Management of Common Postoperative Complications

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Abstract

Postoperative complications are common. Major guidelines have been published on stratifying and managing adverse cardiovascular events and thromboembolic events, but there is often less literature supporting management of other, more common, postoperative complications, including acute kidney injury, gastrointestinal complications, postoperative anemia, fever, and delirium. These common conditions are frequently seen in hospital and can contribute to longer lengths of stay and rising health care costs. These complications are often due to the interplay between both patient-specific and surgery-specific risk factors. Identifying these risk factors, while addressing and optimizing modifiable risks, can mitigate the likelihood of developing these postoperative complications. Often, a multidisciplinary approach, including care team members through all phases of the surgical encounter, is needed. Cardiovascular and thrombotic complications have been addressed in prior articles in this perioperative series. We aim to cover other common postoperative complications, such as acute renal failure, postoperative gastrointestinal complications, anemia, fever, and delirium that often contribute to longer lengths of stay, rising health care costs, and increased morbidity and mortality for patients.

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In 2010, there were an estimated 51.4 million surgical procedures performed in the United States.[1] In healthy patients, postoperative complications occur less than 0.1%,[2] but vary by surgical type and patient risk factors. A systematic review found 14.4% of patients undergoing surgery experienced an adverse event,[3] defined as injury from medical management which prolongs length of stay, causes disability at discharge, or both.[4] Of these, 5.2% were considered potentially preventable.[3] Of the adverse events that occur in the hospital, as many as 39.6% are surgically related.[5] Care of the surgical patient commonly includes preoperative evaluation, often during a clinic visit, for risk stratification and medical optimization before surgery.[6] The preoperative evaluation facilitates identification of these risk factors and can help minimize postoperative complications.

Common surgical complications, including thrombotic and cardiopulmonary events, have been addressed in prior articles in this perioperative series. Although adverse cardiac events are considered major postoperative complications, there are other more common postoperative complications, such as acute renal failure, postoperative gastrointestinal complications, anemia, fever, and delirium that represent significant morbidity for patients, leading to longer lengths of stay and increase cost of care.[7-12] The goal of this review is to address these very common postoperative complications.

ASSESSMENT AND MANAGEMENT OF PATIENTS WITH PERIOPERATIVE RENAL DISEASE

Perioperative renal dysfunction, whether it is acute kidney injury (AKI) or pre-existing chronic kidney disease (CKD), is associated with increased morbidity and mortality.[13-16] AKI is a serious and relatively common postoperative complication, with incidence ranging from 18% to 47% of surgical cases.[17] Immediate complications associated with AKI include development of sepsis, anemia,

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TABLE 1. Risk Factors for the Development of Perioperative Acute Kidney Injury

Patient factors	Procedure factors	Perioperative factors
Older age	Emergency surgery	Hypotension
Functional dependence	Cardiovascular surgery	Hypovolemia
Chronic comorbidities	Cardiopulmonary bypass	Blood loss
Chronic kidney disease	Major surgery	Anemia
Obesity	Intraperitoneal	Use of nephrotoxic agents
Diabetes	Transplant	
Cardiovascular disease	Lung resection	
Hepatobiliary disease	Use of contrast dye	
Pulmonary disease		
Steroid use		
Cancer		
Anemia		
Acute comorbidities		
Critically ill/intensive care patients		
Sepsis		
Increased intra-abdominal pressure		

coagulopathy, and need for mechanical ventilation.[14,15] There are several risk factors for postoperative AKI, including patient-specific, procedure-specific, and perioperative factors as outlined in Table 1. Preexisting CKD confers the greatest risk for postoperative AKI.[7,18] AKI is also a significant risk factor for the development of CKD[13,14] as well as an independent risk factor for cardiovascular mortality.[14]

In patients with CKD, perioperative risk is compounded by the presence of comorbid illnesses (cardiovascular disease, hypertension, diabetes, and autonomic dysfunction) and renal disease–associated conditions (anemia, electrolyte and acid base imbalances, altered volume status, coagulopathy, malnutrition, and bone disease). Preoperatively, clinicians should discuss the patient's wishes regarding dialysis in the event renal function worsens unexpectedly. All patients with CKD require preoperative cardiac risk assessment and risk mitigation.

Patients with known CKD have a particularly high risk for major adverse cardiac events with increased morbidity and mortality.[14,16] In a meta-analysis evaluating perioperative risk of death and cardiac events after elective, noncardiac surgery, CKD was identified as an independent risk factor for postoperative death and cardiac events, with a similar strength of association as diabetes, stroke, and coronary disease. The severity of renal disease directly correlated with the risk of postoperative death.[19]

Postoperative AKI is often multifactorial, related to predisposing risk factors and perioperative events, including hypotension, hypovolemia, sepsis, low cardiac output states (heart failure or anesthesia induced), and administration of radiographic contrast.[13,20] The most common cause of postoperative AKI is renal hypoperfusion as a result of transient hypotension and hypovolemia.[21] Surgical patients are predisposed to hypotension due to preoperative fasting (causing fluid depletion), vasodilatory effect of anesthesia, increased insensible losses, blood loss, and third spacing. Patients thought to have normal gastric emptying should be allowed to ingest clear liquids up to 2 hours before anesthesia.[22] Monitoring hemodynamics (with mean arterial pressure goal of greater than 65 mm Hg)[13] and maintaining euvolemia should be prioritized. Ongoing fluid requirements should be assessed carefully. Volume assessment presents a challenge as intraoperative urine output may not be a reliable indicator of fluid balance and intraoperative oliguria does not predict postoperative AKI due to slowed distribution and reduced clearance

of intravenous fluids infused while patients are under anesthesia.[13]

The type of intravenous fluid administered may play a role in causing or preventing AKI. Balanced crystalloid solutions (electrolyte composition resembling plasma) may be preferred over normal saline to avoid hyperchloremic acidosis, which can cause renal vasoconstriction and reduced glomerular filtration rate.[13,17,23-25] Debate remains regarding the use of colloid solutions, although the use of synthetic colloids, such as hydroxyethyl starches, is not recommended due to the association with renal injury.[13,23,26] The use of albumin remains controversial, although there may be a role in certain patient populations (such as patients who are hypoalbuminemic).[13,23]

The presence of anemia, whether pre- or postoperatively, reduces the blood's oxygen carrying capacity and increases the risk for AKI.[13,27] Preoperative hemoglobin should be optimized ideally to normal range for age and sex, or reasonable goal of greater than 12.0 g/dL[28] before elective surgery to mitigate the effect of surgical blood loss and prevent the need for transfusions.

Nephrotoxic agents, including nonsteroidal anti-inflammatory drugs, aminoglycoside antibiotics, and contrast dye should be avoided, if possible. Clinicians should carefully review all antihypertensives preoperatively and consider the potential risks and benefits in the perioperative period. In patients with well-controlled blood pressure, providers should hold angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers, and diuretics preoperatively.[13,28] Furthermore, medications should be dosed appropriately based on the degree of renal function.

In a 2013 Cochrane Database systematic review of interventions to prevent perioperative kidney injury, there was no benefit in mortality or acute renal injury for various pharmacologic interventions, including dopamine, diuretics, calcium channel blockers, ACE inhibitors, N-acetyl cysteine, atrial natriuretic peptide, sodium bicarbonate, antioxidants, or erythropoietin.[20] However, the search for renoprotective strategies continues. Preoperative treatment with high-dose statin has been shown to be effective in reducing the risk of AKI among patients undergoing coronary catheterization[29,30] and procedures with contrast administration[31] with mixed results in major noncardiac surgery.[14,32] The use of dexmedetomidine has also shown promising results in preventing AKI.[17] Additional studies are needed to clarify the effects and recommendations regarding perioperative use of statins and dexmedetomidine to prevent AKI.

Management strategies to prevent AKI focus on optimizing volume status, renal perfusion, oxygen delivery, and avoidance of nephrotoxins. As noted above, preoperative hemoglobin should be optimized ideally to normal range for age and sex or reasonable goal of greater than 12.0 g/dL.[33] Hold antihypertensives, particularly ACE inhibitors, angiotensin receptor blockers, and diuretics preoperatively in patients with controlled blood pressure. Patients thought to have normal gastric emptying should be allowed to ingest clear liquids up to 2 hours before anesthesia.[22] Monitor fluid status closely and maintain euvolemia. Evidence supports the use of crystalloid intravenous solutions. Avoid nephrotoxins throughout the perioperative period when possible.

MANAGEMENT OF PATIENTS WITH GASTROINTESTINAL COMPLICATIONS

Assessment and Management of Postoperative Nausea and Vomiting

One of the most common postoperative gastrointestinal complications is postoperative nausea and vomiting (PONV). PONV is defined as the presence of nausea, vomiting, or retching that occurs in the post-anesthesia care unit to within 24 hours postoperatively.[34] The incidence of PONV ranges from 30% up to 80% and has been shown to be more dreaded by patients than postoperative pain.[34] The consequences of PONV are significant, ranging from direct patient health effects (discomfort, dehydration, aspiration, infection, wound dehiscence, and anxiety) to prolonged post-

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TABLE 2. Medication Options for the Prevention and Treatment of PONV[a]

Drug family	Examples	Clinical pearls
5-HT_3 antagonists	Ondan-, dola-, grani-, or palonosetron	Equally effective; QT prolongation
NK-1 antagonists	Apre-, caso-, or rolapitant	Oral formulation; high cost
Corticosteroids	Dexamethasone or methylprednisolone	Monitor glucose; short duration not associated with wound infection/healing; tumor lysis can occur (rare)
Butyrophenones	Droperidol, haloperidol, or amisulpride	QT prolongation; risk of sudden cardiac death
Antihistamines	Dimenhydrinate, meclizine, or diphenhydramine	Side effects, especially in the elderly
Anticholinergics	Scopolamine (transdermal)	Side effects, especially in the elderly
Phenothiazines	Perphenazine or prochlorperazine	Sedation; extrapyramidal effects; most effective class for opioid-induced nausea and vomiting
Miscellaneous	Propofol, clonidine, mirtazapine, gabapentin, benzodiazepines, or metoclopramide	Varying efficacy; various side effects including sedation, confusion, fall risk, and respiratory depression

[a]5-HT_3 = 5-hydroxytryptamine; NK-1 = neurokinin; PONV = postoperative nausea and vomiting.

anesthesia care unit stay, unplanned hospitalization, delayed return to work, and increased health care costs.[34,35]

PONV is multifactorial, with etiologies categorized as central, peripheral, and miscellaneous causes.[34] Central factors include cortical and medullary effects; peripheral factors include direct gastrointestinal stimulation, trauma, and the cathartic effects of blood; miscellaneous factors include the varied influences of anesthesia and medications. Nausea and vomiting are also mediated by neurotransmitters, including serotonin, dopamine, histamine, acetylcholine, and neurokinin; these are the receptors at which anti-emetics exert their effects.[34,36]

The 2014 Society of Ambulatory Anesthesia (SAMBA) guidelines provide a framework to identify at-risk patients, and to prevent and treat PONV.[34,35] The basic steps include: 1) identifying at-risk patients; 2) reducing baseline risk factors; and 3) providing prophylaxis and treatment if necessary.

There are several patient-specific and procedure-specific factors that have been shown to increase PONV risk. These include female sex, history of PONV, history of motion sickness, nonsmoking status, younger age, usage of general anesthesia, usage of volatile anesthetics or nitrous oxide, the duration of anesthesia, postoperative opioid use, and specific surgical types (cholecystectomy, gynecologic surgeries, and laparoscopy).[34] Based on this information, the SAMBA guidelines recommend a 4-point risk stratification/scoring tool, which was modified from Apfel et al[34,37]: female sex, 1 point; history of PONV/motion sickness, 1 point; nonsmoker status, 1 point; and postoperative opioid use, 1 point. A score of 0 to 1 is considered low risk (10% to 20%); a score of 2 to 3 is intermediate risk (40% to 60%); and a score of 4 is high-risk (80%).

After risk stratification, the SAMBA guidelines recommend modifying identified risk factors and considering prophylaxis based on risk score and treatment based on the presence of nausea and or vomiting. Reducing baseline risk includes using regional anesthesia rather than general anesthesia if possible, use of total intravenous anesthesia with propofol, avoidance of

nitrous oxide, avoidance of volatile anesthetics, minimization of perioperative opioid use, and ensuring adequate hydration. A multimodal analgesic regimen should be employed to reduce opioid use. Opioid use increases the risk of PONV and predisposes to opioid-induced nausea and vomiting, a subtype of PONV, which can last 72 to 96 hours postoperatively.[36] Based on the above scoring tool, the SAMBA guidelines[34,35] recommend the following: a low risk (score of 0-1) indicates no prophylaxis required; an intermediate risk (score of 2-3) indicates use of prophylaxis with one to two interventions/agents; and a high risk (score of 4) indicates multimodal prophylaxis using two or more interventions/agents.

Specific interventions and agents should be based on patient-specific risk factors, comorbidities, potential for adverse effects, history of previous prophylaxis/treatment success or failure, personal preference, and cost. Interventions that can be used for both prophylaxis and treatment of PONV include medications (Table 2), intravenous hydration, acupuncture, massage, aromatherapy (isopropyl alcohol), and acupressure (P6 stimulation).[34-36] Combination therapy has been shown to be more effective than single-agent therapy; this could also include the simultaneous use of pharmacologic and nonpharmacologic options. Given the variety of neurotransmitters involved in mediating nausea and vomiting, clinicians should use medications from different pharmacologic classes to achieve additive beneficial effects. If prophylaxis was unsuccessful, clinicians should select an anti-emetic agent from a different pharmacologic class than what was previously used.

Assessment and Management of Postoperative Ileus

Postoperative ileus (POI) is broadly defined as the temporary cessation of bowel function, which prevents effective transit of intestinal contents. POI is typically a self-limited physiologic response lasting up to 72 hours postoperatively.[38-40] POI is due to nonmechanical factors (a combination of neurogenic or sympathetic-induced dysmotility, inflammatory-mediated dysmotility, and pharmacologic effects), which effectively differentiates this condition from that of bowel obstruction. Although the incidence of POI varies significantly, it occurs in approximately 20% of surgical cases. Consequently, patients who experience POI remain hospitalized approximately 5 days longer than those who do not experience POI.[38-40]

Clinical signs and symptoms concerning for POI include abdominal pain, distention, abdominal bloating, nausea/vomiting, delayed flatus, and an inability to tolerate oral diet. A key differentiating factor between POI and bowel obstruction is that in cases of bowel obstruction, there is often an initial return of bowel function postoperatively before cessation, which is not seen in POI. There are many specific risk factors associated with the development of POI, including male sex, history of chronic constipation, obesity, the use of general anesthesia, abdominal and pelvic surgery, open surgery (as opposed to laparoscopic), perioperative bleeding, the use of perioperative opioids and other antiperistaltic medications, infectious or inflammatory abdominal complications, delayed enteral nutrition, the use of a nasogastric tube, and bowel wall edema.[38-40]

Prevention of POI is ideal and can be facilitated by epidural anesthesia rather than general anesthesia (if feasible), reduction in intraoperative and postoperative opioid use, minimization of direct intestinal trauma perioperatively, and using a minimally invasive surgical approach.[36] Many of these approaches are components of early recovery after surgery protocols. Other nonpharmacologic interventions have been explored with mixed results, including the preventive benefits of postoperative chewing gum, coffee, and early postoperative ambulation.[41-43]

The diagnostic workup for POI should include a detailed medical and perioperative history and serial abdominal examinations. Basic laboratory studies that should be obtained include complete blood count; electrolytes including calcium, magnesium, and

potassium; creatinine; liver enzymes; and lactate. The initial imaging test of choice is a supine and upright abdominal x-ray to differentiate between POI and bowel obstruction or perforation.[44] Computed tomography scan of the abdomen and pelvis with oral contrast has a high sensitivity and specificity (approximately 90% to 100%) for differentiating POI from bowel obstruction, if clinical concern remains.[44] Treatment of POI aims to lessen patient discomfort and minimize the duration of ileus. This consists of a careful review of current medications and discontinuation of any potentially offending (antiperistaltic) agents, implementation of an opioid-sparing multimodal analgesic regimen, intravenous fluids (with a goal to achieve an euvolemic status), bowel rest, electrolyte replacement, and placement of a nasogastric tube for cases of significant abdominal complaints or frequent/continuous vomiting.[36,38,40] Patients with opioid-induced POI may benefit from medications such as alvimopan and methylnaltrexone (peripheral acting mu-opioid receptor antagonists), which function to block peripheral opioid receptors in the gastrointestinal tract but do not cross the blood-brain barrier and thus do not exert any anti-analgesic effects.[36,45] There are conflicting efficacy results and variable adverse effects reported with agents such as metoclopramide, erythromycin, neostigmine, and propranolol.[38-40]

Assessment and Management of Postoperative Gastrointestinal Stress Ulcers

Gastrointestinal stress-related mucosal disease (SRMD) is another perioperative complication that clinicians should be cognizant of, and similar to POI, prevention of SRMD is the ideal goal. The incidence of perioperative SRMD has been shown to be as high as 15%.[46,47] The pathogenesis of SRMD is multifactorial, consisting of a combination of factors affecting or impairing mucosal protection (alterations in splanchnic blood flow, transient perioperative hypotension/reduced cardiac output, hypovolemia, vasoconstriction, catecholamine release, and pro-inflammatory cytokine release) and stress-related hypersecretion of gastric acid.[46,47]

TABLE 3. Stress Ulcer Prophylaxis Criteria[a]

Major risk factors ≥1	Minor risk factors ≥2
Mechanical ventilation >48 h	Gastrointestinal bleed within 1 y
Coagulopathy: INR[a] >1.5 or platelet count <50 × 10^9/L	Head injury with GCS <10 × 10^9/L
	Hepatic or renal failure
	Hepatic or renal transplant
	Spinal cord injury
	Severe burns (>35% SA)
	Multiple trauma with ISS >16
	Partial hepatectomy
	Septic
	Hydrocortisone dose equivalence of >250 mg
	ICU stay >1 wk
	Occult gastrointestinal bleed

[a]INR = international normalized ratio; ICU = intensive care unit; ISS = injury severity score; GCS = Glasgow Coma Scale; SA = surface area.
Data from the American Journal of Health-System Pharmacy[46] and the Eastern Association for the Surgery of Trauma guidelines.[47]

There has been significant effort to better identify and appropriately provide stress ulcer prophylaxis (SUP) to patients who are at high risk for SRMD and who would benefit most from this intervention. Numerous studies have shown extreme variability in SUP prescribing practice, leading to considerable health care costs, adverse effects, and widespread inappropriate use of management strategies.[48-50] To help standardize prescribing habits, clinicians should use consensus guidelines such as the combined American Society of Health-System Pharmacists and the Eastern Association for the Surgery of Trauma guidelines (Table 3).[46,47] According to their recommendations, patients with either one or more "major" risk factors or two or more "minor" risk factors are suitable candidates for SUP. The consensus guidelines recommend using SUP in the following settings: while a patient is mechanically ventilated, during intensive care unit stay, while not receiving oral nutrition, or for up to 1 week from the time of critical illness.

The most widely used and most effective medication options for SUP include proton

TABLE 4. Intravenous Iron Formulations and Dosing (Off-Label Use)[a]

	Iron dextran	Iron sucrose	Ferric gluconate	Ferumoxytol	Ferric carboxymaltose
Trade name	InFeD	Venofer	Ferrlecit	Feraheme	Injectafer
Maximum FDA-approved single dose	100 mg	400 mg	125 mg	510 mg	750 mg
Dosing	Up to 300 mg slow intravenous push or diluted in 100-250 mL normal saline	100-200 mg intravenous push for 5 doses	125 mg diluted in 100 mL normal saline over 60 min daily for 5 doses maximum per wk	510 mg rapid intravenous push for 2 doses 3-8 d apart	750 mg intravenous infusion or intravenous push for 2 doses 1 wk apart

[a]FDA = US Food and Drug Administration.

pump inhibitors (PPIs) and histamine-2 receptor blockers (H2B). Other less-effective and less- used options include sucralfate (a cytoprotective agent) and prostanoids (such as misoprostol, which decrease gastric acid and bolsters mucosal defenses).[46,47,49,51] Antacids are no longer recommended for SUP given numerous complications, including electrolyte derangements (hypermagnesemia, hypercalcemia, and hypophosphatemia) and evidence for increased gastrointestinal bleeding.[46,47,49,51]

Clinicians should also be aware that the most commonly used SUP agents (PPIs and H2Bs) are not free of potential adverse effects. There is robust evidence supporting the increased risk for nosocomial pneumonia (PPI and H2B), clostridium difficile infection (PPI>H2B association), hypomagnesemia (PPI>H2B association), and bone health complications (PPI).[52-55]

MANAGEMENT OF PATIENTS WITH PERIOPERATIVE ANEMIA

Anemia is another common complication in the postoperative setting, occurring in up to 80% to 90% of individuals undergoing major surgery.[56] Anemia is defined by the WHO as a hemoglobin less than 13 g/dL in males and less than 12 g/dL in females. When identified in the preoperative setting, anemia should be corrected before surgery whenever possible. This approach is well-studied and guideline-supported.[57,58] The safety and feasibility of preoperative intravenous iron therapy makes this the best approach to mitigating perioperative anemia, when feasible. intravenous iron therapy is effective at increasing preoperative hemoglobin levels and can effectively decrease transfusions in noncardiac surgery patients.[59,60] Formulations and off-label dosing can be found in Table 4.

It is also well-known that restrictive transfusion strategies, even in the postoperative setting, are either more beneficial or non-inferior to liberal transfusion strategies. In cardiac surgery, a recommended transfusion threshold of 7.5 g/dL exists based on a number of randomized, controlled trials.[57] A similar recommendation exists based on data for patients undergoing hip fracture surgery, with a recommended transfusion threshold of 8 g/dL.[57,61] This threshold can be extrapolated to all orthopedic surgeries. Furthermore, given that the orthopedic study populations also included patients at risk for cardiovascular disease, this population can also be included in the hemoglobin transfusion threshold of 8 g/dL.[61] Transfusion of blood and blood products in these groups has been shown to increase the risk of postoperative morbidity and mortality in cardiac and noncardiac surgery.[62,63] The reason for this increased risk is unclear, but may be related to the anemia itself. Also, red blood cell transfusions are known to be immunomodulatory and have been shown to increase postoperative infection in cardiac and spinal surgery.[62,64] Another small study found that postoperative transfusion increased the risk of morbidity in patients undergoing radical cystectomy.[65] Yet another study showed an increased rate of atrial fibrillation in patients after coronary artery bypass graft surgery.[66]

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Restrictive transfusion thresholds have proven superior in general to liberal restrictive transfusion thresholds; however, these thresholds are based on the cutoffs used in randomized controlled trials, and individual patient characteristics should also be considered when setting transfusion thresholds. Additionally, insufficient evidence yet exists to support these restrictive guidelines in patients with acute coronary syndrome, severe thrombocytopenia (as higher red blood cell volume increases platelet effectiveness), and chronic transfusion-dependent anemia.[67] There are data suggesting that a restrictive transfusion threshold is equally beneficial in acute coronary syndrome; however, more studies are needed before recommendations can be made.[68]

Iron deficiency anemia is common in the postoperative setting. With adherence to restrictive transfusion strategies patients often do not have iron stores to replenish intraoperative blood loss. Iron therapy in the postoperative setting has been studied, particularly in orthopedic surgery. So far, no significant benefit has been found with the initiation of oral iron therapy in the postoperative setting.[69,70] This is likely due, in part, to increased inflammation and decreased oral iron absorption in the postoperative setting. In patients who have undergone orthopedic surgeries, intravenous iron therapy before hospital discharge led to significantly increased hemoglobin levels at the time of discharge.[71] Further studies are needed to assess the true impact of intravenous iron on outcomes in postoperative anemia, but the safety of intravenous iron therapy makes it a potential option.

Managing anemia in the postoperative setting must be individualized. Given the safety and efficacy, it would be reasonable to give intravenous iron therapy to patients in the postoperative setting with mild to moderate anemia and postoperative iron deficiency. Transfusion outside of guidelines mentioned above should be reserved for those who have hypotension or tachycardia not responding to fluids or are otherwise hemodynamically unstable (eg, symptomatic anemia), those with ongoing blood loss, or those with comorbidities necessitating a lower hemoglobin threshold.[56]

DIAGNOSIS AND MANAGEMENT OF PATIENTS WITH POSTOPERATIVE FEVER

Postoperative fever (defined as a temperature over 38°C) is a very common finding. The pathophysiology of fever is related to a release of cytokines in the body.[72] These cytokines may be related to the inherent stress of surgery or due to more sinister causes, such as infection. Although postoperative fever is frequently benign, its presence cannot be ignored. One of the most useful frameworks for thinking about postoperative fever is to consider the timing of the fever in relation to the surgery: immediate, acute, subacute, and delayed.

Immediate

Immediate postoperative fever is defined as fever occurring intraoperatively or within hours after surgery. Common causes are listed in Table 5. Immediate postoperative fevers are generally self-limited, typically resolving within 2 to 3 days, depending on the type and duration of surgery.[73-75] Rarely, immediate postoperative fever can be due to malignant hyperthermia. Individuals who are genetically susceptible and exposed to certain anesthetic agents (see Table 5) develop an unregulated influx of calcium leading to persistent muscular contraction.[76] Eventually this produces more heat than the body is able to expel and core body temperature can increase to dangerous levels. Findings include hyperthermia, muscular rigidity, tachycardia, hyperkalemia, elevated creatinine kinase, and disseminated intravascular coagulation.[77,78] The only known treatment is dantrolene.

For immediate postoperative fever, one of the most important considerations is what not to do. Given the differential of immediate postoperative fever, one does not need to obtain blood cultures or chest x-rays in this scenario. Empiric antibiotics should also be avoided.

TABLE 5. Causes of Postoperative Fever

Timing of fever	Causes
Immediate postoperative fever (intraoperatively or hours after surgery)	Trauma associated with surgery
	Blood products
	Preoperative medications
	Antibiotics
	Pre-existing infections
	Malignant hyperthermia
	Succinylcholine
	Enflurane
	Desflurane
	Halothane
	Isoflurane
	Sevoflurane
Acute postoperative fever (within the first week after surgery)	Nosocomial infections
	Surgical site infections
	Urinary tract infections
	Aspiration pneumonia
	Ventilator-associated pneumonia
	Catheter site infections
	Myocardial infarction
	Pancreatitis
	Alcohol withdrawal
	Thrombophlebitis
	Deep vein thrombosis
	Pulmonary embolism
	Acute gout
Subacute postoperative fever (between 1 and 4 weeks after surgery)	Infections
	Surgical site infections
	Catheter-associated infections
	C difficile colitis
	Drug reactions
	Beta-lactams
	Sulfa-products
	Heparin
	H2-blockers
	Thrombophlebitis
	Deep vein thrombosis
	Pulmonary embolism
Delayed postoperative fever (more than 4 weeks after surgery)	Bacterial infections (typically indolent types)
	Coagulase-negative staphylococci
	Consider endocarditis

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TABLE 5. Continued

Timing of fever	Causes
	Parasitic infections
	Toxoplasmosis
	Babesiosis
	Viral infections
	Human immunodeficiency virus
	Cytomegalovirus
	Hepatitis viruses

Acute

Acute postoperative fever is defined as fever occurring within the first week after surgery. Common causes are listed in Table 5. Infectious etiologies are very common in this period, although other culprits exist as well.[79-81] Bacterial infections are often due to endogenous skin or bowel flora. Evaluations should be directed at these causes. Consideration should be given to obtaining a chest x-ray, urine culture, blood culture, evaluation of the surgical site, troponin, lipase, and uric acid. When risk factors are present, consider deep vein thrombosis, pulmonary embolism, and alcohol withdrawal.

Subacute

Subacute postoperative fever is defined as fever occurring between 1 and 4 weeks after surgery. Common causes are listed in Table 5. Infectious etiologies are again common in this period, but since patients are typically dismissed from the hospital by this point, one should focus the attention on surgical site infections, catheters, or other invasive devices.[82,83] Evaluation should again focus on possible infections; therefore, one should inspect the surgical site, evaluate any lines, and consider the possibility of *Clostridium difficile* colitis. Clots should also be considered, but drug reactions are also common during this period. Specifically look for use of beta-lactams, sulfa-containing products, heparin products, and H2-blockers.

Delayed

Delayed postoperative fever is defined as fever occurring more than 4 weeks after surgery. Common causes are listed in Table 5. Most delayed postoperative fevers are due to infections. One must keep in mind that bacterial infections in this timeframe will be due to more indolent microorganisms such as coagulase-negative staphylococci. Another important consideration is infective endocarditis, with symptoms taking weeks to months to develop.[84] Viral , fungal, and parasitic infections may need to be considered as well.

In summary, evaluation of postoperative fever must first consider the timing of the fever in relation to surgery. Then the approach can focus on the common causes in that timing category.

MANAGEMENT OF PATIENTS WITH POSTOPERATIVE DELIRIUM

Delirium represents a major challenge in hospitalized patients and in postoperative care. The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) defines delirium as a complex medical syndrome consisting of a disturbance in attention and cognition, not directly caused by another neurocognitive disorder or medical condition, and developing over a short period (such as hours to days).[85,86] Delirium is associated with longer lengths of stay, increased mortality in hospital, and poor prognosis even after discharge.[87,88] The cost associated with delirium is also high, with health care costs of more than $150 billion in 2008 related to delirium.[89]

Delirium is common in surgical patients, with some studies noting a prevalence of 62% in elderly surgical patients.[90,91] However, similar to most aspects of perioperative

medicine, higher-risk surgeries as well as patient risk factors influence the likelihood of developing delirium. In a study of 225 patients undergoing coronary artery bypass grafting or valve replacement, 46% developed delirium.[92] In a large meta-analysis of orthopedic surgery patients, delirium was noted in upwards of 53% of hip fracture patients but only in 28% of elective orthopedic surgery patients.[93] Similar to nonsurgical patients, surgical patients who develop delirium have worse long-term outcomes. For example, patients who develop delirium in the perioperative period have greater declines in cognitive function over the ensuing year compared with similar patients who do not develop delirium.[92]

Multiple risk factors for delirium have been identified. In hospitalized patients, the use of restraints, poor nutrition, polypharmacy, and having an indwelling bladder catheter can predispose patients to delirium.[94] Many of these risk factors also apply to the patient postsurgically, although surgical patients have additional factors which may predispose them to delirium in the postoperative setting. Perioperative analgesic use following surgery, use and duration of anesthesia, blood loss, acute kidney injury, and postoperative infections all can contribute to delirium in the postoperative setting.[91] Furthermore, elderly patients, those with pre-existing cognitive impairment, those undergoing emergent procedures, and patients undergoing hip fracture surgery are at an even higher risk for delirium in the postoperative period.[95]

Several prediction tools for the development of delirium have been described previously.[91,96-98] Common themes among these prediction tools include Mini Mental Status Examination scores lower than 24, preexisting medical comorbidities such as prior stroke or transient ischemic attack, kidney disease, or poor functional status, including poor visual acuity and decreased baseline cognitive status. Although these tools can be helpful to risk stratify patients, many of the markers are nonmodifiable risk factors, making the perioperative management of patients at risk for delirium challenging.

Modifiable risk factors do exist and should be the focus of perioperative evaluation and management. Clinicians should identify medications that can contribute to delirium including anticholinergics, dopamine agonists, corticosteroids, benzodiazepines, hypnotics, narcotics, and antidepressants.[99] For elective surgeries, addressing polypharmacy before a planned procedure can help decrease the likelihood of developing delirium.[100] Additionally, recognizing patients at risk for withdrawal from either drug or alcohol use is crucial to preventing complications from substance withdrawal.[101] Once hospitalized, ensuring urinary catheters are promptly removed, avoiding the use of restraints, avoiding overuse of analgesics, limiting unnecessary room changes, providing frequent reorientation, and encouraging a normal sleep/wake cycle scan also help prevent postoperative delirium.[102,103]

Management of delirium focuses on identifying reversible causes and emphasizing reorientation in a stable environment with consistency of staff and location.[102,104] Nonpharmacologic strategies and addressing modifiable risk factors should be the cornerstone of delirium management. A recent large systematic review did not support the use of haloperidol or second-generation antipsychotics for the management of delirium.[105] These agents should be reserved for patients who are a danger to themselves or others, and for whom de-escalation techniques have proven ineffective.[102] Benzodiazepines may worsen delirium and should not be used unless treating another underlying condition such as alcohol withdrawl.[106,107] Melatonin supplementation may play a role in the prevention of perioperative delirium and, given its limited side-effect profile, is a reasonable option for patients at risk for delirium.[108] Regardless, a multimodal approach, addressing potential reversible causes is still the cornerstone of delirium management in both surgical and nonsurgical patients.

CONCLUSION

The risk factors for many postoperative complications include both patient and surgery-specific variables. Postoperative complications are often due to the interplay of multiple factors. Awareness of these risk factors can aid in the earlier identification and intervention to modify these variables that predispose patients to common postoperative complications. As risk can be both patient- and surgery-specific, mitigation requires a multidisciplinary approach with care team members throughout all phases of the patient's surgical encounter.

Abbreviations and Acronyms: **ACE** = angiotensin-converting enzyme; **AKI** = acute kidney injury; **CKD** = chronic kidney disease; **DSM-5** = Diagnostic and Statistical Manual of Mental Disorders; **EAST** = Eastern Association for the Surgery of Trauma; **H2B** = histamine-2 receptor blockers; **POI** = postoperative ileus; **PONV** = postoperative nausea and vomiting; **PPI** = proton pump inhibitors; **SAMBA** = Society of Ambulatory Anesthesia; **SRMD** = stress related mucosal disease; **SUP** = stress ulcer prophylaxis

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