

Heart Failure in Pregnant Women: Is It Peripartum Cardiomyopathy?

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Peripartum cardiomyopathy is a rare but important cause of maternal morbidity and mortality. Women with peripartum cardiomyopathy often present with symptoms and signs of heart failure. The diagnosis of peripartum cardiomyopathy is made after all other causes of heart failure are excluded. Emphasis is on the immediate recognition of an unwell pregnant or recently pregnant woman, early diagnosis with the use of echocardiography, and the correct treatment of heart failure. (Anesth Analg 2015;120:638–43)

Maternal heart disease is a leading cause of maternal mortality in developed countries.^{1–4} Anesthesiologists are frequently involved in the multidisciplinary management of women with heart disease in pregnancy in the setting of antenatal care and planning for safe birth or in the peripartum period.^{1,5,6} Anesthesiologists may also be involved in the care of these women in the acute presentation phase when a pregnant woman presents with heart failure and requires resuscitation and in the postpartum management decisions involving location and acuity of care. Therefore, it is important that anesthesiologists understand the major causes of heart failure during pregnancy, their presentation, differential diagnosis, and management. This focused review will explore one significant cause of heart failure in pregnancy, peripartum cardiomyopathy (PPCM), within the context of the differential diagnosis of other causes of heart failure.

PPCM is a serious but uncommon form of heart disease associated with pregnancy. It is diagnosed when all other causes of heart failure are excluded.⁷ PPCM may present during the third trimester of pregnancy or in the months after pregnancy.⁸ The incidence of the disease is approximately 1 in 2000 pregnant women, although the incidence varies throughout the world.^{9–11} Mortality in untreated disease ranges between 9% and 50%. Short- and long-term morbidity is substantial, with 36% to 77% of women experiencing a long-term reduction in cardiac function.^{7,12,13} Prognosis depends on the degree of left ventricular dysfunction at diagnosis; women who present with left ventricular end-diastolic diameter >60 mm and a fractional shortening <21% have a reduced likelihood of returning to normal cardiac function.¹⁴

The etiology of the disease is unknown, and this hampers progress regarding specific diagnostic markers and disease-specific drug therapy. Recent work has investigated the role of oxidative stress, angiogenic imbalance, and the cleavage of prolactin to a cathepsin D–cleaved 16-kDa fragment in the pathogenesis of PPCM.¹⁵ This latter work suggests that bromocriptine may be a possible disease-specific therapy for PPCM; however, robust clinical trials are needed before recommending this therapy for women with PPCM.^{8,16} Studies investigating the role of infection, inflammation, autoimmune disease, genetics, cardiovascular risk factors, pregnancy-related factors, and various biochemical substances have also been performed; however, no single factor has been identified as the underlying cause of the disease.^{8,17–19}

DEFINITIONS

Peripartum Cardiomyopathy

PPCM is defined as heart failure with left ventricular systolic dysfunction quantified by echocardiography. It is defined as reduced ejection fraction ($\leq 45\%$), fractional shortening ($\leq 30\%$), or both,⁸ and in some definitions, an end-diastolic dimension >2.7 cm/m² body surface area.^{12,13,20,21} It is important to note that presentation is similar regardless of gestational age.⁹ This uncommon cause of heart failure should be differentiated from other causes of heart failure in pregnant women so that correct management may be instituted (Fig. 1). It is also important that women are not inappropriately labeled as having this rare disease, with no known specific treatment, when there are other more common pathophysiologic conditions to explain the heart failure.

Women who are ultimately diagnosed with PPCM present with nonspecific symptoms and signs of heart failure (Table 1). After all other causes of heart failure, including known precipitants of failure such as fluid overload, tachyarrhythmias, hypertensive heart disease, severe anemia, thyrotoxicosis, sepsis, drug toxicity (including cocaine use), valvular heart disease, congenital heart disease, and previous cardiomyopathy (idiopathic, chemotherapy-associated, human immunodeficiency virus-associated cardiomyopathy) are excluded, the diagnosis of PPCM is made.^{20,22} Some women may have risk factors for PPCM, including advanced maternal age or teenage pregnancy, African ethnicity, pregnancy with multiple fetuses, family history, and multiparity (although PPCM occurs for most women

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Table 1. Cardiac Symptoms, Signs, and Investigations in Pregnant or Recently Pregnant Women

	Key considerations
Symptoms	
Agitation	May indicate hypoxemia
Cough	May indicate pulmonary congestion
Nausea and vomiting	Consider myocardial ischemia as atypical presentations are common in pregnancy
Breathlessness	Cardiac and respiratory causes need to be evaluated; consider pulmonary hypertension
Pain (chest, back interscapular, and epigastric)	Consider myocardial ischemia (coronary occlusion or dissection), ischemic heart disease, aortic dissection (especially Marfan syndrome), and pre-eclampsia
Signs	
Tachypnea	Respiratory rate must be measured
Tachycardia	Resting heart rates >100 bpm should be evaluated
Irregular heartbeat	
Hypotension	Consider systolic and/or diastolic heart failure, right heart failure, sepsis, and hypovolemic
Severe hypertension	Acute pulmonary edema may occur in the setting of critical hypertension (pre-eclampsia)
New heart murmur	Consider valvular heart disease, especially mitral stenosis
Additional heart sound	May be present in heart failure
Wheeze	Consider acute pulmonary edema as well as acute asthma
Febrile	The presence of fever should prompt examination and investigation for sepsis. Consider endocarditis, myocarditis, and rheumatic heart disease
Investigations	
Full blood examination	Assessment of blood smear, hemoglobin, platelet count, and white cell count
B-natriuretic peptide	Commonly elevated in heart failure
Cardiac enzymes	Elevated serum troponin may indicate myocardial ischemia
Arterial blood gases	Hypoxemia and metabolic acidemia may indicate low cardiac output
Chest x-ray	May show cardiomegaly and pulmonary congestion
Electrocardiography	Heart rate and rhythm and ST-segment elevation or depression may indicate myocardial ischemia
Transthoracic echocardiography ^a	Cardiac structure and function, regional wall motion abnormalities, and reduced contractility may indicate ischemia/cardiac assessment of ejection fraction—preserved or reduced?
Computer tomography pulmonary angiography	Ventilation perfusion mismatching in the case of pulmonary emboli
Coronary angiograph with angioplasty with or without stenting	Myocardial infarction and ischemic heart disease—diagnosis and treatment
Cardiac magnetic resonance imaging	Cardiac structure and function/presence of ventricular thrombus

bpm = beats per minute.

^aTransthoracic echocardiography or transesophageal echocardiography.

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with the first or second pregnancy); however, PPCM may occur in otherwise healthy pregnant or recently pregnant women. In the future, a better understanding of cardiac function throughout pregnancy, especially the changes in cardiac function in late pregnancy, may enable us to identify women who have subclinical cardiac dysfunction earlier in pregnancy. Ideally, earlier institution of interventions could reduce the chance of developing clinical cardiac failure.

It is important to emphasize the issue of hypertension as a known cause of heart failure in adults. The development of heart failure that occurs in association with hypertensive conditions of pregnancy, such as pre-eclampsia can be explained by known mechanisms and should therefore not be considered PPCM.^{22,23} Studies that have excluded known causes of heart failure, such as hypertension, demonstrate a clear postpartum peak in the initial presentation of PPCM, most commonly 2 to 62 days after delivery.^{8,9} Because the assessment of cardiac function is not routinely performed before birth, it is possible that some women with subclinical disease are unrecognized. Indeed, some seemingly healthy term-pregnant women have recently been shown to have reductions in both systolic and diastolic function.^{24,25} Standard peripartum management, including routine anesthesia care, IV fluid therapy, and oxytocin therapy, may be detrimental to the cardiac function of these women, and it is possible that they may be at increased risk of developing heart failure in the postpartum period.

Heart Failure

Heart failure is commonly classified into reduced ejection fraction heart failure and preserved ejection fraction heart failure.²⁰ Heart failure may also be classified into acute and chronic failure. Women with PPCM, by definition, present with acute reduced ejection fraction heart failure.²² When the acute reduced ejection fraction heart failure occurs antenatally, there are the additional physiologic stresses because of the changes associated with pregnancy and birth, and additional consideration related to the well-being of the fetus.

KEY ISSUES IN MANAGEMENT

Organizational Issues

When managing critically ill women with heart failure in pregnancy, organizational issues are important to ensure optimal maternal and fetal outcomes.¹ The latest Confidential Enquires into Maternal Death in the United Kingdom concluded that the most important organizational issue pertaining to acute heart failure in pregnant women was the maintenance of clinical skills by all providers. Skills should especially focus on the early recognition of the severely ill pregnant woman.¹ Providers caring for high-risk pregnant women need to be familiar with cardiac arrest in pregnancy protocols.^{26,27} Organizations should encourage the development of functional teams and collaboration among clinicians, nurses, and midwives because multidisciplinary team management and planning

are crucial to the safe care of pregnant women with heart failure in pregnancy.^{26,27}

Recognition of Heart Failure in a Pregnant or Recently Pregnant Woman

Presentation of women with PPCM can be variable and sometimes difficult to differentiate from normal signs and symptoms of pregnancy, and it is important to maintain a high suspicion for the presence of heart failure.^{28,29} Women may present with symptoms of both right and left heart failure, including pulmonary edema, pulmonary embolism, systemic embolism, and ventricular tachyarrhythmias. Acute heart disease must be considered in any pregnant or recently pregnant woman presenting with cardiorespiratory symptoms and signs, including breathlessness, orthopnea, paroxysmal nocturnal dyspnea, tachypnea, or other signs of right or left heart failure.³⁰ Common presenting symptoms include orthopnea, dyspnea, cough, swelling, excessive weight gain, and palpitations.^{9,31} Of key importance is the early use of echocardiography to differentiate heart failure from respiratory disease, especially asthma, in a woman who presents with breathlessness, cough, and wheeze.³²

Diagnosis

Women with PPCM present with signs and symptoms of heart failure. It is important for the anesthesiologist to differentiate between women with the normal symptoms of healthy pregnancy (e.g., occasional shortness of breath on exertion and edema) and women who exhibit symptoms and signs of heart failure (hypoxemia, pulmonary edema, pleural effusions, marked sinus tachycardia, paroxysmal nocturnal dyspnea, cough, and angina) (Table 1). In addition to the usual biochemical, hematological, and radiological tests (e.g., chest radiograph, electrocardiograph, and B-type natriuretic peptide concentration), echocardiography is the most important diagnostic test in any pregnant or recently pregnant woman suspected of heart failure.^{12,20,33,34} Transthoracic echocardiography will enable the assessment of valvular pathology, the diagnosis of congenital heart disease, and the assessment of the effects of chronic hypertension. The measurements required to diagnosis dilated cardiomyopathy (PPCM) can be made. Echocardiographic features of PPCM include ventricular dilatation and hypokinesia; these features are very similar to those found in dilated cardiomyopathy diagnosed in nonpregnant adults.^{8,22} Importantly, echocardiography will also enable classification of heart failure as reduced ejection fraction heart failure, which occurs in PPCM, or preserved ejection fraction heart failure, which often occurs in hypertensive heart failure.

Although echocardiography is the most commonly used modality to assess cardiac function, cardiac magnetic resonance imaging, without gadolinium contrast in the pregnant woman, may also be used to quantify cardiac function and structure and allow more accurate assessment of cardiac volumes and the detection of left ventricular thrombus.⁸ Postpartum cardiac magnetic resonance imaging enables examination with gadolinium, which may demonstrate myocardial fibrosis in some women.³⁵

Stabilization Before Birth

For women who present with heart failure, the focus is on determining whether it is reduced or preserved ejection

fraction heart failure because the treatment differs. It is also important to determine whether the woman has hypertensive disease (pre-eclampsia or chronic hypertension) because both preserved and reduced ejection fraction heart failure may occur in the setting of hypertension. In women who meet the diagnostic criteria for pre-eclampsia complicated by heart failure, management of severe pre-eclampsia with magnesium sulfate for seizure prophylaxis and investigations for multiorgan system disease are necessary.

Stabilization of the woman may be necessary while the diagnosis is being made and includes identifying and managing the precipitating events and planning for delivery.³⁰ It is important to note that there is no specific treatment for the condition.⁷ The broad principles of management of a pregnant woman in heart failure with a dilated cardiomyopathy are followed and should be individualized for each woman depending on severity of presentation and coexisting morbidities.^{30,36,37} In general, acute treatment is aimed at improving symptoms, slowing progression of disease, and improving survival. Strategies include oxygen supplementation to maintain oxygen saturations of $\geq 95\%$ (noninvasive or invasive ventilation [tracheal intubation and ventilation]), the use of positive end-expiratory pressure, diuretics, and vasodilators (e.g., titrated nitroglycerine).^{8,30} Once stabilized, β -adrenergic receptor blockade with metoprolol should be considered.¹²

Critically ill women with signs of low cardiac output (hypoperfusion) or refractory pulmonary edema may require inotropic drugs (e.g., dobutamine and levosimendan), an intra-aortic balloon pump, or ventricular assist devices.^{8,13} Women who require inotropic support should be referred early to a cardiac transplantation unit for consideration of transplantation if clinical improvement does not occur.¹³ Women with dilated cardiomyopathy are at increased risk of thromboembolism, therefore, thromboprophylaxis is essential.

Intrapartum Issues

Multidisciplinary specialty antenatal planning, including input from cardiologists, assists with safe intrapartum management. The cardiovascular effects of neuraxial anesthesia and analgesia, as well as general anesthesia, should be considered when managing women with stabilized heart failure. The specific anesthetic technique should consider the mode of delivery and clinical severity of heart failure. The general management principles are summarized in Table 2.

Postpartum Issues

Close monitoring in the postpartum period, often in the intensive care unit, is essential. Heart function may deteriorate after birth, and in some women, up to a few weeks to months after birth. Cardiac complications leading to death include acute pulmonary edema, tachyarrhythmias, and pulmonary and systemic emboli. In the unfortunate event of death, an autopsy should be requested to help determine the cause.¹

Women with stable disease may be able to breastfeed although some clinicians recommend avoiding breastfeeding because of the possible negative effects of prolactin on cardiac function.⁸ It is also important to consider transfer of drugs into breast milk and whether these drugs are safe for the newborn. Angiotensin-converting enzyme inhibitors are

Table 2. Ten Management Principles for Managing a Woman with Heart Failure in Pregnancy

Management with a core supervising team
Manage with appropriately trained staff in the safest location
Ensure good lines of communication with the woman and the multidisciplinary team
Minimize cardiac work by optimal preload, contractility, lusitropy, heart rate, rhythm, and afterload
Avoid aortocaval compression
Intensive hemodynamic monitoring
If general anesthesia is required, plan strategies to reduce the likelihood of hypertension, hypotension, arrhythmias, acute pulmonary edema, and cardiac arrest
If general anesthesia is required, plan strategies to manage hypertension, hypotension, arrhythmias, acute pulmonary edema, and cardiac arrest
Avoid oxytocin and ergometrine because these cause significant life-threatening cardiac complications
Plan a management strategy for the complication of hemorrhage, including mechanical methods of uterine compression, Bakri balloon tamponade, use of misoprostil, and consideration of hysterectomy

FUNCTIONAL CAUSES**Preload increase****Contractility problem****Lusitropy problem****Rate disturbance****Rhythm disturbance****Afterload problem**

due to

Physiological conditions

Pathological conditions

Pharmacological agents

- including
- tocolysis
- oxytocics
- analgesia and anesthesia
- intravenous fluids
- drug overdose/drug error
- illicit drug use

STRUCTURAL CAUSES**Congenital heart disease**

- uncorrected
- corrected

Acquired heart disease

Pericardial disease

- inflammation
- infection
- edema

Vascular disease

- small vessel - coronary vessels
- large vessel - aorta, pulmonary vessels

Myocardial disease

- cardiomyopathy
- known causes
- inflammatory
- infiltrative
- infective
- hypertrophy
- fibrosis
- edema
- unknown causes
- idiopathic
- peripartum cardiomyopathy

Conductive tissue disease

Valvular disease

- inflammation
- infection
- stenotic, regurgitant lesions

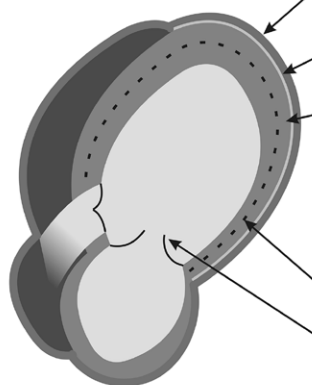


Figure 1. Causes of heart failure in pregnant or recently pregnant women. The causes of heart failure are divided into functional and structural causes. Abnormalities of function can be divided into the six categories of physiologic cardiac function, and the structural abnormalities can be divided into the major cardiac structural categories. Abnormalities of function may independently be a reason for the development of heart failure in pregnant women or may be combined with structural problems to cause heart failure. The diagnosis of peripartum cardiomyopathy is made after the exclusion of all known causes of heart failure.

safe in breastfeeding women and are often commenced in women with dilated cardiomyopathy. Serial echocardiography should be repeated after birth, and women should undergo regular follow-up by cardiologists. Factors predictive of adverse outcomes include ongoing poor left ventricular function, increased left ventricular end-diastolic dimension, and delayed recovery.¹² Poor recovery of ventricular function may signal the need for an implantable cardioverter/defibrillator and cardiac resynchronization therapy.³⁶

Management of Women with a History of PPCM

PPCM may recur in subsequent pregnancies. The reported recurrence rates range from 25% to 100%. Advice to women with a history of PPCM regarding risks associated with subsequent pregnancies should consider: (1) the severity of presentation and the initial clinical course; (2) the degree of cardiac recovery; (3) concurrent medical conditions and risk factors for cardiac disease such as smoking, hypertension, obesity, and anemia;²³ and (4) the availability of tertiary specialist hospital services to manage high-risk pregnant women.

FUTURE DIRECTIONS

The development of databases with strict adherence to the definition of PPCM may help to better understand the epidemiology of PPCM.^{38,39} Because death from cardiac disease is preventable in many cases,⁴⁰ further education and

research into the best strategies to educate women and caregivers (including anesthesiologists) in early recognition of cardiac disease may result in earlier diagnosis and treatment and better outcomes.

Furthermore, the widespread use of bedside echocardiography in pregnant women by anesthesiologists may enable more rapid diagnosis and the timely commencement of treatment, a better understanding of cardiac physiology and pathophysiology, and fewer diagnostic errors, thus leading to a reduction in morbidity and mortality from cardiac disease in pregnant women. ■■

DISCLOSURES

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