle walk can be performed to stratify the need for formal cardiopulmonary exercise testing (45). A stair climb over 22 m or shuttle walk over 400 m falls in the low-risk group; when the stair climb is less than 22 m or shuttle walk under 400 m, cardiopulmonary exercise testing is recommended. Finally cardiopulmonary exercise testing is also recommended when PPO FEV₁ and PPO DLCO is less than 30% or with a positive high-risk cardiac evaluation. With cardiopulmonary exercise testing VO₂ max of less than 10 mL/kg/min (35%), 10 to 20 mL/kg/min (35% to 75%), and greater than 20 mL/kg/min (>75%) are classed as high, moderate, and low risk, respectively (45).

Whereas the role of pulmonary function testing prior to cardiothoracic surgery is well defined, its role in the routine preoperative evaluation for noncardiothoracic surgery is controversial and less well defined.

**Preoperative Pulmonary Optimization**

Strategies to reduce PPC begin prior to surgery with identification of patients with high-risk factors that are potentially modifiable. These include smoking cessation, optimization of nutrition, identification and management of obstructive sleep apnea (OSA) and treating acute exacerbations of COPD.

Smoking is associated with a significant increase in PPC, with rates varying between 4% and 43% based on spirometry findings and the length of prior smoking (46,47). Smoking cessation is associated with a significant reduction (20% to 41%) in postoperative complication rates; however, this is contingent on the duration of abstinence and extent of prior smoking. When surgery is elective, smoking cessation should be initiated 4 weeks prior to surgery (48). As previously reported, low preoperative albumin is associated with a higher PPC. Preoperative enteral nutrition with an immune-repleting diet improves outcomes in malnourished elective gastroenterology oncology patients; they experience a significant decrease in nosocomial sepsis and hospital length of stay (49,50). Enthusiasm for total parenteral nutrition is tempered due to the increased rates of parenteral nutrition, identification and management of obstructive sleep apnea (OSA) and treating acute exacerbations of COPD.

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Obstructive pulmonary disorders are associated with increased risk of PPC, especially when reversible airway obstruction is present (37,52,53). However, Millelidge and Nunn (54) demonstrated that even patients with severe airway obstruction—defined as an FEV₁ less than 1 L—can safely undergo an operative intervention without an increase in postoperative complications. The key element in the management of patients with COPD is the identification and appropriate treatment of the reversible component of the airway disease.

β₂-Agonists have a salutary effect on airway hyperreactivity in obstructive airway disease. When symptom-free mild asthmatic volunteers were intubated under local anesthesia, FEV₁ decreased by 50%; in the group pretreated with a β₂-agonist, the FEV₁ decreased by only 20% (55). However, it is important to note that the incidence of postintubation bronchospasm is still significant, even when β₂-agonists are used as monotherapy (36,57).

Preoperative steroid therapy, even of short duration, has been shown to decrease the incidence of wheezing postintubation (57–59). The concern for negative effects on wound healing and increased infection rates have not been borne out (60). With regard to the use of methylxanthines, a Cochrane review in 2001 showed that neither theophylline nor aminophylline offered any advantage over β₂-agonists in the setting of acute bronchospasm (61).

Finally, there is good evidence in adults that upper and lower airway infections increase airway reactivity and result in demonstrable spirometry abnormalities for 6 to 8 weeks postinfection (62). Elective surgery should ideally be delayed in patients with underlying bronchial hyperreactivity and the underlying infection treated.

**Intraoperative Mechanical Ventilation**

There is well-established evidence that lung protective ventilation strategies that reduce excessive volume/pressure and minimizes atelectasis-related injury in ARDS also reduce postoperative morbidity and mortality (63). However, since the publication of this seminal work, there is compelling evidence supporting the extrapolation of this ventilation strategy in patients without ARDS undergoing intermediate to high-risk surgery. Severgini et al. (64) demonstrated that a protective ventilation strategy (VT: 7 mL/kg ideal body weight, 6 to 8 cm H₂O PEEP, recruitment maneuvers) was associated with better postoperative pulmonary function test, higher arterial oxygenation and lower Clinical Pulmonary Infection Score. In a similarly designed study, Futier et al. (65) showed that a protective ventilation strategy (VT: 6 to 8 mL/kg ideal body weight, 6 to 8 cm H₂O PEEP, recruitment maneuvers) was compared to standard therapy (VT: 10 to 12 mL/kg ideal body weight, 6 to 8 cm H₂O PEEP, no recruitment maneuvers) reduced a composite of major pulmonary and extrapulmonary complications (RR, 0.40; 95% confidence interval [CI], 0.24 to 0.68; p = 0.001). Despite the acceptance of protective ventilation strategies in a broader population group, there are still selected cohorts of patients that receive nonprotective
ventilation. Using data from the Multicenter Perioperative Outcomes Group database in 330,823 patients undergoing intraoperative mechanical ventilation, Bender et al. (66) reported that females, obese patients and those of short stature still have a high incidence of large tidal volume ventilation (>Vt: 10 mL/kg ideal body weight). These data suggest that all intermediate- and high-risk patients presenting for surgery be managed with lung protective ventilation with careful consideration of the short, obese and female patient sub-population.

**NEUROLOGIC SYSTEM**

The incidence of perioperative stroke in patients undergoing noncardiac and nonneurologic surgery is 0.1%, but the associated mortality may be as high as 24% (67). Furthermore stroke mortality during the perioperative period is higher than stroke mortality in the community. Previous data on the incidence of perioperative stroke traditionally reported only clinically overt stroke. However, more sensitive tests, such as diffusion-weight MRI (DW-MRI), can detect a much higher incidence of covert stroke, which is reported to be as high as 10%. Covert stroke can impair quality of recovery and long-term cognitive function (68,69).

The risk factors associated with perioperative stroke vary based on the type of surgical procedure—cardiac versus non-cardiac—and preoperative medical comorbidities. The surgical procedure associated with the highest risk of perioperative neurologic injury is cardiac surgery. Contemporary prospective studies report a 3% incidence of stroke in CABG procedures, 8% in isolated valve surgery, and 11% in combined CABG valve surgery. Advanced age and female gender are additional risk factors for perioperative neurologic injury (70). One of the most important factors for cerebral injury during cardiac surgery is macroembolization of atheromatous debris during aortic manipulation. Every attempt should be made to identify the high-risk patient with a large atheromatous burden by using preoperative CT imaging and epiaortic echocardiography to guide placement of the aortic cannula (71).

Nonsurgical factors associated with perioperative stroke include a history of previous stroke/TIA, atrial fibrillation, renal disease, history of dialysis, age 62 years or older, female gender, cardiac valvular disease, smoking, COPD, and an elevated body mass index. Based on several well-conducted studies, carotid stenosis does not increase the risk of perioperative stroke (72,73); however the evaluation of the patient with carotid stenosis requires a thorough assessment of the cardiovascular system. Patients with carotid artery stenosis are at an increased risk of CAD. Severe correctable CAD is evident in approximately 26% of patients with cerebrovascular disease, whereas only 9% of patients have normal coronary anatomy (74). Despite the increased incidence of CAD in patients with carotid stenosis, the rate of medical complications in patients undergoing carotid endarterectomy (CEA) is low. Paciaroni et al. (75) reported that medical complications occurred in less than 10% of patients who underwent CEA, and only 0.4% had severe complications. Furthermore perioperative nonfatal and fatal MI occurred in only 1% of the patients and was associated with a mortality rate of approximately 0.2%. For a more detailed discussion on the preoperative evaluation of the cardiac patient presenting for noncardiac surgery refer to the discussion above.

There is some evidence suggesting a possible association between perioperative β-blockade and stroke, as previously discussed in this chapter. In the POISE trial (21), the metoprolol arm had a higher incidence of stroke (41 [10.0%] vs. 19 [5.0%] patients; 2.17, 1.26–3.74; p = 0.0053) and mortality (129 [3.1%] vs. 97 [2.3%] patients; 1.33, 1.03–1.74; p = 0.0317) compared to the placebo arm. The association between β-blockade and stroke also appears to be dependent on the type of β-blocker, with atenolol and metoprolol having a higher incidence of stroke compared to bisoprolol (76,77). With the extensive use of β-blockade in the perioperative period, the risk of stroke must be carefully evaluated based on the other pre-existing risk factors.

Timing of surgery after a recent stroke requires an evaluation of risk based on the urgency of the procedure and the risk of recurrent stroke. Acute stroke impairs autoregulation and cerebral blood flow becomes pressure passive. The restitution of autoregulation is thought to occur at 1 to 3 months and, ideally, elective surgery should be delayed beyond this period. For a more detailed discussion on the perioperative care of patients at high risk for stroke during or after noncardiac, nonneurologic surgery the consensus statement published by the Society for Neuroscience in Anesthesiology and Critical Care is an excellent resource (78).

**RENAI SYSTEM**

Acute kidney injury (AKI) and chronic kidney disease (CKD) are important medical problems worldwide. Although the incidence of AKI in hospitalized patients ranges from 3.2% to 20%, patients admitted to an ICU have much higher rates, with estimates between 22% and 67% (79). In the United States, the prevalence of CKD has been increasing; in 1988 to 1994, 10.0% of patients had CKD, whereas in 1999 to 2004, this rose to 13.1% (80). This trend can be partially attributed to greater rates of hypertension, diabetes mellitus, and obesity. Consequently, the preoperative evaluation and management of the patient with renal disease is complicated by the coexistence of multiple medical and surgical problems. Therefore a step-wise logical approach to these patients is required to ensure that important data are not omitted.

**Risk Evaluation and Stratification**

Preoperative renal risk evaluation and stratification are based on the comorbid medical condition of the patient, pre-existing renal function, and the procedure-specific renal risk (Fig. 53.1).

**Comorbidity**

Comorbid conditions that increase the risk of chronic renal insufficiency include a spectrum of cardiovascular, endocrine, hepatic, autoimmune, and congenital disorders. The severity, duration, and appropriate management of the conditions determine the degree of renal dysfunction a patient will develop. Diabetes mellitus (DM) and hypertension are the leading causes of end-stage renal disease (ESRD) (81), with glomerulonephritis and polycystic kidney disease being other major diagnoses. DM affects the kidney by several mechanisms resulting in albuminuria, the nephrotic syndrome, and progressive renal failure. Therapeutic measures shown to slow
Pre-Existing Renal Dysfunction

The aforementioned KDIGO guideline defines CKD broadly as “abnormalities of kidney structure or function, present for longer than 3 months, with implications for health” (79). The severity of dysfunction can be assessed by quantifying the level of albuminuria and the glomerular filtration rate (GFR). In particular, a cutoff GFR of 60 mL/min has been established, as complications of CKD tend to increase below this value (83). The GFR can be estimated using either mathematical models, or by determining the clearance of inulin or other filtration markers. Historically, either the Cockroft–Gault equation or the formula derived from the Modification of Diet in Renal Disease (MDRD) Study have been used to estimate GFR (85). A more recently developed equation from the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) investigators has demonstrated less bias and greater accuracy than the MDRD Study equation (86,87) and is recommended in the KDIGO guideline. These estimates of GFR are based primarily on serum creatinine, however, which limits their utility due to various extra-renal influences on serum creatinine. To address this, the CKD-EPI investigators have incorporated cystatin C, a ubiquitous protein eliminated by glomerular filtration and whose serum level is less dependent on extra-renal factors, into newer equations (88,89). The National Kidney Foundation supports an online calculator for GFR estimation (90). Importantly, assessment of GFR in the perioperative setting is challenging, as significant and rapid changes in GFR will not be reflected immediately by the serum creatinine. Thus, use of the above equations should be limited to situations where steady state has been established.

The presence of pre-existing renal dysfunction has a significant impact on perioperative morbidity and mortality. Mathew et al. (91) performed a systematic review and meta-analysis of 31 studies to assess whether CKD predicts mortality and cardiovascular morbidity in noncardiac surgery; the investigation included a large proportion of studies of vascular procedures. The pooled unadjusted odds ratio of 30-day mortality for patients with CKD compared to those with normal renal function was 2.8. When adjusted for potential confounding factors such as DM, CAD, and HF, the odds ratios remained elevated at over 1.4, though the results were not pooled due to heterogeneity. Cardiovascular events including myocardial infarction, HF, and cardiac arrest were also increased in patients with CKD.

Likewise, Mooney et al. (89) undertook a systematic review and meta-analysis but also included studies of cardiac surgery. The vast majority of studies estimated GFR using either the Cockroft–Gault or MDRD Study equations. At an estimated GFR of less than 60 mL/min/1.73 m², patients had an increased risk of postoperative 30-day and long-term mortality, with multivariable adjusted RR of 2.98 and 1.61, respectively. A graded association was discovered between decreasing estimated GFR and increasing odds for 30-day mortality. Recognizing the association between CKD and perioperative mortality and morbidity, various surgical risk prediction scores, including the NSQIP MICA (10), STS risk models (23,26), and EuroSCORE II (25) incorporate an assessment of renal function.

Procedure-Related Risk

Procedure-related renal risk is an important determinant of perioperative renal injury, though risk assessment has been difficult owing to a wide range of definitions for AKI across studies. Cardiac and major vascular procedures are associated with a high risk of AKI, while for patients undergoing noncardiovascular surgery it is much lower. The incidence of AKI following cardiac surgery has been estimated at up to 30%, with approximately 1% of patients requiring renal replacement.
therapy (RRT) (92,93). The development of AKI is associated with increased mortality and perioperative complications; even relatively small postoperative reductions in estimated GFR (i.e., >25%) confer a fourfold greater risk of death (94).

CPB has several negative effects on renal function, though the exact mechanism of injury has yet to be elucidated (95). Nonpulsatile flow, inadequate renal perfusion pressure, and the induction of an inflammatory response all contribute to renal dysfunction. In a meta-analysis of randomized and observational studies, Nigwekar et al. (96) reported a lower risk of AKI with off-pump CABG compared with on-pump surgery. Although in the observational studies there was a reduced requirement for RRT following off-pump surgery, the randomized trials showed no difference. Furthermore, Chawla et al. (92) reviewed the STS database from 2004 to 2009 and found, in patients with CKD, improved in-hospital mortality and decreased need for RRT with off-pump CABG. This benefit was most pronounced in patients with the lowest baseline estimated GFR. Although off-pump approaches certainly are not feasible for many cardiac operations, this data highlights the positive influence that modification of a surgical technique can have on organ protection.

In open vascular surgery, the location of the arterial reconstruction, the duration of the aortic cross-clamp, and the emergent nature of the procedure are all strong predictors of postoperative renal complications. In a retrospective study of 101 patients who underwent thoracoabdominal aortic aneurysm (AAA) repair, nearly 28% developed postoperative renal dysfunction (97). The rate of renal insufficiency for infrarenal abdominal aortic reconstruction tends to be much lower, and was reported to be 1.7% in one single-center study (98). Unfortunately, the definitions for renal dysfunction in these studies specified high thresholds for postoperative change in serum creatinine, so the true incidence of AKI may be higher using modern definitions. The hypothesized mechanisms of postoperative renal injury are ischemia-reperfusion of the kidneys, atheroembolic injury, intravenous contrast-induced nephropathy, and inflammatory damage.

Measures aimed at modifying surgical technique to reduce the incidence of postoperative renal dysfunction in aortic surgery have been met with mixed success. The most significant advance has been the widespread adoption of endovascular techniques for aortic aneurysm repair. Small studies have suggested that the reduced aortic manipulation and renal ischemia that accompany the endovascular technique are associated with reduced inflammation and postoperative renal injury (99,100). A large retrospective cohort study of 6,614 patients with unruptured AAA discovered lower odds (adjusted odds ratio, 0.42) of acute renal failure associated with endovascular aneurysm repair (EVAR) compared to open repair; however, acute renal failure was identified by diagnostic codes rather than conventional biochemical data (101). Conversely, a cohort study based on NSQIP data (102) and the Dutch Randomized Endovascular Aneurysm Management trial (103) showed no significant differences in renal outcomes between EVAR and open repair; further research will be required to establish whether endovascular techniques are truly renoprotective.

Preoperative Evaluation

AKI and CKD are characterized by retention of nitrogenous waste products, fluid and electrolyte abnormalities, acid–base disorders, and impairment of the hematologic and coagulation systems. The preoperative evaluation of these patients must therefore take into account these specific changes and the increased risk they pose during the perioperative period.

The history and physical examination should be directed toward evaluating the severity of the comorbid conditions and the complications related to the renal dysfunction. Uremic patients are at risk for the development of pericarditis and large pericardial effusions, which can be hemodynamically compromising. The presence of an elevated jugular venous pressure and pulsus paradoxus should alert the clinician to the presence of a pericardial effusion.

Uremia is additionally associated with nausea, vomiting, and recurrent episodes of hiccupping, which may place the patient at increased risk for aspiration. Severe nausea and vomiting may result in dehydration, and a thorough evaluation of the patient’s volume status must be performed. These patients may be on intermittent hemodialysis, peritoneal dialysis, or continuous venovenous RRT. Records of the last dialysis, fluid balance, and body weight must be obtained to help with the assessment of the fluid status.

Anemia in renal failure is multifactorial in nature; bleeding from platelet dysfunction, malnutrition, and decreased erythropoietin production all contribute toward the low red cell mass. Electrolyte abnormalities are common in renal failure; hyperkalemia, hyperphosphatemia, and hypocalcemia are the typical electrolyte profiles seen in renal failure. Inadequately treated hyperkalemia confers the risk of developing malignant cardiac dysrhythmias.

Diagnostic Testing

The diagnostic studies in patients with renal dysfunction are determined by the findings on the history and physical examination. Complete blood count helps to assess the severity of the anemia, morphology of the red blood cells, and the platelet count. Although uremic patients may have normal platelet numbers, they develop an acquired platelet dysfunction that results in an increased risk of bleeding. The pathogenesis of this hemostatic dysfunction is multifactorial and includes the effects of circulating toxins, alteration of the vessel wall, and anemia. To assess the degree of platelet function, a platelet function assay can be performed.

The basic metabolic panel helps to determine the electrolyte profile and allows the anion gap to be calculated. AKI and CKD are commonly characterized by an increased anion gap metabolic acidosis. The BUN can be tracked to assess the efficacy of RRT. Due to the limitations of common parameters such as BUN, serum creatinine, and urine output in diagnosing AKI, significant effort has recently been made in the investigation of various novel biomarkers for detecting kidney damage and predicting AKI. Several molecules have been assessed including interleukin-18, kidney injury molecule-1, liver fatty acid-binding protein, neutrophil gelatinase-associated lipocalin, tissue inhibitor of metalloproteinases-2, and insulin-like growth factor–binding protein 7 (104,105). At present, these are not widely used in the preoperative evaluation of patients but will likely have significant utility in the future.

An electrocardiogram (ECG) should be performed to determine whether ischemia, ventricular hypertrophy, or strain pattern is present. Hyperkalemia is characterized by tall peaked T waves, widened QRS complex, and shortened QT interval.
The ECG of patients with pericardial effusion may demonstrate small QRS complexes and the presence of electrical alternans—change in QRS amplitude with each heartbeat. A chest radiograph may reveal signs of pulmonary edema, cardiomegaly, or a large pericardial effusion.

In conclusion, available data convincingly demonstrate that patients with CKD or who develop AKI have worse outcomes than those with normal renal function. Unfortunately, none of the pharmacologic strategies proposed to protect the kidneys in the perioperative period have shown clear benefit (106). Thus, it is important to identify patients at risk for worsening renal function to be able to appropriately counsel those patients and anticipate complications. With definitions for AKI becoming more standardized, such as the AKI Network and KDIGO (107) definitions, future research should be able to provide more robust findings.

SUMMARY

High-risk surgical patients present a unique challenge to the perioperative physician. Because of their multiple comorbidities and the increasing complexity of surgery being performed, their perioperative risk is disproportionately higher than the general surgical population. To appropriately manage these patients, risk factors must be identified and stratified following completion of the clinical, laboratory, and special investigations. Risk-modification strategies may be implemented preoperatively if they are likely to have a beneficial effect during the operative course. Otherwise, they can be initiated postoperatively as part of the long-term care plan for the patient.

Key Points

- Assessment of the high-risk patient begins with preoperative identification, stratification, and modification of risk factors.
- No preoperative test should be performed unless it is likely to influence patient treatment.
- In noncardiac surgery, the ACC/AHA algorithm provides a structured and cost-effective evaluation strategy.
- Scoring systems in cardiac surgery assist with risk profiling, predicting mortality, and resource use.
- Systematic reviews have now defined patient and surgery-specific risk for PPC.
- It is important to assess and treat reversible airway obstruction in chronic obstructive airway disease.
- Patients with CKD are at elevated risk for perioperative morbidity and mortality irrespective of coexisting medical problems.
- The risk of AKI in patients with chronic renal insufficiency is determined by comorbidities, baseline renal function, and procedure-specific risk.
- Effective interventions to prevent AKI in patients at risk have proven elusive. Strategies should be aimed at optimizing renal perfusion and managing the metabolic and hematologic derangements in patients with CKD.
- The prevention of secondary neuronal injury must be the focus of perioperative intervention.

References


46. Chalon S, Moreno H Jr, Benowitz NL, et al. Nicotine impair endothe-


56. Groeben H, Peters J. Corticosteroids and inhaled salbu-

57. Silvanus MT, Groeben H, Peters J. Corticosteroids and inhaled salbu-


59. Pien LC, Grammer LC, Patterson R. Minimal complications in a surgi-


62. Pien LC, Grammer LC, Patterson R. Minimal complications in a surgi-


64. Maslow AD, Regan MM, Israel E, et al. Inhaled albuterol, but not intra-


67. Ng JL, Chan MT, Gelb IW. Perioperative stroke in noncardiac, nonneuro-


69. Ng JL, Chan MT, Gelb IW. Perioperative stroke in noncardiac, nonneuro-

70. Taggart DP, Westaby S. Neurological and cognitive disorders after coro-

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