Anesthetic Management of Cesarean Delivery for a Parturient With Previous Myocardial Infarction and Coronary Artery Stents
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Stem Case and Key Questions Content
A 40-year-old G4P3003 at 32 weeks gestation is admitted to the labor floor for blood pressure control. She has a history of chronic hypertension and has now been diagnosed with superimposed preeclampsia. She had a non-ST elevation myocardial infarction at 29 weeks gestation, and she says she had stents placed at an outside hospital, but does not know what kind. She has been on aspirin since stent placement. She was taking clopidogrel but stopped 3 days ago when her medication ran out. Her OB history is significant for one previous cesarean delivery for arrest of labor. Three years ago she was diagnosed with insulin-dependent diabetes. She has been smoking throughout her pregnancy.

1. What else would you like to know on history?

You call the hospital where her stents were placed and the medical records department faxes her catheterization report to you. She has two bare metal stents in the right coronary artery. Her EKG is normal sinus rhythm with Q waves in II, III, and aVF. Echo shows EF 50%, mild LVH, and mild inferior hypokinesis of left ventricle. Hemoglobin 10, hematocrit 30, platelets 332.

2. How long does she need to be on antiplatelet therapy and which medications should she be taking? Are the guidelines different for pregnant women?

3. The obstetrician would like to control her blood pressures and prolong her pregnancy until she is closer to term. The delivery plan is repeat cesarean. However, if her blood pressures cannot be controlled, she may be delivered in the next few days. How should her antiplatelet medication be managed until she delivers?
4. How are high risk pregnant patients managed at your institution? Are multidisciplinary meetings held to coordinate their care? What are the challenges in managing the care and coordinating a delivery plan for these patients?

Despite repeated doses of labetalol, her elevated blood pressures persist and she is called for cesarean delivery the next day. On physical exam, her blood pressure is 168/100 mmHg, heart rate 90 beats per minute. She is 153 kg and her BMI is 60 kg/m². She has a Mallampati 3 airway with good mouth opening, full dentition, full neck range of motion, a thyromental distance of 6 cm, and is able to prognath. Cardiopulmonary exam is unremarkable.

5. What type of anesthesia will you administer for cesarean delivery? Would your plan change if she was delivered one week later?

6. Would you use thromboelastography (TEG) to assess platelet function in this patient?
7. If you choose a neuraxial technique, which technique would you choose and why? What dose of neuraxial or epidural medication would you use? What test dose would you use for this patient?

8. If a general anesthetic is chosen, how would you manage induction?

9. Do you want blood products available? When would you transfuse platelets or packed red blood cells?

You elect for general anesthesia and are able to intubate the patient easily. The baby is delivered 12 minutes after incision. Five minutes after delivery, the obstetrician informs you that there is poor uterine tone and requests additional uterotonics. EBL is 1400 ml.

10. What uterotonics will you give for uterine atony? Do the side effects of oxytocin preclude administering it as a first line agent for uterine atony?

11. The tone improves but then you see ST segment depressions on her EKG. What do you do now?

12. Would you consider use of TTE intraoperatively to evaluate this patient?

13. The depressions resolve. Do you extubate the patient? Where should she go postoperatively?

14. Where are high risk pregnant patients cared for postpartum at your institution? Who manages their care?
I. Acute Myocardial Infarction During Pregnancy

Epidemiology
Acute myocardial infarction (MI) during pregnancy occurs in 1 in 10,000 to 1 in 30,000 deliveries (1,2). Pregnancy increases the risk of MI by 3-4 fold (1). Seventy-two percent of patients are older than 30 years of age and 38% are older than 35 years of age (3). The mortality rate from acute MI is higher (18%) within 24 hours before or after delivery compared to the antepartum (9%) and postpartum periods (9%) (3). In-hospital mortality of women who experience an MI during pregnancy is 7.3% (2).

Risk Factors
The risk factors for coronary artery disease and myocardial infarction during pregnancy include chronic hypertension, diabetes, obesity, maternal age greater than 30 years, hypercholesterolemia, family history of early myocardial infarction, and smoking (2-6). In addition, a previous transient ischemic attack or stroke, arrhythmia, NYHA class > II functional status, left heart obstruction, and EF < 40% can be associated with cardiac arrest, as well as pulmonary edema and arrhythmias (7). Acute coronary spasm and dissection can also occur during pregnancy. Angiography and autopsy have shown that 43% of pregnant women who had an MI during pregnancy had atherosclerosis, 21% had coronary thrombus, 16% had dissection, and 29% had normal coronaries (8).

Cardiovascular Changes During Pregnancy and Risk of Myocardial Infarction
The hemodynamic changes during pregnancy may contribute to the increased risk of MI during pregnancy (1,9). Both heart rate and stroke volume increase, thus increasing cardiac output, ventricular wall tension, and oxygen demand (9). Cardiac output continues to increase during labor and immediately postpartum with autotransfusion. In addition, the physiologic anemia of pregnancy decreases oxygen delivery, however this may be offset by increased blood flow. Hypercoagulability of pregnancy may increase the risk of coronary thrombus in the setting of coronary artery disease (9).

Revascularization During Pregnancy
There are no specific guidelines for interventions for acute MI during pregnancy. However, literature suggests that thrombolytics are associated with both fetal and maternal hemorrhage, increased maternal mortality (1.2%) and pregnancy loss (5.8%) (10,11). Currently, angioplasty and stent placement, followed by antiplatelet medications are preferred and have been reported as successful, without maternal or fetal complications (4-6,12-17).

Antiplatelet Therapy During Pregnancy
The 2014 American College of Cardiology/American Heart Association Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery provides recommendations for perioperative management of antiplatelet therapy for patients.
with coronary stents who are on dual antiplatelet therapy (18). However, at this time, there are no specific considerations for pregnant women undergoing noncardiac surgery who have coronary stents and are on dual antiplatelet therapy. The guidelines recommend that elective surgery be delayed for at least 1 month of dual antiplatelet therapy for bare metal stents and 12 months of dual antiplatelet therapy for drug-eluting stents (18). Second generation drug-eluting stents have been developed to be thromboresistant, biocompatible, and bioabsorbable (19). Thus, dual antiplatelet therapy may be required for only 6 months (18,19).

If surgery must occur prior to these time periods, the risks and benefits of continuing dual antiplatelet therapy versus continuing aspirin alone versus discontinuing dual antiplatelet therapy must be individualized to each patient (18). Discontinuation of dual antiplatelet therapy is associated with an increased risk of stent thrombosis (18). For bare metal stents, thrombosis occurs due to restenosis with neointimal hyperplasia (20). Drug-eluting stents inhibit neointimal hyperplasia, but then re-endothelialization occurs more slowly and thrombosis can occur due to presence of the partially exposed stent (20).

Currently, recommended dual antiplatelet therapy is the use of aspirin combined with a P2Y12 receptor antagonist (clopidogrel (thienopyridine) or ticagrelor (cyclopentyltriazolopyrimidine)) (21). The fetal effects of P2Y12 inhibitors are unknown, however adverse fetal effects have not been reported. The FDA classifies clopidogrel as class B (22) and ticagrelor as class C (23). Low dose (60-150 mg/day) aspirin during the second and third trimesters of pregnancy appears safe (24). The safety of administering aspirin during the first trimester or in higher doses has not been well established.

II. Anesthetic Management of Delivery

Multidisciplinary Management
The literature emphasizes that multidisciplinary care for parturients with coronary artery disease and stents is important to successful care (9,13,17). The services of obstetrics, cardiology, neonatology, and anesthesiology are needed to plan timing and method of delivery (induction, spontaneous labor, or scheduled cesarean delivery), anesthetic technique (neuraxial or general anesthesia), and coordination of antiplatelet therapy with surgery and use of neuraxial techniques for analgesia and anesthesia. Postoperative care in an intensive care unit may be needed. Lack of interprofessional communication has been reported as a risk factor for maternal mortality (25).

Preoperative Anesthesia Evaluation
The preoperative anesthesia evaluation for a parturient with known history of or risk factors for myocardial infarction includes cardiac history (MI, transient ischemic attack, stroke, arrhythmias), current New York Heart Association functional classification, physical exam, EKG (arrhythmias, evidence of prior infarct), and echo for evaluation of ejection fraction and left heart function.
obstruction (mitral valve area < 2 cm², aortic valve area < 1.5 cm², or peak left ventricular outflow gradient > 30 mmHg) (7,9,26). Determining whether she has bare metal or drug-eluting stents and when they were placed guides the management of dual antiplatelet therapy.

Vaginal Delivery
Epidural analgesia for labor pain is regarded as the most effective and least depressant method of pain relief (27). For the parturient with coronary artery disease, effective analgesia can avoid the tachycardia and increased oxygen demand associated with pain during contractions (9,17,28). An assisted second stage of delivery may be done to shorten maternal expulsive efforts (17). Antiplatelet therapy, however, must be considered prior to performing a neuraxial technique.

Neuraxial Techniques for the Pregnant Patient Receiving Antiplatelet Therapy
According to the American Society of Regional Anesthesia and Pain Medicine (ASRA) guidelines, neuraxial techniques may be done when patients are taking aspirin 81 mg PO daily (29). Clopidogrel is to be held for 7 days prior to neuraxial techniques (29). Laboratory tests available to evaluate platelets include platelet count (quantitative assessment only) and bleeding time (now considered to be inconsistent and insensitive) (30). Thromboelastography (TEG) measures all phases of coagulation, including initial fibrin formation (reaction time in minutes, r), subsequent clot formation via fibrin cross-linking (k time in minutes), and clot strength (maximum amplitude in millimeters, MA), which reflects both platelet quantity and function, as well as fibrinogen levels (31). However, normal physiologic changes of pregnancy include hypercoaguability, thus normal TEG values for pregnant women will be different than those currently established. TEG values for healthy pregnant women have been reported (32), however standard reference ranges have not been established (33). In addition, there is limited information regarding TEG values for pregnant patients on antiplatelet therapy (31) and what those values should be to reflect adequate antiplatelet therapy during pregnancy. A modified thromboelastography assay has been used to evaluate platelet function specifically for patients receiving aspirin or clopidogrel (30). Although this assay may reflect platelet inhibition by these medications (30), there are no published reports about the assay being used for pregnant women.

Anesthetic Technique for Cesarean Delivery
Hemodynamic stability to maintain oxygenation and coronary perfusion is essential regardless of the anesthesia technique performed for cesarean delivery. Neuraxial techniques for cesarean delivery have been performed with favorable maternal and fetal outcomes (4,9,12,17). In order to avoid a sudden sympathectomy after administration of intrathecal medications, a modified combined spinal epidural technique can be used. An initial low dose of spinal medication is administered, then epidural medications are given incrementally until an adequate anesthetic level is obtained. This technique decreases the likelihood of hypotension, tachycardia, and need for vasopressors (34).
General anesthesia has been reported in the literature for parturients with ischemic heart disease requiring emergency deliveries or for parturients on thienopyridine antiplatelet therapy (11,16,28,35). Rapid sequence induction is required due to risk of aspiration, however the stimulation is associated with catecholamine release, hypertension, and tachycardia. Use of a remifentanil infusion during induction has been reported to decrease the stress response from intubation, maintaining mean arterial pressures and heart rate near baseline values (36). This opioid is also rapidly metabolized by the fetus (37). Emergence and extubation can also be associated with hemodynamic changes that may precipitate myocardial ischemia in the parturient with coronary artery disease.

Blood Products
Although there are no specific guidelines regarding the optimal hematocrit for a parturient with a history of ischemic heart disease and MI, a lower threshold for intraoperative red blood cell transfusion may be considered, especially if the patient is on dual antiplatelet therapy and is at risk for increased blood loss. A lower threshold for intraoperative platelet transfusion may be considered for patients on antiplatelet therapy as well, particularly thienopyridines (5). Platelet transfusions have been given preemptively, prior to cesarean delivery, for a parturient requiring emergency cesarean delivery while taking clopidogrel (16).

Uterotonics
Uterotonics are essential to maintain uterine tone and decrease blood loss postpartum. Oxytocin is considered a first line agent for prevention of uterine atony. Although it has been given as an intravenous bolus (38), administering it as an infusion diluted in crystalloid decreases the incidence of peripheral vasodilation and subsequent hypotension and reflex tachycardia (9,39,40). Oxytocin is also known to cause coronary vasoconstriction and ST segment changes (41), which would further compromise coronary blood flow to an already ischemic myocardium.

Second line agents include methylergonovine maleate and carboprost tromethamine. The latter may be preferred, due to the known hypertensive side effect of methylergonovine maleate (40). Misoprostol can be given sublingual or per rectum for prevention and treatment of uterine atony and postpartum hemorrhage (42,43). Side effects may include shivering, fever, nausea, vomiting, and diarrhea, however there are no known cardiovascular side effects.

Intraoperative Use of Transthoracic Echocardiography
Transthoracic echocardiography (TTE) can be used by anesthesiologists as a noninvasive point-of-care modality to narrow differential diagnoses and guide therapy (44,45) and may have utility in the obstetric population. Rapid obstetric screening echocardiography (ROSE) is a focused TTE exam that emphasizes basic pattern recognition for a general assessment of volume status, contractility, right heart function, relative size, and response to vasopressors (46). This information used in conjunction
with a clinical assessment can be used to guide therapy. Low-frequency phased array probes are compatible with ultrasound machines used for regional anesthesia and central line placement. TTE training workshops for anesthesiologists have been developed for learning image acquisition and interpretation (47), and training with simulation may improve performance in correct identification of anatomy, quality of images, and time for image acquisition (48).

**Postpartum**
Immediately postpartum, autotransfusion from relief of vena cava compression, decreased lower extremity pressure, and decreased vascular capacitance dramatically increases preload, increasing cardiac output to more than 100% above prelabor values (49). Cardiac output remains elevated above prelabor values for 24 hours postpartum, thus the parturient is still at risk for cardiac events during this time period, such as myocardial ischemia and infarction, as well as in-stent thrombosis (3,18). Admission to an intensive care unit or other monitored setting allows for early diagnosis of perioperative cardiac events and prompt intervention if required.

**Footnotes**
[a] In December 2014, the FDA announced that the pregnancy letter categories A, B, C, D and X, would be replaced by the Pregnancy and Lactation Labeling Rule. The labeling changes went into effect on June 30, 2015. Any new drugs submitted after that date use the new format, while previously approved drugs are being phased in gradually.


[b] The FDA-assigned pregnancy categories as used in the Drug Formulary are as follows:
**Category A:** Adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of a risk in later trimesters).

**Category B:** Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in humans, and the benefits from the use of the drug in pregnant women may be acceptable despite its potential risks. Or animal studies have not been conducted and there are no adequate and well-controlled studies in humans.

**Category C:** Animal reproduction studies have shown an adverse effect on the fetus, there are no adequate and well-controlled studies in humans, and the benefits from the use of the drug in pregnant women may be acceptable despite its potential risks. Or animal studies have not been conducted and there are no adequate and well-controlled studies in humans.

**Category D:** There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.
Category X: Studies in animals or humans have demonstrated fetal abnormalities or there is positive evidence of fetal risk based on adverse reaction reports from investigational or marketing experience, or both, and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit. http://www.fda.gov/drugs/drugsafety/ucm245470.htm. Last accessed 2/15/16.

References