

PERIPARTUM CARDIOMYOPATHY

Definition

Peripartum cardiomyopathy is a distinct cardiomyopathy the cardiac phenotype of which resembles dilated cardiomyopathy.¹⁻⁴

The NHLBI has defined peripartum cardiomyopathy as development of heart failure with LVEF<45%, fractional shortening <30%, or both, with or without an LVEDD>2.7 cm/m² body surface area, in the last month of pregnancy or within 5 months, in the absence of an identifiable cause of heart failure or recognizable heart disease prior to the last month of pregnancy.⁵

The ESC has defined peripartum cardiomyopathy as an idiopathic cardiomyopathy without any other cause of HF, that occurs mainly during the peripartum period or in the months following delivery, termination, or miscarriage. It is a diagnosis of exclusion. The left ventricle may not be dilated but the ejection fraction is nearly always reduced below 45%.^{3,4}

Epidemiology

The incidence of peripartum cardiomyopathy varies from 1 in 1000–5000 in the USA and Europe to 1 in 1000 in South Africa, 1 in 300 in Haiti, and 1 in 100 in Nigeria.^{1,2,6,7}

Aetiology

Peripartum cardiomyopathy continues to be a cardiomyopathy of unknown cause. Various pathophysiologic mechanisms have been proposed such as excessive prolactin (reduced myocardial STAT3 protein levels and activated oxidative stress-cathepsin D-16 kDa prolactin cascade), cytokine-mediated inflammation, viral myocarditis, and autoimmune mechanisms. A toxic role of late-gestational hormones such as prolactin on the maternal vasculature in the context of a cardiac predisposition (the vasculo-hormonal hypothesis) is also being considered.² Prolonged tocolysis, advanced maternal age, high gravidity/parity, multipregnancy, race, socioeconomic status, gestational hypertension, and cocaine abuse are risk factors associated with the development of peripartum cardiomyopathy. A role for genetics in the development of peripartum cardiomyopathy has been supported by multiple reports, with a genetic cause of disease identified in up to 20% of studied patients.⁸ The most notable example of this is mutations in the sarcomeric gene titin (TTN). FLNC, DSP, and BAG3 have also been implicated. the identity and relative abundance of these variants is remarkably similar to that seen in idiopathic dilated cardiomyopathy.⁸⁻¹¹

Presentation

Clinical presentation is extremely variable, from mild symptoms that can be attributed to pregnancy to acute heart failure. Elevated JVP, S3 and basal rales can be normal in pregnancy. Most often patients present with NYHA III or IV symptoms. Patients may also present with ventricular arrhythmias, systemic embolism due to LV thrombus or pulmonary embolism. Most cases occur in the puerperium,¹² but the disease may well present before and up to months after delivery.²

Investigations

Diagnosis is being put by exclusion (Table 1 and Figure 1).

- **ECG** is seldom normal, usually displaying ST-T abnormalities or LV hypertrophy voltage criteria.
- **Echocardiography** is essential for LV assessment.
- **MRI** allows more accurate measurements, but gadolinium crosses the placenta and is not recommended during pregnancy.¹³
- **BNP** and **NT-proBNP** levels are raised.

Differentiation between post-partum cardiomyopathy, and severe gestational hypertensive complications may be difficult.⁶

Therapy

After delivery peripartum cardiomyopathy is treated conventionally.

During pregnancy precautions are needed:

Furosemide in congestion. Caution is needed in preeclampsia due to concern for decreased placental perfusion). Furosemide is preferred to *thiazides* that may carry a possible risk of birth defects or fetal thrombocytopenia (see Chapter on Pregnancy). *Spirolactone* may cause feminization of male fetus. No data are available for *eplerenone*.

Hydralazine and nitrates to maintain a systolic blood pressure <110 mm Hg. **Amlodipine** and **methyldopa** can also be used. **ACEI and ARB** are teratogenic.

b-1 selective beta blockers such as **metoprolol** that are compatible with breast feeding are used. Neonates should be monitored for bradycardia, hypoglycemia and growth retardation. b-2 receptor blockade has anti-tocolytic action and carvedilol may be teratogenic at high doses.¹²

Digoxin may be used.

Bromocriptine (2.5 mg twice daily for 2 weeks, followed by 2.5 mg daily for 4 weeks or even 2.5 mg daily for one week), a dopamine D2 receptor agonist, is associated with a high rate of full LV recovery and low morbidity and mortality.¹⁴ It should be added to standard heart

failure therapy (Table 2).

Subcutaneous **LMWH** are used in LVEF<30% or AF.

In acute heart failure **dobutamine** and **dopamine** may be used. *Norepinephrine* decreases placental blood flow.

CRT with or without ICD is considered in patients who fulfill criteria 6 months following presentation.

Recovery occurs within the first 6 months.¹⁵ However, therapy with standard heart failure medications should not be discontinued after restoration of LV function.⁸

Delivery

Unless there is deterioration in the maternal or foetal condition, there is no need for early delivery. Urgent delivery, irrespective of gestation, may need to be considered in women presenting or remaining in advanced HF with haemodynamic instability. In general, spontaneous vaginal birth is preferable in stable women, but assisted second stage is recommended to reduce maternal efforts and shorten labor. Caesarean section is preferred for patients who are critically ill and in need of inotropic therapy or mechanical support.¹³ Limited studies suggest breastfeeding is safe.¹

Genetic Testing

The genetic predisposition to peripartum and dilated cardiomyopathy may be the same, and genetic counseling and testing should be considered for women with PPCM, following guidelines developed for dilated cardiomyopathy.¹⁰

Prognosis

Peripartum cardiomyopathy is associated with considerable mortality for the mother (up to 8%), and the child. Around a third of children born to women have an adverse neonatal outcome and their mortality rate was approximately 5-times that of children born to controls.⁷ However, the prognosis is better than with other causes of dilated cardiomyopathy with normalization of LV function in 40 to 70% of patients, mostly occurring within 2 to 6 months after diagnosis, although later recovery as well as deterioration, up to 3 years, is also possible.^{2,7,15-17} The ESC EORP PPCM Recovery Score accurately predicts LV recovery at 6 months (Figure 2).¹⁸ Maternal mortality rates range widely, up to 30%, depending on the ethnic background and geographic region.¹⁹ With contemporary therapy, reported mortality is 2-15% at 6-12 months.^{3,17} Up to 13% of patients may have major events or persistent severe cardiomyopathy.¹⁵ Caucasians and those diagnosed postpartum are most likely to recover. **Subsequent pregnancies** carry risk of relapse, and dedicated counseling and monitoring are

essential (Table 3).¹ Outcomes for subsequent pregnancies after peripartum cardiomyopathy are better for women who have fully recovered heart function after their initial presentation. However, the normalization of left ventricular function does not guarantee a favorable outcome.²⁰ In general, a subsequent pregnancy carries a recurrence risk for post-partum cardiomyopathy of 20–50%.^{20,21} Factors associated with lack of recovery at initial assessment a LVEDD >5.6 cm, the presence of LV thrombus, and African-American race. Pregnancy is discouraged in women with LVEF<25% at diagnosis that has not been normalized at 2 months.^{13,16} However, even if the LVEF is normalized, there is still a need for counseling because of the risk of recurrence with a new pregnancy.^{6,22} Patients who decide to become pregnant again should undergo baseline echocardiography and determination of serum BNP level before or early in pregnancy. Patients should be followed with repeat echocardiography during the early second and third trimesters, during the last gestational month, and early after delivery and at any time if new symptoms of heart failure develop. Early termination of an unintentional pregnancy should be considered to prevent worsening of LV function and potential maternal mortality, especially in patients with persistent LV dysfunction.

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