Peripartum Cardiomyopathy
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Peripartum cardiomyopathy (PPCM) is an uncommon disorder associated with pregnancy in which the heart dilates and weakens, leading to symptoms of heart failure. PPCM may be difficult to diagnose because symptoms of heart failure can mimic those of pregnancy. Affected women may recover normal heart function, stabilize on medicines, or progress to severe heart failure requiring mechanical support or heart transplantation. Even when the heart recovers, another pregnancy may be associated with a risk of recurrent heart failure. Important research is underway to understand the cause of PPCM and to develop new treatments.

Definitions
Cardiomyopathy (literally heart muscle disease) is a general term used to describe an abnormality of heart muscle function that can lead to symptoms of heart failure. Patients with cardiomyopathy may also be at risk for abnormal heart rhythms (arrhythmias) and even sudden death. PPCM is a form of dilated cardiomyopathy in which the heart chambers enlarge or dilate and the muscle weakens, leading to reduced blood flow and increased heart pressures in the heart.

PPCM is diagnosed when the following 3 criteria are met:
1. Heart failure develops in the last month of pregnancy or within 5 months of delivery.
2. Heart pumping function is reduced, with an ejection fraction (EF) less than 45% (typically measured by an echocardiogram as described below).
3. No other cause for heart failure with reduced EF can be found.

PPCM is rare in the United States, Canada, and Europe, with an estimated case rate of 1 per 2500 to 4000 live births. This translates to 1000 to 1300 woman developing PPCM each year in the United States. Most patients (80%) present within 3 months of delivery, with the minority presenting in the last month of pregnancy (10%) or 4 to 5 months postpartum (10%). Some specialists believe that the definition of timing is too strict and that patients who develop symptoms of heart failure during the second or early third trimester should also be diagnosed with PPCM. In some countries, PPCM is much more common (eg, 1 in 1000 live births in South Africa and up to 1 in 300 live births in Haiti). This may be related to differences in diet, lifestyle, other medical conditions, or genetics.

Heart failure is a common cardiac condition in which the heart is unable to pump blood at a sufficient rate to meet the demands of the body. Most patients who develop heart failure have had a prior injury or stress on the heart that caused the heart to weaken. In the
case of PPCM, the stress is presumed to be pregnancy, but the mechanisms are poorly understood. Other potential contributors include high blood pressure, heart attack, heart valve dysfunction, exposure to toxins such as alcohol or chemotherapy, or a genetic mutation that leads to heart failure in adulthood. Other medical conditions such as diabetes mellitus, obesity, and chronic kidney disease can worsen heart failure.

**Risk Factors**

Several risk factors are associated with PPCM. These include the following:

- Older maternal age
- Multiparity (1 or more prior pregnancies)
- Multifetal pregnancy (eg, twins)
- African descent
- High blood pressure
- Prior toxin exposure (eg, cocaine)
- Use of certain medications to prevent premature labor

It is important to note that although PPCM is more likely to occur in a woman over the age of 30 who is pregnant with twins and has had prior pregnancies, PPCM can also occur in a young woman who is pregnant with her first child.

**What Is the Cause of PPCM?**

The underlying cause of PPCM has not been clearly defined. Heart biopsies performed in women with PPCM have shown inflammation in 10% to 75% of cases. This may be attributable to a prior viral illness or abnormal immune response, although there is no evidence that antiviral or immunosuppression medications improve outcomes. Other potential causes of PPCM include nutritional deficiencies, coronary artery spasm, small-vessel disease, and defective antioxidant defenses. Genetics may also play a role in the tendency to develop PPCM.

**Symptoms**

The major symptoms of PPCM are those of heart failure and include fatigue, shortness of breath, and fluid retention. Because there is a significant overlap between symptoms related to pregnancy, especially toward the end of the third trimester or after delivery, and heart failure (Table 1), the diagnosis may be initially missed or delayed.

- Fatigue is the sensation of feeling tired or weak and being unable to perform usual daily activities such as showering or dressing without stopping to rest. Fatigue can be worse in the afternoon or after engaging in a strenuous activity.
- Shortness of breath can be defined as breathlessness with activities such as walking a block on flat ground or up 1 flight of stairs. As heart failure progresses, patients may become short of breath while eating, talking, or resting. Some patients will also develop difficulty breathing at night, causing them to wake up with cough or congestion or requiring them to sleep on pillows or in a recliner to breathe.
- Fluid retention can manifest as swelling in the legs (also called edema); swelling in the abdomen with bloating, pain, loss of appetite, or feeling full; chest congestion leading to cough and shortness of breath (as discussed above); increased urination at night; and weight gain.
- Patients with heart failure caused by PPCM may also complain of palpitations or skipped beats, racing heart, lightheadedness, or almost fainting. Rarely, patients with PPCM may present with symptoms related to a blood clot that breaks away from the heart and goes to a vital organ such as the brain, causing a stroke, or coronary artery, causing a heart attack. Blood clots to the lungs may cause shortness of breath, lightheadedness, racing heart, or coughing up blood.

In most patients, heart failure symptoms can be relieved or stabilized with medications, along with changes in lifestyle and diet (see Management below).

**Evaluation**

The evaluation of PPCM begins with a complete medical history and physical examination. The keys to the medical history are ruling out heart disease that may have predated pregnancy; identifying other potential causes or precipitants of heart failure, including a family history of heart disease; and defining symptom severity. Similarly, the physical examination may help to uncover other noncardiac conditions associated with cardiomyopathy while assessing for signs of reduced heart function and fluid retention. In addition, the history and physical examination may detect complications associated with PPCM such as loss of circulation to a limb caused by a blood clot.

Laboratory blood tests are a standard part of the evaluation of any patient with the diagnosis of cardiomyopathy or heart failure, including patients with PPCM. This includes tests to assess kidney, liver, and thyroid function; tests to assess electrolytes, including sodium and potassium; and a complete blood count to look for anemia or evidence of infection. In addition, markers of cardiac injury and stress such as troponin and B-type natriuretic peptide can be used to assess level of risk. Laboratory tests may also be done to rule out other causes of cardiomyopathy such as lupus and human immunodeficiency virus.

<table>
<thead>
<tr>
<th>Table 1. Is it Pregnancy or Heart Failure?</th>
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<tbody>
<tr>
<td>Shortness of breath</td>
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<tr>
<td>Fatigue</td>
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<tr>
<td>Leg swelling</td>
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<tr>
<td>Abdominal pain, bloating</td>
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<tr>
<td>Weight gain</td>
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<td>Cough, chest pain</td>
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<tr>
<td>Palpitations, tachycardia</td>
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<tr>
<td>High blood pressure</td>
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Other tests that are typically performed in patients with PPCM include the following:

- Chest x-ray to look for enlargement of the heart and fluid in the lungs.
- Chest computed tomography (CT) scan to rule out blood clots in the lungs, which can occur during or immediately after pregnancy and cause symptoms similar to those of PPCM such as chest pain, shortness of breath, and palpitations.
- Electrocardiogram (heart tracing) to assess heart rate and rhythm, to look for abnormal electric conduction, and to rule out a heart attack.
- Echocardiogram (heart ultrasound) to assess the size and function of the heart and to exclude other causes of heart failure such as valve dysfunction or a congenital heart defect. Once a diagnosis of PPCM is made, follow-up echocardiograms are typically performed to assess the response to medical therapy and to monitor for heart recovery. The primary measure of heart function is the left ventricular EF. This is the percentage of blood ejected from the heart with each beat; it normally ranges from 50% to 70%. Many laboratories report an estimated EF (eg, 45%–50%); others provide a calculated EF (eg, 47%) using a formula.
- Cardiac catheterization with coronary angiography, an invasive procedure, to assess the severity of heart failure and to rule out blockages or dissection of the coronary arteries. At the same time, a heart biopsy can be performed to look for an alternative cause of cardiomyopathy.
- Other imaging studies to look for inflammation or scarring of the heart muscle, including cardiac magnetic resonance imaging (MRI) and nuclear heart scans. Cardiac magnetic resonance imaging can also be used to look for blood clots in the heart.

**Management**

Medications are used to stabilize heart function, to improve blood flow to vital organs, and to reduce fluid overload. They can also be used to prevent or treat complications such as blood clot formation and abnormal heart rhythms. The choice and safety of medications depends on whether the patient presents during or after pregnancy (Table 2).

- Vasodilators: These medications relax blood vessels, making it easier for the heart to eject blood, and lower pressures in the heart and lungs. During pregnancy, the vasodilator of choice is hydralazine, which can be given alone or with nitrates. After pregnancy, angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers can be used safely in place of hydralazine/nitrates and may help the heart to heal. ACE inhibitors or angiotensin receptor blockers should not be taken during pregnancy because they can cause birth defects. Vasodilators can lower blood pressure and may be associated with lightheadedness or fatigue.
- Diuretics: These medications cause the kidneys to excrete salt and water and help to relieve symptoms related to fluid retention such as shortness of breath, abdominal bloating, and edema. Diuretics can also lower blood pressure and lead to loss of potassium, causing muscle cramps and dehydration. Blood pressure, kidney function, and electrolytes should be monitored while on diuretic therapy.
- β-Blockers: Patients with PPCM and heart failure have increased levels of catecholamines (adrenaline and related hormones), which can increase heart rate, blood pressure, and overall heart and vascular stress. β-Blockers are used to block these effects and can result in decreased heart rate and blood pressure. Over time, β blockers help the heart to heal and recover normal EF. They also protect the heart against abnormal heart rhythms. Certain β-blockers are safer than others during pregnancy.
- Digitalis: Digitalis is derived from the foxglove plant and has been used for more than 200 years to treat heart failure. Digitalis strengthens the pumping ability of the heart and may lower stimulation of catecholamines. Digitalis can also be used to slow the heart rate in patients with an arrhythmia called atrial fibrillation. Digitalis can be used safely during and after pregnancy with the monitoring of blood levels.
- Spironolactone: Like ACE inhibitors, spironolactone can be used safely after pregnancy to treat heart failure and to help the heart to heal. Spironolactone is a mild diuretic that causes the kidneys to retain potassium, so kidney function and potassium levels need to be monitored during therapy.
- Anticoagulants: Patients with PPCM are at increased risk of developing blood clots, especially if the EF is very low. In these cases, medications are used to thin the blood. During pregnancy, heparin can be given as an injection under the skin or as a continuous intravenous infusion. After pregnancy, warfarin can be taken safely as a pill once a day. Like ACE inhibitors, warfarin should not be taken during pregnancy because of the risk of birth defects. Both heparin and warfarin require close monitoring of blood clotting parameters to avoid bleeding.
- Antiarrhythmics: In patients who experience arrhythmias, medications may be needed to stabilize the heart rate and rhythm. During pregnancy, β-blockers,
sotalol, and intravenous procainamide can be used. Amiodarone is a third-line agent that can be given intravenously or orally during or after pregnancy, but it may be toxic to the fetus and requires careful monitoring of liver, thyroid, and lung function.

Some patients with PPCM will develop severe symptoms of heart failure and require more aggressive treatment in an intensive care setting. Intravenous medications, including inotropes to increase the pumping function of the heart and vasodilators and diuretics to relieve congestion, are commonly used. Supplemental oxygen is usually provided by a nasal cannula or face mask, and a catheter may be placed into the heart to monitor pressures and heart output. For patients who do not respond to these interventions, mechanical support with a balloon pump or temporary heart pump (sometimes called a ventricular assist device) may be necessary. Mechanical support is generally continued until native heart function improves (bridge to recovery) or the patient undergoes heart transplantation (bridge to transplantation). In recent reports, heart transplantation was required in only approximately 5% of PPCM patients, with excellent posttransplantation survival.

Delivery and Breastfeeding
Decisions on the timing and type of delivery (eg, vaginal versus caesarian section) should be made in consultation with a multidisciplinary team, including specialists from cardiology, obstetrics, anesthesia, and pediatrics. Early delivery is not required if the mother and fetus are stable. In 1 study, preterm birth occurred in 25% of patients. Patients with PPCM may choose to breastfeed after delivery, but this should be discussed with their caregivers. ACE inhibitors, β-blockers, and diuretics are generally considered safe in this setting.

Rhythm Management
An implantable cardioverter-defibrillator (ICD) is indicated after delivery if the patient continues to have serious arrhythmias or the heart function remains significantly reduced (typically an EF less than 35%) despite optimal medical therapy. The implantable cardioverter-defibrillator is placed under the skin with wires leading into the right side of the heart to provide backup pacing if the heart rate goes too slow or internal shock if the heart rate goes too fast in a life-threatening rhythm called ventricular tachycardia or fibrillation.

Diet and Activity
Standard treatment for heart failure includes maintaining a low-salt diet and restricting fluid intake to less than 2 L/d. Alcohol and smoking should also be avoided. Patients may be asked to weigh themselves daily and report significant changes (eg, increase of more than 3–4 pounds over 1–2 days) because this may require adjustment of diuretics. Activity level depends on the severity of symptoms and should be discussed with one’s physician.

Prognosis and Follow-Up
Older studies suggested that approximately 50% of patients with PPCM recover normal heart function, 25% have persistently reduced heart function but remain stable on medications, and 25% progress to severe heart failure. More recent research suggests that outcomes of PPCM have improved, with survival rates as high as 90% to 95% with contemporary medical and device therapy (Figure). Although early improvement in EF (ie, within the first 3–6 months) predicts a good outcome, some women will have slow, gradual improvement in EF over years. The decision of when to stop medications after the heart fully recovers, usually defined as an EF greater than 50%, remains controversial. Most physicians, however, agree that ACE inhibitors and β-blockers should be continued for at least 1 year after normalization of EF.

Risk of Subsequent Pregnancy
One of the most important questions asked by women with a history of PPCM is whether they can safely get pregnant again. The risk of a subsequent pregnancy depends on the recovery of heart function after the diagnosis of PPCM. For women with persistently reduced EF, there is a substantial risk of recurrent heart failure and even death. For women with recovered EF, the risk is much lower and can be further stratified by a stress echocardiogram. If the EF is normal at rest and increases with stress (eg, normal contractile reserve), the risk of recurrent PPCM or heart failure appears to be minimal. Any decision to become pregnant again after a prior diagnosis of PPCM should
be made after consultation with a cardiologist and high-risk obstetrician. If a woman chooses to move forward, medications that are potentially toxic to the fetus (eg, ACE inhibitors) should be stopped, and serial monitoring for signs of heart failure or reduced EF during the pregnancy is critical.

Research and Future Directions
There is active research into understanding the cause of PPCM and developing new therapies. Treatments that alter the immune system such as intravenous γ-globulin and immunoabsorption have been tried but are not proven. Recently, investigators have focused on the role of prolactin in PPCM. Prolactin is a hormone released from the pituitary gland late in pregnancy and after delivery that stimulates the production of breast milk. Prolactin, however, may have adverse effects on the heart muscle by limiting its blood supply and causing cell death. Bromocryptine is a medication that inhibits the pituitary secretion of prolactin, and early studies suggest that it may be beneficial in the treatment of PPCM. More research is needed to determine its safety and efficacy.

Disclosures
None.

References

Additional Resources
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