Update in Perioperative Medicine

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Update to ACC/AHA guidelines on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery

Stents: recent study found no difference in risk for major adverse cardiac events (MACEs) between drug-eluting stents (DESs) and bare metal stents; DESs may be more effective than bare metal stents at 3 to 6 mo and beyond (may not be necessary to wait 12 mo after placement of DES before performing noncardiac surgery); second-generation DESs more effective than first-generation DESs; major complication was bleeding; incidence of bleeding and MACEs highest in first 6 wk; antiplatelet therapy had no effect on incidence of bleeding or MACEs; β-blockade: systematic review by Wijeysundera et al (2014) — concluded that β-blockade ≤1 day prior to surgery decreased risk for nonfatal MI or death; β-blockers, angiotensin-converting enzyme inhibitors, and statins: Botto et al (2014) concluded that intensification of cardiovascular therapy associated with improved outcomes at 1 yr B-type natriuretic peptide (BNP): Rodseth et al (2014) found that postoperative measurement plus preoperative measurement stronger predictor of outcomes at 30 days and 6 mo than preoperative measurement alone; elevation of postoperative BNP stronger predictor than revised cardiac risk index score of ≥3 or preoperative BNP; management of elevated postoperative BNP uncertain; meta-analysis by Young et al (2014) concluded that BNP has high rule-out value (ie, normal value indicates complications unlikely); however, high BNP not strong predictor of complications

Aortic stenosis (AS): Andersson et al (2014) found higher incidence of major cardiac events and mortality in patients with AS undergoing emergency surgery compared with control group; outcomes in patients with AS undergoing elective surgery not much worse than those in control group

Pulmonary studies

Preoperative inspiratory muscle training: systematic review by Mans et al (2015) showed decrease in all postoperative pulmonary complications (risk ratio 0.48); no significant effect on length of stay observed; systematic review by Snowdon et al (2014) found reduced time to extubation and decreased pulmonary complications, but no effect on length of stay

Pulmonary hypertension: Hip Fracture Accelerated Surgical Treatment and Care Track (HIP ATTACK) investigators performed case-controlled trial of 132 patients with pulmonary hypertension undergoing total hip arthroplasty; pulmonary hypertension associated with fewer complications compared with previous studies (substantial increase observed only with arrhythmias); investigators concluded that in selected patients, risk for pulmonary hypertension may not be as high as previously thought

Continuous positive airway pressure (CPAP): review of 10 trials in Cochrane database (not limited to obstructive sleep

Educational Objectives

The goals of this program are to prevent comorbid complications in the perioperative setting and to improve treatment of bronchospasm in patients with asthma. After hearing and assimilating this program, the clinician will be better able to:

1. Cite recent data on the role of β-blockade in the perioperative setting.
2. List strategies that may reduce risk for pulmonary complications in patients undergoing surgery.
3. Select appropriate bridging anticoagulation therapy.
4. Explain the perioperative risk associated with carotid artery stenosis, estimated glomerular filtration rate, and HbA1c.

5. Explain the pharmacologic basis for the use of selective ligands of GABA receptors in the treatment of asthma.

Faculty Disclosure

In adherence to ACCME Standards for 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, members of the faculty and planning committee reported nothing to disclose.
Acute kidney injury: Intra-abdominal surgery known risk factor for AKI. Choi et al (2014) found in 336 cases that AKI is associated with lower eGFR (45-59 mL/min) after exploratory laparotomy compared to standard care (90%).

Bridging anticoagulation: perioperative anticoagulation can be managed by continuing with oral anticoagulation, cessation of oral medication and bridging with heparin or low-molecular-weight heparin, or cessation of anticoagulation; current ACC guidelines recommend bridging in high-risk patients; meta-analyses of patients on oral anticoagulant therapy undergoing implantation of cardiac devices showed that bridging regimen associated with significant increase in risk for bleeding (no effect on thromboembolic events observed); no difference in incidence of bleeding or thromboembolism observed between patients who stopped oral anticoagulation and patients who continued with oral anticoagulation; studies concluded that continuing with oral anticoagulation may be preferred in patients undergoing implantation of cardiac devices; anticoagulation management in elective surgery — Douketis et al (2014) examined patients with atrial fibrillation taking either dabigatran or warfarin; bridging therapy associated with significant increase in risk for major bleeding

Carotid artery stenosis: Sonny et al (2014) performed trial using retrospective cohort methodology; examined internal carotid peak systolic velocity on duplex studies (substitute for stenosis); no significant increase in risk for postoperative stroke or MI observed; study concluded that preoperative ultrasonography of carotid arteries may not be necessary in asymptomatic patients

Kidney disease: chronic kidney disease known predictor of perioperative outcomes; estimated glomerular filtration rate (eGFR) more useful than serum creatinine for predicting adverse postoperative events; retrospective cohort study divided eGFR into 6 stages; correlation between eGFR and perioperative MACEs demonstrated; most notable increase in odds ratio (1.8 to 3.9) observed from stage 3a (eGFR 45-59 mL/min) to stage 3b (eGFR 30-44.9 mL/min); study concluded that patients at eGFR stage ≥3b at highest risk

Acute kidney injury: intra-abdominal surgery known risk factor for developing acute kidney injury (AKI); Kim et al (2014) demonstrated that risk for AKI varied by type of operation (eg, risk ratio 0.23 for appendectomy and 1.34 for ileostomy); rate of 30-day mortality increased in patients who developed AKI (from 1.4% after exploratory laparotomy to 31.6% after gastric bypass); aspirin, clonidine, and risk for AKI — randomized controlled trial by Garg et al (2014) demonstrated that preoperative administration of aspirin and clonidine had no effect on incidence of AKI; however, post hoc analysis revealed that aspirin increased risk for major bleeding and bleeding-associated AKI and clonidine increased risk for hypotension (which also increased risk for AKI)

Diabetes: Underwood et al (2014) analyzed impact of preoperative HbA1c on clinical outcomes in patients undergoing non-cardiac surgery; compared with control group, patients with HbA1c of 8% to 10% had longer lengths of stay, but no differences observed for all other outcomes (eg, AKI, 30-day mortality, wound healing); according to National Institute of Health and Care Excellence guidelines, data insufficient to support routine testing of HbA1c in healthy adults with diabetes undergoing noncardiac surgery; increased risk for infection and cardiovascular events observed in subset of patients with elevated HbA1c undergoing orthopedic and vascular surgery

Geriatric studies: pilot trial compared accelerated care and standard care in patients undergoing repair of fractured hip (standard care involves repairing hip within 72 hr of time of fracture); in study, accelerated arm underwent repair within 6 hr and standard arm underwent repair within 24 hr; outcomes better in accelerated group; rate of mortality increased by 13% in standard group; rate of MI higher in standard group than in accelerated group (23% vs 13%); frailty scores — most frailty scores complex and labor intensive; study tested validity of 2 simple frailty scores that included age, sex, race, albumin, serum creatinine, hematocrit, body mass index, and either Charleston comorbidity index or ASA classification; simple scores outperformed complex scores; study concluded that frailty can be approximated easily in preoperative setting and with fewer resources

Impaired sensorium: Gajdos et al (2014) found that preoperative impaired sensorium (defined as acute change in mental status within 48 hr of surgery) associated with significant increase in risk for postoperative morbidity and mortality for all outcome measures

Selective Pharmacologic Targeting to Alleviate Bronchospasm

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Bronchoconstrictive disease: prevalence of asthma in United States 7% to 10%; ≤55% of Americans with asthma have poorly controlled symptoms, even if their care meets standards

GABA<sub> receptor</sub>: ligand-gated ion channel best known as inhibitor of neurotransmission; consists of pentamer generally containing 2 α and 2 β subunits and 1 γ subunit; activation of GABA<sub> receptors acutely relaxes airway smooth muscle, which has generated excitement about potential new class of short-acting bronchodilators; however, concern exists that activation of GABA<sub> receptors may lead to unwanted CNS side effects; a subunits — 6 types possible; usually, synaptic receptors inside CNS (which usually contain α<sub>1</sub>, α<sub>2</sub>, or α<sub>3</sub> subunits) mediate large-amplitude phasic inhibitory currents, whereas extrasynaptic receptors outside CNS (which usually contain α<sub>4</sub>, α<sub>5</sub>, or α<sub>6</sub> subunits) mediate low-amplitude tonic inhibitory currents; airway smooth muscle receptors contain only α<sub>1</sub> and α<sub>3</sub> subunits; goal to activate these receptors and relax airway smooth muscle, and avoid activating receptors that may have sedative CNS side effects

Novel α<sub>4</sub> ligands: selective modulators of GABA<sub>4</sub> channels, CM-D and XA-G, have been developed with goal of enhanced selectivity for α<sub>4</sub> subunits; electrophysiology studies in oocytes expressing GABA<sub> receptors subunits demonstrated that applying these novel α<sub>4</sub> ligands resulted in significant increase in current augmentation; ex vivo organ bath experiments — compared effects in tracheal rings from wild-type mice and knockout mice; when novel α<sub>4</sub> subunit ligand added to organ bath, relaxation demonstrated in wild-type mice but not in knockout mice; XA-G more potent than CM-D; analogous experiments using human airway smooth muscle showed significant relaxation using these novel ligands

Augmentation of β<sub>2</sub> agonists: first-line agents for asthma (eg, albuterol) demonstrate dose-response curve for relaxation of smooth muscle; experiments applying low doses of CM-D and XA-G demonstrated ≈1 logarithmic left shift of albuterol dose response curve
Delivery by inhalation: in bronchoconstriction mouse model, XA-G administered by inhalation resulted in decreased airway resistance

**Conclusion:** novel selective α4 subunit ligands shown to cause acute relaxation of airway smooth muscle in ex vivo and in vivo models; ligands potentiate relaxation induced by albuterol; this finding may be clinically important given increasing resistance to β agonists, especially in patients with severe asthma on long-acting β agonists; activation of receptor hypothesized to result in relative hyperpolarization of contracted airway smooth muscle, which would limit influx of calcium through voltage-sensitive pathways; selectivity anticipated to limit CNS side effects, although α4β7 receptors exist in CNS; >5% of GABA_A receptors in CNS contain α4; some α4β7 receptors could be synaptic and have clinical consequences; α4β7 receptors exist in thalamus and dentate gyrus; selective ligands inactive against α4β7; however, ligands also active against α4 receptors, which are present in cerebellum, but clinical effects unclear; current research focusing on developing derivatives degraded in periphery and incapable of crossing blood-brain barrier

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PERIOPERATIVE MEDICINE/
SELECTIVE PHARMACOLOGIC TARGETING TO ALLEVIATE BRONCHOSPASM

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1. A systematic review showed that administration of β-blockers in the perioperative setting was associated with a reduction in the incidence of:
   (A) Nonfatal myocardial infarction (MI)  (C) Stroke
   (B) Hypotension  (D) Death

2. A recent study looked at the use of clonidine and aspirin in the perioperative setting. Which of the following conclusions of this study is correct?
   (A) Clonidine had no effect on incidence of nonfatal MI
   (B) Clonidine was associated with increased risk for nonfatal cardiac arrest **
   (C) Aspirin had no effect on incidence of nonfatal MI
   (D) Aspirin had no effect on incidence of major bleeding

3. In a meta-analysis of patients undergoing vascular surgery, statins were associated with a reduction in risk for all the following, EXCEPT:
   (A) MI  (C) Kidney injury
   (B) Stroke  (D) All-cause mortality

4. Which of the following is the strongest predictor of surgical outcomes at 30 days and 6 mo?
   (A) Revised cardiac risk index score ≥3
   (B) Preoperative B-type natriuretic peptide (BNP)
   (C) Elevation of postoperative BNP **

5. A systematic review showed that preoperative respiratory training was associated with which of the following?
   (A) Reduction in time to extubation **
   (B) Reduced incidence of nonpulmonary complications
   (C) Decreased length of stay
   (D) Reduced incidence of thromboembolic events

6. A study of patients who underwent gastrectomy showed that smoking cessation for a minimum of _______ conferred benefit.
   (A) 1 wk  (B) 2 wk  (C) 4 wk  (D) 8 wk

7. Two meta-analyses looked at patients on oral anticoagulant therapy undergoing implantation of cardiac devices. The studies concluded that _______ may be preferred in patients undergoing implantation of cardiac devices.
   (A) Stopping oral anticoagulant therapy  (C) Bridging with heparin
   (B) Continuing with oral anticoagulant therapy **  (D) Bridging with low-molecular-weight heparin

8. A study showed that a preoperative HbA1c of 8% to 10% was associated with an increase in:
   (A) Incidence of acute kidney injury  (C) Length of stay
   (B) Time to wound healing  (D) Rate of 30-day mortality

9. Which of the following GABA A receptor subunits is found in airway smooth muscle?
   (A) α 1  (B) α 3  (C) α 5 **  (D) α 6

10. Selective α 4 ligands of GABA A receptors are active against α 6 receptors, which are located in the:
    (A) Thalamus  (C) Cerebellum
    (B) Dentate gyrus  (D) None of the above

Answers to Audio Digest Anesthesiology Volume 57, Issue 35: 1-D, 2-D, 3-C, 4-B, 5-B, 6-C, 7-D, 8-A, 9-C, 10-A