Evidence and Guidelines for Managing Cardiovascular Disease

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Risk for perioperative major adverse cardiac events (MACE): 5 million cardiovascular (CV) deaths or nonfatal myocardial infarctions (MI) occur annually; little known about prediction and prevention of MACE; guidelines from 2007 available; new guidelines expected in 2014; recent study — retrospective analysis of coronary angiography of patients suffering postoperative MI showed demand ischemia in 55%, thrombotic events in 26%, and normal angiograms in 19%; suggests that perioperative MI multifactorial problem, with demand ischemia representing predominant etiology; planned prospective observational study — evaluation via computed tomography (CT) angiography of patients with ≥3 CV risk factors undergoing noncardiac surgery; designed to document major vascular outcome 30 days and 1 yr after surgery and provide data about etiology of perioperative MI

Risk after recent MI: American College of Cardiology (ACC)/American Heart Association (AHA) Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery state that waiting 4 to 6 wk after MI to perform elective surgery reasonable; recent retrospective study supports waiting 8 wk after MI; although ACC/AHA guidelines date from 2007, basic tenets reiterated in subsequent publications; questions addressed by guidelines — whether delay of surgery needed in unstable patient; whether patient medically and surgically optimized; whether further CV tests warranted; whether modification of perioperative monitoring and care plans needed; 2007 guidelines provided updates of 2002 guidelines; every recommendation given level of evidence, from A (indicating multiple trials and populations) to C (relying on expert opinion), and designated from class 1 (positive recommendation) to class 3 (negative recommendation in which risk outweighs benefit); class 1 recommendations given for drugs, interventions, and therapies that should be implemented; class 3 therapies not recommended and potentially harmful; in class 2a and 2b, risk-benefit ratios less well defined

Approach to patients: take history and establish presence of active cardiac conditions, functional capacity (FC), whether change in symptoms or medication has occurred, current medications, and presence of pacemaker or implantable cardiac defibrillator (ICD); perform physical examination (PE) and routine tests; assess cardiac risk factors and surgical risk; active cardiac conditions — patient should undergo evaluation and treatment before noncardiac surgery if present; include unstable coronary syndromes, decompenated congestive heart failure (CHF), significant arrhythmias, or severe valvular disease; FC — if poor, perioperative and long-term cardiac risk increased (estimated through use of metabolic equivalents [METs]); determine whether patient can perform >4 MET capacity (eg, climbing stairs, walking uphill, golfing, bowling)

PE and routine tests: perform careful CV examination and assess comorbidities; perioperative electrocardiography (ECG) — class 1 indication in patients with ≥1 cardiac risk factor undergoing vascular surgery, or with coronary artery, peripheral artery, or cerebrovascular disease and undergoing intermediate-risk surgery; class 2a if undergoing vascular surgery (no risk factors); class 2b with ≥1 clinical risk factor and undergoing intermediate-risk surgery; class 3 (not recommended) in asymptomatic patients undergoing low-risk surgery

Risks: clinical risk factors — prospective validated predictors of perioperative MACE (eg, perioperative MI, cardiac death, cardiac arrest); derived from Revised Cardiac Risk Index (RCRI; risk factors include history of ischemic heart disease, CHF, cerebrovascular disease, diabetes mellitus, and renal insufficiency); risks of surgery — vascular surgery considered high risk (risk of MACE >5%); intermediate-risk (1%-5%) procedures include intraarterial, thoracic, carotid, head and neck, orthopedic, and prostate procedures; low-risk (<1%) surgeries include endoscopy, superficial procedures, cataracts, breast, and ambulatory surgery; guidelines follow algorithm and consider need for emergency vs elective surgery, active cardiac conditions, FC, risk factors, and risk of surgery to determine whether patients ready for surgery vs need further testing or change in plan

Stress testing: provokes cardiac stress during imaging, with goals of assessing FC of heart, identifying perioperative MI or arrhythmias, and estimating perioperative and long-term prognosis; cardiac risk directly related to extent that myocardium affected; class 1 guideline for patients with active cardiac conditions; reasonable and may be considered for patients with high risk and poor FC or poor FC and 2 clinical risk factors, or 2 clinical risk factors with good FC and undergoing vascular surgery; class 3 for patients with no risk factors undergoing intermediate- or low-risk surgery; patients with abnormal ECG or who cannot exercise require pharmacologic stress perfusion imaging or dobutamine echocardiography; contra indications — avoid pharmacologic tests with adenosine or dipyridamole if patient bronchospastic, has carotid occlusion, or taking theophylline; avoid dobutamine echocardiography in patients with serious arrhythmias, hypertension, or poor echocardiographic imaging; recent data — show patients undergoing intermediate- and high-risk surgery who undergo noninvasive cardiac stress testing have increased 1-yr survival and increased length of hospital stay; retrospective study — shows many patients undergo unnecessary cardiac tests

Educational Objectives

The goals of this program are to improve perioperative management of patients with cardiovascular disease and the treatment of hypotension in obstetric patients. After hearing and assimilating this program, the clinician will be better able to:

1. Perform an appropriate preoperative evaluation of patients with cardiovascular disease.
2. Cite guidelines for scheduling elective noncardiac surgery after percutaneous coronary intervention (PCI).
3. Outline recent requirements and recommendations for perioperative β-blockade.

4. Explain the role of nitric oxide in the response of the uterine artery to ephedrine.
5. Choose the most appropriate vasopressor for obstetric anesthesia.

Faculty Disclosure

In adherence to ACCME Standards of Commercial Support, Audio-Digest requires all faculty and members of the planning committee to disclose relevant financial relationships within the past 12 months that might create any personal conflicts of interest. Any identified conflicts were resolved to ensure that this educational activity promotes quality in health care and not a proprietary business or commercial interest. For this program, the faculty and planning committee reported nothing to disclose.
Revascularization: indications identical whether or not surgery planned; class 1 indication before noncardiac surgery; useful for patients with stable angina and left main coronary-artery stenosis, 3-vessel disease, or 2-vessel disease with significant proximal left anterior descending (LAD) coronary artery stenosis plus either low ejection fraction (EF) or ischemia on stress test; recommended for unstable angina, non-ST-elevation MI (NSTEMI), or acute STEMI; retrospective study — patients undergoing revascularization after MI benefited, compared with patients receiving percutaneous coronary intervention (PCI)

Perioperative PCI: of no value in preventing perioperative cardiac events for noncardiac surgery unless independently indicated; 2009 data show 5% of patients receiving stents undergo surgery ≤1 yr after stent placement

Risks: restenosis — scar formation at angioplasty site or within stent; drug-eluting stent (DES) decreased restenosis rate to 4%-6%; stent thrombosis — stent surface must re-endothelialize to maintain nonthrombogenic surface (time required not known for DES [may fail to endothelialize, thus necessitating dual antiplatelet therapy for life]); thrombosis outside perioperative period rare but catastrophic (death rate ≥40%)

Perioperative guidelines after PCI: angioplasty — delay elective surgery ≥2 wk, then proceed with aspirin therapy (ASA); bare-metal stents (BMS) — delay 30 to 45 days, then proceed with ASA; DES — delay elective surgery ≥1 yr, and continue ASA during perioperative period; recent data indicate optimal timing for elective surgery after BMS 46 to 180 days (>180 days for DES; risk equivalent to waiting 1 yr)

Antiplatelet therapy: many patients (20%-50% of population) resistant to clopidogrel (Plavix) or ASA because of genetic factors or drug interactions; prasugrel (Effient) — new thienopyridine with increased potency, consistency, and risk for life-threatening bleeding; speaker recommends discontinuation 10 days before surgery (vs 5 days for clopidogrel); cangrelor — not yet approved by Food and Drug Administration (FDA); rapid-acting, reversible, intravenous platelet inhibitor, with half-life of 9 min; provides coverage during preoperative period after clopidogrel or prasugrel discontinued

Perioperative β-blockade: as of January 1, 2012, all surgical patients on β-blockers required to be given 2 doses of β-blockers in perioperative period (within 24 hr of surgery and on postoperative day 1 or 2); if β-blockers withheld for either, pay-for-performance measures require documentation of contraindication to therapy (ie, heart rate [HR] <50 bpm, systolic blood pressure [BP] <100 mm Hg, or patient receiving inotropic or vasopressor agents) ACC Foundation/AHA guidelines: metoprolol found to decrease MACE by ≥20% and MI by 30%, but doubled stroke rate, increased mortality by 33%, doubled significant hypotension, and tripled significant bradycardia

Revised guidelines (2009): class 1 indication — continuation of β-blockers in patients currently receiving them; class 2 indications — β-blockers titrated to HR and BP probably recommended for patients with potential CAD undergoing vascular surgery; class 3 indications — routine use of high doses without titration; patients with absolute contraindications; key points in 2009 revisions — titration important; fixed-dose strategy not recommended; β-blocker withdrawal associated with increased risk for MI

Recent data: atenolol shows reduced mortality, compared with metoprolol; chronic β-blockade associated with better outcome than acute β-blockade; acute surgical anemia influences cardioprotective effect of β-blockade; genetic variation in patients alters response to β-blockade (future studies should include genetic testing)

Risks: consider hemodynamic effects; avoid bradycardia and hypotension; search for other causes of tachycardia before adding β-blockers; start β-blockade well before planned procedure; routine administration not advocated

Statin therapy: effects — increases endothelial nitric oxide; promotes and restores endothelial function; anti-inflammatory; stabilization of plaque; decreased platelet aggregation; significantly decreases risk in patients with CAD; meta-analysis shows association with significant reductions in atrial fibrillation, MI, and hospital length of stay; adverse side effects — hepatotoxicity, rhabdomyolysis, and possible increase in blood loss; guidelines — continue administration for patients already taking statins; reasonable to use in patients undergoing vascular surgery, and those with risk factors undergoing intermediate-risk surgery

a2-agonists: associated with reduction in cardiac event rates in noncardiac surgery patients; have no class 1 or 2a indications; 2b indications — consider for control of hypertension in patients with known CAD or ≥1 clinical risk factor and undergoing surgery (guidelines may change with results from new study)

Postoperative testing: important for identification of patients at risk for perioperative MI; guidelines — for patients with high or intermediate surgical risk or CAD, perform ECG at baseline and on postoperative days 1 and 2 (most cost effective); troponin measurement — obtain for patients with ECG changes or chest pain (class 1 indication); peak troponin T level during first 3 postoperative days in patients undergoing noncardiac surgery significantly associated with 30-day mortality; postoperative measurement increases detection of myocardial injury in high-risk patients by factor of 3

Role of Phenylephrine and Other Vasoactive Drugs in Obstetric Anesthesia

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Hypotension in pregnancy: significant problem after neuraxial anesthesia; therapeutic options include fluid loading, pharmacologic treatment, and positioning; uterine perfusion heavily dependent on arterial pressure; controversy has existed over which vasopressors have least effect on fetus

Ephedrine: mixed-action drug; derived from plants with both α- and β-agonist effects; repeated dosing potentially depletes patient stores of catecholamines, thus decreasing effect; should be avoided in patients taking monoamine oxidase inhibitors (MAOI) due to potential for hypertensive crisis

Phenylephrine: direct-acting pure α-agonist; large doses can cause reflex bradycardia

Vasopressors and pregnancy: pregnant ewe model — presented in 1970 study; showed ephedrine best at preserving uterine blood flow, compared with other vasopressors; later study showed ephedrine preserved blood flow with no change in fetal pH, while pure α-agonists caused largest decrease to uterine blood flow; differential response of uterine artery to ephedrine (ie, less vasoconstriction) attributed to endothelium; levels of nitric oxide found to increase during pregnancy and prevent vasoconstriction from ephedrine (blocking synthesis abolishes differential effect)

Studies in humans: fetal heart-rate tracings show periods of increased metabolism or stress after doses of ephedrine; approximately linear relationship observed between dose of ephedrine given and amount of increase in fetal heart rate; ephedrine crosses placenta (directly affects fetus); as no change seen in fetal pH, significance of effect unclear; study of prophylactic use of ephedrine found 30 mg minimum effective dose to preserve normotension after spinal anesthetic without observable effects on fetus (small patient sample); meta-analysis of 7 studies concluded women receiving phenylephrine delivered babies with higher umbilical cord pH levels, compared with those receiving ephedrine; higher base excess seen in phenylephrine group, but with no change in occurrence of true acidosis (pH <7.2), and no change in APGAR scores; acidosis study — found lower pH and higher difference between pCO2 of umbilical artery and umbilical vein with infusion of ephedrine than with phenylephrine; ephedrine appeared to stimulate metabolism in healthy fetuses
without observable clinical effects, but ability of compromised fetus to tolerate increased stress questioned; higher arterial pH and better arterial-venous pCO₂ differential seen in phenylephrine group; dose-response relationship seen between amount of ephedrine administered to mother and fetal CO₂ production

**Treatment plan:** main goal to maintain maternal homeostasis (also benefits fetus); best results observed when maternal BP maintained at 100% baseline level; infusions — some centers begin phenylephrine infusion with spinal anesthesia, but most use bolus administration; *American Society of Anesthesiologists guidelines — both phenylephrine and ephedrine acceptable drugs, but in absence of maternal bradycardia, phenylephrine possibly preferable

**Conclusions:** ephedrine originally considered best obstetric vaso-pressor due to preservation of uterine blood flow; ephedrine causes fetal acidosis (generally well tolerated in healthy pregnancy, but no data available on effects on compromised fetuses); phenylephrine leads to better fetal metabolic markers, and, in absence of contraindications, preferred choice; superiority of infusion vs bolus dosing unclear, but goal to maintain 100% preinduction BP

**Acknowledgements**

Dr. Roth was recorded at the *UCSD Anesthesiology Update 2013*, held January 16-19, 2012, in San Diego, CA, and sponsored by the University of California, San Diego, School of Medicine, Department of Anesthesiology. Dr. Cummings was recorded at the *Survey of Current Issues in Surgical Anesthesia*, held December 2-6, 2013, in Naples, FL, and sponsored by the Cleveland Clinic Anesthesiology Institute. For information on upcoming meetings sponsored by the University of California, San Diego, School of Medicine, Department of Anesthesiology, please visit cme.ucsd.edu, and for those sponsored by the Cleveland Clinic, visit ccfcmc.org (or check our website, Audio-Digest.org, under “Upcoming Meetings”). The Audio-Digest Foundation thanks the speakers and the sponsors for their cooperation in the production of this program.

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**Estimated time to complete the educational process**

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<th>Activity</th>
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<tr>
<td>Review Educational Objectives</td>
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<td>Take posttest</td>
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1. Which of the following is the predominant etiology of postoperative myocardial infarctions?
   (A) Thrombotic event
   (B) Arrhythmia
   (C) Decreased pO₂
   (D) Demand ischemia

2. There is _______ evidence for perioperative stress testing in patients with no risk factors who are undergoing intermediate-or low-risk surgery.
   (A) Class 3
   (B) Class 2b
   (C) Class 2a
   (D) Class 1

3. Recent data suggest that elective surgery should be delayed for _______ after placement of drug-eluting stents (DES).
   (A) 14 to 30 days
   (B) 30 to 45 days
   (C) 45 to 180 days
   (D) >180 days

4. All the following are true about the investigational drug cangrelor, except:
   (A) Administered orally
   (B) Has a half-life of 9 min
   (C) Reversible
   (D) Rapidly acting

5. Choose the true statement about perioperative β-blockade.
   (A) Class 1 indication for patients with coronary artery disease who are undergoing vascular surgery
   (B) Improved outcomes are associated with fixed-dose strategies
   (C) Metoprolol is associated with decreased mortality, compared with atenolol
   (D) Chronic β-blockade is associated with better outcome then acute β-blockade

6. Which of the following is a potential side effect of phenylephrine?
   (A) Reflex bradycardia
   (B) Reflex tachycardia
   (C) Hypertensive crisis in patients taking monoamine oxidase inhibitors
   (D) Catecholamine depletion

7. The differential response of the uterine artery to ephedrine is caused by:
   (A) Oxytocin
   (B) Human chorionic gonadotropin
   (C) Nitric oxide
   (D) Elevated pCO₂

8. What is the minimum effective dose of ephedrine required to maintain normotension after spinal anesthesia?
   (A) 10 mg
   (B) 20 mg
   (C) 30 mg
   (D) 40 mg

9. Umbilical artery pH levels are higher in babies of women who received phenylephrine during delivery, compared with those whose mothers who received ephedrine.
   (A) True
   (B) False

10. Neonatal metabolic markers are most stable when maternal blood pressure is maintained at _______ of the baseline level.
    (A) 80%
    (B) 90%
    (C) 100%
    (D) 110%

Answers to Audio-Digest Anesthesiology Volume 56, Issue 09: 1-C, 2-D, 3-D, 4-D, 5-B, 6-C, 7-B, 8-A, 9-D, 10-B