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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/m^2. 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 you chose a general anesthetic, how would you induce this patient?

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

13. Where are high risk pregnant patients cared for postpartum at your institution? Who manages their care?

Model Discussion Content
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. Hypercoaguability 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 2007 American College of Cardiology/American Heart Association Task Force on Practice Guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery provides recommendations for management of antiplatelet therapy while patients with cardiac stents are on dual antiplatelet therapy.[18] However, at this time, there are no specific considerations for pregnant patients with coronary stents undergoing noncardiac surgery. The guidelines recommend that elective surgery with a risk of perioperative or postoperative bleeding be delayed until at least 12 months of dual antiplatelet therapy (aspirin and a thienopyridine) has been given after drug-eluting stent placement and 1 month after bare metal stent placement.[18] If surgery must occur prior to these time periods, it is recommended that aspirin be continued if possible.[18] Discontinuation of dual antiplatelet therapy is associated with an increased risk of coronary thrombosis, myocardial infarction, and death.[18] For bare metal stents, thrombosis occurs due to restenosis with neointimal hyperplasia.[19] 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.[19]
The fetal effects of thienopyridines are not known, however there have been no reports of adverse fetal effects. The FDA classifies clopidogrel and ticlopidine as class B.[a,20,21] Low dose (60-150 mg/day) aspirin during the second and third trimesters of pregnancy appears safe.[22] 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. The Confidential Enquiry into Maternal and Child Health (CEMACH) report notes that lack of inter professional communication is a risk factor for maternal mortality.[23]

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 obstruction (mitral valve area < 2 cm^2, aortic valve area < 1.5 cm^2, or peak left ventricular outflow gradient > 30 mmHg).[7,9,24] 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.[25] For the parturient with coronary artery disease, effective analgesia can avoid the tachycardia and increased oxygen demand associated with pain during contractions.[9,17,26] 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.[27] Clopidogrel is to be held for 7 days and ticlopidine for 14 days prior to neuraxial techniques.[27] Laboratory tests available to evaluate platelets include platelet count (quantitative assessment only) and bleeding time (now considered to be inconsistent and insensitive).[28] 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.[29] 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,[30] however standard reference ranges have not been established.[31] In addition, there is limited information regarding TEG values for pregnant patients on antiplatelet therapy[29] 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.[28] Although this assay may reflect platelet inhibition by these medications,[28] 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] Combined spinal epidural anesthesia, in which an initial low dose of spinal medication is given, then epidural medications are administered until anesthetic level is adequate, or epidural anesthesia only, both allow for slow administration of medications, thus decreasing the likelihood of

hypotension, tachycardia, and the need for vasopressors.[32]
General anesthesia has been reported in the literature for parturients with ischemic heart disease requiring emergency deliveries or for parturients on thienopyridine antiplatelet therapy.[11,16,26,33] 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.[34] This opiod is also rapidly metabolized by the fetus.[35] 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,[36] administering it as an infusion diluted in crystalloid decreases the incidence of peripheral vasodilation and subsequent hypotension and reflex tachycardia.[9,37,38] Oxytocin is also known to cause coronary vasoconstriction and ST segment changes,[39] 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.[38] Misoprostol can be given sublingual or per rectum for prevention and treatment of uterine atony and postpartum hemorrhage.[40,41] Side effects may include shivering, fever, nausea, vomiting, and diarrhea, however there are no known cardiovascular side effects.

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% of prelabor values.[42] Cardiac output remains elevated above prelabor values for 24 hours postpartum, thus the parturient is still at risk for cardiac events, such as myocardial ischemia and infarction, during this time period, 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.
Footnote [a] The FDA-assigned pregnancy categories as used in the Drug Formulary are as follows:**Category A**: Adequate and well-controlled studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of 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 pregnant women. **Category C**: Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and

well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks. **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 potential benefits may warrant use of the drug in pregnant women despite potential risks. **Category X**: Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.
http://depts.washington.edu/druginfo/Formulary/Pregnancy.pdf. Last accessed 2/9/14.

References

1. James AH, Jamison MG, Biswas MS, Brancazio LR, Swamy GK, Myers ER. Acute myocardial infarction in pregnancy: A United States population-based study. Circulation 2006;113:1564-71.
2. Ladner HE, Danielsen B, Gilbert WM. Acute myocardial infarction in pregnancy and the puerperium: A population-based study. Obstet Gynecol 2005;105:480-4.
3. Roth A, Elkayam U. Acute myocardial infarction associated with pregnancy. J Am Coll Cardiol 2008;52:171-80.
4. von Steinburg SP, Klein E, Langwieser N, Kastrati A, Schneider KT, Zohlnhöfer D. Coronary stenting after myocardial infarction during twin pregnancy – a case report. Hypertens Pregnancy 2011;30:485-9.
5. Sebastian C, Scherlag M, Kugelmass A, Schechter E. Primary stent implantation for acute myocardial infarction during pregnancy: use of abciximab, ticlopidine, and aspirin. Cathet Cardiovasc Diagn 1998;45:275-9.
6. Boztosun B, Olcay A, Avci A, Kirma C. Treatment of acute myocardial infarction in pregnancy with coronary artery balloon angioplasty and stenting: use of tirofiban and clopidogrel. Int J Cardiol 2008;127:413-6.
7. Siu SC, Sermer M, Colman JM, et al. Prospective multicenter study of pregnancy outcomes in women with heart disease. Circulation 2001;104:515-21.
8. Roth A, Elkayam U. Acute myocardial infarction associated with pregnancy. An Intern Med 1996;38:369-72.
9. Smith RL, Young SJ, Greer IA. The parturient with coronary heart disease. Int J Obstet Anesth 2008;17:46-52.
10. Turrentine M. Braems G, Ramirez M. Use of thrombolytics for the treatment of thromboembolic disease during pregnancy. Obstet Gynecol Surv 1995;50:534-41.
11. Pierre-Louis B, Singh P, Frishman WH. Acute inferior wall myocardial infarction and percutaneous coronary intervention of the right coronary during active labor: a clinical report and review of the literature. Cardiol Rev 2008;16:260-8.
12. Sanchez-Ramos L, Chami YG, Bass TA, DelVAlle GO, Adair CD. Myocardial infarction during pregnancy: management with transluminal coronary angioplasty and metallic intracoronary stents. Am J Obstet Gynecol 1994;171:1392-3.
13. Kamran M, Suresh V, Ahluwalia A. Percutaneous transluminal coronary angioplasty (PTCA) combined with stenting for acute myocardial infarction in pregnancy. J Obstet Gynaecol 2004;24:701-2.
14. Balmain S, McCullough CT, Love C, Hughes R, Heidemann B, Bloomfield P. Acute myocardial infarction during pregnancy successfully treated with primary percutaneous coronary intervention. Int J Cardiol 2007;116:e85-7.

15. Al-Aqeedi RF, Al-Nabti AD. Drug-eluting stent implantation for acute myocardial infarction during pregnancy with use of glycoprotein IIb/IIIa inhibitor, aspirin, and clopidogrel. J Invasive Cardiol 2008;20:E146-9.
16. Myers GR, Hoffman MK, Marshall ES. Clopidogrel use throughout pregnancy in a patient with a drug-eluting coronary stent. Obstet Gynecol 2011;118:432-3.
17. Duarte FP, O'Neill P, Centeno MJ, Ribeiro I, Moreira J. Myocardial infarction in the 31st week of pregnancy – case report. Rev Bras Anestesiol 2011;61:225-7.
18. Fleisher LA, Beckman JA, Brown KA. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Anesth Analg 2008;106:685-712.
19. Howard-Alpe GM, de Bono J, Hudsmith L, Orr WP, Foex P, Sear JW. Coronary artery stents and non-cardiac surgery. Br J Anaesth 2007;98:560-74.
20. Plavix (clopidogrel bisulfate tablets). October 2009. http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020839s044lbl.pdf. Last accessed 2/9/14.
21. Ticlopidine hydrochloride tablets. September 1999. http://www.accessdata.fda.gov/drugsatfda_docs/anda/99/75161_Ticlopidine%20Hydrochloride_Prntlbl.pdf. Last accessed 2/9/14.
22. CLASP: a randomised trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9364 pregnant women. CLASP (Collaborative Low-dose Aspirin Study in Pregnancy) Collaborative Group. Lancet 1994;343:619-29.
23. Why Mothers Die 2000-2002. The Confidential Enquiry into Maternal and Child Health (CEMACH). http://www.hqip.org.uk/assets/NCAPOP-Library/CMACE-Reports/33.-2004-Why-Mothers-Die-2000-2002-The-Sixth-Report-of-the-Confidential-Enquiries-into-Maternal-Deaths-in-the-UK.pdf. Last accessed 2/9/14.
24. Oakley C, Child A, Jung B, et al. Expert consensus document on management of cardiovascular diseases during pregnancy. Eur Heart J 2003;24:761-81.
25. ACOG Committee Opinion #295: pain relief during labor. Obstet Gynecol 2004;104:213.
26. Gil S, Atiénzar C, Filella Y, Fernández M, Borrás R, Miranda A. Anaesthetic management of acute myocardial infarction during labour. Int J Obstet Anesth 2006;15:71-4.
27. Horlocker TT, Wedel DJ, Rowlingson JC, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition). Reg Anesth Pain Med 2010;35:64-101.
28. Collyer TC, Gray DJ, Sandhu R, Berridge J, Lyons G. Assessment of platelet inhibition secondary to clopidogrel and aspirin therapy in preoperative acute surgical patients measured by Thrombelastography Platelet Mapping. Br J Anaesth 2009;102:492-8.
29. Orlikowski CE, Payne AJ, Moodley J, Rocke DA. Thrombelastography after aspirin ingestion in pregnant and non-pregnant subjects. Br J Anaesth 1992;69:159-61.
30. Karlsson O, Sporrong T, Hillarp A, Jeppsson A, Hellgren M. Prospective longitudinal study of thromboelastography and standard hemostatic laboratory tests in healthy women during normal pregnancy. Anesth Analg 2012;115:890-8.
31. de Lange NM, Lancé MD, de Groot R, Beckers EA, Henskens YM, Scheepers HC. Obstetric hemorrhage and coagulation: an update. Thromboelastography, thromboelastometry, and conventional coagulation tests in the diagnosis and prediction of postpartum hemorrhage. Obstet Gynecol Surv 2012;67:426-35.
32. Teoh WH, Thomas E, Tan HM. Ultra-low dose combined spinal-epidural anesthesia with intrathecal bupivacaine 3.75 mg for cesarean delivery: a randomized controlled trial. Int J Obstet

Anesth 2006;15:273-8.
33. Cuthill JA, Young S, Greer IA, Oldroyd K. Anaesthetic considerations in a parturient with critical coronary artery disease and a drug-eluting stent presenting for caesarean section. Int J Obstet Anesth 2005;14:167-71.
34. Steinlechner B, Dworschak M, Birkenberg B, Lang T, Schiferer A, Moritz A, Mora B, Rajek A. Low-dose remifentanil to suppress hemodynamic responses to noxious stimuli in cardiac surgery: a dose-finding study. Br J Anaesth 2007;98:598-603.
35. Kan RE, Hughes SC, Rosen MA, Kessin C, Preston PG, Lobo EP. Intravenous remifentanil: placental transfer, maternal and neonatal side effects. Anesthesiology 1998;88:1467-74.
36. Butwick AJ, Coleman L, Cohen SE, Riley ET, Carvalho B. Minimum effective bolus dose of oxytocin during elective Caesarean delivery. Br J Anaesth 2010;104:338–43.
37. Bhattacharya S, Ghosh S, Ray D, Mallik S, Laha A. Oxytocin administration during cesarean delivery: Randomized controlled trial to compare intravenous bolus with intravenous infusion regimen. J Anaesthesiol Clin Pharmacol 2013;29:32-5.
38. Dyer RA, van Dyk D, Dresner A. The use of uterotonic drugs during caesarean section. Int J Obstet Anesth 2010;19:313-9.
39. Svanström MC, Biber B, Hanes M, Johansson G, Näslund U, Bålfors EM. Signs of myocardial ischaemia after injection of oxytocin: a randomized double-blind comparison of oxytocin and methylergometrine during Caesarean section. Br J Anaesth 2008;100:683-9.
40. Sood AK, Singh S. Sublingual misoprostol to reduce blood loss at cesarean delivery. J Obstet Gynaecol India 2012;62:162-7.
41. Firouzbakht M, Kiapour A, Omidvar S. Prevention of post-partum hemorrhage by rectal Misoprostol: A randomized clinical trial. J Nat Sci Biol Med 2013;4:134-7.
42. Gaiser R. Physiologic Changes of Pregnancy. In: Chestnut DH, Polley LS, Tsen LC, Wong CA, eds. Chestnut's Obstetric Anesthesia: Principles and Practice. 4th ed. Philadelphia, PA: Mosby Elsevier, 2009.