Perioperative Medication Management

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3. level 3 studies, which meet none of the evidence criteria for that study type or are derived from expert opinion, commentary, or consensus.

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1. Screening

Ask all preoperative patients about medication intake.

1.1 Ask preoperative patients about all prescription medications.

Recommendations

- Ask the patient to bring in the actual medications or a list with the names, doses, and frequencies.
- Review medications used with all patients to determine the indication for the drug, the possible effects (both risks and benefits) of each medication perioperatively, and whether or not the patient has adhered to the medication and dosage.

Evidence

- In a study of 304 patients admitted to a general internal medicine inpatient unit, 25% of drugs in use were not recorded, and 61% of patients had at least one drug unrecorded. These drugs included medications that require management in the perioperative period, including cardiovascular agents and NSAIDs (1).
- A cross-sectional study compared patient-reported medication use with medications documented in the medical records of 312 outpatients. Discrepancies were found in 76% of patients; 51% were taking unrecorded medications, 29% were not taking a recorded medication, and 20% were taking a different dosage from what was recorded (2).
- A cross-sectional study compared medication lists generated in the clinic (using pill bottles and patient reports) with medications found in the home in 50 patients who were newly referred to a geriatrics clinic. Overall, 48% of patients were taking at least one medication that they did not report and 19% were taking at least one prescription medication that they did not report (3).

Rationale

- Patients are often on numerous medications, some of which they may not take and others that they may not need.
- Patients may forget to inform the physician of a medication they are taking.
- Patients taking multiple medications may be at increased risk for potential adverse drug interactions.

1.2 Ask all preoperative patients about OTC and herbal medication use.

Recommendations

- Review OTC and herbal medication use with the patient to prevent any potential adverse effects, and highlight the paucity of human data on many herbal medications.
- Stop herbal medications before surgery.

Evidence

- A 2014 systematic review of the effect of preoperative aspirin on outcomes of coronary artery bypass surgery included 8 randomized trials and 19 observational trials. Aspirin increased postoperative bleeding in randomized trials (difference of means, 132 mL; \( P=0.002 \)) and observational studies (difference in means, 133 mL; \( P=0.003 \)), transfusion requirements in randomized trials (difference in means, 0.67; \( P=0.02 \)) and observational studies (difference in means, 0.19; \( P=0.02 \)), and the need for reoperation for bleeding in randomized trials (OR, 1.76 [CI, 1.05 to 2.93]) but not in observational studies (OR, 1.13 [CI, 0.91 to 1.42]) (4).
- A 2001 systematic review of the use of herbal medications in the perioperative period found no randomized trials but summarized the findings of case series and observational studies of the most commonly used products, including echinacea, ephedra, garlic, ginkgo, ginseng, kava, St. John's
wort, and valerian. The review noted that complications during the perioperative period can arise from direct and pharmacodynamic or pharmacokinetic effects of medications. Effects described included immunostimulatory effects from echinacea; tachycardia, hypertension, and vasoconstriction from ephedra; platelet dysfunction from garlic; platelet inhibition and bleeding from ginkgo and ginseng; CNS effects from kava; drug metabolism changes from St. John's wort; and sedation from valerian (5).

- A 2001 systematic review of drug interactions between the seven top-selling herbal medicines and prescribed drugs included 17 clinical trials and 41 case reports or case series. Garlic, ginkgo, and ginseng had interactions with warfarin and appeared to cause bleeding. St. John's wort decreased levels of many drugs (e.g., digoxin, warfarin, oral contraceptive, and cyclosporine) and precipitated serotonin syndrome, and kava had dopaminergic antagonistic properties (6).

- A prospective cohort study evaluated the relationship between traditional and herbal medication use and perioperative events in 601 patients undergoing elective surgery. In the multivariate analysis, patients who were prescribed Chinese herbal medications were more likely to have preoperative events (adjusted RR, 2.21 [CI, 1.14 to 4.29]) but not intraoperative or postoperative events compared with patients who did not take herbal medications. Use of traditional Chinese herbal medicines appeared to cause hypokalemia; patients taking ginseng did not have prolonged PTTs, and those taking ginger did not have elevated INRs or prolonged PTTs (7).

- A cross-sectional study evaluated the use of alternative medication in 2560 patients awaiting elective surgery. Overall, 39.2% admitted to using some form of alternative medicine supplements; 44.4% did not consult with their primary physicians, and 56.4% did not inform the anesthesiologists (8).

- A cross-sectional study evaluated the use of alternative medicines among 3106 patients seen in a preoperative clinic. Herbal medications were used by 22%, and 51% used vitamins (9).

- A cross-sectional study evaluated herbal medication use among 2723 patients in the UK before anesthesia. Overall, 131 patients (4.8%) were taking herbal medications, but it was recorded on the patient's chart in only two cases (10).

- A cross-sectional study evaluated self-reported use of herbal medications in 2186 patients undergoing elective surgery. Overall, 57% had ever taken herbal medications, 38% had taken herbal medications in the last 2 years, and 16% used herbal medicines during the month of surgery. Use was higher among those undergoing gynecologic procedures (OR, 1.68 [CI, 1.29 to 2.18]) and those with a self-perception of good health (OR, 1.32 [CI, 1.04 to 1.69]) and was lower in black patients (OR, 0.69 [CI, 0.51 to 0.95]), patients with pulmonary symptoms (OR, 0.77 [CI, 0.62 to 0.94) or diabetes (OR, 0.46 [CI, 0.32 to 0.68]), and patients undergoing vascular surgery (OR, 0.19 [CI, 0.07 to 0.48]) (11).

**Rationale**
- Many patients are using OTC and herbal meditations that can have potential drug interactions, and many are used for symptomatic relief only.

**Comments**
- Vitamin E and alternative therapies may potentially interact with warfarin (12).

### 1.3 Screen for conditions that may affect drug metabolism

**Recommendations**
- Ask about any history of liver, kidney, or thyroid disease.
- Obtain lab tests as indicated to evaluate renal (BUN/creatinine), hepatic (transaminases, bilirubin), and thyroid (TSH, T₄) function in appropriate patients.

**Evidence**
• Consensus.

Rationale
• Hepatic and renal insufficiency may lead to increased levels of drugs metabolized by those systems.
• Hyperthyroidism may accelerate metabolism in general.
2. Diagnosis

Confirm the diagnostic indication for therapy, and perform a risk-benefit analysis of continuing, stopping, or starting a drug preoperatively.

2.1 Determine the nature and extent of comorbid conditions to assess the need for and timing of drug therapy.

Recommendations

- Assess patients for:
  - Left ventricular dysfunction by history (known heart failure, dyspnea, paroxysmal nocturnal dyspnea, orthopnea), physical exam (tachypnea, jugular venous distension, S3, rales, edema), and diagnostic tests (echocardiography, when indicated). Optimize medications (diuretics, ACE inhibitors, β-blockers, digoxin) for heart failure to prevent perioperative decompensation.
  - CAD (clinical risk factors, history of MI, angina, chest pain, dyspnea, ischemic changes on ECG), and continue or start antianginal medications to minimize perioperative ischemia.
  - Stage II-III hypertension (systolic BP ≥160 mm Hg, diastolic BP ≥100 mm Hg), and start, continue, or add medications and adjust doses to obtain better control to minimize perioperative BP lability.
  - Valvular heart disease based on history (rheumatic fever, murmurs), physical exam (murmur), and diagnostic tests (echocardiography) when indicated, and initiate appropriate endocarditis prophylaxis based on the cardiac condition and type of surgical procedure.
  - Bronchospasm (COPD or asthma), and optimize pulmonary status with bronchodilators and steroids as indicated.
  - Any change in sputum quantity or quality that may suggest an infection requiring antibiotic treatment in patients with COPD.
  - Symptoms (hot or cold intolerance or weight loss or gain) and signs (goiter, tremor) of thyroid disease, particularly hyperthyroidism; start or continue appropriate treatment such as propylthiouracil, β-blockers, or thyroid as needed.
  - Renal insufficiency (risk factors, BUN/creatinine) and liver disease (history of hepatitis, alcohol and drug use, abdominal exam, liver function tests) because these conditions may alter drug metabolism.
  - Risk profile for DVT, including age, history, comorbid conditions, immobility, and surgical procedure, and prescribe an appropriate regimen for prophylaxis.
  - Optimize glycemic control in patients with diabetes before surgery, using oral medication or insulin as needed, and consider perioperative insulin in patients undergoing major surgery.
  - Be willing to use medications with known potential for adverse effects during surgery if these drugs are essential to the patient's health.

- See module Preoperative Evaluation.
- See module Perioperative Management of Diabetes Mellitus.
- See module Perioperative Management of Heart Failure.
- See module Perioperative Management of Hypertension.
- See module Perioperative Management of Hyperthyroid Patients.
- See module Perioperative Management of Hypothyroid Patients.
- See module Preoperative Cardiac Risk Assessment and Management.
- See module Venous Thromboembolism Prophylaxis in the Surgical Patient.

Evidence
• The 2007 ACC/AHA guidelines for perioperative evaluation recommended assessing for the presence of active cardiac conditions. The guideline recommended continuing β-blockers in patients who are already receiving them and considering β-blockers in patients at high risk for cardiac complications or those undergoing high-risk surgery (13).

• A 2008 systematic review of the effect of perioperative β-blockers on mortality included 33 trials with 12,306 patients and found that treatment with β-blockers did not lead to improved all-cause or cardiovascular mortality. Treatment was associated with a decrease in nonfatal MI (NNT, 63) and an increase in nonfatal stroke (NNH, 293) (14; 15).

• A retrospective cohort study evaluated the impact of β-blocker discontinuation after vascular surgery among 140 patients who were treated with β-blockers perioperatively, among whom 8 were taken off the medication postoperatively. Withdrawal was associated with increased cardiovascular mortality (0% vs. 25%, P=0.005) and postoperative MI (16).

• In a case-controlled study of patients with deep sternal site infections after CABG, those patients with diabetes and a preoperative glucose level >110 mg/dL had a higher risk for deep sternal wound infections (OR, 1.4 [CI, 0.4 to 4.8]; P=0.6) (17).

• A 2012 noninferiority randomized, controlled trial compared liberal (120 mg/dL to 180 mg/dL) with tight (90 mg/dL to 120 mg/dL) glucose goals in 189 patients with diabetes undergoing CABG. There were no differences in rates of infection between the groups, but the liberal group had fewer episodes of hypoglycemia (18).

• A 2011 randomized, controlled trial compared liberal (120 mg/dL to 180 mg/dL) with tight (90 mg/dL to 120 mg/dL) glucose goals (achieved with insulin infusion) in 82 patients undergoing CABG. There were no differences in the rates of major adverse events between the groups, but there were more episodes of hypoglycemia in the tight-control group (NNH, 1.6) (19).

• A prospective cohort study evaluated the relationship between hypokalemia and perioperative complications in 2402 patients who underwent elective CABG. Perioperative arrhythmias were seen in 53.7% of patients. Patients with preoperative hypokalemia were more likely to have serious perioperative arrhythmia (OR, 2.2 [CI, 1.2 to 4.0]) (20).

Rationale
• Untreated or uncontrolled medical illness may have a more deleterious impact on outcome than the medications used to treat it.

Comments
• Preoperative treatment can prevent thyroid storm in hyperthyroid patients.

• Consider the consequences of discontinuing a drug (e.g., for uncontrolled hypertension, uncontrolled diabetes, exacerbation of asthma).

2.2 Consider the risk associated with the particular surgical procedure when planning medication use.

Recommendations
• Consider using intravenous (as opposed to subcutaneous) insulin for better glucose control in diabetics undergoing complex, high-risk surgical procedures (e.g., CABG).

• Avoid the use of sliding-scale insulin in preference for long-acting and prandial regimens.

• Consider supplemental steroid coverage when indicated, based on the type of surgery and the likelihood of adrenal suppression.

• Consider perioperative β-blockers in patients with multiple cardiac risk factors (RCRI >2) undergoing intermediate- to high-risk noncardiac surgery or vascular surgery.
• Use appropriate DVT prophylaxis based on the risk of the surgical procedure along with the patient's age and underlying risk factors.

• Use appropriate endocarditis prophylaxis based on the risk associated with the specific type of surgery and the patient's underlying cardiac disease.

• Consider the risk for bleeding based on the procedure in determining the use of perioperative anticoagulation.

• Consider the risk for postoperative wound infection based on the type of surgery, and use appropriate antibiotic prophylaxis.

• See table Surgical Risk Stratification and Associated VTE Incidence.

Evidence

• A 2012 guideline from the American College of Chest Physicians provided evidence-based guidelines for the assessment of risk and the use of VTE prophylaxis, and recommended different DVT prophylaxis based on the risk associated with the procedure (21).

• The 2007 ACC/AHA guidelines for perioperative evaluation recommended assessing for the presence of active cardiac conditions. The guideline recommended continuing β-blockers in patients who are already receiving them and considering β-blockers in patients at high risk for cardiac complications or those undergoing high-risk surgery (13).

• A 2008 systematic review of the effect of perioperative β-blockers on mortality included 33 trials with 12,306 patients and found that treatment with β-blockers did not lead to improved all-cause or cardiovascular mortality. Treatment was associated with a decrease in nonfatal MI (NNT, 63) and an increase in nonfatal stroke (NNH, 293) (14; 15).

• A study used a prospective database with over 200,000 surgical patients to identify factors predicting cardiac events. In the logistic regression analysis, the type of surgery was predictive of cardiac events; particularly high risk was seen with aortic (OR, 4.96 [CI, 3.55 to 6.93]), upper abdominal (OR, 4.02 [CI, 2.89 to 5.60]), and brain (OR, 4.04 [CI, 1.79 to 9.13]) procedures, and low risk was seen with breast procedures (OR, 0.20 [CI, 0.08 to 0.50]) (22).

• A 2012 noninferiority randomized, controlled trial compared liberal (120 mg/dL to 180 mg/dL) with tight (90 mg/dL to 120 mg/dL) glucose goals in 189 patients with diabetes undergoing CABG. There were no differences in rates of infection between the groups, but the liberal group had fewer episodes of hypoglycemia (18).

• A 2011 randomized, controlled trial compared liberal (120 mg/dL to 180 mg/dL) with tight (90 mg/dL to 120 mg/dL) glucose goals (achieved with insulin infusion) in 82 patients undergoing CABG. There were no differences in the rates of major adverse events between the groups, but there were more episodes of hypoglycemia in the tight-control group (NNH, 1.6) (19).

• A 2002 narrative review of corticosteroid supplementation for adrenal insufficiency noted that major surgery is associated with increased levels of stress and requires more intensive steroid supplementation than less stressful procedures (23).

Rationale

• Different surgical procedures have varying levels of risk with respect to stress, DVT, endocarditis, bleeding, and wound infection.

Comments

• A patient on chronic anticoagulation with warfarin may require “bridging therapy” before a procedure associated with a high risk for thromboembolism, as opposed to just discontinuing it several days before a low-risk procedure (24).
2.3 Use lab testing preoperatively to measure drug levels, assess potential drug toxicity, and assess control of a disease.

**Recommendations**

- Measure drug levels to assess adherence and efficacy when indicated for seizures, arrhythmias, or other chronic illness.
- Obtain drug levels when toxicity is suspected.
- Obtain liver or kidney function tests for potentially hepatotoxic or nephrotoxic drugs.
- Obtain glucose levels perioperatively to assess control of diabetes and adjust therapy.
- Obtain thyroid function tests (TSH, T₄) preoperatively to assess thyroid status if significant hyperthyroidism or hypothyroidism is suspected.
- See table [Laboratory and Other Studies for Drug Prescribing in the Surgical Patient](#).

**Evidence**

- Consensus.

**Rationale**

- Knowledge of drug levels may be useful, especially when adherence needs to be confirmed or toxicity is suspected.
- Drug absorption, distribution, metabolism, and elimination may be altered by anesthesia or analgesic drugs; therefore, dose, frequency, and mode of administration may need to be adjusted to achieve therapeutic and avoid toxic levels.
- Uncontrolled diabetes is associated with poor wound healing, and more intensive therapy may decrease morbidity.
- Untreated hyperthyroidism may be related to the development of thyroid storm perioperatively.

**Comments**

- Some of the lab tests may need to be monitored both intraoperatively (glucose) and postoperatively (glucose, BUN/creatinine, potassium, certain drug levels), as well as preoperatively.
3. Consultation

Consider consultation with all physicians involved in patients' care to define their medical condition and prescription medication needs. Consult appropriate medical subspecialists for help in managing perioperative medication use.

3.1 Discuss underlying medical conditions, the need for current medication or alternatives, and an anesthetic plan with the anesthesiologist and the patient's primary and specialist physicians.

Recommendations
- Consult the patient’s physician to obtain detailed information about medical problems and medications and to ascertain whether a particular drug may be indicated or contraindicated.
- Consider a medical subspecialty and/or anesthesiology consultation if there are questions about a patient's fitness for surgery, need for further diagnostic tests before surgery, or need to modify medications.

Evidence
- Mainly consensus.
- A 2003 narrative review discussed interactions between anesthetic agents and other drugs (25).

Rationale
- More information regarding the stability and severity of the patient’s disease may be needed to decide on the use or modification of specific drugs.
- The anesthesiologist should be aware of the patient's medications and the potentially important drug interactions with anesthetics.

3.2 Consult medical subspecialists to help determine the benefits and risks of stopping a medication before surgery, identify possible safer alternatives, or start medications in the perioperative period.

Recommendations
- Consult specialists as needed and ensure communication among all consultants.
- Consider consultation with a cardiologist:
  - To manage chronic anticoagulation in patients with heart disease
  - To determine the need for specific therapy in patients with risk factors for CAD
  - To treat perioperative arrhythmias
  - To manage antplatelet agents in patients with recent stents
- Consider consultation with a nephrologist to adjust medications in patients with chronic or acute kidney disease.
- Consider consultation with a neurologist:
  - To manage antiepileptic medications
  - To optimize the timing of antplatelet therapy in patients with cerebrovascular disease
- Consider consultation with an endocrinologist:
  - For help with the perioperative management of insulin or oral hypoglycemic agents in patients with diabetes
- To advise regarding stress-dose steroids

**Evidence**
- Consensus.

**Rationale**
- Medical specialists may be helpful in making a decision about withholding a medication in the perioperative period.
- Treatment of a condition after surgery may be different from that in the nonsurgical setting.

**Comments**
- It is important to consult with the anesthesiologist about agents used in the operating room and the surgeon about the extent and complications of a given procedure to determine implications for medication management.
- A 2013 Cochrane review of computerized drug-dosage advice found some benefits in anticoagulation dosing and the correct administration of some antibiotics (26).
4. Hospitalization

Consider hospitalization for serious comorbid illness or preoperative adjustment of specific medical regimens that would be difficult to perform on an outpatient basis. 

4.1 Consider hospitalization to adjust perioperative medication in patients with severe comorbid illness or drug toxicity.

Recommendations

- Consider hospitalization preoperatively for:
  - Anticoagulant “bridge therapy” with warfarin to heparin or LMWH
  - Toxicity with warfarin, digoxin, or other drugs requiring monitoring
  - Uncontrolled diabetes (diabetic ketoacidosis/hyperosmolar state) for intravenous insulin
  - Bowel prep in an elderly, debilitated patient to minimize risk for dehydration
  - Detoxification of an alcoholic or drug abuser
  - Instituting certain antiarrhythmic therapy
  - Abrupt discontinuation of a drug that may trigger an exacerbation of a chronic illness, such as asthma, arrhythmia, or seizure
  - New illness or exacerbation of a chronic illness (pneumonia, COPD, angina) requiring inpatient observation, monitoring, or treatment not available in the outpatient setting

Evidence

- Consensus.

Rationale

- Certain regimens are difficult or impossible to follow at home due to the nature of the regimen itself, potential side effects, or the lack of finances or drug coverage to obtain the medication as an outpatient.
5. Therapy

Continue or institute drug therapy when there is clear diagnostic indication after thorough risk-benefit assessment and discussion with the patient, and discontinue or adjust medications that may have potentially adverse effects. Consider the use of non-drug therapy whenever possible to minimize the potential for drug interactions or adverse effects.

5.1 Continue necessary therapies for chronic medical problems.

Recommendations

- Continue current medications perioperatively unless they are likely to have an adverse effect or significant drug interactions.
- Consider necessary dose adjustments mandated by anesthesia or surgery.
- In patients with diabetes:
  - Hold metformin for 1 or more days before surgery
  - Advise patients on other oral medications to continue them up until the morning of surgery
  - Plan to use dextrose-containing intravenous solutions in patients who have been on sulfonylureas
  - Never withhold basal insulin
  - In patients receiving insulin, adjust insulin dosage before the surgical procedure to avoid hypoglycemia
- In patients with hypertension:
  - Continue β-blockers, clonidine, and calcium-channel blockers in the preoperative period, including on the day of surgery
  - Discontinue ACE inhibitors, ARBs, and diuretics on the morning of surgery if possible
  - Consult established guidelines and carefully consider need for bridging anticoagulant therapy depending on risk for thromboembolic events.
- Provide appropriate prophylaxis as indicated to prevent DVT, endocarditis, ischemia, and wound infection.
- Discuss the need for a given drug with the patient.
- See table Perioperative Cardiovascular Medication Management.
- See table Perioperative Rheumatologic Medication Management.
- See table Perioperative Pulmonary Medication Management.
- See table Perioperative Endocrine Medication Management.
- See table Perioperative Neurologic Medication Management.
- See table Perioperative Psychiatric Medication Management.
- See table Perioperative Gastrointestinal Medication Management.
- See table Perioperative HIV Medication Management.
- See table Perioperative Herbal Medication Management.
- See module Perioperative Management of Diabetes Mellitus.
- See module Perioperative Management of Hypertension.
Evidence

- A 2012 guideline from the American College of Chest Physicians recommended the use of VTE prophylaxis for all patients undergoing surgery, with specific interventions dependent upon the surgical risk (21).
- Withdrawal syndromes after cessation of antihypertensive agents have occurred with β-blockers, methyldopa, clonidine hydrochloride, guanabenz, and betanidine sulfate, with signs and symptoms ranging from nervousness, tachycardia, headache, and nausea to exacerbation of myocardial ischemia (β-blockers) or hypertension (clonidine, methyldopa) in the post-treatment period (27).

Rationale

- Specific medications are necessary to control various medical conditions.
- Prophylactic medications can reduce perioperative morbidity and mortality.
- Adherence will be improved if the patient understands how the medications are to be taken perioperatively, especially if it differs from the usual regimen, and the importance of the drug therapy and the risk of withholding treatment.

Comments

- Abrupt discontinuation of clonidine resulted in 14 of 14 patients developing excessive increases in heart rate and BP and 7 of 14 having subjective symptoms (28).
- After clonidine withdrawal, both systolic and diastolic blood pressures increased to values significantly greater than during clonidine administration (29).
- β-blocker discontinuation after vascular surgery was associated with increased cardiovascular mortality (0% vs. 25%, P=0.005) and postoperative MI in 8 patients who discontinued β-blockers postoperatively compared with 132 patients who continued β-blockers (16).

5.2 Adjust drug doses or substitute drugs as needed in the perioperative setting.

Recommendations

- Adjust doses as necessary to maintain therapeutic levels of crucial drugs (e.g., phenytoin and theophylline) and avoid toxicity.
- Withhold or discontinue medications (e.g., anticoagulants or oral hypoglycemic agents) with significant potential for adverse events.
- Consider alternative drugs (longer acting or of a related class) or routes of administration (intravenous or transdermal for nitrates or clonidine if NPO) when necessary.
- Be aware of potential drug interactions when prescribing additional medications, especially with drugs that have a low therapeutic index (e.g., warfarin, digoxin, or hypoglycemic agents).
- See table Perioperative Cardiovascular Medication Management.
- See table Perioperative Rheumatologic Medication Management.
- See table Perioperative Pulmonary Medication Management.
- See table Perioperative Endocrine Medication Management.
- See table Perioperative Neurologic Medication Management.
- See table Perioperative Psychiatric Medication Management.
- See table Perioperative Gastrointestinal Medication Management.
- See table Perioperative HIV Medication Management.
• See table Perioperative Herbal Medication Management.

Evidence
• A 2005 systematic review of warfarin interactions with drugs and foods included 181 studies, of which 84% were of poor quality, mostly case reports. Most interactions (72%) potentiated the effects of warfarin. The review presented a long list of culprit medications (30).

• A randomized trial compared insulin plus metformin to insulin alone in 200 postoperative patients with diabetes who had undergone CABG. The primary outcome was levels of lactate. After 2.5 days, lactate levels did not differ between the groups and no patient in either group developed lactic acidosis (31).

• A 2003 narrative review discussed interactions between anesthetic agents and other drugs (25).

Rationale
• Anesthetic agents may alter hepatic metabolism and renal excretion.

• Surgical patients may be NPO for several days and, therefore, unable to take their usual medications orally.

• Medications may potentiate the effects of anesthetic or analgesic drugs.

• Continuation of these medications may have a more deleterious effect on surgical outcome than their withdrawal would on the underlying disease.

• Patients on multiple medications are at risk for multiple-drug interactions that may be additive, antagonistic, or difficult to predict.

5.3 **Start new medications prophylactically when appropriate to minimize risk for DVT, endocarditis, wound infection, myocardial ischemia, or gastric aspiration.**

Recommendations
• Provide DVT prophylaxis to all patients undergoing surgery, and choose a specific strategy based on risk stratification:
  • Consider both drug and mechanical measures in prescribing prophylactic regimens for all patients undergoing surgery
  • Base the choice of VTE prophylaxis on risk factors associated with the procedure, patient comorbidities, and bleeding risk
  • Closely monitor perioperative patients for complications of VTE prophylaxis
  • Determine the appropriate duration of VTE prophylaxis

• Provide endocarditis prophylaxis to patients with:
  • Prosthetic valves
  • Complex congenital heart disease (not repaired or repaired within the past 6 months)
  • Previous endocarditis
  • Heart transplant with valvular heart disease
  • Patients undergoing specific dental and upper respiratory tract procedures

• Consider perioperative β-blockade titrated to heart rate and BP:
  • For patients undergoing vascular surgery who are known to have CAD or ischemia on preoperative testing or who are at high risk for cardiac complications
  • For some patients undergoing intermediate-risk surgery who are known to have CAD or who are at high risk for cardiac complications
  • In patients already receiving β-blockers for the treatment of other conditions
• Provide prophylaxis for surgical wound infection for most procedures, including major intra-abdominal, intrathoracic, intracranial, and vascular surgery.
• Provide gastric aspiration prophylaxis for morbidly obese or pregnant patients.
• See table VTE Prophylaxis Regimens by Surgical Procedure.
• See table Perioperative Cardiovascular Medication Management.
• See table Perioperative Rheumatologic Medication Management.
• See table Perioperative Pulmonary Medication Management.
• See table Perioperative Endocrine Medication Management.
• See table Perioperative Neurologic Medication Management.
• See table Perioperative Psychiatric Medication Management.
• See table Perioperative Gastrointestinal Medication Management.
• See table Perioperative HIV Medication Management.
• See table Perioperative Herbal Medication Management.

Evidence
• A 2012 guideline from the American College of Chest Physicians recommended the use of VTE prophylaxis for all patients undergoing surgery, with specific interventions dependent upon the surgical risk (21).
• A 2011 guideline from the American Society of Anesthesiologists on preoperative fasting and the use of drug agents to reduce the risk for pulmonary aspiration recommended against the routine use of gastric acid blockers in surgical patients. The guideline did not address the use of medications in patients at increased risk for aspiration (32).
• The 2009 update of the 2007 ACC/AHA guidelines on perioperative cardiac evaluation recommended continuing β-blockers in patients who are already receiving them and considering β-blockers in patients at high risk for cardiac complications or those undergoing high-risk surgery (33).
• A 2008 guideline from the ACC/AHA recommended prophylaxis only for patients at increased risk for bacteremia and with increased risk for infective endocarditis, with amoxicillin as the first-line agent for most patients requiring dental prophylaxis (34).
• A 2008 systematic review of the effect of perioperative β-blockers on mortality included 33 trials with 12,306 patients and found that treatment with β-blockers did not lead to improved all-cause or cardiovascular mortality. Treatment was associated with a decrease in nonfatal MI (NNT, 63) and an increase in nonfatal stroke (NNH, 293) (14).
• A 2012 review of antimicrobial prophylaxis in surgery was published in The Medical Letter (35).

Rationale
• Surgical patients are potentially at risk for complications that can be minimized by appropriate prophylaxis.

5.4 Substitute non-drug alternatives if appropriate.

Recommendations
• Discontinue medications used to treat benign or self-limited symptoms.
• Avoid medications in the perioperative setting if there are non-drug alternatives.
• Consider using hot or cold packs instead of analgesics or anti-inflammatory drugs for pain or arthralgias.
- Consider intermittent pneumatic compression instead of heparin for DVT prophylaxis to avoid potential bleeding problems or if anticoagulants are contraindicated
- If time permits, initiate diet and lifestyle changes before surgery to minimize the use of antihypertensive, hypoglycemic, or lipid-lowering medications.
- Provide patient education and reassurance to decrease anxiety and sedative requirements.

**Evidence**
- Consensus.

**Rationale**
- Alternative modalities may be less likely to cause adverse effects.
6. Patient Counseling

Involve patients in decision making with respect to medication use in surgery, especially when controversy exists or there are several alternatives.

6.1 Explain to the patient the potential harms vs. benefits of any medication prescribed perioperatively.

Recommendations
- Discuss the harms and benefits of any medication proposed, prescribed, or withheld in the perioperative period.
- Discuss the plan for continuing or restarting medications postoperatively or after discharge.

Evidence
- Consensus.

Rationale
- Patients should understand the reasons for taking or stopping their medications or for substituting other non-drug therapies when available.

6.2 Review with the patient any medications that should be discontinued or have dose adjustments before surgery.

Recommendations
- Inform patients of medications that should be discontinued more than 24 hours before surgery:
  - MAO inhibitors
  - Chlorpropamide
  - Warfarin
  - Newer oral anticoagulants (dabigatran, rivaroxaban, apixaban)
  - Antiplatelet agents (depending on indication and surgical procedure)
  - NSAIDs (depending on half-life)
  - Metformin (for radiocontrast procedures only)
  - Herbal medications
- Review the list of medications that should be discontinued within 24 hours of surgery:
  - Oral hypoglycemics (including metformin)
  - Some NSAIDs
  - Heparin
  - Diuretics (optional)
  - ACE inhibitors and ARBs (optional, depending on indication and blood pressure)
- Review the list of medications that may need modification of dosage perioperatively:
  - Insulin
  - Corticosteroids
- Discuss the importance of adherence to a preoperative medication regimen.
- Discuss the rationale behind the use of prophylactic medications, including harms, benefits, and options.

Evidence
• Consensus.

Rationale

• Patient participation in perioperative medication management is crucial to successful outcome and minimization of adverse events.
7. Follow-up

Recognize that medication use in the perioperative period requires ongoing assessment, patient education, and dosage adjustments.

7.1 Adjust medication doses as dictated by perioperative circumstances.

Recommendations
- Review the intraoperative anesthetic record for agents used and evidence of hypotension.
- Monitor medication levels and adjust doses during the perioperative period.
  - Adjust medication dosing based on perioperative renal insufficiency
  - Adjust medication dosing based on perioperative hepatic dysfunction
  - Monitor blood glucose and oral intake in patients with diabetes
- See module Perioperative Management of Diabetes Mellitus.
- See module Perioperative Management of Patients with Liver Disease.

Evidence
- A 1994 narrative review discussed the effect of anesthetic agents on renal function, noting that inhalational anesthetics, opioids, barbiturates, and benzodiazepines may reduce glomerular filtration rate and urine output (36).
- A cross-sectional study compared renal and hepatic function after the administration of sevoflurane and isoflurane in patients undergoing surgery who had normal baseline renal function. There were no differences between the anesthetic agents (37).

Rationale
- Various medications and hypotension may alter renal blood flow and thereby warrant dosage alterations in the postoperative period.
- Various anesthetics and hypotension may alter hepatic blood flow, particularly in patients with underlying hepatic dysfunction, and thereby warrant medication adjustments postoperatively.

Comments
- The etiology of postoperative renal and hepatic dysfunction is multifactorial and often related to factors other than a specific anesthetic agent. Hypotension, preexisting renal or hepatic dysfunction, aminoglycosides, and type of surgery have all been implicated as risk factors.

7.2 Use alternative agents or routes of administration as necessary.

Recommendations
- Consider alternatives to oral or enteral medications in patients who are NPO or have decreased bowel function postoperatively.
- Use intravenous preparations of the medication, if available, or a different drug in the same class.

Evidence
- Consensus.

Rationale
- Patients may not be able to take their usual medications postoperatively.
- Postoperative ileus may result in decreased absorption of medication.
- After GI or major abdominal surgery, patients are unable to take medications orally and may require a parenteral substitute until GI function returns.
• The patient may experience decompensation or exacerbation of various cardiovascular conditions if medications (or substitutes) are not continued.

7.3 Continue prophylactic medication (such as anticoagulants), β-blockers, and antibiotics postoperatively as appropriate. BC

Recommendations
• Continue DVT prophylaxis until the patient is ambulatory or discharged, or no longer depending on the procedure.
• Continue perioperative β-blockers, if used, beyond discharge in most patients.
• Consider giving an additional dose of antibiotics for surgical wound prophylaxis for a long surgical procedure.

Evidence
• A 2012 guideline from the American College of Chest Physicians recommended DVT prophylaxis until the patient is ambulatory and, in major orthopedic surgery, for a minimum of 10 to 14 days and possibly extended prophylaxis for up to 35 days (38).
• A 2012 review from The Medical Letter on antimicrobial prophylaxis for surgery recommended intraoperative repeat antibiotic dosing during procedures lasting longer than 3 hours, at intervals of one to two times the half-life of the antibiotic (35).

Rationale
• Ongoing risk for DVT is based on patient and procedural factors.
• Patients who are candidates for perioperative β-blockers also have indications for long-term therapy.
• If the duration of surgery was longer than 4 hours, the initial dose of antibiotics may be insufficient prophylaxis.

7.4 Remember to restart necessary medications that were stopped preoperatively to minimize potential complications. C

Recommendations
• Watch for:
  • Hyperglycemia if insulin or hypoglycemic medications were stopped before surgery, and slowly reintroduce them as the patient resumes oral feeding
  • Evidence of thromboembolism if anticoagulation was stopped or reduced preoperatively, and restart anticoagulants and antiplatelet agents when the surgeon feels there is no significant risk for bleeding
  • Evidence of heart failure if diuretics or ACE inhibitors were discontinued preoperatively, and restart them as soon as possible postoperatively
  • Restart medications for underlying conditions as soon as possible after surgery, substituting parenteral dosage forms if needed if the patient cannot take oral medications.

Evidence
• Consensus.

Rationale
• Glucose levels will increase due to the stress of surgery, dextrose-containing intravenous fluids, and increasing oral intake.
• The risk for an embolic or thrombotic event will decrease if the “unprotected period” off anticoagulation or antiplatelet therapy is minimized; however, the risk for postoperative bleeding may be increased if anticoagulation is resumed too quickly.
• Without their usual medications, some patients with left ventricular dysfunction may decompensate in the perioperative period.
References


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Perioperative Medication Management


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Glossary

**ACC**
American College of Cardiology

**ACE**
angiotensin-converting enzyme

**AHA**
American Heart Association

**ARB**
angiotensin receptor blocker

**BP**
blood pressure

**BUN**
blood urea nitrogen

**CABG**
coronary artery bypass graft(ing)

**CAD**
coronary artery disease

**CI**
confidence interval

**CNS**
central nervous system

**COPD**
chronic obstructive pulmonary disease

**DVT**
deep venous thrombosis

**ECG**
electrocardiography

**GI**
gastrointestinal

**HIV**
human immunodeficiency virus

**INR**
international normalized ratio

**LMWH**
low-molecular-weight heparin

**MAO**
monoamine oxidase

**MI**
myocardial infarction

**NNH**
number needed to harm

**NNT**
number needed to treat

**NPO**
nothing by mouth
**NSAID**
nonsteroidal anti-inflammatory drug

**OR**
odds ratio

**OTC**
over the counter

**PTT**
partial thromboplastin time

**RCRI**
Revised Cardiac Risk Index

**RR**
risk ratio

**T₄**
thyroxine

**TSH**
thyrotropin

**VTE**
venous thromboembolism
# Tables

## Laboratory and Other Studies for Drug Prescribing in the Surgical Patient

<table>
<thead>
<tr>
<th>Test</th>
<th>In Whom to Order</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug levels (e.g., digoxin, antiarrhythmics, antiepileptics, theophylline)</td>
<td>Patients on antiepileptics (phenytoin, phenobarbital, valproic acid), antiarhythmics (digoxin, quinidine), theophylline, and other drugs with a narrow therapeutic range. Obtain if toxicity suspected or if levels have not recently been checked. Some postoperative patients may need levels of aminoglycosides or vancomycin.</td>
<td>Drug levels may vary perioperatively due to interactions with anesthetic and analgesic agents.</td>
</tr>
<tr>
<td>Glucose</td>
<td>All patients with diabetes. Patients with prediabetic states (impaired glucose tolerance, impaired fasting glucose)</td>
<td>Evaluate diabetic control and adjust medications based on risk for perioperative hypoglycemia or hyperglycemia in diabetics.</td>
</tr>
<tr>
<td>Electrolytes (potassium)</td>
<td>Patients on diuretics, ACE inhibitors, or ARBs; patients with CKD or hyporenin-hypoaldosteronism</td>
<td>Assess for possible hypokalemia (diuretics) or hyperkalemia (ACE inhibitors, renal insufficiency, hyporenin-hypoaldosteronism).</td>
</tr>
<tr>
<td>BUN/Creatinine</td>
<td>Patients with CKD or acute kidney injury, patients taking potentially nephrotoxic drugs, patients with risk factors for renal disease.</td>
<td>Renal function may be unstable after intra- or postoperative hypotension, which may lead to renal insufficiency. Renal function may affect drug dosing.</td>
</tr>
<tr>
<td>Liver function tests</td>
<td>Patients on hepatotoxic drugs, patients with history of liver disease.</td>
<td>Dosing adjustments may be necessary for certain drugs metabolized by the liver.</td>
</tr>
<tr>
<td>CBC</td>
<td>Patients on drugs with bone marrow toxicity or drugs that cause hemolysis or thrombocytopenia</td>
<td>Heparin can commonly cause thrombocytopenia.</td>
</tr>
<tr>
<td>Thyroid function tests (free T₄, TSH)</td>
<td>Patients with known hyperthyroidism or hypothyroidism in whom levels have not recently been checked, or in whom medication doses have changed</td>
<td>Uncontrolled hyperthyroidism may increase surgical risk.</td>
</tr>
<tr>
<td>PT/INR/PTT</td>
<td>Patients on warfarin or heparin.</td>
<td>Assess level of anticoagulation, both preoperatively and postoperatively. Drug interactions and altered diet can interact with warfarin and affect the INR.</td>
</tr>
<tr>
<td>Bleeding time</td>
<td>Patients on antiplatelet agents who are undergoing certain high-risk surgeries. Not needed in most patients</td>
<td>Assess only if the patient has been on antiplatelet agents (ASA or NSAIDs) and risk for bleeding would be a factor (neurosurgery, surgery without direct access to the bleeding site) (rarely used).</td>
</tr>
</tbody>
</table>

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; ASA = acetylsalicylic acid (aspirin); BUN = blood urea nitrogen; CBC = complete blood count; CKD = chronic kidney disease; INR = international normalized ratio; NSAID = nonsteroidal anti-inflammatory drug; PT = prothrombin time; PTT = partial thromboplastin time; T₄ = thyroxine; TSH = thyrotropin.
**Perioperative Cardiovascular Medication Management**

### **β-blockers** (propranolol, metoprolol, atenolol, bisoprolol)

**Recommendation:** Continue in patients already receiving. Consider starting in high-risk patients undergoing vascular or high-risk noncardiac surgery.

**Comments:** To avoid withdrawal symptoms. To prevent perioperative cardiac events (target heart rate 55-65 beats/min), although while ischemia and nonfatal MI are reduced, stroke risk and overall mortality may be increased.

**Evidence:**

- A 2014 systematic review of the effect of perioperative β-blockers compared with placebo in patients with at least one risk factor for heart disease who were undergoing noncardiac surgery included eight trials. Overall, patients receiving β-blockers had a lower risk for MI (RR, 0.73 [CI, 0.61 to 0.86]), an increased risk for stroke (RR, 2.17 [CI, 1.35 to 3.50]), and no difference in mortality (RR, 0.91 [CI, 0.60 to 1.36]) (39).

- A 2010 systematic review of esmolol in patients undergoing noncardiac surgery included 32 randomized trials. Patients receiving esmolol had fewer episodes of cardiac ischemia (OR, 0.16 [CI, 0.05 to 0.54]) but similar rates of MI (OR, 0.23 [CI, 0.01 to 6.09]), arrhythmias (OR, 0.52 [CI, 0.23 to 1.18]), hypotension (OR, 0.41 [CI, 0.22 to 0.79]), and bradycardia (OR, 1.42 [CI, 0.74 to 2.74]) (40).

- A 2008 systematic review of the effect of perioperative β-blockers on mortality included 33 trials with 12,306 patients and found that treatment with β-blockers did not lead to improved all-cause or cardiovascular mortality. Treatment was associated with a decrease in nonfatal MI (NTT, 63) and an increase in nonfatal stroke (NDH, 293) (41).

- A retrospective, multicenter, cohort study evaluated the impact of perioperative β-blocker therapy on patients who underwent noncardiac surgery. The impact on mortality varied according to cardiac risk. In very low-risk patients (RCRI score, 0), β-blockers increased the risk for in-hospital mortality (adjusted OR, 1.43 [CI, 1.29 to 1.58]), and in those with an RCRI score of 1, there was a trend toward increased mortality with β-blockers (adjusted OR, 1.13 [CI, 0.99 to 1.30]). There was no impact on mortality in patients with RCRI scores of 2 (adjusted OR, 0.90 [CI, 0.75 to 1.08]). In patients at higher risk, β-blockers prevented mortality, with an adjusted OR of 0.71 (CI, 0.56 to 0.91) in patients with an RCRI score of 3, and 0.57 (CI, 0.42 to 0.76) in patients with an RCRI score of 4 (42).

- A retrospective cohort study compared outcomes in patients who received bisoprolol with those who received β-selective β-blockers (metoprolol or atenolol) in the perioperative setting. In the multivariate analysis, bisoprolol was associated with fewer perioperative strokes than atenolol or metoprolol (OR, 0.20 [CI, 0.04 to 0.99]) (43).

- A retrospective cohort study compared outcomes in 1011 patients who received perioperative atenolol with outcomes in 2776 patients who received perioperative metoprolol at the San Francisco Veterans Affairs hospital. Patients receiving metoprolol had higher 1-year mortality in the propensity-matched analysis than those receiving atenolol (OR, 2.1 [CI, 1.5 to 2.9]) (44).

- A retrospective cohort study evaluated the impact of the timing of perioperative β-blocker initiation on 940 vascular surgery patients. Perioperative β-blockers, when started at least 1 week before surgery, were more beneficial than when started less than 1 week preoperatively (44; 39).

- A retrospective cohort study evaluated the impact of β-blocker discontinuation in 140 patients who underwent vascular surgery. In the multivariate analysis, discontinuation after surgery was associated with increased mortality (adjusted OR, 17.0; P=0.01) and postoperative MI (adjusted OR, 17.7; P=0.003) (46).

### **Calcium-channel blockers** (nifedipine, amlodipine, diltiazem, verapamil)

**Recommendation:** Continue. Consider starting diltiazem prophylactically for CABG.

**Comments:** Rare withdrawal syndrome, potential effects on anesthetic agents; potential antiarrhythmic, anti-ischemic, and renal protective effects with CABG.

**Evidence:**

- A 2003 systematic review of the impact of calcium-channel blockers on patients undergoing noncardiac surgery included 11 studies. Calcium-channel blockers reduced ischemia (RR, 0.49 [CI, 0.30 to 0.80]) and SVT (RR, 0.52 [CI, 0.37 to 0.72]); most benefit was with diltiazem (45).

- Small studies have evaluated the effect of diltiazem in patients undergoing CABG and have documented anti-ischemic and antiarrhythmic protection (46; 47; 48; 49; 50) and prevention of decrease in renal function (51).

- A randomized trial compared nifedipine with nitroglycerine in 104 patients undergoing CABG. The nifedipine group had fewer MIs (4% vs. 12%, P<0.001) (52).

- A 1985 narrative review stated that calcium-channel blockers may potentiate hemodynamic and MAC depressive effects of inhalation anesthetics and neuromuscular blockers (53).

- Two of 16 patients on diltiazem and 2 of 100 patients on nifedipine experienced life-threatening coronary vasospasm following discontinuation of the drug at the time of coronary revascularization (54), but 0 of 81 patients on nifedipine in another study had no adverse effects after acute withdrawal (55).
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<th><strong>Perioperative Medication Management</strong></th>
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**Nitrates**

**Recommendation:** Continue. May start iv nitrates intra- or postoperatively. Do not use prophylactically during surgery

**Comments:** May be a marker for in-hospital mortality; intraoperatively may reduce ischemia or have no benefit in noncardiac surgery

**Evidence:**

- A retrospective cohort study used the Oxford Record Linkage Study to examine relationships between inturcurrent cardiovascular drug therapy and cardiac death within 30 days of surgery under general anesthesia. Nitrates were associated with increased cardiac death (adjusted OR, 4.79 [CI, 1.01 to 22.72]) (56)

- A randomized trial compared prophylactic intraoperative nitroglycerin infusion vs. placebo in 45 patients undergoing noncardiac surgery. There was no difference in incidence of perioperative ischemia between the groups (57)

- A randomized trial compared preoperative isosorbide dinitrate infusion vs. placebo in 100 patients undergoing CABG. The rate of perioperative MI did not differ between the groups (22% vs. 18%) (58)

**Sympathomlytics; α2-agonists for perioperative prophylaxis**

**Evidence:**

- A 2002 systematic review of clonidine for the prevention of perioperative myocardial ischemia included seven studies. Clonidine reduced perioperative ischemia, with a pooled OR of 0.49 (CI, 0.34 to 0.71) (60)

**ACE inhibitors** (captopril, enalapril, lisinopril, ramipril)

**Recommendation:** Controversial—continue with caution (avoid hypovolemia)

**Comments:** Potential for hypotension with induction of anesthesia and increased vasoconstrictor requirements; many anesthesiologists recommend withholding it on the morning of surgery; other physicians base recommendations on indication for the drug and current BP (continue for HF and uncontrolled hypertension; otherwise, discontinue)

**Evidence:**

- A 2003 systematic review of the effects of ACE inhibitors and ARBs in patients undergoing cardiothoracic surgery included 29 studies. Perioperative use of ACE inhibitors or ARBs was associated with mortality (OR, 1.20 [CI, 1.06 to 1.35]) and acute kidney injury (OR, 1.17 [CI, 1.01 to 1.36]), although there was heterogeneity in the kidney-injury outcome (61)

- A 2008 systematic review of withholding or administering ACE inhibitors and ARBs in the perioperative period included five studies with 434 participants. The preoperative administration of ACE inhibitors or ARBs increased intraoperative hypotension requiring vasopressors (RR, 1.50 [CI, 1.15 to 1.96]), but there were insufficient data to assess other outcomes (62)

- A randomized trial compared discontinuation of ramipril, continuation of ramipril, and continuation of pralipril with prophylactic low-dose vasopressin in 47 patients on ramipril who were undergoing CABG. Patients who continued ramipril had lower BP with anesthesia induction which stayed low; those who received vasopressin had a drop in BP followed by recovery (63)

- A prospective observational study evaluated the effect of ACE-inhibitor or ARB therapy in patients undergoing noncardiac surgery. Patients on ACE-inhibitor or ARB therapy did not have increased rates of perioperative MI or renal failure, although those who were also receiving diuretics had more frequent hypotension (64)

- A prospective observational study evaluated the impact of perioperative ACE inhibitors in 4224 patients undergoing CABG. Compared with no ACE-inhibitor treatment, continuous therapy (OR, 0.64 [CI, 0.46 to 0.88]) and the addition of a postoperative ACE inhibitor (OR, 0.63 [CI, 0.40 to 0.97]) were associated with lower risks for cardiovascular events. Compared with continuous therapy, withdrawal of ACE inhibitors was associated with cardiac (OR, 1.27) and renal (OR, 1.15) events (65)

- A 2003 narrative review stated that induction of anesthesia in a patient with preoperative fasting, volume depletion, sympathetic blockade, and reduced venous capacitance may cause hypotension in patients on ACE inhibitors whose angiotensin II response to hypotension is blocked. Vasopressors and fluids should be readily available (66)

**Angiotensin II receptor blockers/antagonists** (losartan, valsartan, candesartan, irbesartan)

**Recommendation:** Uncertain, although they are usually continued

**Comments:** Potential for hypotension with induction of anesthesia and decreased responsiveness to pressors
### Perioperative Medication Management

#### Evidence:
- **Diuretics** (furosemide, spironolactone, hydrochlorothiazide)
  - **Recommendation**: Optional (can continue on morning of surgery or stop, either on morning of surgery or day before)
  - **Comments**: Avoid hypokalemia and hypovolemia acutely (although these problems are less likely once steady-state has been reached); check K+, BUN/Cr

<table>
<thead>
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<td>A 2013 systematic review of the effects of ACE inhibitors and ARBs in patients undergoing cardiothoracic surgery included 29 studies. Perioperative use of ACE inhibitors or ARBs was associated with mortality (OR, 1.20 [CI, 1.06 to 1.35]) and acute kidney injury (OR, 1.17 [CI, 1.01 to 1.36]), although there was heterogeneity in the kidney injury outcome (61)</td>
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#### Diuretics

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</table>

#### Digoxin (digoxin)

| Recommendation: Continue. May be used prophylactically for arrhythmias (pre- or postoperatively) in cardiothoracic surgery |
| Comments: Check serum level to avoid toxicity (which is enhanced by other drugs, stress, acidosis, hypoxia, electrolyte abnormalities, catecholamines); unclear effect on supraventricular arrhythmias |

<table>
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<tr>
<th>Evidence:</th>
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<tbody>
<tr>
<td>A prospective cohort study evaluated predictors of supraventricular arrhythmias in 4181 patients undergoing noncardiac surgery who were initially in sinus rhythm. Among patients who underwent intrathoracic surgery, digoxin was associated with a lower risk for arrhythmias (OR, 0.20 [CI, 0.04 to 0.80]) (68)</td>
</tr>
<tr>
<td>A randomized trial compared digoxin to diltiazem in 70 patients after pneumonectomy. The diltiazem group had fewer supraventricular arrhythmias (0% vs. 32%, P&lt;0.005) (69)</td>
</tr>
<tr>
<td>A randomized trial compared digitalis with control in 120 patients on propranolol who were undergoing CABG. The digitalis group had a lower rate of postoperative supraventricular arrhythmias (3.1% vs. 21.4%, P&lt;0.005) (70)</td>
</tr>
<tr>
<td>A randomized trial compared the combination of digitalis plus atenolol vs. digitalis alone, atenolol alone, or neither in 160 patients undergoing CABG. The rate of postoperative atrial fibrillation was 5% in the combination group, 17.9% in the digitalis group, 15.4% in the atenolol group, and 25% in the control group; the difference between combination therapy and control was statistically significant (71)</td>
</tr>
</tbody>
</table>

#### β-blockers/α-β blockers

| Recommendation: Continue. Do not start for acute HF |
| Comments: To avoid withdrawal symptoms |

<table>
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<tr>
<th>Evidence:</th>
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</thead>
<tbody>
<tr>
<td>A randomized trial compared perioperative bisoprolol with placebo in 165 patients with HF undergoing noncardiac surgery. There was no difference in mortality between the groups (34.5% with bisoprolol and 24.4% with placebo, P=0.17) (72)</td>
</tr>
</tbody>
</table>

#### Antihypertensives

| Evidence: A 2005 narrative review discussed symptoms associated with withdrawal of antihypertensive medications (73) |

<table>
<thead>
<tr>
<th>Diuretics</th>
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<tbody>
<tr>
<td>Recommendation: Optional</td>
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</tbody>
</table>
### Perioperative Medication Management

**Comments:** Avoid hypokalemia and hypovolemia acutely (although these problems are less likely once steady-state has been reached); check K+, BUN/Cr

<table>
<thead>
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<th>β-blockers</th>
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<tbody>
<tr>
<td><strong>Recommendation:</strong> Continue</td>
</tr>
<tr>
<td><strong>Comments:</strong> To avoid withdrawal symptoms. To prevent perioperative cardiac events</td>
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</tbody>
</table>

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<th>α-β blockers (labetalol)</th>
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<tbody>
<tr>
<td><strong>Recommendation:</strong> Continue. May be started intra- or postoperatively for perioperative hypertension</td>
</tr>
<tr>
<td><strong>Comments:</strong> May attenuate hemodynamic responses to intubation; also used for pheochromocytomas, perioperative hypertension, and deliberately induced hypotension, an anesthetic technique usually for neurosurgery</td>
</tr>
</tbody>
</table>

**Evidence:**
A randomized trial compared labetalol to nicardipine before intubation or for treatment of hypertension in 130 patients undergoing general anesthesia. Mean arterial BP was higher in the labetalol groups than in the nicardipine groups. The rate of tachycardia was lower in the labetalol groups, but there were no differences in other adverse events (74).

<table>
<thead>
<tr>
<th>Calcium blockers</th>
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<tbody>
<tr>
<td><strong>Recommendation:</strong> Continue</td>
</tr>
<tr>
<td><strong>Comments:</strong> Rare withdrawal syndrome; potential effects on anesthetic agents; potential antiarrhythmic, anti-ischemic, and renal protective effects with CABG</td>
</tr>
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</table>

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<thead>
<tr>
<th>ACE inhibitors/ARBs</th>
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<tbody>
<tr>
<td><strong>Recommendation:</strong> Uncertain</td>
</tr>
<tr>
<td><strong>Comments:</strong> Potential for hypotension with induction of anesthesia and increased vasoconstrictor requirements</td>
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<tr>
<th>Sympatholytics (centrally acting α₂-agonists—clonidine)</th>
</tr>
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<tbody>
<tr>
<td><strong>Recommendation:</strong> Continue. May start prophylactically in high-risk cardiac patients with contraindications to β-blockers</td>
</tr>
<tr>
<td><strong>Comments:</strong> To avoid withdrawal syndrome (rebound hypertension, tachycardia); may decrease ischemia, shivering, anesthesia-analgesia requirement, sedative hypnotic effect, decrease sympathetic tone</td>
</tr>
</tbody>
</table>

**Evidence:**
Case reports have described a withdrawal syndrome after perioperative cessation of clonidine (75; 76).

<table>
<thead>
<tr>
<th>α-blockers (doxazosin, terazosin)</th>
</tr>
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<tbody>
<tr>
<td><strong>Recommendation:</strong> Continue. Start treatment for pheochromocytoma at least 5 days preoperatively. Consider stopping before cataract surgery</td>
</tr>
<tr>
<td><strong>Comments:</strong> May be used for pheochromocytoma (with or without β-blockade, depending on type); may be associated with floppy iris syndrome</td>
</tr>
</tbody>
</table>

**Evidence:**
A case series reviewed 113 patients undergoing surgical excision of pheochromocytoma. Patients receiving preoperative α-blockade required more intra- and postoperative fluids and that calcium-channel blockers were as effective and safer when used as the primary mode of antihypertensive therapy (77).

**Intraoperative floppy iris syndrome** is a clinical syndrome observed during cataract surgery reported in patients taking systemic α₂ adrenergic receptor antagonists. It has been most strongly linked to the use of tamsulosin (78). Medication washout periods of up to 2 weeks and specific surgical procedures have been attempted to reduce risk of complications from α₂ adrenergic receptor antagonists in the setting of cataract surgery (79).

<table>
<thead>
<tr>
<th>Vasodilators (hydralazine)</th>
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<tbody>
<tr>
<td><strong>Recommendation:</strong> Continue. May be started intraoperatively or postoperatively to treat hypertension. Indicated for treatment of preeclampsia/eclampsia</td>
</tr>
</tbody>
</table>
Perioperative Medication Management

<table>
<thead>
<tr>
<th>Comments:</th>
<th>May reduce intraoperative and postoperative hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence:</td>
<td>Hydralazine pretreatment in 10 patients reduced the incidence of intubation hypertension (80)</td>
</tr>
<tr>
<td>A case series described the effect of the combination of hydralazine and propranolol in 110 patients undergoing carotid endarterectomy. All patients receiving the therapy had good control of postoperative hypertension (81)</td>
<td></td>
</tr>
</tbody>
</table>

### Antiarrhythmics

**Class Ia (quinidine, procainamide, disopyramide, lidocaine)**

**Recommendation:** Continue; can substitute iv lidocaine or procainamide perioperatively

**Comments:** Check levels; negative inotropes, can prolong QT and prolong neuromuscular blockade

**Evidence:** Consensus

**Class Ic (flecainide, encainide, propafenone, moricizine)**

**Recommendation:** Continue

**Comments:** Negative inotropic effect

**Evidence:** Consensus

**Class III**

**Amiodarone**

**Recommendation:** Continue. May be started prophylactically for arrhythmias in cardiac surgery

**Comments:** Check level; long half-life; may cause bradycardia, atrioventricular dissociation, and vasodilation. May prevent atrial arrhythmias post-CABG

**Evidence:**

A 2005 systematic review of amiodarone prophylaxis in patients undergoing cardiac surgery included 10 trials with 1744 participants. Amiodarone decreased postoperative atrial fibrillation or flutter (RR, 0.64 [CI, 0.55 to 0.75]), ventricular tachyarrhythmias (RR, 0.42 [CI, 0.28 to 0.63]), and stroke (RR, 0.39 [CI, 0.21 to 0.76]) (92)

The PAPABEAR study was a randomized, controlled trial comparing amiodarone with placebo in 601 patients undergoing cardiac surgery. The amiodarone group had fewer atrial tachyarrhythmias (16.1% vs. 29.5%, \( P<0.001 \)) overall, with a similar effect in various subgroups, including younger as well as older patients, patients undergoing CABG alone or with valve surgery, and patients taking or not taking β-blockers (83)

A review of 17 anesthetics administered to 16 patients on amiodarone found dangerous interactions in patients undergoing CABG and hemodynamically significant bradyarrhythmias in patients undergoing noncardiac surgery (84)

**Sotalol**

**Recommendation:** Continue or can start prophylactically

**Comments:** Prophylactically may decrease atrial arrhythmias after CABG

**Evidence:**

A 2002 systematic review of amiodarone compared with sotalol for the prevention of atrial fibrillation in patients undergoing cardiac surgery included 10 studies. Both active drugs were superior to placebo, and there was no significant difference between them (85)

A randomized trial compared sotalol with atenolol in 253 patients undergoing cardiac surgery. Postoperative atrial fibrillation occurred in fewer patients taking sotalol (10% vs. 22%, \( P=0.13 \)) (86)
### Lipid-lowering agents

#### Statins

| Recommendation: Continue, as recommended by ACC/AHA guidelines (33), or start prophylactically, especially in patients undergoing cardiovascular procedures and vascular surgery, despite manufacturer's recommendation to discontinue preoperatively |
| Comments: Potential benefits to continuing: may prevent perioperative MI, atrial fibrillation, death. Potential theoretical benefits: plaque stabilization, rebound, may reduce inflammatory response to bypass surgery. Potential theoretical reasons to discontinue: may increase risk for myopathy and hepatotoxicity, may be associated with delirium in the elderly |
| Evidence: |
| A 2013 Cochrane review of perioperative statins in statin-naive patients undergoing vascular surgery included six studies. Statins had no effect on mortality (RR, 0.73, [CI, 0.31 to 1.75]), although though there were few patients in the analysis (87) |
| A 2012 Cochrane review of preoperative statins in patients undergoing cardiac surgery included 11 trials with 984 participants. Preoperative statin therapy was associated with a lower risk for postoperative atrial fibrillation (OR, 0.40 [CI, 0.29 to 0.55]) but had no effect on mortality (OR, 0.98 [CI, 0.14 to 7.10]) or stroke (OR, 0.70 [CI, 0.14 to 3.63]) (88) |
| A 2010 systematic review of the effect of preprocedural statins on outcomes included 21 trials with 4805 participants. Preprocedural statin therapy significantly reduced postprocedural MI overall (RR, 0.57 [CI, 0.46 to 0.70]) and after percutaneous coronary intervention and noncardiac surgery, but not after CABG. Statin therapy did not reduce all-cause mortality (RR, 0.66 [CI, 0.37 to 1.17]) but did reduce post-CABG atrial fibrillation (RR, 0.54 [CI, 0.43 to 0.68]) (89) |
| Although statins are thought to have a beneficial effect on inflammation, a small placebo-controlled trial failed to show that atorvastatin, initiated within 7 days preoperatively, was associated with clinically significant reductions in levels of C-reactive protein (90) |
| A retrospective cohort analysis of 284,158 patients aged 65 and older undergoing elective surgery found that statin use was associated with an increased risk for postoperative delirium (91) |
| A 2012 narrative review based on a literature review suggested that statin withdrawal is associated with worse outcomes in acute coronary syndrome, ischemic stroke, and noncardiac surgery, emphasizing the importance of resumption of statins after surgery (92) |

#### Bile sequestrants (colestipol)

| Recommendation: Discontinue the day before or morning of surgery |
| Comments: May decrease bioavailability of other drugs and fat-soluble vitamins |
| Evidence: |
| A 1994 narrative review noted that bile sequestrants result in decreased bioavailability of thiazide diuretics, digitalis preparations, β-blockers, coumarin anticoagulants, thyroid hormones, fibric acid derivatives, and certain oral hypoglycemic agents (93) |
Perioperative Medication Management

Niacin

Recommendation: Unknown

Comments: May cause liver enzyme elevations

Evidence:

No data in perioperative period

Fibrac acid derivatives (gemfibrozil)

Recommendation: Unknown

Comments: May cause myopathy, especially in combination with statins

Evidence:

No data in perioperative period

Anticoagulants

Heparin (unfractionated)

Recommendation: Discontinue on morning of surgery (4-6 hours before) if full anticoagulation and restart at least 12 hours postoperatively if adequate hemostasis (or as per surgeon and type of procedure). Continue or start if for prophylaxis (mini-dose 5000 IU sc q8-12h)

Comments: Minimize risk for perioperative bleeding as well as period of time without full anticoagulation protection; check PTT preoperatively if on full-dose anticoagulation. If used prophylactically, it should not interfere significantly with the coagulation mechanism

Evidence:

Based on recommendations from the 2012 ACCP guideline on antithrombotic therapy and prevention of thrombosis, 9th ed. (21)

LMWH (enoxaparin, dalteparin)

Recommendation: Continue or start for prophylaxis: can start 12 hours before, 2 hours before, 6 hours after, or the following morning. Discontinue 24 hours preoperatively if on full-dose anticoagulation. If neuraxial anesthesia is planned, do not give LMWH for at least 12 hours before surgery or at least 2 hours after removal of a spinal needle or epidural catheter

Comments: Discontinue before neuraxial anesthesia due to potential risk for perispinal hematoma. Effective for prophylaxis, particularly in orthopedic surgery and high-risk to very high-risk patients. Consider extended prophylaxis for 3-5 weeks postoperatively after total-hip arthroplasty and surgery for abdominal or pelvic cancer

Evidence:

Based on recommendations from the 2012 ACCP guideline on antithrombotic therapy and prevention of thrombosis, 9th ed. (21)

A 2002 systematic review evaluated preoperative compared with postoperative treatment with LMWH in patients undergoing elective hip surgery. The rate of postoperative DVT was 19.2% in patients who received preoperative LMWH, 12.4% in those who received perioperative LMWH, and 14.4% in those who received postoperative LMWH. Rates of bleeding were higher in the perioperative group (6.3%) than in the other groups (94)

Several studies have addressed LMWH as bridging anticoagulation (95; 96; 97)

Pentasaccharides (fondaparinux)

Recommendation: Start 6 hours after total hip or knee replacement or hip fracture surgery for DVT prophylaxis. Watch for postoperative bleeding; inhibits factor Xa and has a 15-hour half-life

Comments: Effective DVT prophylaxis for major orthopedic surgery

Evidence:

Based on recommendations from the 2012 ACCP guideline on antithrombotic therapy and prevention of thrombosis, 9th ed. (21)
Perioperative Medication Management

| A 2002 systematic review of fondaparinux compared with enoxaparin in patients undergoing total hip or knee replacement and hip-fracture surgery included four trials with 7344 participants. Patients receiving fondaparinux had a lower risk of VTE by day 11 (6.8% vs 13.7%, P<0.001), with higher rates of major bleeding but similar rates of clinically relevant bleeding |

**Warfarin**

Recommendation: Discontinue preoperatively depending on indication:
Stop 3-5 days before elective surgery (depending on INR) to minimize bleeding.
Check INR preoperatively; ideally ≤1.5.
For urgent procedures, can use low-dose oral or sc vitamin K to reduce INR within 24-36 hours; if emergency, use fresh frozen plasma or prothrombin complex concentrate.
If high risk for embolic event, use bridging therapy with unfractionated or LMWH.
Restart after procedure when deemed safe by surgeon.
Start the night before orthopedic surgery if for DVT prophylaxis; goal is INR 2-3 by postoperative day 3-5

Comments: Minimize risk for perioperative bleeding as well as period of time without full anticoagulation protection. Consider the indication for anticoagulation and risk for an embolic event when not anticoagulated. Check PT/INR preoperatively

**Evidence:**
Based on recommendations from the 2012 ACCP guideline on antithrombotic therapy and prevention of thrombosis, 9th ed. (21)

A 2012 systematic review of periprocedural heparin bridging therapy included 34 studies, of which 1 was a randomized trial. The rate of thromboembolic events did not differ between bridged and nonbridged patients (OR, 0.80 [CI, 0.32 to 1.54]), but bridged patients had a higher rate of major bleeding (OR, 3.60 [CI, 1.52 to 8.50]) (22)

**Novel Oral Anticoagulants**

**Evidence:** Based on recommendations regarding new antithrombotic drugs (100) from the 2012 ACCP guideline on antithrombotic therapy and prevention of thrombosis, 9th ed.

**Oral thrombin inhibitors (dabigatran)**

Recommendation: If discontinuing anticoagulation preoperatively, stop dabigatran 1-4 days before surgery: 24 hours before surgery with normal renal function and for procedures with low bleeding risk; add an additional day if there is impaired renal function and an additional 1-2 days for procedures with high bleeding risk or spinal/epidural anesthesia

**Evidence:** Consensus; manufacturer's recommendations; review (101)

**Oral Xa inhibitors (rivaroxaban, apixaban)**

Recommendation: If discontinuing anticoagulation preoperatively, stop rivaroxaban and apixaban at least 1 day before surgery if renal function is normal and for procedures with low bleeding risk. Add an additional day if there is impaired renal function or if the procedure has a high bleeding risk

**Evidence:** Consensus; manufacturer's recommendations; review (101)

**Antiplatelet agents**

**Evidence:** Reviews of perioperative management of anticoagulant and antiplatelet therapy (102; 103; 104; 105; 106; 107) and use in CABG (108)

**Comment:** The role of preoperative platelet function testing is controversial

**Aspirin**

Recommendation: Uncertain; often discontinued but depends on indication (TIA, CAD/ACS), procedure (risk for bleeding and access to the site), and surgeon's preference. If discontinuing, usually stop 5-10 days before surgery and consider restarting 24-48 hours postoperatively. Before elective surgery, dual antiplatelet therapy with aspirin and clopidogrel, prasugrel, or ticagrelor is recommended for at least 4-6 weeks after placement of a bare metal stent and at least 12 months after a drug-eluting stent, if possible, to minimize the chance of stent thrombosis postoperatively

Comments: Consider indication for therapy and risk for bleeding:
Irreversible platelet inhibitor
Prolongs bleeding time but not necessarily correlated with bleeding complications
<table>
<thead>
<tr>
<th>Medication</th>
<th>Recommendation</th>
<th>Evidence</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ticlopidine</td>
<td>Discontinue. Usually stop 10-14 days preoperatively. Can start postoperatively to improve graft patency in vascular surgery</td>
<td>A 2013 narrative review of antiplatelet therapy and cardiac surgery stated that patients who have received ticagrelor should wait 5 days after the last dose before undergoing surgery, although it is likely that surgery can be safely performed 3 days after discontinuing ticagrelor (106)</td>
<td>Irreversibly inhibits ADP-induced platelet-fibrinogen binding and subsequent platelet-platelet interactions. Postponing elective noncardiac surgery for 2-4 weeks after coronary stenting should permit completion of the mandatory antiplatelet regimen (aspirin and ticlopidine), thereby reducing the risk for stent thrombosis and bleeding complications; otherwise one must balance the risk for thrombosis with premature discontinuation with the risk of bleeding if the drugs are continued (this drug is rarely used)</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>Discontinue. Usually stop 5-7 days preoperatively</td>
<td>A 2012 narrative review based on a literature review advised individualizing the plan for perioperative aspirin but suggested continuation if used for secondary prevention, noting that the risk for withdrawal and thromboembolic events was probably greater than the risk for bleeding (except in specific surgeries) (410)</td>
<td>Inhibitor of ADP-induced platelet aggregation; irreversible platelet inhibitor</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>Discontinue. Usually stop 7 days preoperatively</td>
<td>A 2012 systematic review of the impact of thienopyridines on patients undergoing surgery included 37 studies (31 cardiac surgery and 6 noncardiac surgery). Exposure to thienopyridines within the 5 days before surgery was not associated with postoperative MI (OR, 0.98 [CI, 0.72 to 1.34]) but was associated with stroke (OR, 1.54 [CI, 1.08 to 2.20]) and mortality (OR, 1.38 [CI, 1.13 to 1.69]) (111)</td>
<td>Inhibits P2Y11 ADP-induced platelet aggregation; irreversible platelet inhibitor</td>
</tr>
<tr>
<td>Ticagrelor</td>
<td>Discontinue. Usually stop 5 days preoperatively</td>
<td>A 2013 narrative review of antiplatelet therapy and cardiac surgery stated that patients who have received ticagrelor should wait 5 days after the last dose before undergoing surgery, although it is likely that surgery can be safely performed 3 days after discontinuing ticagrelor (106)</td>
<td>Even though ticagrelor is a reversible platelet inhibitor, the package insert recommends stopping it 5 days before surgery rather than earlier</td>
</tr>
<tr>
<td>CABG-related TIMI major bleeding was greater in patients taking prasugrel than in patients taking clopidogrel (13.4% vs. 3.2%; HR, 4.73) (114)</td>
<td>Consensus, manufacturer's recommendation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG-related TIMI major bleeding was greater in patients taking prasugrel than in patients taking clopidogrel (13.4% vs. 3.2%; HR, 4.73) (114)</td>
<td>Consensus, manufacturer's recommendation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombosis - related complications; irreversible platelet inhibitor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evidence:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rates of major adverse cardiac events were lower in the aspirin group (1.8% vs. 9.0%, P=0.02) with no difference in bleeding complications, although the study was not powered to evaluate bleeding complications (109)</td>
<td>A randomized trial compared low-dose aspirin with placebo in high-risk patients undergoing noncardiac surgery. Rates of major adverse cardiac events were lower in the aspirin group (1.8% vs. 9.0%, P=0.02) with no difference in bleeding complications, although the study was not powered to evaluate bleeding complications (109)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>It may have beneficial effects</td>
<td>Discontinuation may be associated with a rebound effect</td>
<td>A 2012 narrative review based on a literature review advised individualizing the plan for perioperative aspirin but suggested continuation if used for secondary prevention, noting that the risk for withdrawal and thromboembolic events was probably greater than the risk for bleeding (except in specific surgeries) (410)</td>
<td>Recommendation: Discontinue. Usually stop 5-7 days preoperatively</td>
</tr>
</tbody>
</table>
### Perioperative Medication Management

#### Evidence:
In 40 consecutive patients undergoing noncardiac surgery within 6 weeks of coronary stent placement, there were 7 MIs, 11 major bleeding episodes, and 8 deaths, most occurring within 2 weeks of stent placement (115). Of 6 patients with major bleeding who died, 3 did not have ticlopidine withheld.

A randomized trial compared ticlopidine with placebo after saphenous vein bypass surgery. The ticlopidine group had better long-term graft patency, with no significant difference in overall mortality or major ischemic events (116).

#### Cilostazol

**Recommendation:** Discontinue. Usually stop 3-5 days preoperatively (half-life 12 hours).

**Comments:** Reversible cAMP PDE III inhibitor

**Evidence:**
In a study of 16 patients, cilostazol was considered to be as effective as warfarin and suitable for postoperative antithrombotic therapy after ePTFE bypass surgery (117).

#### Dipyridamole

**Recommendation:** Uncertain

**Comments:** Reversible platelet adhesion inhibitor (half-life 10 hours); may increase risk for bleeding when combined with aspirin

**Evidence:**
A randomized trial compared aspirin, aspirin plus dipyridamole, and placebo in 1112 patients undergoing CABG. Aspirin plus dipyridamole decreased rates of early saphenous vein aortocoronary occlusion compared with placebo (12.9% vs. 18%), with a trend toward reduction with aspirin alone (118).

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ACC = American College of Cardiology; ACCP = American College of Chest Physicians; ACE = angiotensin-converting enzyme; ACS = acute coronary syndrome; ADP = adenosine diphosphate; AHA = American Heart Association; ARB = angiotensin receptor blocker; BP = blood pressure; BUN = blood urea nitrogen; CABG = coronary artery bypass grafting; CAD = coronary artery disease; cAMP = cyclic adenosine monophosphate; CI = confidence interval; Cr = creatinine; DVT = deep venous thrombosis; EPS = extrapyramidal symptoms; ePTFE = expanded polytetrafluoroethylene; HF = heart failure; HR = hazard ratio; iv = intravenous; INR = international normalized ratio; IU = international unit; LMWH = low-molecular-weight heparin; MAC = minimum alveolar concentration; MI = myocardial infarction; NNT = number needed to harm; NNH = number needed to treat; OR = odds ratio; PAPABEAR = Prophylactic Amiodarone for the Prevention of Arrhythmias that Begin Early After Revascularization, Valve Replacement, or Repair (trial); PDE = phosphodiesterase; PT = prothrombin time; PTT = partial thromboplastin time; q8-12h = every 8-12 hours; RCRI = Revised Cardiac Risk Index; RR = risk ratio; sc = subcutaneous; SVT = supraventricular tachycardia; TIA = transient ischemic attack; TIMI = thrombolysis in myocardial infarction; VTE = venous thromboembolism.
### Perioperative Rheumatologic Medication Management

#### NSAIDs

<table>
<thead>
<tr>
<th>Recommendation: Controversial</th>
</tr>
</thead>
<tbody>
<tr>
<td>If discontinuing, stop 1-3 days before, depending on half-life</td>
</tr>
<tr>
<td>May start postoperatively for pain relief</td>
</tr>
</tbody>
</table>

**Comments:** Reversible platelet inhibitors. Disadvantages—potential for bleeding and renal insufficiency. Advantages—may decrease requirement for opioids and improve early postoperative analgesia

**Evidence:**
- A 2005 systematic review of the effect of preoperative coxibs on clinical outcomes included 22 studies with 2246 participants. Preoperative coxibs reduced postoperative pain, analgesic consumption, and patient satisfaction compared with placebo in the majority of studies. There was no significant difference in intraoperative blood loss (119)
- A large case-control analysis found that the risk for acute MI was 1.52 for patients who stopped taking NSAIDs 1-29 days before the index date compared with nonusers. Current and past NSAID use (discontinued ≥60 days before) was not associated with an increased risk for acute MI (120)
- A 1994 narrative review highlighted controversies in the perioperative use of NSAIDs and recommended the selective use of NSAIDs in combination with opioid analgesics and local anesthetics for perioperative management of pain (121)

#### COX-2 inhibitors

<table>
<thead>
<tr>
<th>Recommendation: Uncertain; discontinue valdecoxib</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comments: No effect on platelets but potential for renal dysfunction as with NSAIDs</td>
</tr>
</tbody>
</table>

**Evidence:**
- A 2005 systematic review of the effect of preoperative coxibs on clinical outcomes included 22 studies with 2246 participants. Preoperative coxibs reduced postoperative pain, analgesic consumption, and patient satisfaction compared with placebo in the majority of studies. There was no significant difference in intraoperative blood loss (119)
- A randomized trial compared the combination of parecoxib and valdecoxib with placebo in 462 patients undergoing CABG. Pain control was better in the coxib group than in the placebo group, but there was an increased incidence of serious adverse events (19% vs. 9.9%, P=0.015) (122)

#### Opioids (codeine, oxycodone, methadone)

<table>
<thead>
<tr>
<th>Recommendation: Continue until morning of surgery; then decision is up to the anesthesiologist to determine narcotic use intraoperatively</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comments: Need to continue adequate pain management and prevent withdrawal symptoms; however, if given immediately preoperatively, will alter analgesic/narcotic dose requirement intraoperatively</td>
</tr>
</tbody>
</table>

**Evidence:**
- Consensus

#### Methotrexate (methotrexate)

<table>
<thead>
<tr>
<th>Recommendation: Continue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comments: Caution with renal insufficiency; mixed results but most likely no problems with wound healing or postoperative infections</td>
</tr>
</tbody>
</table>

**Evidence:**
- A randomized trial compared continuation of methotrexate with cessation of methotrexate in 388 patients with RA on methotrexate who were undergoing elective orthopedic surgery. Results were also compared with outcomes in surgical patients who were not on methotrexate. Patients who continued methotrexate had a lower risk of surgical complication or postoperative infection than patients who discontinued (2% vs. 15%, P<0.003) or patients who were not on methotrexate (10.5%) (123)
- A retrospective case series reported outcomes in 15 patients with RA taking methotrexate who underwent 39 surgeries. No postoperative complications related to methotrexate were observed (124)
Two small studies of 32 (125) and 38 (126) patients with RA undergoing orthopedic procedures suggested that methotrexate may increase postoperative infections, and it should be temporarily discontinued before surgery.

A 2010 narrative review of the perioperative management of medication for RA recommended continuing methotrexate perioperatively (127)

**Biologic response modifiers** (etanercept, infliximab, anakinra, rituximab, adalimumab)

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Hold for two half-lives or at least one administration interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comments</td>
<td>Potentially increased risk for infection</td>
</tr>
<tr>
<td>Evidence</td>
<td>A 2013 systematic review of infectious risk in patients treated with TNF blocking agents and undergoing surgery included 14 studies, of which 13 were retrospective. There was an increased risk for infection in 4 of 6 studies in which patients received TNF blocking agents compared with not receiving them. However, none of the other studies that compared continued vs. discontinued treatment at surgery found an increased risk for infection when the medication was continued perioperatively (128)</td>
</tr>
</tbody>
</table>

A 2010 narrative review of the perioperative management of immunosuppressive medication suggested waiting four to five half-lives before surgery and restarting treatment after recovery from surgery (127)

CABG = coronary artery bypass graft(ing); COX-2 = cyclo-oxygenase 2; MI = myocardial infarction; NSAID = nonsteroidal anti-inflammatory drug; RA = rheumatoid arthritis; TNF = tumor necrosis factor.
### Perioperative Pulmonary Medication Management

#### Inhaled β-agonists

**Recommendation:** Continue or start if bronchospasm is present  
**Comments:** To maintain bronchodilator effect  
**Evidence:**

- A randomized trial compared nebulized salbutamol with saline in 53 patients at high risk for postoperative infection who were undergoing upper abdominal surgery. There was no difference in the rate of postoperative chest infection between the salbutamol group and saline group (129).  
- A randomized trial compared salbutamol with salbutamol plus corticosteroids in 31 patients with partially reversible airway obstruction. Patients in the combination-therapy group were less likely to have wheezing after intubation (77% to 80% vs. 6.7%, \( P=0.0058 \)) (130).  
- A 2007 narrative review discussed the perioperative management of patients with COPD (131).

#### Inhaled anticholinergics

**Recommendation:** Continue  
**Comments:** To maintain bronchodilator effect  
**Evidence:**

A randomized trial compared prophylactic treatment with either an inhaled β-2 adrenergic agonist or an inhaled cholinergic antagonist or a placebo inhalation in 42 patients undergoing intubation for surgery. Both bronchodilators resulted in lower lung resistance after intubation compared with placebo (132).

#### Inhaled steroids

**Recommendation:** Continue or consider starting if bronchospasm is present  
**Comments:** To maintain anti-inflammatory and bronchodilator effects

#### Leukotriene antagonists (montelukast, zafirlukast) and lipoxygenase inhibitors (zileuton)

**Recommendation:** Continue?  
**Comments:** No data in perioperative setting

#### Systemic steroids for asthma/COPD

**Recommendation:** Continue/increase; may start prophylactically if patient had been on steroids in the recent past  
**Comments:** Give stress doses of hydrocortisone if suspected suppression of hypothalamic-pituitary-adrenal axis  
**Evidence:**

A retrospective cohort study evaluated risks associated with preoperative corticosteroids in 172 patients with asthma. Overall, 5.2% of patients developed postoperative bronchospasm and 3.6% had postoperative infections (133).

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COPD = chronic obstructive pulmonary disease.
## Perioperative Endocrine Medication Management

### Insulin

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modify and follow fingersticks: options include 1/2-2/3 NPH dose, or iv regular insulin infusion</td>
<td>Type 1 diabetics require perioperative insulin to prevent ketoacidosis. Hypoglycemia is more dangerous than hyperglycemia. Tight control perioperatively is not clearly defined, and it may or may not result in better outcome</td>
</tr>
</tbody>
</table>

**Evidence:**
- A prospective, randomized study of insulin-requiring diabetic patients undergoing orthopedic surgery found better diabetic control in those receiving an infusion of 2 U/h of regular insulin than those receiving two thirds of their daily maintenance dose of NPH; however, two of eight patients receiving the infusion needed a reduction in dose and increased dextrose infusion to avoid hypoglycemia (134)
- A study of 65 NIDDM patients undergoing major surgery showed that those receiving sc or continuous iv insulin had better glucose control than those in the routinely managed group. The iv insulin group also required a smaller insulin dose and only had one hypoglycemic event (135)
- A cohort study evaluated the impact of continuous insulin infusion with tighter glucose control on surgical outcomes in patients undergoing cardiac surgery. Continuous insulin therapy was associated with lower rates of hospital mortality (57% reduction) and deep sternal wound infections (66% reduction) after CABG (136)
- A cohort study compared outcomes in diabetic patients undergoing cardiac surgery who were treated with sc insulin or continuous insulin infusion. In the multivariate analysis, continuous insulin infusion was associated with a lower risk for death (OR, 0.43; P=0.001) (137)
- A pre-post study evaluated the impact of an insulin-infusion protocol with a target glucose level of 80-150 mg/dL in postoperative cardiothoracic surgery patients. The protocol resulted in significantly improved glycemic control without significantly increasing the risk for hypoglycemia (138)

**Sulfonylureas**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinue</td>
<td>Stop 12-72 hours before surgery depending on half-life of drug and type of procedure to minimize possibility of hypoglycemia</td>
</tr>
</tbody>
</table>

**Evidence:**

**Meglitinides** (repaglinide, nateglinide)

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probably discontinue, although uncertain</td>
<td>Minimize possibility of postoperative hypoglycemia (although unlikely as a single agent)</td>
</tr>
</tbody>
</table>

**Evidence:**

**Biguanides** (metformin)

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinue 24-48 hours before major surgery; can stop on morning of radiologic procedure using iv contrast media</td>
<td>To minimize the rare possibility of lactic acidosis; less risk with iv contrast procedures, especially with normal renal function</td>
</tr>
</tbody>
</table>

**Evidence:**
- A 1999 systematic review of metformin-associated lactic acidosis found that almost all reported cases occurred in patients with decreased renal function or other contraindications to the drug (140)
### Thiazolidinediones (rosiglitazone, pioglitazone)

**Recommendation:** Probably discontinue on morning of surgery although uncertain

**Comments:** Insulin sensitizers; possibility of postoperative hypoglycemia; potential for liver dysfunction (based on problems with troglitazone)

**Evidence:**

Consensus

### a-glucosidase inhibitors (acarbose, miglitol)

**Recommendation:** Uncertain

**Comments:** Probably minimal risk for hypoglycemia based on mechanism that minimizes increase in postprandial glucose

**Evidence:**

Consensus

### Thyroxine

**Recommendation:** Continue (or start preoperatively, although hypothyroid patients tolerate surgery well in most cases)

**Comments:** Has long half-life, iv preparation available; risk of surgery with mild-moderate hypothyroidism is low

**Evidence:**

A retrospective cohort study compared surgical outcomes in 59 patients with mild to moderate hypothyroidism and matched controls. There were no differences in outcomes (141)

### Antithyroid drugs (propylthiouracil, methimazole)

**Recommendation:** Continue or start preoperatively

**Comments:** Inhibit synthesis of thyroxine, prevent conversion from T<sub>4</sub> to T<sub>3</sub>

**Evidence:**

A randomized study of 30 untreated hyperthyroid patients showed that methimazole and thyroxine normalized T<sub>3</sub> and decreased risk for postoperative hypothyroidism compared with metoprolol alone (142)

### β-blockers

**Recommendation:** Continue or start preoperatively

**Comments:** Decrease adrenergic activity, decrease peripheral conversion of T<sub>4</sub> to T<sub>3</sub>

**Evidence:**

In 130 patients undergoing subtotal thyroidectomy, preoperative propranolol and metoprolol both prevented thyroid storm. Metoprolol offered additional advantages of shortened preoperative preparation time, simplicity of dosage, and shorter postoperative stay compared with propranolol (143)

Preoperative treatment with metoprolol alone compared favorably to methimazole and thyroxine in preventing thyroid storm and perioperative complications (142)

### Potassium iodide (potassium iodide)

**Recommendation:** Continue or start preoperatively for clinical hyperthyroidism

**Comments:** Prevent release of T<sub>4</sub> and T<sub>3</sub>

**Evidence:**

An observational study reported outcomes in 10 patients who were undergoing surgery for Grave’s disease. Potassium iodide and propranolol for 10 days normalized T<sub>3</sub> and T<sub>4</sub> better than either drug alone
<table>
<thead>
<tr>
<th>Glucocorticoids</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommendation:</strong> Continue/increase</td>
</tr>
<tr>
<td><strong>Comments:</strong> Give stress doses of hydrocortisone if suspected suppression of hypothalamic-pituitary-adrenal axis. Adrenal suppression secondary to glucocorticoid therapy is variable and may last 9-12 months. ACTH stimulation test results may not correlate with clinical outcome</td>
</tr>
<tr>
<td><strong>Evidence:</strong></td>
</tr>
<tr>
<td>A 2008 systematic review of perioperative stress-dose steroids included nine studies. Hemodynamics did not differ between patients on stress-dose steroids and those on chronic doses (145)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Oral contraceptives</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommendation:</strong> Continue (with DVT prophylaxis) or discontinue several weeks before surgery and use alternative method for contraception</td>
</tr>
<tr>
<td><strong>Comments:</strong> Possible risk for pregnancy may outweigh risk for DVT. Oral contraceptives increase DVT risk, although absolute risk is low in young, healthy women. Oral contraceptives reduced antithrombin III and anti-Xa levels</td>
</tr>
<tr>
<td><strong>Evidence:</strong></td>
</tr>
<tr>
<td>A 2001 systematic review evaluated the risk for VTE associated with third-generation oral contraceptive pills. Third-generation oral contraceptive pills were associated with a higher risk for VTE than second-generation oral contraceptive pills (adjusted OR, 1.7 [CI, 1.4 to 2.0]) (146)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Postmenopausal HT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommendation:</strong> Discontinue at least 30 days before surgery (if possible)</td>
</tr>
<tr>
<td><strong>Comments:</strong> Increases risk for VTE and CAD</td>
</tr>
<tr>
<td><strong>Evidence:</strong></td>
</tr>
<tr>
<td>A 2012 systematic review for the U.S. Preventive Services Task Force included nine fair-quality trials with most of the results reported from the Women’s Health Initiative, which had 11 years of follow-up. The results of this analysis included the finding that estrogen plus progestin therapy increased the number of cases of invasive breast cancer (8 more per 10,000 women-years), stroke (9 more per 10,000 women-years), and DVT (12 more per 10,000 women-years). This analysis reported risks for both combined estrogen and progesterin therapy as well as for estrogen-only therapy (147)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tamoxifen (tamoxifen)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommendation:</strong> Consult oncologist before any decision to discontinue</td>
</tr>
<tr>
<td><strong>Comments:</strong> Increased DVT risk but need to clarify risk-benefit ratio</td>
</tr>
<tr>
<td><strong>Evidence:</strong></td>
</tr>
<tr>
<td>A 2013 systematic review for the U.S. Preventive Services Task Force of medications to reduce the risk for primary breast cancer included seven studies. Tamoxifen increased thromboembolic events more than raloxifene (NNH, 250) (148)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Raloxifene (raloxifene)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommendation:</strong> Discontinue at least 3 days preoperatively</td>
</tr>
<tr>
<td><strong>Comments:</strong> Increased DVT risk similar to HT and greatest in first 4 months of use; selective estrogen-receptor modulator</td>
</tr>
<tr>
<td><strong>Evidence:</strong></td>
</tr>
<tr>
<td>The MORE trial was a randomized trial comparing raloxifene with placebo in over 7000 women with osteoporosis. Raloxifene increased the risk for DVT (RR, 3.1) (149)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Alendronate (alendronate)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommendation:</strong> Discontinue at least 1 day before surgery</td>
</tr>
</tbody>
</table>
Comments: Stop due to specific administration guidelines: unable to remain NPO; bisphosphonate that inhibits osteoclast-mediated bone resorption

Evidence:

Must be taken with at least 6-8 oz of water and patient should not lie down for at least 30 minutes and until after the first food of the day (as per manufacturer’s recommendations)

A case report of a patient developing hypocalcemic tetany after bowel prep with Fleet Phospho-Soda suggested that patients taking bone metabolism regulators may not be able to respond appropriately to hypocalcemic stressors (150)

ACTH = adrenocorticotropic hormone; CABG = coronary artery bypass grafting; CAD = coronary artery disease; CI = confidence interval; DVT = deep venous thrombosis; HT = hormone therapy; iv = intravenous; MORE = Multiple Outcomes of Raloxifene Evaluation; NIDDM = non-insulin-dependent diabetes mellitus; NNH = number needed to harm; NPH = neutral protamine Hagedorn (insulin); NPO = nothing by mouth; OR = odds ratio; RR = risk ratio; sc = subcutaneous; T<sub>3</sub> = triiodothyronine; T<sub>4</sub> = thyroxine; VTE = venous thromboembolism.
### Perioperative Neurologic Medication Management

**Recommendation:** Continue (except before neurosurgery aimed at removing epileptic foci); may start prophylactically before intracranial surgery

**Comments:**

To prevent perioperative seizures; may be useful for short-term prophylaxis with intracranial aneurysms or cerebral tumors

Non-oral formulations may be substituted perioperatively (151):

- Commercial alternatives are available for clonazepam, diazepam, lacosamide, levetiracetam, lorazepam, midazolam, nitrazepam, phenobarbital, phenytoin, and valproic acid.
- Alternatives requiring preparation are available for carbamazepine, clonazepam, lamotrigine, oxcarbazepine, primidone, and topiramate.
- There are no alternatives for ethosuximide, felbamate, retigabine, stiripentol, tiagabine, vigabatrin, and zonisamide

**Evidence:**

- A review discusses numerous drug interactions between anticonvulsants and anesthetic agents (152)
- A retrospective analysis of 387 neurosurgical patients at low risk for seizures with intracranial aneurysms found that postoperative anticonvulsant medication given for an average of 3 days controlled seizures (153)
- A study of 128 patients undergoing craniotomy for intracerebral tumors recommended short-term preventive treatment with antiepileptic drugs in patients without preoperative seizures (154)

**Phenytoin**

**Recommendation:** Continue

**Comments:** Check level; CNS depressant; may reduce requirement for general anesthetics

**Evidence:** Consensus

**Phenobarbital**

**Recommendation:** Continue

**Comments:** Check level; CNS depressant; avoid rebound; may reduce requirement for general anesthetics

**Evidence:** Consensus

**Carbamazepine**

**Recommendation:** Continue

**Comments:** Check level

**Evidence:**

- Discontinuation of carbamazepine was associated with increased frequency of seizures (maximal increase in the first 2 weeks) in patients with a history of epilepsy and incompletely controlled seizures (156)

**Valproic acid**

**Recommendation:** Continue

**Comments:** Check level; CNS depressant; may reduce requirement for general anesthetics

**Evidence:**

- Valproic acid did not increase complications of hemostasis during therapeutic resections for epilepsy, and it should not be discontinued before craniotomy (157)
**Carbidopa/levodopa**

**Recommendation:** Uncertain; either continue or discontinue the night before surgery

**Comments:** Withdrawal may worsen symptoms of Parkinsonism or precipitate a neuroleptic malignant-like syndrome; may have drug interactions; can cause arrhythmias (treated with β-blockers), hypo- or hypertension

**Evidence:**

> Three patients with Parkinson's disease developed a neuroleptic malignant-like syndrome after discontinuation of carbidopa-levodopa or on a drug holiday (158)

**For myasthenia gravis (pyridostigmine, neostigmine)**

**Recommendation:** Continue (may reduce dose if not severe)

**Comments:** Despite potential medication side effects (bradycardia, salivation), withdrawal may worsen muscle weakness and increase risk for respiratory complications

**Evidence:**

> In a review of 324 thymectomies, excessive incidence of respiratory insufficiency and airway-associated morbidity was potentially related to prolonged mechanical ventilation and withdrawal of anticholinesterase medication (159)

Myasthenia gravis patients treated with pyridostigmine show a resistance to the effects of succinylcholine (160) and vecuronium (161)

Myasthenic patients are sensitive to nondepolarizing relaxants, but intermediate-acting nondepolarizing relaxants (atracurium and vecuronium) are eliminated rapidly and can be titrated and reversed (162)

**For Alzheimer’s disease (tacrine, donepezil)**

**Recommendation:** Discontinue

**Comments:** Intravenous administration of tacrine may prolong action of succinylcholine; po use may cause resistance to nondepolarizing muscle relaxants

**Evidence:**

> Tacrine depresses cholinesterase activity and prolongs the duration of the neuromuscular block (163)

Donepezil has a possible synergistic effect with succinylcholine-type muscle relaxants; discontinue 2-3 weeks before surgery due to its long half-life (164)

---

CNS = central nervous system; EEG = electroencephalogram; po = oral.
Perioperative Psychiatric Medication Management

Overview: Based on a 2006 systematic review (165), a multidisciplinary group of clinicians made the following recommendations:

Patients who use lithium, MAO inhibitors, tricyclics, and clozapine have serious drug-drug interactions and qualify for American Society of Anesthesiologists Physical Status 3. From the perspective of physical risk, they require discontinuation; however, from the perspective of withdrawal risk and psychiatric relapse, they need intensive, integrated anesthetic/psychiatric management.

For ASA Physical Status 2 patients on SSRIs who are physically and mentally stable, the risk of withdrawal seems to justify their continuation. Patients with higher physical or psychiatric risks should be seen in consultation.

Physical and psychiatric risks of patients using antipsychotics and other antidepressants are enhanced and should be considered to be ASA Physical Status 2 from a physical perspective. From a withdrawal perspective, they should be seen by their psychiatrists.

### TCAs (amitriptyline, nortriptyline, imipramine, desipramine)

**Recommendation:** Uncertain; continue or taper and discontinue at least several days before elective surgery

**Comments:** Anticholinergic effects, widened QRS and QT, arrhythmias, drug interactions, withdrawal syndrome

**Evidence:**

Most anesthesiologists surveyed continued TCAs despite theoretical concerns. Reported complications in surgical patients are extremely rare (166)

Because effects of long-term TCAs last several days after cessation of the drug and the mechanisms for interactions have been identified, continuation of therapy perioperatively is reasonable provided due caution is used (167)

TCA withdrawal syndromes are characterized by GI or somatic distress, sleep disturbances, mood fluctuations, and movement disorders, most likely due to rebound excess cholinergic activity (168)

### MAO inhibitors (pargyline, phenelzine)

**Recommendation:** Usually stop 10-14 days before surgery (although some anesthesiologists feel they can be continued with precautions)

**Comments:** Potential drug interactions. The newer class (RIMA) allows selective rapidly reversible inhibition of type A-MAO. If continued perioperatively, avoid foods with high amounts of tyramine

**Evidence:**

Newer studies found the risk for pharmacokinetic drug reactions to be lower for tranylcypromine than for phenelzine, and anesthesia without discontinuation of MAO inhibitors may be safe after careful evaluation of the patient’s perioperative and psychiatric risk (169)

There were no differences in hemodynamics or complications in 27 patients undergoing ECT or elective surgery while on MAO inhibitors (170)

Surgical case reports include a death after cardiac surgery with MAO inhibitors and fentanyl plus midazolam (171), two cases of urgent cardiac surgery using fentanyl without adverse effects (172), a successful case in a patient refusing to stop an MAO inhibitor and TCA (173), and cardiovascular collapse in a patient who discontinued an MAO inhibitor 20 days before surgery (174)

Nonsurgical case report and reviews: Interactions with sympathomimetics can cause hypertension and with meperidine result in hyperpyrexia, hallucinations, coma (175; 176)

### SSRIs (fluoxetine, sertraline, paroxetine, citalopram, fluvoxamine)

**Recommendation:** Continue with caution

**Comments:** Associated with withdrawal syndrome if stopped; inhibit cytochrome P450 enzymes; can increase INR; may be associated with increased risk for bleeding

A abrupt discontinuation can result in a syndrome characterized by specific physical and psychological symptoms. Incidence, timing, and severity of symptoms vary related to plasma elimination and clinical characteristics (177)

**Evidence:**

A retrospective study of 72,540 patients on SSRIs compared with 457,876 not taking SSRIs found that receiving SSRIs in the perioperative period was associated with a higher risk for adverse events (mortality, readmission at 30 days, transfusions); however, an unmeasured covariate may have explained the result (178)

A retrospective cohort study evaluated the association between the use of SSRIs and bleeding. SSRIs were associated with an increased risk for transfusion (adjusted OR, 3.71 [CI, 1.35 to 10.18]) in patients...
undergoing orthopedic surgery (179)

In users of coumarins and antiplatelet agents, use of SSRIs was associated with increased bleeding risks (180; 181)

### Phenothiazines, butyrophenones, risperidone, ziprasidone, olanzapine

**Recommendation:** Continue

**Comments:** Can enhance CNS depression, lower seizure threshold, cause ECG abnormalities, arrhythmias, hypotension, neuroleptic malignant syndrome; discontinuation associated with withdrawal dyskinesia and rebound agitation

**Evidence:**

Consensus

### Benzodiazepines

**Recommendation:** Continue; may be started preoperatively (by the anesthesiologist) or postoperatively for sedation

**Comments:** May decrease anesthetic requirement. Chronic use may increase requirement for opiates. Abrupt discontinuation may cause a withdrawal syndrome

**Evidence:**

- An abstinence syndrome with anxiety, mood swing, depression, and thinking disorder developed 24 hours after abruptly stopping oxazepam, which the patient had been taking for 2 months (182)
- Abrupt withdrawal of sedation with midazolam, propofol, or lorazepam in critically ill patients may precipitate withdrawal symptoms (183)
- Subjects treated with midazolam preoperatively self-report improved postoperative psychological and pain recovery (184)
- Preoperatively, midazolam premedication was associated with a significantly lower anxiety level and higher sedation level but did not prolong the discharge time (185)

### Lithium (lithium)

**Recommendation:** Uncertain; continue or stop 2-3 days before surgery

**Comments:** Check level; can cause ECG changes, prolonged action of muscle relaxants, NDI

**Evidence:**

- Case reports of patients treated with lithium carbonate in preoperative preparation of Grave’s disease showed successful surgical outcome with no significant adverse effects (190; 191; 192)

ASA = American Society of Anesthesiologists; CI = confidence interval; CNS = central nervous system; ECG = electrocardiography; ECT = electroconvulsive therapy; GI = gastrointestinal; INR = international normalized ratio; MAO = monoamine oxidase; NDI = nephrogenic diabetes insipidus; OR = odds ratio; QRS = electrocardiographic complex; QT = electrocardiographic interval; RIMA = reversible inhibition of monoamine oxidase; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant.
## Perioperative Gastrointestinal Medication Management

### H2 blockers

**Recommendation:** Continue or start prophylactically

**Comments:** May be protective for stress ulcers and aspiration

**Evidence:**

See PPIs for aspiration protection ([193; 194; 195])

Prophylactic ranitidine prevented postoperative gastroduodenal complications in high-risk neurosurgical patients ([196])

Prophylactic IV ranitidine had a beneficial effect on postoperative infectious complications in patients following acute colorectal surgery ([197])

### PPIs

**Recommendation:** Continue or start prophylactically

**Comments:** May be protective for stress ulcers and aspiration

**Evidence:**

Two consecutive doses of rabeprazole, lansoprazole, or omeprazole or a single dose of ranitidine on the morning of surgery reduced gastric volume and acidity, potentially protecting against aspiration pneumonitis ([193; 194; 195])

In CABG patients in postoperative intensive care, better gastric pH control and potential prevention of gastric stress ulcers was achieved with famotidine or ranitidine compared with cimetidine or antacids ([198])

A study of 2252 ICU patients found mechanical ventilation and coagulopathy to be the most important risk factors for stress-induced GI bleeding; in the absence of these two risk factors, clinically important GI bleeding was rare (0.1%), and prophylaxis can be safely withheld ([199])

### Immunomodulators/Immunosuppressants

**Purine analogues: azathioprine, 6-mercaptopurine**

**Recommendation:** Continue or hold on day of surgery

**Comments:** Theoretical risk for perioperative myelotoxicity (thiopurines—renal elimination)

**Evidence:**

The use of azathioprine, 6-mercaptopurine, or infliximab did not increase postoperative infections in several studies of patients with IBD undergoing abdominal surgery ([200; 201; 202]); however, one study of 343 patients reported an increased risk of postoperative intra-abdominal septic complications, primarily in patients with known risk factors ([203])

### Cyclosporine (cyclosporine)

**Recommendation:** Continue

**Comments:** Minimize graft rejection

**Evidence:**

A 2006 systematic review including five studies with azathioprine, five with cyclosporine, and three with infliximab showed no increased risk for total or infectious complications ([204])

Several studies found no significant increase in perioperative complications in patients on cyclosporine ([205; 206])

Chronic cyclosporine therapy in postcardiac transplant patients undergoing noncardiac surgery did not clinically prolong the anesthetic effect ([207]).
Fourteen patients with cardiac transplants undergoing noncardiac surgery received cyclosporine alone or with azathioprine or prednisone. There were no deaths and two cases of wound infection. (208)

CABG = coronary artery bypass grafting; GI = gastrointestinal; H2 = histamine-2; iv = intravenous; IBD = inflammatory bowel disease; ICU = intensive care unit; PPI = proton-pump inhibitor.
# Perioperative HIV Medication Management

## Antiretroviral agents

**Recommendation:** Continue up to surgery, stop together, then restart together

**Comments:** Theoretical advantage to minimize emergence of resistant viral strains; may affect cytochrome P450 system

**Evidence:**

Consensus (209; 210)

Midazolam should be avoided or used at a reduced dosage with saquinavir, which significantly decreases its clearance (211)

HIV patients with CD4 counts < 200 cells/μL were more likely to get sepsis postoperatively (despite antibiotics and antiretrovirals) than patients with higher CD4 counts (212)

---

CD4 = cluster of differentiation 4; HIV = human immunodeficiency virus.
## Perioperative Herbal Medication Management

<table>
<thead>
<tr>
<th>Herbal Medication</th>
<th>Recommendation</th>
<th>Comments</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>St. John's wort</strong></td>
<td>Discontinue at least 5 days before surgery</td>
<td>Inhibits serotonin, norepinephrine, and dopamine reuptake; long half-lives of active ingredients: hypericin (43.1 hours), hyperforin (9 hours); induces cytochrome P450 enzymes, alters metabolism of other drugs</td>
<td>Cyclosporine levels were decreased in transplant recipients (213; 214)</td>
</tr>
<tr>
<td><strong>Ginkgo biloba</strong></td>
<td>Discontinue at least 36 hours before surgery</td>
<td>Inhibits platelet aggregation; active ingredient, terpenoids, have half-lives of 3-10 hours</td>
<td>Ginkgo has been associated with spontaneous intracranial bleeding (217; 218; 219; 220), hyphema (221), and postoperative bleeding following laparoscopic cholecystectomy (222)</td>
</tr>
<tr>
<td><strong>Ginseng</strong></td>
<td>Discontinue at least 24 hours before surgery (based on half-life) or 7 days before due to platelet inhibition</td>
<td>Inhibits platelet aggregation; alters coagulation cascade; may cause hypoglycemia; ginsenosides have half-lives of 0.8-7.4 hours</td>
<td>Ginseng lowered postprandial glucose levels in both diabetics and nondiabetics (223)</td>
</tr>
<tr>
<td><strong>Garlic</strong></td>
<td>Discontinue at least 7 days before surgery</td>
<td>Inhibits platelet aggregation</td>
<td>Components of garlic exerted their effects at various stages in the process of platelet aggregation (226)</td>
</tr>
<tr>
<td><strong>Kava</strong></td>
<td>Discontinue at least 24 hours before surgery</td>
<td>Dose-dependent CNS effects including sedation; may be associated with liver injury; kavalactone half-life is 9 hours</td>
<td>Dose-dependent CNS effects including sedation; may be associated with liver injury; kavalactone half-life is 9 hours</td>
</tr>
</tbody>
</table>
### Case report of coma attributed to an alprazolam-kava interaction (228)

#### Echinacea
- **Recommendation:** Discontinue (as far in advance of surgery as possible)
- **Comments:** Short-term immunostimulatory effects but long-term use has potential for immunosuppression; pharmacokinetics not studied
- **Evidence:**
  - Expert opinion warned against concomitant use of echinacea and immunosuppressive drugs because of the probability of decreased effectiveness, especially in patients awaiting transplants (229)
  - Long-term use (>8 weeks), however, has the potential for immunosuppression and the possibility of impaired wound healing and opportunistic infections (5; 230)

#### Saw palmetto
- **Recommendation:** Discontinue
- **Comments:** Increases bleeding time
- **Evidence:**
  - Case report of intraoperative hemorrhage with a prolonged bleeding time that normalized after stopping the herb (231)

#### Ma huang (ephedra)
- **Recommendation:** Discontinue
- **Comments:** Sympathomimetic effects
- **Evidence:**
  - Reports to the FDA of adverse effects of ephedra alkaloids included hypertension, palpitations, tachycardia, stroke, seizure, and death (232)

#### Valerian
- **Recommendation:** Taper and discontinue slowly weeks before surgery (if physically dependent) or continue until the day of surgery
- **Comments:** May potentiate sedative effects of anesthetics and adjuvants; may be associated with withdrawal symptoms; pharmacokinetics not studied but probably short-lived
- **Evidence:**
  - Inhibits breakdown of GABA and produces dose-dependent sedation and hypnosis (233; 234)
  - Case report of valerian withdrawal: a patient presenting with delirium and cardiac complications after surgery, responding to benzodiazepine treatment (235)

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CNS = central nervous system; FDA = Food and Drug Administration; GABA = $\gamma$-aminobutyric acid.
# Surgical Risk Stratification and Associated VTE Incidence

<table>
<thead>
<tr>
<th>Patient Risk</th>
<th>Risk Factor Stratification</th>
<th>VTE Incidence without Prophylaxis</th>
</tr>
</thead>
</table>
| Low          | Minor surgery in patients under age 40 with no additional risk factors | Calf vein DVT: 2%  
Proximal vein DVT: 0.4%  
Clinical PE: 0.2%  
Fatal PE: 0.002% |
| Moderate     | Nonmajor surgery in patients aged 40-60 with no clinical risk factors  
Minor surgery lasting <30 minutes in patients with clinical risk factors  
Major surgery in patients under age 40 with no clinical risk factors | Calf vein DVT: 10%-20%  
CellTxTL::Proximal DVT: 2%-4%  
CellTxTL::Clinical PE: 1%-2%  
CellTxTL::Fatal PE: 0.1%-0.4% |
| High         | Nonmajor surgery in patients over age 60 or with clinical risk factors  
Major surgery in patients over age 40 or with clinical risk factors | Calf vein DVT: 20%-40%  
CellTxTL::Proximal DVT: 4%-8%  
CellTxTL::Clinical PE: 2%-4%  
CellTxTL::Fatal PE: 0.4%-1% |
| Very high    | Major surgery in patients over age 40 with history of VTE, cancer, or certain hypercoagulable states  
Hip or knee arthroplasty  
Hip fracture surgery  
Major trauma  
Spinal cord injury | Calf vein DVT: 40%-80%  
CellTxTL::Proximal DVT: 10%-20%  
CellTxTL::Clinical PE: 4%-10%  
CellTxTL::Fatal PE: 0.2%-5% |

DVT = deep venous thrombosis; PE = pulmonary embolism; VTE = venous thromboembolism.
# VTE Prophylaxis Regimens by Surgical Procedure

<table>
<thead>
<tr>
<th>General Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low risk (A)</strong>*</td>
</tr>
<tr>
<td>Early ambulation postoperatively (adequate for patients at very low risk)</td>
</tr>
<tr>
<td>IPC sleeves</td>
</tr>
<tr>
<td>Graduated elastic stockings</td>
</tr>
<tr>
<td><strong>Moderate risk (A)</strong></td>
</tr>
<tr>
<td>Graduated elastic stockings</td>
</tr>
<tr>
<td>IPC sleeves (preferable), or</td>
</tr>
<tr>
<td>Enoxaparin, 40 mg sc qd, or</td>
</tr>
<tr>
<td>Dalteparin, 5000 IU sc, or</td>
</tr>
<tr>
<td>Unfractionated heparin, 5000 IU sc q12h</td>
</tr>
<tr>
<td><strong>High risk (A)</strong></td>
</tr>
<tr>
<td>Unfractionated heparin, 5000 IU sc q8h, or</td>
</tr>
<tr>
<td>Enoxaparin, 40 mg sc qd, or</td>
</tr>
<tr>
<td>Dalteparin, 5000 IU sc qd</td>
</tr>
<tr>
<td><strong>Very high risk (C)</strong></td>
</tr>
<tr>
<td>Unfractionated heparin, 5000 IU sc q8h, plus graduated elastic stockings and/or IPC sleeves, or</td>
</tr>
<tr>
<td>Enoxaparin, 40 mg sc qd (extended duration), plus graduated elastic stockings and/or IPC sleeves, or</td>
</tr>
<tr>
<td>Dalteparin, 5000 IU sc qd (extended duration), plus graduated elastic stockings and/or IPC sleeves</td>
</tr>
<tr>
<td><strong>Rivaroxaban, 10 mg po qd</strong></td>
</tr>
</tbody>
</table>

**Comments**

- IPC sleeves alone are best reserved for patients at high risk for hemorrhage (e.g., trauma patients, patients undergoing procedures with a high incidence of bleeding such as radical prostatectomy, patients with factor deficiencies, craniotomy).
- Graduated elastic stockings and IPC sleeves must be placed before surgery and worn continuously through the intraoperative and postoperative period until the patient is ambulatory.
- The rate for symptomatic or asymptomatic total VTE in general surgery is ~25% without prophylaxis.

**Evidence**

- A 2012 guideline from the American College of Chest Physicians provided guidance based on pooled VTE prophylaxis data on surgical and trauma patients (21; 38).
- A 1992 meta-analysis of studies from 1984 to 1991 compared LMWH vs. unfractionated heparin for postoperative VTE prophylaxis. Among general-surgery patients there was no improvement in the benefit-to-risk ratio for LMWH compared with unfractionated heparin. In orthopedic surgery, the absolute risk reduction for VTE was significant for LMWH vs. unfractionated heparin (236).
- Hip fracture patients who were repaired within 2 days of hospitalization and had more than 5 physical or occupational therapy sessions had a shorter length of stay, fewer medical complications, and were more likely to return to the community (237).
A prospective randomized trial compared intermittent pneumatic calf compression with no treatment in patients undergoing major abdominal surgery. There was no difference in the incidence of VTE between the two groups (238).

In a review of VTE prophylaxis with unfractionated heparin in two specific surgical populations, unfractionated heparin was effective in reducing the incidence of fatal PE and proximal DVT (239).

**Orthopedic Surgery**

**Total hip or knee replacement (A) (treat for at least 10-14 days)**

<table>
<thead>
<tr>
<th>LMWH (preferred)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enoxaparin, 30 mg sc q12h or 40 mg sc qd, or</td>
</tr>
<tr>
<td>Dalteparin, 5000 IU sc qd, or</td>
</tr>
<tr>
<td>Fondaparinux, 2.5 mg qd</td>
</tr>
</tbody>
</table>

**Warfarin adjusted to a target INR of 2-3**

| Rivaroxaban 10 mg, po qd¹ |
| Apixaban 2.5 mg bid¹ |
| Dabigatran 110 mg qd¹ |

**Unfractionated heparin**

| Aspirin (may be less effective than other options) |

**Adjuvant prophylaxis with IPC (with or without graduated elastic stockings) may provide additional benefit (C)***

**Hip fracture surgery**

<table>
<thead>
<tr>
<th>LMWH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enoxaparin, 30 mg sc q12h (C), or</td>
</tr>
<tr>
<td>Fondaparinux, 2.5 mg qd (A)</td>
</tr>
</tbody>
</table>

**Unfractionated heparin**

| Warfarin adjusted to a target INR of 2-3 |
| Aspirin (may be less effective than other options) |

**Extended prophylaxis (A)**

<table>
<thead>
<tr>
<th>LMWH (preferred)</th>
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<tbody>
<tr>
<td>Enoxaparin, 40 mg sc qd, or</td>
</tr>
<tr>
<td>Dalteparin, 5000 IU sc qd</td>
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</tbody>
</table>

**Warfarin with a goal INR of 2-3**

**Comments**

| Dextran or IPC alone is not recommended |

| Enoxaparin 40 mg qd has not been approved for prophylaxis for total knee replacement, but may be as effective and is less costly than 30 mg q12h |
The risk for VTE extends beyond the hospital stay; extended prophylaxis for 4–6 weeks may reduce the incidence of clinically important VTE events.

<table>
<thead>
<tr>
<th>Evidence</th>
</tr>
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<tbody>
<tr>
<td><strong>Without prophylaxis, the rates for symptomatic and asymptomatic VTE in total hip replacement include total DVT, 45%-57%; proximal DVT, 23%-36%; total PE, 0.7%-30%; and fatal PE, 0.1%-0.4%. In total knee replacement, rates are total DVT, 40%-84%; proximal DVT, 9%-20%; total PE, 1.8%-7%; and fatal PE, 0.2%-0.7%. In hip fracture patients without prophylaxis, rates are total DVT, 36%-60%; proximal DVT, 17%-36%; total PE, 4.3%-24%; and fatal PE, 3.6%-12.9%</strong></td>
</tr>
</tbody>
</table>

| A 2012 guideline from the American College of Chest Physicians evaluated pooled VTE prophylaxis data on surgical and trauma patients and provided recommendations on VTE prophylaxis (21) |
| A 2002 meta-analysis of four randomized controlled trials found that fondaparinux significantly reduced the incidence of VTE by day 11 (182/2682 = 6.8%) compared with enoxaparin (371/2703 = 13.7%) with an odds ratio of 0 ([CI, 0.458-0.631] P<0.001) among patients undergoing major orthopedic surgery. This beneficial effect was consistent across all types of surgery and all subgroups. Major bleeding occurred more frequently in the fondaparinux-treated group (2.7%) than in the enoxaparin group (1.7%) (P=0.008) (20) |
| A 2001 systematic review and meta-analysis demonstrated that among patients undergoing total hip or knee replacement, extended-duration prophylaxis (for 3042 days) significantly reduced the frequency of symptomatic VTE. The reduction in risk is equivalent to about 20 asymptomatic events per 1000 patients treated (240) |

| RECORD 3 trial included 2531 patients undergoing knee arthroplasty. A 10- to 14-day course of treatment with rivaroxaban significantly reduced the total event rate compared with an equal duration of treatment with enoxaparin (1.1% and 3.7%, respectively; P<0.001) (241). In the RECORD 2 trial involving 2509 patients undergoing total hip arthroplasty, a 31- to 39-day course of rivaroxaban significantly reduced the total event rate compared with a 10- to 14-day course of enoxaparin followed by 21 to 25 days of placebo (2.0% and 9.3%, respectively; P=0.0001) (242) |

**RECORD 3 trial included 2531 patients undergoing knee arthroplasty. A 10- to 14-day course of treatment with rivaroxaban significantly reduced the total event rate compared with an equal duration of treatment with enoxaparin (9.6% and 18.9%, respectively, P<0.001) (243). In the RECORD 4 trial involving 3148 patients undergoing knee arthroplasty, a 10- to 14-day course of treatment with rivaroxaban significantly reduced the total event rate compared with an equal duration of enoxaparin at the higher 30-mg twice-daily dose (6.9% and 10.1%, respectively; P=0.012) (244). In both the RECORD 2 and 3 trials, rivaroxaban significantly reduced the incidence of symptomatic VTE compared with enoxaparin. Rivaroxaban did not increase major bleeding in any of the trials, but a pooled analysis of all four trials revealed a small but significant increase in major plus clinically relevant nonmajor bleeding with rivaroxaban |

| A pooled analysis compared newer agents (apixaban, rivaroxaban and dabigatran) with enoxaparin for the prevention of VTE after total hip or knee replacement. The study found that rivaroxaban was superior to enoxaparin for the prevention of major VTE with RR, 0.32 [CI, 0.15-0.67] and that apixaban and dabigatran were equivalent. There were no statistically significant differences in major bleeding when comparing newer drugs with enoxaparin (245) |

| Patients undergoing total hip replacement were randomly assigned to enoxaparin vs. placebo. Venography was the endpoint for DVT. Four patients (10.8%) receiving enoxaparin developed DVT, whereas 20 (51.3%) had DVT in the placebo group. The observed major bleeding rate was 4% in both groups. This showed the efficacy of enoxaparin for preventing DVT in this patient group (246) |

| Investigators compared enoxaparin and warfarin for the prevention of VTE after total hip arthroplasty. Inpatient programs providing treatment with either enoxaparin, 30 mg sc q12h, or adjusted-dose warfarin for a mean of 7.3 days afforded protection against VTE, with overall rates of morbidity and mortality of 3.7% and 0.6%, respectively, and a very low rate of major bleeding complications (0.9%) for 3 months after total hip arthroplasty. During the hospitalization, the patients managed with enoxaparin had a lower rate of VTE than those managed with adjusted-dose warfarin (P=0.008). This benefit was lost after the medication was discontinued, with no difference in the prevalence of VTE between the two groups at 3 months after discharge from hospital (247) |

| A large, randomized trial compared aspirin, 160 mg, vs. placebo until post-op day 35 in patients undergoing repair of fractured hips. The group assigned to aspirin had lower rates of VTE (DVT or PE), with a number needed to treat of 111 after 35 days. Patients were allowed to have other forms of VTE prophylaxis, which makes the results difficult to interpret and apply (248) |

| In a survey of members in the American Association of Hip and Knee Surgeons, warfarin was the most common drug treatment used for total hip and total knee arthroplasties, followed by IPC sleeves and LMWH (249) |

| A consecutive patient study of 360 patients undergoing total hip arthroplasty showed that continuing warfarin (0.5%) after discharge for 4 weeks was more effective than placebo (9.4%) in the incidence of VTE (250) |

| In another study of prolonged out-of-hospital prophylaxis after total hip replacement, the LMWH reviparin was compared with an adjusted dose oral anticoagulant (acenocoumarol). Symptomatic thromboembolic events occurred in 2.3% (15/643) of the reviparin group and 3.3% (21/636) of those receiving acenocoumarol. Major bleeding was reported in 1.4% (9/643) of the reviparin group and 3.7% (24/643) in those on the adjusted-dose oral therapy (251) |

| In a trial of 89 patients undergoing total hip or knee replacement, investigators evaluated the efficacy of graded compression stockings. All patients had the pressure gradient generated by the compression stockings evaluated, and 98% of the stockings failed to produce the ideal pressure gradient. Reversed gradient was observed in 54%, and this resulted in a higher incidence of DVT. The overall rate of DVT was 16.7% by venography (252) |
### Gynecologic Surgery

**Low risk (C)**
- Early mobilization alone is recommended for low-risk patients undergoing short procedures for benign disease

**Moderate to high risk (surgery for benign disease without additional risk factors)**
- Unfractionated heparin, 5000 IU sc q12h (A), or
- LMWH
  - Enoxaparin, 40 mg sq qd, or
  - Dalteparin, 5000 IU sc qd (C)

**IPC (C)**
- **Very high risk (malignancy) (C)**
  - IPC and/or unfractionated heparin, 5000 IU sc q8h, or
  - LMWH
    - Enoxaparin, 40 mg sc qd, or
    - Dalteparin, 5000 IU sc qd

**Comments**
- IPC sleeves must be placed before surgery and worn continuously through the intraoperative period and postoperative period until the patient is ambulatory; IPC may be combined with LMWH
- Extended prophylaxis after discharge may be considered for select very high-risk patients who are not ambulating or are considered to still be at risk for development of VTE; LMWH: enoxaparin (40 mg sc qd), dalteparin (5000 IU sc qd), or warfarin (goal INR 2-3) is suggested but has not been studied in clinical trials in this patient population
- The rate for symptomatic or asymptomatic total VTE in gynecologic surgery is ~16%

**Evidence**
- LMWH and IPC appear to be similarly effective in the postoperative prophylaxis of VTE in high-risk gynecologic-oncology patients. The use of LMWH is not associated with an increased risk for bleeding complications when compared with IPC (252)

### Neurosurgery

**Craniotomy (A)**
- IPC alone (preferred except in high-risk patients), or
- IPC plus
  - Unfractionated heparin, 5000 IU sc q12h, or enoxaparin, 40 mg sc qd

**Spinal cord injury (C)**
- IPC plus
  - Enoxaparin, 30 mg sc q12h, or
  - Heparin, 5000 IU sc q8h for 2 weeks, then

- Enoxaparin, 40 mg sc qd, or warfarin (goal INR 2-3) continued during the rehabilitation phase
Comments
Continuing prophylaxis into the rehabilitation phase is indicated in spinal cord injury but the duration has not been established
The rate for symptomatic or asymptomatic total VTE in neurologic surgery is ~22%

Evidence
A randomized, prospective, double-blind trial of 150 patients undergoing craniotomy for brain tumor compared enoxaparin, 40 mg sc qd, with unfractionated heparin, 5000 IU sc q12h. All patients wore graduated compression stockings plus IPC devices and had compression ultrasonography to evaluate VTE at discharge. The overall rate of asymptomatic VTE was 9.3% and there were no significant differences between the groups (254)

Urologic Surgery

Transurethral prostatectomy (C)

Early ambulation alone is recommended for patients undergoing transurethral prostatectomy or other low-risk procedures

Moderate risk (major open urologic procedures, e.g., nephrectomy) (B)

Unfractionated heparin, 5000 IU sc q12h

LMWH

Enoxaparin, 40 mg sc qd, or

Dalteparin, 5000 IU sc qd

IPC

Very high risk (e.g. radical prostatectomy) (C)

IPC and or graduated elastic stockings plus

Unfractionated heparin, 5000 IU q8h, or

Enoxaparin, 40 mg sc qd, or dalteparin, 5000 IU sc qd

Evidence
A 2012 guideline from the American College of Chest Physicians evaluated pooled VTE prophylaxis data on surgical and trauma patients and provided recommendations on VTE prophylaxis (21)
A review of VTE prophylaxis with unfractionated heparin in general, orthopedic, and urologic surgery found that it was effective in reducing the incidence of fatal PE and proximal DVT (239)
In a prospective study of 36 patients undergoing urologic surgery for malignancy, patients received dalteparin for 3-7 days and no clinically evident VTE developed (255)

Major Trauma

LMWH

Enoxaparin, 40 mg sc qd, or

Dalteparin, 5000 IU sc qd, or

Unfractionated heparin, 5000 IU q8h

Patients at high risk for bleeding:

Initial IPC and elastic stockings followed by

LMWH when possible (C)
Comments

Patients with clinical risk factors for VTE should receive prophylaxis, if possible (A)

Enoxaparin is preferred if no contraindication for use such as intracranial bleeding, incomplete spinal cord injury with paraspinal hematoma, continued uncontrolled bleeding, or coagulopathy

Continue prophylaxis until patient is ambulatory

If VTE risk continues after discharge, consider extended prophylaxis with LMWH or warfarin

Evidence

Among 344 randomly assigned major trauma patients, 136 who received low-dose heparin (5000 IU sc q12h) and 129 who received enoxaparin (30 mg sc q12h) had venograms adequate for analysis. Sixty patients given heparin (44%) developed DVT, and 40 patients given enoxaparin (31%) had DVT. The rates of proximal DVT were 15% and 6%, respectively. LMWH was more effective than low-dose heparin in preventing VTE after major trauma (255)

*Letters in parentheses indicate strength of recommendation:
  A = Strength of recommendation based on preponderance of data derived from level 1 studies, which meet all of the evidence criteria for that study type;
  B = Strength of recommendation based on preponderance of data derived from level 2 studies, which meet all of the evidence criteria for that study type;
  C = Strength of recommendation based on preponderance of data derived from level 3 studies, which meet all of the evidence criteria for that study type.

1 U.S. FDA approval for this indication pending

bid = twice daily; CI = confidence interval; DVT = deep venous thrombosis; FDA = Food and Drug Administration; INR = international normalized ratio; IPC = intermittent pneumatic compression; LMWH = low-molecular-weight heparin; PE = pulmonary embolism; po = orally; q8h = every 8 hours; q12h = every 12 hours; qd = every day; RR = risk ratio; sc = subcutaneous; VTE = venous thromboembolism.