Q: Does elevated blood pressure at the time of surgery increase perioperative cardiac risk?

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A: Elevated blood pressure by itself has not been shown to increase the incidence of perioperative cardiac events, although conclusions depend on the specific outcomes measured. However, target-organ damage caused by chronic hypertension does confer increased cardiac risk.

Proceed when hypertension is mild or moderate
Current guidelines based on ample evidence indicate no benefit to delaying surgery in patients with mild or moderate hypertension (systolic blood pressure < 180 mm Hg and diastolic blood pressure < 110 mm Hg) without associated cardiovascular abnormalities.1,2

Outcomes less clear with severe hypertension
In contrast, scant evidence is available to guide the clinician on the proper course of action in patients who present with severe elevations in blood pressure at the time of surgery.

Prys-Roberts and colleagues in 1971 compared the development of ischemia on continuous electrocardiographic recording among treated and untreated hypertensive patients who presented for elective surgery, with normotensive patients serving as controls.3 The 7 untreated hypertensive patients had a mean arterial pressure (MAP) of 129.5 mm Hg; the 9 treated patients had a MAP of 129.0 mm Hg. Myocardial ischemia was documented in 3 of 9 treated patients, 5 of 7 untreated patients, and none of the 15 control patients. No adverse cardiac events occurred in any group. Every patient who experienced ischemia had a 50% or greater decrease in MAP after induction of anesthesia. Although the study was observational in nature and included few patients, it represents the only such study to include patients with an extreme elevation of blood pressure.

Authors of larger studies in which hypertension was not identified as a predictor of cardiovascular complications acknowledged the lack of inclusion of patients with severe hypertension. In an evaluation of hypertensive patients with differing levels of blood pressure control who presented for surgery, Goldman and Caldera found that only five had diastolic blood pressure greater than 110 mm Hg.4 In this study, no increase in the incidence of perioperative myocardial infarction or death was observed in any group regardless of treatment or blood pressure control.

Target-organ damage carries high risk
Hypertension is causally linked to occult and symptomatic coronary artery disease, heart failure, renal insufficiency, and cerebrovascular disease. These diseases place the patient at higher risk for adverse cardiac events, and constitute four of the six criteria for the Revised Cardiac Risk Index (RCRI), which is the current recommended tool for assessing perioperative cardiac risk.5 Patients with longstanding uncontrolled hypertension, especially those with severe hypertension, are at greater risk for target-organ damage.

More controversial is the appropriate course in these patients with uncontrolled or severe hypertension. Guidelines recommend antihypertensive treatment, although no evidence suggests that treatment modifies cardiac risk. Also, it remains to be determined whether blood pressure control needs to be achieved over a period of weeks or if gaining control in the immediate preoperative period is sufficient.

Severe hypertension: Assess for target-organ damage
A reasonable strategy for managing patients with severe or uncontrolled hypertension therefore starts with an assessment of target-organ damage (Figure).6

If the extent of target-organ damage is unknown or if an assessment cannot be performed before elective surgery, then surgery should be postponed until the cardiac risk can be determined. If a patient has one or more of the RCRI criteria, conventional wisdom is to treat with beta-blockade.5 A gain, the optimal timeframe for achieving control of blood pressure is not known. Whether treatment by itself (regardless of the achieved blood pressure) is adequate to reduce risk, or whether treatment must result in a blood pressure decline into the range defined as mild or moderate hypertension, is also not known.

Finally, if a patient has no evidence of end-organ damage and is otherwise fit, there is no evidence to suggest that surgery should be cancelled until better blood pressure control is obtained.

* Dr. Kroen reported that he has no commercial affiliations or financial interests that pose a potential conflict of interest with this article.
Teamwork is essential

Close communication between the surgeon, anesthesiologist, and medical consultant is necessary to elaborate the need for close invasive arterial pressure monitoring, as well as aggressive treatment of blood pressure to prevent the precipitous drop in MAP that can lead to ischemia.

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Q: When is it appropriate to stop antiplatelet therapy in a patient with a drug-eluting stent prior to noncardiac surgery?

A: The US Food and Drug Administration recommends that combined antiplatelet therapy (aspirin plus clopidogrel) be continued for at least 3 months after placement of a sirolimus-eluting stent and at least 6 months after placement of a paclitaxel-eluting stent. Current guidelines from the American College of Cardiology/American Heart Association (ACC/AHA) and from the American College of Chest Physicians recommend 9 to 12 months of dual-antiplatelet therapy after placement of either stent. Multidisciplinary discussions are necessary if surgery is considered prior to completion of 1 year of combined antiplatelet therapy. Antiplatelet therapy must also be reinstituted as soon as possible after surgery in suitable patients.

Drug-eluting stents: Less restenosis, more late thrombosis

In the first decade of interventional cardiology practice (1977–1987), the restenosis rate at 6 months after balloon angioplasty was 32% to 40%.1 This was in addition to a high acute closure rate that often required repeat interventions. This led to the introduction of bare-metal stents (BMS) in 1986, but the 6-month restenosis rate with these stents remained as high as 17% to 32%.1

Drug-eluting stents (DES) were designed to address the high rates of in-stent restenosis associated with BMS. DES, which now constitute about 90% of all stents placed in the United States, have reduced the restenosis rate to less than 10%.1 However, late stent thrombosis, which occurs more than 30 days after stent placement, is thought to occur more frequently with DES than with BMS, and results in death or infarction in 60% of patients.2

Extended dual-antiplatelet therapy is recommended in patients with DES because of the delayed endothelial regeneration caused by drug elution within the stent’s local environment. This creates a microenvironment conducive to platelet thrombus formation.

With adequate antiplatelet therapy, however, the rate of stent thrombosis is less than 1% with DES.3 A pooled analysis of 10 randomized trials showed no difference in rates of stent thrombosis between DES and BMS when patients were on appropriate combined antiplatelet therapy.2 Although another recent clinical trial found no significant difference in the incidence of late stent thrombosis between patients receiving DES or BMS, it did find higher rates of major adverse cardiovascular events with DES compared with BMS in the year following clopidogrel discontinuation and showed that late stent thrombosis occurred up to 18 months after stent placement.4 A study of 2,006 patients who were followed for at least 1 year after stent placement found that late stent thromboses developed in patients on stable aspirin monotherapy while no thromboses occurred in patients on combined antiplatelet therapy.5

Limited data from noncardiac surgeries

In addition to the above issues, perioperative management also must take into account the “prothrombotic rebound” phenomenon upon stopping antiplatelet therapy (which has never been studied) as well as the prothrombotic state portended by the surgery itself. Noncardiac surgeries performed within 3 to 6 weeks of coronary artery stent placement were associated with an increased incidence of major adverse cardiovascular events.6–9

No published studies have addressed the issue of perioperative stent thrombosis in patients with DES undergoing noncardiac surgeries; the only study we know of that has done so is a retrospective analysis conducted at the Cleveland Clinic and presented in pre-

* All authors reported that they have no commercial affiliations or financial interests that pose a potential conflict of interest with this article.
Two patients developed myocardial infarction (on post-stenting in 35 patients. No patients died in this study. Days of stenting in 13 patients and within 180 days of surgery. Clopidogrel was discontinued within 90 days before surgery. Clopidogrel were both discontinued a median of 10 days before surgery. Eighty-eight patients (77%) had all antiplatelet medication. The median time to surgery in this study continued antiplatelet therapy for at least 4 months after stent placement. Also, the study's retrospective design and small size are major limiting factors. The risk of thrombosis after DES placement rises proportionally with the length of the stent and is also increased in patients undergoing treatment for in-stent restenosis and bifurcations. Premature discontinuation of antiplatelet therapy is the most important predictor of stent thrombosis after DES implantation.

Discussion with the surgeon to verify that continuing antiplatelet therapy is truly a significant risk for bleeding is imperative. A spin-in can be continued for coronary artery bypass graft and cataract surgeries, and most vascular surgeons are comfortable with continuing antiplatelet therapy perioperatively. Studies of perioperative bleeding in patients on antiplatelet therapy have yielded varied results and have been conducted mainly in cardiac surgery patients. Only a few studies address antiplatelet therapy and noncardiac surgery. One study of 40 consecutive patients reported 7 myocardial infarctions, 11 major bleeding episodes, and 8 deaths, with stent thrombosis accounting for most of the fatal events. In another study of patients who had received stents within the prior year, antiplatelet therapy was not interrupted perioperatively or was interrupted only briefly; of the study's 103 patients, 46 suffered complications and 5 died.

Despite uncertainties, some recommendations emerge from the discussion above. Coronary revascularization should be undertaken only if the patient's clinical characteristics dictate it, irrespective of the surgery. If revascularization is inevitable, consider BMS or optimized plain balloon angioplasty. There is no evidence that preoperative revascularization in an asymptomatic patient changes postoperative outcomes.

All patients should be optimized with beta-blockade. If surgery is required urgently, a multidisciplinary risk-benefit analysis should be done with the surgeon at the helm. Every effort should be made to continue dual-antiplatelet therapy if possible. If the surgical team has reservations about hemorrhagic risk and surgery is indicated, consider referral to a tertiary surgical center with more experience. A cardiologist should be an integral part of any decisions related to discontinuing antiplatelet therapy because high-risk patient and stent characteristics are best interpreted by a cardiologist. Wherever feasible, discontinuation of clopidogrel 5 days before surgery and aspirin 7 days before surgery appears reasonable, but this largely depends on the surgeon's preference. Multiple reports of very late stent thrombosis in patients with DES (> 1 year after placement) suggest that antiplatelet therapy must be reinstated as soon as possible after surgery.

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9. Vicenzi MN, Meilzter T, Hitzinger B, Halaj M, Fleisher LA, Metzler H. Coronary artery stenting and non-cardiac surgery—a preliminary form. The median time to surgery in this cohort of 114 patients was 236 days after DES placement. Eighty-eight patients (77%) had all antiplatelet agents discontinued prior to surgery. A spin-in and clopidogrel were both discontinued a median of 10 days before surgery. Clopidogrel was discontinued within 90 days of stenting in 13 patients and within 180 days of stenting in 35 patients. No patients died in this study. Two patients developed myocardial infarction (on post-operative days 3 and 7, respectively); neither of these patients had DES thrombosis by postoperative catheterization. One patient developed major bleeding. While encouraging, these data alone are not sufficient to demonstrate that discontinuation of antiplatelet therapy in patients with DES is safe. Most patients in this study continued antiplatelet therapy for at least 4 months after stent placement. Also, the study's retrospective design and small size are major limiting factors. 
Q: Should statins be discontinued preoperatively?

A: Although discontinuation of 3-hydroxy 3-methylglutaryl coenzyme A reductase inhibitors (statins) preoperatively has largely become routine practice, recent literature indicates that this action may be inappropriate.

Historical reasons for statin interruption

The rationale for stopping statins preoperatively has been unclear. Statin manufacturers recommend discontinuing these agents a few days prior to elective major surgery, claiming the potential for major surgery to cause rhabdomyolysis in patients predisposed to renal failure. A part from a small number of case reports, there is minimal evidence that statin therapy increases the risk of postoperative rhabdomyolysis. A retrospective cohort study of 981 consecutive patients undergoing major elective vascular surgery assessed the effect of statin exposure on the risk of myopathy. In addition to no cases of rhabdomyolysis, there was no increased risk of myopathy in statin users.

Most research on statins in the perioperative setting has focused on their role in cardiovascular risk reduction. Well known for their powerful lipid-lowering role, statins also appear to prevent plaque rupture, optimize endothelial function, and provide anti-inflammatory effects. These effects are referred to as the “pleiotropic effect” of statins. In contrast to these drugs’ lipid-lowering effects, which take several weeks to months to occur, their pleiotropic effects are thought to take place within hours to days. It is likely one or more of the pleiotropic mechanisms that improves outcomes when statins are given in the setting of acute coronary syndromes.

Clinical trial evidence: reduction in perioperative risk with statin continuation

The few clinical trials assessing perioperative statin use have evaluated patients undergoing major noncardiac surgery (largely vascular procedures) and the incidence of perioperative complications such as death, myocardial infarction (MI), and other ischemic events such as angina and stroke. All trials assessing the association between statin exposure and reduction in perioperative complication rates have shown positive results, with adjusted risk reductions ranging from 30% to 78% in each study’s primary end point.

The first trial to investigate statin use and perioperative risk reduction was a retrospective, case-control study of 2,816 patients undergoing vascular surgery. It demonstrated a greater than fourfold reduced risk of perioperative mortality with statin use. A retrospective study using a large database of 780,591 patients evaluated whether lipid-lowering therapy was associated with reduced mortality in the setting of major noncardiac surgery. Using propensity matching analysis, the authors found significantly less in-hospital mortality for patients receiving lipid-lowering therapy (odds ratio: 0.62; 95% CI, 0.58 to 0.67; P < .001).

The only prospective trial to date was a randomized, double-blind study of 100 patients undergoing elective vascular surgery. Patients were randomized to atorvastatin 20 mg/day or placebo, with therapy starting a mean of 31 days before surgery and continuing for 45 days. The primary end point was a composite of death from cardiac causes, nonfatal MI, unstable angina, and ischemic stroke. At 6 months, a significant reduction in the primary end point was noted in the statin group (P = .031). Limitations of this single-center trial were its small sample size, a low event rate, and a broad composite end point.

Statin withdrawal may be risky

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Statin withdrawal may be risky

Although never studied directly, information would suggest that perioperative statin withdrawal in higher-
risk patients may be detrimental. Considering the proven benefits of these medications in the setting of myocardial ischemia, and recognizing that major surgery poses an increased risk for such an event, it may be prudent to have statin therapy continued during this time of potential need.

Given the current evidence, we recommend continuing statin therapy perioperatively for patients already receiving it. This recommendation includes taking the medication on the day of (or evening before) surgery to maximize the potential benefit. Future research is needed to address whether statin therapy should be initiated in high-risk patients as a means of decreasing perioperative cardiovascular risk.

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Q: What is the appropriate means of perioperative risk assessment for patients with cirrhosis?

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A: There are no prospective data to answer this question definitively, but the body of available evidence suggests that the model for end-stage liver disease (MELD) score offers the most prognostic information.

Data are from small, retrospective studies
Although only a small minority of patients undergoing surgery suffers from cirrhosis, patients with clinically significant chronic liver disease do have a higher rate of perioperative morbidity and mortality than the general population, due to an excess of bleeding episodes, infection, encephalopathy, and renal failure, among other causes. Complications of chronic liver disease, including gastrointestinal bleeding, ascites, and thrombocytopenia, also may worsen outcomes.

Intuitively, more advanced liver disease should be accompanied by worse perioperative outcomes. While multiple studies have found this to be true, the available data are from small, retrospective studies with heterogeneous populations, and thus offer limited data from which to extrapolate.

Two common scoring schemes
Two commonly used clinical scoring schemes have both been found to correlate with postoperative mortality.

The Child-Turcotte-Pugh (CTP) classification categorizes patients into three groups (A, B, and C) based on points assigned according to five clinical and laboratory measures (Table). Multiple studies have shown the CTP classification to correlate with perioperative mortality. A retrospective study from 1984 reported postoperative mortality rates of 10%, 31%, and 76% among patients in classes A, B, and C, respectively, after various abdominal surgeries. A 1997 study of 92 patients yielded similar results, leading to a general conclusion that surgery is reasonably safe for patients in CTP class A and all but contraindicated for patients in class C. Class B constitutes a group of patients at substantially increased risk of mortality.

The CTP scheme has a number of limitations, however. Most notably, it is derived from clinical experience, it is subject to “floor” and “ceiling” effects (values at one extreme of a range are grouped with values at the other extreme), and it uses subjective criteria (ascites and encephalopathy).

The MELD score was developed to predict mortality in patients with chronic liver disease undergoing transjugular intrahepatic portosystemic shunting,
but it has since been found to have predictive value in other clinical settings. The score relies solely on objective measurements—creatinine, bilirubin, and the international normalized ratio—but its formula is cumbersome (Figure). Fortunately, online MELD score calculators (such as www.unos.org/resources/MeldPeldCalculator.asp?index=98) obviate the need to perform the calculations.

A number of studies have examined the predictive value of the MELD score in the perioperative setting, although these studies have been small and retrospective. The largest assessed 131 patients who underwent 140 inpatient procedures, including 67 intra-abdominal and 29 orthopedic surgeries.4 Fifty-nine of the surgeries were considered “nonelective.” Mortality at postoperative day 30 was correlated with MELD score and was higher in general surgical patients than in the cohort as a whole. The authors presented a “rule of thumb” in which each 1-point increase in the MELD score up to 20 points is associated with a 1% increase in mortality, and each 1-point increase beyond 20 points is associated with a 2% mortality increase.

This study looked at the MELD score upon admission; no study has assessed whether intervening upon the individual components of the MELD score to improve the score changes surgical outcomes.

Another retrospective study (N = 53) concluded that patients with a MELD score greater than 14 have substantially poorer outcomes after abdominal surgery than do patients with lower scores.5 However, the small numbers of patients in studies such as this result in wide confidence intervals for the outcomes.

MELD score vs CTP classification
A number of studies have compared the MELD score with the CTP classification. However, accurate retrospective calculation of the CTP score is probably very difficult, and comparisons based on such calculations may be imprecise. A higher score in both scoring systems is accompanied by excess and increasing mortality, but because the MELD score is based on objective data and provides a more continuous assessment of liver disease, it may be a superior method of risk stratification.

Factors beyond scoring systems also matter
The likelihood of complications is also affected by nonclinical factors. Emergent operations, abdominal surgeries, certain types of anesthesia, and biliary obstruction all increase patient risk, while laparoscopy is associated with lower risk. Appropriate measures should also be taken to optimize the patient’s status before surgery, although little evidence exists to suggest that the postoperative course is improved by interventions such as paracentesis or plasma transfusion. Furthermore, while cirrhosis may be a patient’s most prominent clinical issue, clinicians must not overlook the possibility of heart disease, lung disease, or other comorbidities that would independently alter the patient’s risk profile.

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Q: Who is at risk for developing acute renal failure after surgery?

A: Patients who are at risk of developing acute renal failure (ARF) after cardiac surgery are usually older than 65 years of age; have diabetes, underlying renal disease, or cardiovascular disease; and have undergone recent coronary angiography or other procedures requiring intravenous contrast.

Perioperative ARF has clinical consequences
In most clinical studies, ARF has been defined as a greater than 25% to 50% increase in serum creatinine from baseline within 1 week after surgery. Monitoring serum creatinine is the most commonly used method to observe changes in renal function perioperatively. Unfortunately, an elevated creatinine level is a late indicator of renal injury, and even a minor increase should be regarded as clinically important and followed closely.⁶

ARF requiring dialysis develops in 1% to 5% of patients after cardiac surgery, and is strongly associated with perioperative morbidity and mortality.² A prospective multicenter trial of patients who had myocardial revascularization found that mortality in patients with renal dysfunction not requiring dialysis was 19%, compared with 63% in those who needed dialysis.³ In patients without renal dysfunction after cardiac surgery, mortality was 0.9%.³ Postoperative ARF also confers an increased risk of mortality in follow-up more than 5 years after cardiac surgery.⁴ Only about 15% of patients who develop ARF at the time of cardiac surgery fully recover.¹

ARF risk score developed for open-heart surgery
A recent retrospective study of more than 33,000 patients who underwent open-heart surgery at the Cleveland Clinic offers the first solid evidence of risk factors for ARF.⁵ A bout 70% of the study population was male, and 89% was Caucasian. The primary outcome was ARF that required dialysis during the postoperative period. A risk score was derived to calculate the risk for developing ARF (Table). Patient-specific risk factors for ARF after cardiac surgery included higher serum creatinine level (> 1.2 mg/dL), diabetes, chronic obstructive pulmonary disease, previous cardiac surgery, markers of severe cardiovascular disease, and female gender. The major intraoperative factor was longer cardiopulmonary bypass time. Age, weight, race, peripheral vascular disease, and cerebrovascular disease were excluded from the scoring model on the basis of the statistical analysis done by the authors.

Each risk factor was assigned a number of points, and the points were then computed to calculate a total score (Table). The risk for developing ARF was directly related to the number of risk factors. The risk
score ranged from 0 to 17 points. Four risk categories of increasing severity (scores 0 to 2, 3 to 5, 6 to 8, and 9 to 13) were determined arbitrarily by the authors.

The frequency of ARF among these categories varied between 0.4% for the lowest risk score to 21.5% for the highest score.

This study involved a large cohort of patients, sufficient to generate and validate a postoperative ARF score that incorporated multiple independent risk factors. Limitations included the single-center data source and the retrospective observational design. Nevertheless, the study provided a valuable tool for both determining the risk of ARF for individual patients and planning future clinical trials.

**Clinical score needed for noncardiac surgery**

Currently, a risk score for ARF has only been developed for patients who have had cardiac surgery; no sufficiently powered study has yet been done for those undergoing noncardiac surgery. The Section of Hospital Medicine and the Department of Nephrology and Hypertension at the Cleveland Clinic are currently conducting a large retrospective cohort study in patients undergoing elective noncardiac surgery.

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**Q: Why treat anemia in the preoperative period of joint replacement surgery with erythropoietin?**

**A: Recombinant human erythropoietin (epoetin alfa) is an effective therapy approved by the US Food and Drug Administration (FDA) to treat preoperative anemia in patients undergoing knee or hip replacement surgery.**

**Anemia is linked to poor outcomes**

Anemia in the preoperative period is a known predictor of adverse outcomes in surgical patients. Carson et al. studied 125 consecutive patients who declined blood transfusions and found that operative mortality was 16 times greater in patients with hemoglobin levels less than 8 mg/dL than in patients with higher hemoglobin levels. Other studies suggest that it is not the anemia itself that is associated with increased mortality, but the practice of treating anemia with blood transfusions.

**Blood transfusion used most often, alternatives needed**

Allogenic blood transfusion is the most commonly used technique in the United States to correct perioperative anemia. Although several methods are available to reduce the need for blood transfusion, the use of allogenic blood remains very high; for example, 47,456 units of blood products were used in the perioperative period of various orthopedic surgeries at the Cleveland Clinic in 2004.

In the next decade, with the aging of the population, the number of major joint replacements to be performed annually will increase, likely leading to an increased need for blood transfusions. This issue highlights the importance of developing effective alternatives to allogenic blood transfusions.
increase in the demand for blood products. Due to the fluctuating supply and the costs and risks associated with the administration of blood products, searching for potential alternatives to transfusions is imperative.

Because blood loss associated with orthopedic surgery is predictable, the application of a carefully designed blood management program is appropriate. However, the usefulness of autologous donations and cell saver machines is limited by incomplete utilization of predonated blood and high cost. Furthermore, allogenic blood transfusions carry certain risks, in particular ABO incompatibility caused by administrative error and transfusion-related lung injuries. Exposure to leukocytes in allogenic blood can also cause immunosuppression. In a large prospective study of 6,301 patients undergoing noncardiac surgery, Dunne et al concluded that the incidence of perioperative anemia in surgical patients is high and is related to an increase in blood utilization. These factors are associated with an increased risk for perioperative infection and other adverse outcomes (including death) in surgical patients.

In a large study by Bierbaum et al, blood management data were collected prospectively on patients who had undergone total hip replacement and knee replacement. Fifty-seven percent of the patients undergoing hip replacement and 39% of the patients undergoing knee replacement received blood transfusions. Patients who were transfused were more likely to have infections, fluid overload, and an increased length of hospitalization compared with patients who did not receive transfusions. The Orthopedic Surgery Transfusion Hemoglobin European Overview study from 225 centers in Europe produced similar results. In this study, allogenic transfusion was associated with a higher rate of wound infection than autologous transfusion (4.2% vs 1%, respectively).

Treatment of anemia and blood conservation

Treatment of perioperative anemia has been shown to decrease the need for transfusion and to improve perioperative outcomes such as postoperative infections, length of stay, and mortality in patients undergoing joint replacement surgery. The efficacy of preoperative erythropoietin therapy for increasing patients’ hemoglobin concentrations and reducing exposure to allogenic red blood cell transfusion in orthopedic surgery has been demonstrated in several double-blind randomized clinical trials. Synthetic erythropoietin was approved by the FDA and has been used for almost 9 years in orthopedic surgeries as a method to improve hemoglobin levels in anemic patients undergoing surgery, and thus to decrease blood transfusions. Several centers in the United States have adopted this novel therapy to reduce the use of blood transfusions.

At the Cleveland Clinic, patients selected for a blood conservation protocol (Figure) with erythropoietin are eligible for four subcutaneous injections of epoetin alfa (600 U/kg) at days 21, 14, 7, and 0 before surgery, as well as oral iron.
ervative erythropoietin treatment are hemoglobin of less than 10 g/dL, iron deficiency anemia, recent gastrointestinal bleed (within 3 months), uncontrolled hypertension, seizure disorder, predonation of blood, blood dyscrasias, and history of thromboembolism.

Reticulocyte count, hemoglobin, and blood pressure should be checked prior to each injection. Iron deficiency may occur during erythropoietin therapy. Normal ferritin but low transferrin saturation may be observed due to an inability to mobilize iron stores rapidly enough to keep pace with the increased erythropoiesis. Supplemental oral or intravenous iron supports erythropoiesis and prevents iron store depletion.

Summary

Treatment of anemia in the perioperative period of major orthopedic surgery decreases the need for blood transfusion and improves perioperative outcomes. Use of epoetin alfa in this setting is FDA-approved and provides significant benefit to qualified and carefully chosen patients.

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Q: Obstructive sleep apnea: What to do in the surgical patient?

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A: A diverse surgical outcomes appear to be more frequent in patients with known obstructive sleep apnea syndrome (OSAS). Aesthetic, sedative, and analgesic drugs should be used with extreme caution in patients with known or suspected OSAS, and close perioperative monitoring of high-risk patients is recommended.

Epidemiology
In Western countries, the prevalence of OSAS is about 5%. The estimated prevalence in surgical patients is 1% to 9%, though it may be even more common in certain populations.2

Disruption of sleep architecture

Sleep studies in patients who undergo major abdominal or cardiac surgery have demonstrated suppression of rapid eye movement (REM) sleep and slow-wave sleep after surgery. The REM sleep returns or rebounds in the late postoperative period (when oxygen may have been discontinued). This return of REM sleep was linked to significant respiratory abnormalities in a group of elderly patients who underwent abdominal vascular surgery.3 In REM sleep, the neural drive to the pharyngeal muscles is at a minimum, and the atonia of antigravity muscles predisposes to airway instability, causing episodic hypoxemias. Reductions in REM and slow-wave sleep

* Both authors reported that they have no commercial affiliations or financial interests that pose a potential conflict of interest with this article.
and the lack of inherent rhythmicity are more pronounced after major surgery than after minor surgery and laparoscopic surgery.

Sedatives, analgesics, and the residual effects of anesthetic agents may worsen OSAS by decreasing pharyngeal tone, thereby increasing upper airway resistance and attenuating the ventilatory and arousal responses to hypoxia, hypercapnia, and obstruction.

In a study of patients who underwent hip and knee replacement, up to one third with OSAS developed substantial respiratory or cardiac complications, including arrhythmias, myocardial ischemia, unplanned transfers to the intensive care unit (ICU), and reintubation.4 In another small prospective study evaluating the incidence of arrhythmias in patients with OSAS who underwent coronary artery bypass graft surgery, those with an oxygen desaturation index of 5 or greater (defined as the number of desaturations > 4% per hour) had a relative risk of 2.8 for the development of atrial fibrillation postoperatively.3

**Preoperative assessment**

Physical examination may reveal characteristic stigmata of OSAS, which include:

- A short, thick neck
- Nasal obstruction
- Tonsillar hypertrophy
- A narrow oropharynx that precludes visualization of the soft palate
- Retrognathia
- Obesity.

In patients with these characteristics and a history of daytime somnolence, snoring, or observed apneas, a presumptive diagnosis of OSAS can be made in the absence of a sleep study. Because the severity of these historical items correlates with the severity of sleep study-proven OSAS, use of a simple screening questionnaire for OSAS appears reasonable.6 None, however, have been validated for use in the preoperative setting.

Clinical suspicion for sleep apnea may first arise intraoperatively. The degree of difficulty in visualizing the faucial pillars, the soft palate, and the base of the uvula predicts difficulty with intubation and should increase the suspicion of OSAS.6 A narrow airway obstruction out of proportion to the apparent degree of sedation, and a pronounced tendency for upper airway obstruction during or upon recovery from anesthesia, can suggest undiagnosed sleep apnea as well.

**Perioperative monitoring and interventions**

Continued inpatient monitoring is advised for the following types of patients with OSAS: those having abdominal or other major surgery, those with significant expected pain or opioid requirements, those with severe OSAS (requiring continuous positive airway pressure [CPAP] at home) at baseline, and those with observed obstruction or episodic desaturations in the recovery room.7

Routine ICU admission after surgery may not be necessary except in patients with coexisting cardiopulmonary disease or a difficult airway. Patients at increased perioperative risk from OSAS should be extubated while awake and after full reversal of neuromuscular blockade is verified.

Benzodiazepines should be avoided altogether and narcotic use should be limited. Alternative forms of analgesia, such as nonsteroidal anti-inflammatory drugs, nerve blocks, or local analgesics, should be considered. If narcotics are required for pain control, patients should be in a monitored setting. Patient-controlled analgesia with no basal rate may help limit dosing.

General anesthesia with a secure airway is preferable to deep sedation without a secure airway, particularly for procedures that may compromise the airway mechanically. Respiratory arrest has been reported in patients with OSAS receiving epidural opioids at 2 to 3 days postoperatively.8 If neuraxial analgesia is planned, local anesthetics alone should be preferred over opioids in combination. Case series and limited data suggest that the use of CPAP in the perioperative setting for known cases of OSAS may help reduce postoperative complications.

Until additional information is available to guide decision making, screening for OSAS should be incorporated as part of the preoperative assessment of patients undergoing surgery.

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The optimal drug, dose, and duration of pharmacologic therapy to prevent venous thromboembolism (VTE) is not known. However, mechanical prophylaxis combined with some form of heparin, in most cases low-molecular-weight heparin (LMWH), is strongly recommended.

**VTE risk is elevated in bariatric surgery patients**

Patients undergoing bariatric surgery are at increased risk for VTE. The reported frequency of thromboembolic complications from bariatric surgery, including deep venous thrombosis (DVT) and pulmonary embolism (PE), is as high as 2.4%.1 PE was the most frequently reported cause of death within 30 days of a bariatric procedure in reports from the International Bariatric Surgery Registry.2 All patients undergoing bariatric surgery have at least two risk factors for VTE (obesity and surgery), and most have one or more additional risk factors.

**Combine multiple strategies whenever possible**

Mechanical prophylaxis alone is never adequate. Early ambulation should always be encouraged in addition to mechanical prophylaxis measures. The Seventh American College of Chest Physicians Conference on Antithrombotic and Thrombolytic Therapy recommends that pharmacologic prophylaxis be combined with the use of graded compression stockings and/or intermittent pneumatic compression devices in high-risk patients undergoing general surgery.3

**Consider weight-adjusted LMWH dosing**

The optimal form and duration of pharmacologic prophylaxis against VTE in morbidly obese patients is not known. Prophylaxis with LMWH is generally recommended, but there is a general lack of consensus on the timing, dose, and duration of treatment. No randomized controlled trials have evaluated the optimal LMWH dosage in severely obese patients.

When the LMWH enoxaparin is used in fixed doses, there is a strong negative correlation between total body weight and enoxaparin’s anticoagulant effect based on anti-Xa assay levels.4 Weight-adjusted doses may be better than fixed doses for obese patients.

One retrospective study compared two dosages of enoxaparin—30 mg or 40 mg subcutaneously every 12 hours—for patients undergoing Roux-en-Y gastric bypass surgery (97.5% of the surgeries were open procedures).5 Enoxaparin was administered 2 hours before surgery and continued until the patient was fully ambulatory or discharged from the hospital. As detailed in the Table, patients in the 40-mg group had a statistically significantly lower risk of postoperative DVT or PE compared with those in the 30-mg group. Operating room time and length of stay were greater.

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**Q: What is the optimal venous thromboembolism prophylaxis for patients undergoing bariatric surgery?**

**A:**

The optimal drug, dose, and duration of pharmacologic therapy to prevent venous thromboembolism (VTE) is not known. However, mechanical prophylaxis combined with some form of heparin, in most cases low-molecular-weight heparin (LMWH), is strongly recommended.

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in the 30-mg group, however, which makes the results of this study less compelling. Nevertheless, the decreased effectiveness of LMWH in obese patients suggests that weight-based dose adjustments should be indicated.

Consider extended pharmacologic prophylaxis
Extended pharmacologic prophylaxis may be needed in patients undergoing bariatric surgery, particularly those with multiple risk factors for VTE. The PROBE study (Prophylaxis against VTE Outcomes in Bariatric Surgery Patients Receiving Enoxaparin) was a multicenter retrospective survey that assessed the frequency of symptomatic DVT or PE in morbidly obese bariatric surgery patients who received six different prophylactic regimens of enoxaparin. Among the 668 patients in this analysis, 7 VTE events occurred—6 PEs (0.9% incidence) and 1 DVT (0.1% incidence). All but one episode of VTE occurred after the cessation of prophylaxis; therefore, extended prophylaxis may have some benefit. However, no trials have evaluated the optimal dose or duration of treatment.

Summary: What the current evidence suggests
Patients undergoing bariatric surgery are at increased risk for VTE and frequently have multiple significant risk factors. Mechanical prophylaxis measures should always be used, and early ambulation should always be encouraged. A lack of randomized controlled trial data precludes specific guidelines for pharmacologic VTE prophylaxis. Increased, weight-based doses of LMWH should be considered, starting preoperatively or as soon as possible after the operation. Extended prophylaxis, particularly for patients at the highest risk for VTE, should also be considered. Further study is needed to define the optimal regimen for pharmacologic VTE prophylaxis for bariatric surgery patients.

REFERENCES

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Q: Do hip fractures need to be repaired within 24 hours of injury?

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A: Patients with unstable medical conditions or with impaired cardiopulmonary function should have operative repair delayed to return them to their healthiest baseline prior to surgery. Otherwise, patients should proceed to operative repair as soon as practically possible.

The case for operating immediately
Early operation (ie, 8 to 24 hours from admission) has been associated with a reduction in the incidence of nonunion of fracture and avascular necrosis of the femoral head, improved long-term functional status, and decreased rates of urinary tract infections, decubitus formation, pneumonia, and venous thromboembolism.1–3

Retrospective uncontrolled studies show that failure to repair hip fractures within 24 hours is associated with increased mortality. As there are no randomized prospective studies comparing delayed surgery with expeditious surgery, it is not known whether surgical delay adversely affects outcomes directly or if delay in surgery is simply a reflection of underlying morbidities that adversely affect outcomes. The literature does show that early operation improves pain control,
which decreases the incidence of delirium and reduces length of hospital stay.

**Delay surgery when comorbidities are significant**

Patients with hip fractures often have comorbidities such as diabetes, congestive heart failure, coronary artery disease, anemia, malnutrition, dehydration, electrolyte disturbances, and rhabdomyolysis with renal failure. These problems may contribute to the event leading to the fracture (neuropathy, visual impairment, weakness) or may be related to immobility after the fracture. Such conditions, if not assessed and treated preoperatively, may lead to perioperative complications such as myocardial ischemia and infarction, delirium, and nutritional compromise, increasing in-hospital and overall mortality and delaying weight bearing and rehabilitation. Therefore, a delay in surgical intervention of 24 to 48 hours after admission is appropriate to correct such metabolic disturbances and to optimize chronic medical conditions in an attempt to improve overall outcomes.

Several studies note no significant difference in the incidence of postoperative mortality between immediate and delayed hip fracture repair when controlling for the severity of medical conditions. In a retrospective study, Grimes et al evaluated 8,383 patients with hip fractures that were repaired surgically between 1983 and 1993. In unadjusted analyses, a delay in surgery greater than 24 hours from admission was associated with increased long-term mortality compared with prompt surgery (ie, < 24 hours from admission); however, after adjustment for demographic variables and for the severity of underlying medical problems, no significant association was found. Mortality at 30 days and postoperative morbidity measures were similar, although a longer time to surgery was associated with the development of decubitus ulcers.

A recent retrospective study of more than 120,000 admissions in the United Kingdom noted that delay of 2 or more days was associated with increased mortality, but the magnitude of this effect was reduced with adjustment for comorbidities.

Many agree that uncontrolled medical comorbidities and postoperative complications increase the risk of death in association with hip fracture, but the effect of optimization of these comorbidities on outcomes had not been assessed until a recent prospective cohort study. Researchers evaluated 571 patients with hip fractures from four New York hospitals and categorized their medical abnormalities as either major (more likely to require correction prior to surgery) or minor (less likely to require correction prior to surgery). The odds ratio of having a complication was increased in the presence of a major abnormality but not in the presence of a minor abnormality. If a major abnormality was present on admission but only minor abnormalities were present at the time of surgery (ie, the major abnormality was corrected), no increased risk was noted.

**Conclusion**

Medical comorbidities contribute to morbidity and mortality after hip fracture repair. Existing evidence suggests that brief surgical delay (up to 72 hours) does not adversely affect health or functional outcomes in patients with hip fracture, and may allow for stabilization of uncontrolled medical conditions prior to surgery. Further studies are needed, however, to characterize the group of patients who would benefit from operative delay for medical optimization.

**REFERENCES**


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Q: Is postoperative atrial fibrillation in patients undergoing noncardiothoracic surgery an important problem?

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A: Although the data on postoperative atrial fibrillation (AF) in patients undergoing noncardiothoracic surgery are sparse and largely observational, postoperative AF appears to have significant clinical and financial ramifications.

Burden is significant
The incidence of postoperative supraventricular arrhythmia (SVA), including atrial fibrillation (AF), appears highly variable and dependent on the population under study. The burden of this problem is considerable, however. Postoperative atrial arrhythmias affect about 1 million elderly Americans annually. These events are associated with significantly longer hospital stays, increased morbidity, and inflated health care costs.

Despite a lower incidence, the overall burden of postoperative atrial tachyarrhythmias is higher with noncardiac surgery compared with cardiac surgery, due to larger volumes.

Findings from largest prospective study
The largest and most rigorously conducted prospective study on the incidence of all atrial arrhythmias in major, nonemergent, noncardiac surgery evaluated 4,181 patients aged 50 years or older who were in sinus rhythm preoperatively. This study included some patients undergoing thoracic surgery, which is associated with significantly higher rates of postoperative SVA than is noncardiothoracic surgery. Serial electrocardiograms were obtained, preoperative clinical data were collected, and postoperative cardiac enzyme levels and clinical outcomes were measured.

Postoperative SVA occurred in 317 patients (7.6%). The incidence of AF was 3.7% in the postoperative period and 4.1% in the intraoperative and postoperative periods combined. SVA was associated with a 33% increase in the length of hospital stay.

Of the nonmodifiable factors identified preoperatively, male sex, age 70 years or older, significant valvular heart disease, history of SVA, asthma, congestive heart failure (CHF), premature atrial complexes on electrocardiography, American Stroke Association class III or IV, and type of procedure were independent predictors of new SVA in the postoperative period. Of the surgical procedures, abdominal aortic aneurysm repair and abdominal, vascular, and intrathoracic procedures were particularly associated with an elevated risk of postoperative SVA.

Postoperative cardiac complications such as CHF, cardiac ischemia, myocardial infarction, ventricular tachycardia, cardiac arrest, and postoperative hypotension, as well as noncardiac events such as pneumonia, bacteremia, infection, urinary tract infection, stroke, pulmonary embolism, and gastrointestinal bleeding, were independently correlated with development of SVA. This study also suggested that the use of beta-blockers and calcium channel blockers appeared to have no effect on the development of SVA postoperatively.

Additional studies
In a prospective study of 462 patients in the intensive care unit (ICU) after noncardiothoracic surgery, the incidence of new-onset atrial arrhythmias was 10.2%. Most arrhythmic events occurred in the first 2 days, and patients with arrhythmic events had a higher mortality rate, a longer ICU stay, and a longer hospital stay than those without arrhythmic events, although most deaths were the result of sepsis and cancer and not the rhythm disturbance per se.

One of the earliest studies on postoperative AF was conducted in patients undergoing cancer surgery. AF appeared to be precipitated by sepsis, pneumonia, CHF, cardiac ischemia, pulmonary embolism, and hypokalemia. Advanced age and male sex were key risk factors, a finding that has been confirmed in subsequent studies. In this study, which appears to have major limitations (including a small sample size and being limited to a surgical ICU setting), AF did not have major clinical sequelae.

In a prospective study from the United Kingdom that included 226 patients undergoing colorectal surgery, 29 (13%) had significant arrhythmias on electrocardiographic monitoring, with AF being the most common arrhythmia. Electrolyte disturbances were often present, and patients frequently required rapid administration of antiarrhythmic agents.

In another prospective study from the United
Kingdom, this one of 51 patients undergoing colorectal surgery, 13 (26%) developed a postoperative arrhythmia, most often A F. Significant univariate correlates of A F in this study were age, hypertension, preoperative and postoperative potassium levels, and postoperative pulmonary edema. Thirty-one percent of all patients who developed the arrhythmia had sepsis, compared with 18% of controls ($P = .38$).

A retrospective study of 13,696 patients undergoing noncardiothoracic surgery over 2 years revealed an A F incidence of 0.37% (51 patients). Most of those affected had cardiac risk factors at the time of surgery, a positive fluid balance, or electrolyte or arterial oxygen saturation abnormalities.

**Bottom line on incidence and clinical predictors**

The incidence of postoperative A F/SVA in patients undergoing major noncardiothoracic surgery is difficult to estimate but varies from approximately 0.37% to 26%, depending on the population studied and the rigor of postoperative monitoring. Advanced age, electrolyte imbalances, infection and sepsis, CHF, pulmonary embolism, and hypotension appear to predict the development of this arrhythmia quite consistently.

**Effect on mortality unknown**

The effect of A F/SVA on mortality is debatable. Most studies indicate that it appears to prolong the length of hospital stay and also contributes significantly to morbidity, although no definitive conclusions can be drawn since the majority of the data is retrospective. Larger prospective studies stratifying patients by surgical type, anesthesia type, and preoperative cardiac risk factors are required to better quantify this problem and perhaps develop reproducible risk indices.

**REFERENCES**


**Q: How can postoperative ileus be prevented and treated?**

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**A:** A multifaceted approach that addresses the mechanical and chemical pathophysiology of ileus appears appropriate, although there is a paucity of prospective data to support it.

Postoperative ileus (POI) describes a period of impaired gastrointestinal (GI) motility without mechanical obstruction that occurs after surgery. It is characterized by abdominal distension, delayed passage of gas and bowel movement, lack of bowel sounds, and accumulation of gas and fluid in the bowel, creating symptoms of nausea and vomiting. Ileus can last from 2 days to more than 1 week, and contributes to delayed enteral nutrition. It is a common and clinically important problem that also contributes to prolonged patient discomfort and hospitalization.

**Multimodal approach to treatment**

Several contributors have been linked to inhibition of GI motility, including the nervous system, neurotransmitters, local factors, hormones, inflammation, anesthesia, and narcotic analgesics. Current research therefore suggests a multifaceted approach to prevention and treatment of POI.

Minimally invasive surgery, use of regional anes-

* Dr. Singh reported that she has no commercial affiliations or financial interests that pose a potential conflict of interest with this article.
therapeutic agents (specifically thoracic epidural anesthesia), treatment of prolonged electrolyte abnormalities (eg, hypokalemia, hyponatremia, and hypomagnesemia), and reduction of opioid use in the postoperative period have all been suggested to be beneficial in preventing POI. Minimal manipulation of the intestines can help to reduce the inflammatory cascade of cytokines and prostaglandins in the bowel wall that has been associated with significant intestinal muscle dysfunction.

**Individualize other options**

In the past, early ambulation was thought to enhance intestinal motility, but study results are inconclusive, and the benefits are derived mostly from a reduction of other pulmonary and thromboembolic complications.

Treatment of POI has usually been supportive, consisting of nasogastric decompression and intravenous fluids. Recent studies have also questioned the utility of nasogastric decompression, concluding that it does not shorten time to first bowel movement and, in fact, may contribute to postoperative complications such as fever, pneumonia, and atelectasis.

Athough the findings from these studies do not support routine use of nasogastric decompression, the clinician must decide which patients may benefit from symptomatic relief.

A variety of pharmacologic agents has been tried as potential treatments for POI. Metoclopramide and other prokinetic agents decrease emesis and enhance motility by acting as dopamine antagonists and cholinergic stimulants. The macrolide antibiotic erythromycin also acts as a motilin agonist, and stimulates activity in the gut migrating motor complex, theoretically enhancing bowel activity. Although nonsteroidal anti-inflammatory drugs (NSAIDs) may reduce the inflammatory response to surgery as well as decrease the need for opiates, careful consideration should be given to their use in light of their effects on platelets and their association with GI bleeding. In early clinical trials, the investigative mu-opioid receptor antagonist alvimopan was shown to reduce opioid-induced bowel dysfunction in patients receiving chronic opioid therapy without disrupting centrally mediated opioid analgesia. Studies evaluating other opioid antagonists (eg, naloxone), adrenergic blockers, parasympathetic agonists (eg, neostigmine), and laxatives as possible stimulators for the GI tract have been inconclusive; these agents have either been associated with prominent side effects or been shown to be ineffective in reducing POI.

Early postoperative feeding, before ileus resolves, has been promoted as a way to decrease the duration of POI, and several studies have demonstrated that early postoperative nutrition reduces gut permeability, enhances immunocompetence, and decreases the stress response to surgery.

Chewing gum in the postoperative setting has been shown to enhance bowel motility, with earlier passage of flatus and defecation compared with controls. The mechanisms appear to be vagal cholinergic stimulation and the release of gastrin, pancreatic polypeptide, and neurotensin, all of which affect GI motility.

Massage of the abdominal wall daily after colectomy has been shown in a randomized trial to decrease postoperative pain and ileus.

Other potential treatments being evaluated include electrical stimulation of the bowel wall, mechanical massage, acupuncture, and atilmotin, a synthetic human motilin.

**Bottom line: A core approach plus tailored supportive measures**

Currently, treatment of POI can best be achieved by using a multimodal approach that combines several therapies. Minimizing the use of opioids and handling of intestines, as well as other supportive options (eg, gum chewing, early ambulation and/or feeding, use of NSAIDs) can be individualized at the physician’s discretion to improve POI. There are currently no therapies approved for POI by the US Food and Drug Administration, but ongoing research is expected to define the potential of emerging pharmacotherapies to reduce the incidence and severity of POI.

**REFERENCES**


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