Cardiovascular Disasters in Pregnancy

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KEYWORDS

• Pregnancy • Pulmonary embolus • Aortic dissection • Cardiomyopathy
• Acute myocardial infarction • Arrhythmia • Cardiac arrest
• Perimortem cesarean section

KEY POINTS

- During pregnancy, the D-dimer level is likely to be elevated; however, a negative D-dimer is still reliably negative in a patient with low pretest probability.
- Life-threatening pulmonary embolism can be treated with tissue plasminogen activator, despite the relative contraindication of pregnancy.
- Aortic dissection is more common in pregnancy and in the immediate postpartum period than their nonpregnant counterparts.
- Cardiac disease in pregnancy is becoming more common, because of the increasing incidence of advanced maternal age, obesity, hypertension, and diabetes mellitus and improved treatments for congenital heart disease.
- Percutaneous coronary intervention is first-line therapy for pregnant patients with acute myocardial infarction.
- Displacement of the uterus is imperative to a successful resuscitation.
- Drug and electricity doses are unchanged in resuscitation of the pregnant patient.
- Perimortem cesarean section must be completed within 5 minutes of loss of circulation.

INTRODUCTION

The normal changes that occur during pregnancy are demanding on the cardiovascular system. Total cardiac output increases about 50% from a combination of increased blood volume and pulse along with a decrease in peripheral resistance. These changes can place significant stress on a normal heart. Physiologic changes are even more dangerous to individuals with underlying cardiac disorders. Cardiac arrest can occur in previously asymptomatic women who are experiencing this type of cardiac stress. In its 2010 guidelines,[1] the American Heart Association summarized

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the scope of cardiac arrest in pregnancy, citing figures from the Confidential Enquiries into Maternal and Child Health data set[2]: "The overall maternal mortality rate was calculated at 13.95 deaths per 100 000 maternities. There were 8 cardiac arrests with a frequency calculated at 0.05 per 1000 maternities, or 1:20,000." The report notes that the frequency of cardiac arrest during pregnancy is rising. Despite being younger and healthier than many patients with cardiac arrest, pregnant women have more dismal outcomes than their nonpregnant counterparts. One case series described a survival rate of only 6.9%.[3] Many cardiopulmonary pathologies can lead to the endpoint of cardiac arrest during pregnancy. The most significant of these are discussed in this article.

VENOUS THROMBOEMBOLISM

Venous thromboembolism (VTE) is significantly more common in pregnancy, than in nonpregnant women. The number of deaths from thrombosis and thromboembolism is estimated at 1.94 per 100,000 pregnancies.[1] Pregnancy in general is a hypercoagulable state, and certain conditions in pregnant women (eg, lupus anticoagulant and antiphospholipid syndrome) can increase the risk of VTE even further. Diagnosis of deep vein thrombosis (DVT) and pulmonary embolism (PE) is more challenging in pregnancy, because standard tests may be unreliable or dangerous.

D-dimer, a blood test used to aid in the diagnosis of DVT and PE, represents a breakdown product of cross-linked fibrin. It is highly sensitive but lacks specificity in healthy, nonpregnant individuals. During pregnancy, it becomes even less specific. A negative D-dimer is still reliably negative in a patient with low pretest probability, but is a result that is less likely to be obtained. This is because the D-dimer level is usually elevated in normal pregnancies. It typically rises throughout pregnancy, peaking around the time of delivery. Although reported rates of negative D-dimer throughout the stages of pregnancy vary widely, it is clear that the usefulness of the D-dimer to rule out VTE decreases as pregnancy progresses.[4–6] An alternative strategy is to use "trimester-adjusted" D-dimer value to rule out VTE. Kline and associates[4] proposed threshold values of 750 ng/dL in the first trimester, 1000 ng/dL in the second, and 1250 ng/dL in the third. The trimester-adjusted D-dimer measurement is a promising theory that has not yet been tested.

Imaging in pregnancy is obviously problematic because of the goal of avoiding exposure of the mother and fetus to radiation. Diagnosing DVT is still relatively straightforward because ultrasound confers no radiation. This test is an excellent starting point even if PE is the primary concern. If DVT is present, the treatment decision has been made, and there is no need for computed tomography (CT) or ventilation/perfusion (V/Q) scan. After the patient is hospitalized, an echocardiogram can be obtained to assess for complications of PE. However, a negative ultrasound cannot definitively rule out DVT because pelvic DVT is more common in pregnancy than in the nonpregnant state and is likely to be missed on ultrasound. In addition, a negative ultrasound in no way rules out PE.

The use of CT versus V/Q for diagnosis of PE is a matter of perennial debate. The data are quite clear, although the optimal decision is less so. Helical CT delivers radiation to the woman, which is of added concern given the sensitivity of the breast tissue during pregnancy. However, CT exposes the fetus to significantly less radiation. One study found that in the third trimester (when the radiation dose to the fetus is highest), helical CT delivers 0.13 mGy, V/Q scanning 0.37 mGy, and pulmonary arteriography 0.50 mGy.[7] Perfusion scanning has the advantage of delivering 30 to 40 times less radiation to the breast tissue. This is particularly relevant in young, pregnant women, whose

breasts have a high cell turnover rate and are highly susceptible to the effects of ionizing radiation.[8] One study of 205 pregnant patients found equivalent negative predictive values (99%–100%) for CT and V/Q. Of the patients who underwent CT, 13% had other clinically significant abnormalities.[9] The bottom line is this: V/Q scan exposes the mother to less radiation but exposes the fetus to more. CT may reveal alternate pathology. The dose of radiation for both is within "acceptable" limits. However, given that any amount of radiation increases the lifetime risk of cancer, the decision must be made on a case-by-case basis. For example, in a patient at higher-than-average risk for breast cancer, a V/Q scan may be the better choice. The patient must be involved in the discussion and given information in a clear, factual manner.

Magnetic resonance imaging (MRI) is emerging as another tool for the diagnosis of PE.[10] The obvious advantage is its lack of ionizing radiation. Disadvantages include the length of time that an ill, unstable patient needs to be away from the emergency department (ED); the need for the patient to lie supine (potentially problematic in a pregnant patient, because of compression of the inferior vena cava); and the uncertainty of the effects of MRI on the fetus. No harmful effects to the fetus have been reported in magnetic fields up to 1.5 T.[11,12] At this point, clinical data regarding the sensitivity and specificity of MRI for PE remain limited, so MRI should not be used to definitively exclude this condition.

After PE has been diagnosed, additional testing including electrocardiography, measurement of troponin, and echocardiography is indicated, as with nonpregnant patients. If these tests show massive PE, administration of tissue plasminogen activator can be considered on a case-by-case basis.

After the definitive diagnosis of DVT or submassive PE has been made, there are two treatment options. Heparin has been used traditionally and is a category C drug in pregnancy. However, it has significant drawbacks, including the need for a drip, frequent blood draws, and therefore hospitalization. Its major use is when delivery is imminent and greater control is desired. Lovenox, a low-molecular-weight heparin and a category B drug, has largely replaced heparin for long-term treatment of thrombotic disease. Coumadin is one of the few category X drugs, capable of producing a teratogenic syndrome. This drug must not be prescribed to pregnant women. Although pregnancy is a relative contraindication for the administration of tissue plasminogen activator, in the setting of cardiac arrest, it might be an appropriate intervention. The successful use of fibrinolytics in pregnant women has been reported for massive, life-threatening PE[13–15] and ischemic stroke.[16] Despite the lack of specific data in pregnancy, pregnant women in cardiac arrest with suspected PE should be treated in accordance with Advanced Cardiovascular Life Support (ACLS) guidelines. These state that in patients in cardiac arrest with known or presumed PE, thrombolytics improve survival to discharge and neurologic outcomes, despite the increased potential for bleeding.[17–19]

AORTIC DISSECTION

Aortic dissection is the second most common cause of maternal death.[1] It is more common than venous thromboembolic disease and occurs more commonly during pregnancy or the immediate postpartum period. Half of the dissections in women younger than 40 occur during pregnancy.[20] Arterial dissections are thought to be related to hormonal and hemodynamic effects on the intima and media of the arterial wall.[21,22]

The diagnosis is challenging, for the same reasons discussed in the VTE section. The D-dimer level is often used as a screening tool, but its reliability has not been validated in nonpregnant patients and its use becomes more complex given the higher

baseline levels during pregnancy, as previously discussed. Imaging is required for definitive diagnosis of aortic dissection. As in nonpregnant patients, CT, MRI, and transesophageal electrocardiography (TEE) can be used. Transabdominal ultrasound sometimes shows, but does not reliably exclude, dissection. The gravid abdomen makes this examination even more challenging. TEE is ideal if it is available, because it avoids radiation and can be done in the ED or operating room and has no associated radiation. CT with intravenous contrast is an effective diagnostic tool but delivers a large dose of radiation and the intravenous contrast material. MRI is problematic for any patient with a dissection, because of the length of the study and the location of the imaging suite outside the ED, but it does have the advantage of no radiation. In most hospitals, where TEE is frequently not immediately available, CT becomes the test of choice. Treatment focuses on reducing blood pressure and pulse to decrease shear stress on the aorta. β-Blockers are generally considered safe in pregnancy (**Table 1**). Treatment is the same as for nonpregnant patients, including antihypertensives and vascular or cardiothoracic surgery. An obstetrician should be consulted to monitor fetal well-being.

CARDIAC DISEASE

According to the Confidential Enquiries into Maternal and Child Health report, cardiac disease accounts for 2.27 deaths per 100,000 pregnancies and its incidence has been increasing since 1991.[2] Acquired heart disease complicates 1% to 4% of pregnancies and causes a significant amount of morbidity and mortality. In the developing world (and among immigrants living in Western countries), mitral stenosis from rheumatic fever is the predominant cause. In the United States, congenital heart disease is much more common, likely because of the quality of medical care, which enables these patients to survive past childhood. In addition, the prevalence of obesity, hypertension, diabetes, and hypercholesterolemia in the United States increases the frequency of coronary artery disease. As the number of pregnancies in women at an advanced maternal age continues to rise, this issue is becoming ever more relevant.

Table 1
Select cardiac drugs in pregnancy

Action	Medication	Considerations
Afterload reduction	Hydralazine	Often chosen first in pregnancy
	Nitrates	Commonly used and considered safe, but pose a theoretic risk of cyanide toxicity (nitroprusside)
	ACE inhibitors	CANNOT be used in pregnancy, but first choice in postpartum patients
Preload	Loop diuretics	Most likely necessary
	Nitrates	Commonly used and considered safe, but pose a theoretic risk of cyanide toxicity (nitroprusside)
β-Blockers	Metoprolol	Considered safe; some evidence of IUGR
Vasopressors	Dobutamine	Best studied in pregnancy
Antiarrhythmics	Adenosine	No clear evidence, presumed safe
	Amiodarone	Reports of fetal thyroid and neurologic abnormalities
	Procainamide	No clear evidence, considered safer than amiodarone
	Verapamil	Does not pose large risk

Abbreviations: ACE, angiotensin-converting enzyme; IUGR, intrauterine growth retardation.
Data from Refs.[50–52]

When evaluating patients with cardiac disease in the ED, it is helpful to understand the conditions that are most likely to lead to poor maternal and fetal outcomes. A prospective study of 562 women with 617 pregnancies validated four predictors of cardiac events (**Table 2**).[23] The presence or absence of these risk factors should never be given precedence over the clinical picture, but they should be viewed as a "red flag" for a patient with the potential to rapidly deteriorate. Specific problems that merit discussion include valvular problems, cardiomyopathy, and acute myocardial infarction (AMI).

Valvular diseases that complicate pregnancy have structural and infectious origins. Not surprisingly, the degree of risk to mother and fetus increases with the severity of valvular dysfunction. Most adverse events occur in patients with moderate to severe mitral or aortic stenosis.[24] Infective endocarditis is a rare but potentially lethal disease in the setting of pregnancy. The risk factors are similar to those in nonpregnant patients.[25]

Cardiomyopathy in young women may be caused by a viral infection (including HIV); toxicologic sources (alcohol, cocaine, doxorubicin); pregnancy itself (peripartum cardiomyopathy), or, less commonly, ischemia induced by coronary artery disease. Women with ejection fractions less than 40% to 45% are at the highest risk.[26,27] Although some patients present with a known diagnosis of cardiomyopathy, the astute emergency physician must maintain a high level of suspicion for this diagnosis in the pregnant patient with dyspnea, fatigue, and pedal edema. The challenge is that these signs and symptoms are frequently present in normal, healthy pregnancies. Further compounding the diagnostic challenge, multiple other conditions can lead to similar symptoms, including pulmonary causes (asthma, PE); infection (pneumonia); cardiac (AMI); anemia; and preeclampsia. The differential diagnosis can be narrowed in large part by the history and physical examination. Ancillary tests, including electrocardiography, imaging, and laboratory studies, also are frequently required.

Brain natriuretic peptide (BNP) may be helpful in ruling in or out a diagnosis of decompensated heart failure. BNP is secreted by the heart when it is overworked, as occurs in cardiac failure. A value less than 100 pg/mL is considered normal, effectively excluding decompensated heart failure. Values between 100 pg/mL and 300 pg/mL indicate potential cardiac disease, whereas values greater than 300 pg/mL indicate the presence of congestive heart failure.[28] Although the BNP level doubles during a normal pregnancy, in part because of increased blood volume, the value should still be less than 100 pg/mL.[29] BNP may have predictive value beyond aiding with the differentiation of the causes of dyspnea. Tanous and colleagues[30] used the BNP value to predict adverse events from a cardiac cause in pregnant women. They determined

Table 2
Predictors of cardiac events in patients with acquired heart disease

Risk Factor	Point Value
New York Heart Association Class II–IV heart failure or cyanosis	1
Previous cardiac event (CVA, TIA, ACS) or arrhythmia	1
Left heart obstruction (MV area <2 cm^2, AV area <1.5 cm^2, peak LV outflow gradient >30 mm Hg)	1
Ejection fraction <40%	1

Abbreviations: ACS, acute coronary syndrome; AV, aortic valve; CVA, cerebrovascular accident; LV, left ventricular; MV, mitral valve; TIA, transient ischemic attack.

Risk of cardiac event: 0 points, 4%; 1 point, 26%; >1 point, 62%.

Data from Siu SC, Sermer M, Colman JM, et al. Prospective multicenter study of pregnancy outcomes in women with heart disease. Circulation 2001;104:515–21.

that a BNP value greater than 100 pg/mL is a sensitive (but not specific) predictor of cardiac events. They also noted patients at greatest risk were those with left ventricular dysfunction.[30]

Management of the pregnant patient with cardiomyopathy depends on the severity of the disease. In general, the approach is the same as for nonpregnant patients with heart failure. Data supporting any particular treatment regimen are limited. Severe diseases may require intervention to control the airway. Noninvasive ventilation strategies should be considered early and may help to avoid intubation. Medication strategies are aimed at reducing afterload and increasing pump function. Although the safety of various medications during pregnancy must be considered (see **Table 1**), the drugs that should be used are essentially unchanged. The major exception is that angiotensin-converting enzyme (ACE) inhibitors are absolutely contraindicated in pregnancy. Patients with decompensated heart failure require admission to the hospital, and obstetrics and cardiology should be consulted early.

Among women of reproductive age, AMI occurs three to four times more often in those who are pregnant versus those who are not pregnant.[31] Management is essentially unchanged in pregnancy. One major exception is thrombolysis, which is relatively contraindicated in pregnancy. Percutaneous coronary intervention (PCI) is first-line therapy for patients with ST-elevation AMI.[32] If PCI is not available at the treating facility, strong consideration should be given to transfer after discussion with a cardiologist, an obstetrician, and the patient. Aspirin,[33,34] β-blockers,[35,36] and nitrates[37] can all be used. Heparin does not cross the placenta, but careful consideration should be given to its use in patients with potential for severe bleeding (placenta previa or abruption, threatened miscarriage).[38] Clopidogrel is generally considered safe, but it causes a significant bleeding risk during delivery.[38] Statins, ACE inhibitors, and angiotensin II receptor blockers are absolutely contraindicated and should all be postponed until after delivery.[39]

Cardiac disease in pregnancy encompasses a huge spectrum of pathologic conditions. However, their management is very similar to that used in nonpregnant patients. Key differences include avoidance of ACE inhibitors in patients with decompensated heart failure and PCI instead of thrombolysis if it is available. Involve consultants early and intervene aggressively, remembering that the health of the fetus depends on a healthy mother.

CARDIAC DYSRHYTHMIAS

Of all the dangerous cardiac conditions discussed, dysrhythmias are the most commonly encountered during pregnancy.[23,40] They occur in women with structurally normal hearts and in women with cardiac abnormalities. Palpitations are a frequent presenting complaint, and the work-up for many of those patients is benign. However, life-threatening dysrhythmias must be excluded. The precise cause of the high frequency is unclear, but the increased stress put on the heart by hormonal and hemodynamic shifts seems to be contributing factors. In addition, thyroid disease is more common during pregnancy than in the nonpregnant state. The source of cardiac dysrhythmia usually can be diagnosed through the history and electrocardiography alone. In some patients, prolonged monitoring and echocardiography are required.

Diagnosis of dysrhythmia generally warrants consultation with a cardiologist and an obstetrician. In general, dysrhythmias in a pregnant woman are managed the same way as in a nonpregnant patient. The exception is in the choice of medication; many antiarrhythmic drugs are teratogenic.

Supraventricular tachycardia is common in pregnancy. Adenosine can be used safely in usual doses. Atrial fibrillation can be managed with rhythm control, rate control, or cardioversion.[41]

Cardioversion is considered safe in all stages of pregnancy.[42–44] Dysrhythmia in the fetus is rare but reported, so a viable fetus should be monitored.[45] Sedation should be used during cardioversion, but during the third trimester it increases the risk of aspiration, airway edema, and decreased functional reserve capacity, causing rapid hypoxia. Cardioversion in the operating room should be considered. If the duration of atrial fibrillation is uncertain or more than 48 hours, low-molecular-weight heparin is preferred for anticoagulation. If antiarrhythmic drugs are required, there are very few data to recommend one drug over another (see **Table 1**). Virtually all of these drugs cross the placenta. Indications for temporary or permanent pacing in patients with symptomatic bradycardias are the same as in nonpregnant patients, and transcutaneous and transvenous pacing can be used.[46]

CARDIAC ARREST

Cardiac arrest during pregnancy has many possible causes, including all of the disease states discussed previously. Initial management includes obtaining intravenous access above the diaphragm, administering 100% oxygen, and relieving compression of the inferior vena cava. Aortocaval compression can be relieved by several methods. The gravid uterus can be displaced manually by either a one-handed push from the patient's right side or a two-handed pull from the left. A left lateral tilt can be created by placing a wedge under a backboard, with a goal angle of 30 degrees (such that the patient does not slide off the board). Effective cardiac compressions can be delivered with this patient positioning. These techniques for uterine displacement improve maternal hemodynamics.[1]

The importance of effective cardiac compression is highlighted in the recent guidelines that changed the long-standing resuscitation algorithm from the ABCs to the C, A, B.[47] When cardiac compressions need to be administered to a pregnant patient, the gravid uterus can interfere with the procedure and upwardly displace the internal organs. Therefore, the location for delivery of effective compressions needs to change: compressions should be delivered slightly higher on the sternum.[1]

The pregnant patient's airway undergoes significant physiologic changes and exhibits increased mucosal edema, secretions, and friability, which are important to recognize because they can lead to a potentially difficult airway. Progesterone decreases sphincter tone, and upward displacement of the abdominal organs increases the risk of aspiration. Breathing is affected by the upward shift of the diaphragm, leading to a decrease in functional residual capacity, intrapulmonary shunting, increased metabolic demand, and thus faster desaturation.

Defibrillation should not be delayed in the coding pregnant patient. Doses for defibrillation are unchanged from the recommended ACLS doses for the nonpregnant patients.[1] Although case reports have described potential harm to the fetus and induction of fatal fetal arrhythmias from high doses of electricity, in a dead or dying patient, these theoretic risks in no way override the benefit of standard defibrillation practices. If fetal monitoring is in place when cardiac arrest occurs, it is reasonable to disconnect the monitor to eliminate the risk of electric arcing.

ACLS guidelines indicate the medications to be given during cardiac arrest. Although there is limited evidence as to their effectiveness, they should still be given in pregnancy as in any patient experiencing an arrest. The doses do not change.

When a patient is in cardiac arrest, the initial management goals are resuscitation and identifying and aggressively treating reversible causes of the arrest. Several mnemonics have been designed to help with that assessment (**Table 3**). However, it may be more helpful to think of three main categories: (1) hypovolemia, (2) pump failure, and (3) obstruction. Hypovolemia can be caused by massive hemorrhage (external and internal, as from disseminated intravascular coagulation or placental abruption or previa) or vasodilation (septic shock, thyroid storm). Pump failure can result from cardiomyopathy, AMI, or arrhythmia. Obstruction can be the result of pulmonary embolus or pericardial tamponade. Ultrasound can be very useful in assessing these categories. The traditional focused assessment with sonography for trauma examination can diagnose free fluid or pericardial effusion. The subcostal view may be problematic because of the gravid uterus, but other cardiac views (eg, the apical or parasternal long/short) can be helpful to estimate ejection fraction or evaluate for pericardial effusion, right ventricular outflow obstruction, and coordinated cardiac motion. If lack of coordinated cardiac motion is observed or if the mother does not respond to intervention and lacks return of spontaneous circulation, perimortem cesarean section must be considered immediately.

Perimortem cesarean section is a daunting procedure, but one that can be lifesaving for mother and baby. Any pregnant patient with a fundal height at the level of the umbilicus (20 weeks) may benefit from perimortem cesarean section, regardless of fetal viability. One case series reported that 12 of 20 women had return of spontaneous circulation immediately after delivery.[48] Hospitals should have a protocol in place to activate all necessary resources for an emergency cesarean section. Cardiac arrest in a pregnant patient should prompt immediate activation of that protocol (Class I, LOE B recommendation). Cesarean section should be started at 4 minutes after onset of maternal cardiac arrest (Class IIb, LOE C recommendation). Although maternal and fetal outcomes are best when the cesarean section is performed within that window, maternal survival has been reported up to 15 minutes after the onset of arrest, and neonatal survival up to 30 minutes after the onset of arrest. If there is an obvious nonsurvivable maternal injury, or if resuscitation seems futile, it may be appropriate to perform the section immediately, particularly if the fetus is viable.[1]

Table 3
Reversible causes of cardiac arrest in pregnancy

Hs & Ts	BEAU CHOPS
Hypovolemia	Bleeding/DIC
Hypoxia	Embolism
Hydrogen ions (acidosis)	Anesthetic complications
Hyper/hypokalemia	Uterine atony
Hypothermia	Cardiac disease
Hyper/hypoglycemia	Hypertension/eclampsia
Tablets/toxins	Other
Cardiac tamponade	Placental abruption/previa
Tension pneumothorax	Sepsis
Thrombosis (MI)	
Thromboembolism (PE)	
Trauma	

Abbreviations: DIC, disseminated intravascular coagulation; MI, myocardial infarction; PE, pulmonary embolism.

Data from 2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care - Part 7.2: management of cardiac arrest. Circulation 2005;112: IV-58–IV-66.

Therapeutic hypothermia is quickly becoming the standard of care for postarrest nonpregnant patients. Its use in pregnancy is essentially unstudied. One case report documented favorable maternal and fetal outcomes after a term delivery in a patient who suffered arrest early in her pregnancy.[49] The use of therapeutic hypothermia is reasonable to consider, using the same criteria as for nonpregnant patients (Class IIB, LOE C recommendation). Fetal bradycardia is a potential complication, so monitoring is recommended (Class I, LOE C recommendation).[1]

SUMMARY

Cardiovascular emergencies are rare in pregnancy, but when they occur, they are frightening for the patient and the provider. Caring for the critically ill pregnant patient can be quite anxiety provoking, and it is helpful to take a step back and remember that survival of the fetus depends on the health of the mother. Although there are important subtle differences in the treatment of conditions, such as pulmonary embolus, decompensated heart failure, and AMI, the diagnosis and overall goals of management remain the same. Involve consultants early and intervene aggressively but appropriately.

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