Present concepts of the aetiology, diagnosis and treatment of peripartum cardiomyopathy

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Abstract
Peripartum cardiomyopathy (PPCM) is defined as a disorder of unknown aetiology that occurs between one month antepartum and five months postpartum in women without pre-existing heart disease. While the reported incidence of PPCM appears to be increasing, the early stage of PPCM can easily be missed, because many symptoms and signs of pregnancy are similar to those of early congestive heart failure (e.g. dyspnoea, abdominal discomfort, fatigue). It shares many clinical characteristics with idiopathic dilated cardiomyopathy but occurs at a younger age and is associated with a relatively better prognosis. Maternal mortality ranges between 9 and 15% in different geographical regions. The acute form of PPCM is a clinical syndrome with reduced cardiac output, tissue hypoperfusion, increase in the pulmonary capillary wedge pressure and tissue congestion. Patient monitoring should be initiated as soon as possible with the types and level of monitoring required for any individual patient depending on the severity of cardiac decompensation and the response to initial therapy. Until the precise mechanisms underlying the aetiology of PPCM are identified, at present treatment is directed toward symptomatic relief and improvement of cardiac function and similar to other forms of congestive heart failure.

Introduction
The occurrence of heart failure during the peripartum period was first described in the 18th century, but cardiomyopathy was not identified as its cause until an article by Gouley et al was published in 1937. PPCM is defined as a disorder of unknown pathogenesis in which left ventricular dysfunction and symptoms of heart failure occur between the last month of pregnancy and the first five months postpartum. PPCM is an exclusion diagnosis based on the absence of an identifiable cause of heart failure or recognisable heart disease prior to the last month of pregnancy. Diagnosis requires echocardiographic evidence of left ventricular systolic dysfunction. Heart failure occurring earlier in pregnancy may be caused by previously unsuspected dilated cardiomyopathy unmasked by the haemodynamic and hormonal stress of pregnancy. Other possible causes of heart failure during the peripartum period, such as infectious, toxic, or metabolic disorders and ischaemic or valvular heart disease need to be considered. Complications of late pregnancy, including toxaemia and amniotic or pulmonary embolism, which may mimic heart failure, should be ruled out before the diagnosis of PPCM is made.

Epidemiology of PPCM
The incidence of PPCM is difficult to estimate, because population-based estimates are not available and the diagnosis is not always straightforward. Incidence rates reported in individual studies are based on the experience at particular institutions and may reflect referral bias as well as individual practice patterns. Reports on the incidence of PPCM vary from 1:100 to 1:15 000 between geographical regions and tend to be associated with low socio-economic standards. PPCM is a rare condition in Europe but a frequent disease in Sahelian Africa. The highest incidence of pregnancy associated heart failure in the world (1:100) has been reported from the Zaria province of Nigeria. However, the incidence of PPCM might have been overestimated due to the absence of echocardiography, possibly resulting in other causes of systolic heart failure being diagnosed as PPCM. Fett et al described an incidence of 1:3 000 in Johannesburg, Desai et al documented it as 1:1 000 in 1995 in Durban.
Aetiology and pathogenesis

Most authors agree that PPCM is a distinct entity, rather than a clinically silent underlying cardiomyopathy unmasked by the haemodynamic stresses of pregnancy. However, there is considerable uncertainty with regards to the aetiology of human PPCM. Although it is termed idiopathic, a number of mechanisms have been proposed as potential aetiological agents, including nutritional deficiencies, genetic disorders, viral or autoimmune aetiologies, hormonal problems, volume overload, alcohol or physiologic stress of pregnancy. The rare incidence of PPCM at a single institution and the absence of relevant animal models have limited research and understanding of the pathogenic mechanisms involved. While early reports suggested that PPCM was more prevalent in women over 30 years of age, caused by heat, hypertension, hard physical exertion during pregnancy, sodium diet, selenium deficiency or maternal cocaine abuse, these were based primarily on case reports and have not been proven in systematic studies that include a large number of patients.

Fett et al investigated selenium deficiency and malnutrition in PPCM patients from Haiti and reported that neither a macro-nutrient deficiency (protein and iron) nor a micro-nutrient deficiency (vitamin A, vitamin B-12, vitamin C, vitamin E, beta-carotene, selenium) played a significant role in the incidence and prevalence of PPCM in this population. Several authors have suggested that multiparity may be a risk factor for PPCM, but a recent study by Elkayam et al does not support a strong association of multiparity in the United States because almost 40% of the cases occurred in association with a first pregnancy and more than 50% following the first two pregnancies. Common associated conditions in this cohort were gestational hypertension (43%), tocolytic therapy (19%), and twin pregnancy (13%).

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Several reports have documented the occurrence of chimerism of the haematopoietic lineage cells from the foetus to the mother during pregnancy. It is postulated that foetal cells may escape into the maternal circulation and remain there without being rejected, due to weak immunogenicity of the paternal haplotype of the chimeric cells or to the naturally occurring immunosuppressive state of the mother, or both. If chimeric haematopoietic cells such as dendritic cells take up residence in cardiac tissue during the immunosuppressed pregnant state and, following postpartum when there is recovery of immune competence, these chimeric cells are recognised as nonself by the maternal immune system, and a pathologic autoimmune response may ensue. Prior exposure to paternal major histocompatibility complex antigens expressed by spermatozoa or previous immunisation from prior pregnancies may play a role in inducing the extent of local tissue inflammatory responses. Cytokines and similar signalling molecules are then released, leading to non-specific bystander myocarditis and myocarditis. The association of PPCM with high titres of auto-antibodies against select cardiac tissue proteins (e.g. adenine nucleotide translocator, branched chain [alpha]-keto acid dehydrogenase) supports abnormal immunologic activity as a possible cause of PPCM.

Loss of myocytes due to apoptosis occurs in patients with end-stage cardiomyopathy, but its importance in pathogenesis is unknown. Support for the role of apoptosis in PPCM has been provided by a study that utilised transgenic mice with cardiac-restricted overexpression of Galpha(q). These mice exhibit a lethal form of PPCM accompanied by apoptosis. Hayakawa et al confirmed the role for apoptotic mechanisms by the demonstration of a reduction in cardiac myocyte apoptosis by caspase inhibition through the administration of the polycaspase inhibitor IDN-1965 which was associated with improved left ventricular function and survival in pregnant Galpha(q) mice. These findings suggest that cardiac myocyte apoptosis plays a causal role in the pathogenesis of cardiomyopathy. The apoptosis signalling surface receptor Fas/APO-1 is known to trigger cell death in a variety of cell types. Sliwa et al observed significantly higher plasma levels of Fas/APO-1 in PPCM patients compared with healthy age and parity matched volunteers. The same group also reported significantly elevated plasma levels of TNF-alpha in PPCM patients, which has been implicated in the pathogenesis of idiopathic dilated cardiomyopathy.

Several lines of evidence suggest that PPCM may be the result of myocarditis due to a viral illness or an autoimmune aetiology. Bultmann et al detected viral genomes in endomyocardial biopsy specimen in eight of 26 PPCM patients (30.7%) but also in 10 of 33 control subjects (30.3%). The detected viruses (PVB 19, HHV 6, EBV, HCMV) have been suspected as aetiological agents but such viruses also have a high prevalence in healthy populations, making it difficult to interpret these findings. Kuhl et al amplified viral genomes in endomyocardial biopsies of 165 (67.4%) of 245 patients with idiopathic dilated cardiomyopathy and found a similar spectrum of viruses (EV=9.4%, ADV=1.6%, PVB19=51.4%, HHV-6=21.6%, EBV=52.0%, HCMV=8.8%), including n=45 cases (27.3%) with multiple infections. The role of endomyocardial biopsy remains controversial. PPCM has also been implicated to be due to other infectious disease agents, such as Chlamydia pneumoniae or enterovirus through a process called “molecular mimicry” in which the infectious agents bear protein that share sequence homology to normal cardiac tissue proteins.
Thus, immune response against these mimics initiates immune responses against normal cardiac tissues leading to myocyte loss. Stress-activated pro-inflammatory cytokines such as tumour necrosis factor alpha (TNF-alpha) or interleukin-1 have been implicated in the pathophysiology of idiopathic dilated cardiomyopathy and Sliwa et al reported significantly higher plasma levels of TNF-alpha and interleukin-6 in PPCM patients as compared to age and parity matched healthy controls.23

Clinical presentation

Normal pregnancy is associated with an expansion of blood volume, an increase in metabolic demands, relative anaemia and changes in vascular resistance that are associated with ventricular dilatation and increase in cardiac output. These physiologic changes are due to an increase in preload and heart rate accompanied by a decrease in afterload, peaking during the second trimester of pregnancy. This presents a challenge because many women in the last month of a normal pregnancy experience dyspnoea, fatigue, and pedal oedema. Symptoms identical to those noted for early congestive heart failure. PPCM may therefore not be recognised, leading to an underestimated incidence.24 The diagnosis of PPCM rests on the echocardiographic identification of new onset left ventricular systolic dysfunction during the peripartum period. Decompensation of patients with subclinical valvular, ischaemic or myopathic heart disease usually occurs during the second trimester. Elkayam et al report that 7% of their US patients were diagnosed within one month before delivery and 75% of patients were diagnosed during the first month postpartum25 while Sliwa et al observed onset of symptoms in the South African patients primarily during the postpartum period,23,26 which is in accordance with findings by Fett et al in Haitian patients.27,28 The symptoms and signs are similar to those in patients with idiopathic dilated cardiomyopathy29 and can be complicated by thromboembolic events and arrhythmia. Echocardiography usually demonstrates features of dilated cardiomyopathy (DCM) with impaired ejection fraction, global dilatation and sometimes thinned out walls.

Diagnosis of acute heart failure due to PPCM

PPCM is one cause of acute heart failure (AHF). The diagnosis of PPCM is often delayed and it is important for the clinician to consider this diagnosis in prospective patients, before potentially preventable major complications develop. It is often life-threatening and requires urgent treatment. AHF due to PPCM can occur due to decompensation of pre-existing stable PPCM or as a first manifestation of PPCM. AHF is a clinical syndrome with reduced cardiac output, tissue hypoperfusion, increase in the pulmonary capillary wedge pressure and tissue congestion.30 The diagnosis of AHF is based on the symptoms and clinical findings in combination with appropriate investigations such as ECG, chest X-ray, biomarkers and echocardiography. Systematic clinical assessment of the peripheral circulation, venous filling and peripheral temperature are important. Right ventricular filling in decompensated heart failure may be evaluated from the central jugular venous pressure (CVP). Caution is necessary in the interpretation of high measured CVP in AHF, as it may be a reflection of decreased venous compliance together with decreased RV compliance. Left sided filling pressure is assessed by chest auscultation, with the presence of wet rales in the pulmonary fields usually indicating raised pressure. The confirmation, classification of severity and clinical follow-up of pulmonary congestion and pleural effusions in non-pregnant patients should be done using the chest X-ray. Cardiac palpitation and auscultation for ventricular and atrial gallop rhythms (S3, S4) should be performed. The ECG often shows non-specific findings such as tachycardia and non-specific ST-T wave changes.

Chest X-ray and other imaging should be performed early for all patients with AHF to evaluate pre-existing chest or cardiac conditions and to assess pulmonary congestion. It is used both for confirmation of the diagnosis and to monitor response to therapy, but the threshold for radiological examinations should be high in pregnant patients. Chest X-ray may show venous congestion or pulmonary oedema but the distinction from inflammatory or infectious lung disease is not trivial. Chest CT scan with or without contrast angiography and scintigraphy may be used to clarify pulmonary pathology and diagnose pulmonary embolism.25 In women who are still pregnant, careful decision-making about procedures that expose the patient to radiation is mandatory. A number of laboratory tests should be used in all AHF patients: full blood count, urea and electrolytes, blood glucose and CRP. Thyroid dysfunction should be excluded. In severe heart failure, additionally INR and arterial blood gas should be performed. Transaminases, urinalysis and plasma B-type natriuretic peptide (BNP) or NT-proBNP can be considered. Arterial blood gas analysis allows assessment of oxygenation (pO2), respiratory adequacy (pCO2), acid base balance (pH) and base deficit and should be performed in all patients with severe heart failure. Non-invasive measurement with pulse oximetry and end-tidal CO2 can often replace arterial blood gas analysis, but not in very low output, vasoconstricted shock states.26 In a study of 100 PPCM patients Sliwa et al documented a positive correlation between plasma CRP levels at baseline with LV end-diastolic (r=0.33, P=0.0026) and end-systolic (r=0.35, P=0.0012) diameters and inversely with LVEF (r=-0.27, P=0.015).30

BNP is released from the cardiac ventricles in response to increased wall stretch and volume overload and has been used to exclude or identify congestive heart failure (CHF) in patients.27 In normal pregnancies, median BNP values are <20 pg/mL, and stable throughout gestation. In comparison, plasma BNP levels are elevated in severe pre-eclampsia. This may reflect ventricular stress and/or subclinical cardiac dysfunction associated with pre-eclampsia.31
Decision-making cut-off points of 300 pg/ml for NT-proBNP and 100 pg/ml for BNP have been proposed. Various clinical conditions may affect the BNP concentration, e.g. renal failure and sepsicaemia. If elevated levels are detected, further diagnostic tests are required, but otherwise BNP has a good negative predictive value to exclude heart failure.\textsuperscript{3} It is important to note that the diagnosis of PPCM requires echocardiography and that increased levels of plasma BNP or NT-proBNP carry important prognostic information, but the exact role of BNP remains to be determined.\textsuperscript{30} Echocardiography is an essential tool for the evaluation of the functional and structural changes underlying or associated with AHF. The most important measurement of ventricular function is the left ventricular ejection fraction for distinguishing patients with cardiac systolic dysfunction from those with preserved systolic function. Echocardiography with Doppler imaging should be used to evaluate and monitor valvular structure and function, regional and global left and right ventricular function, possible pericardial pathology and mechanical complications. Cardiac output can be estimated by appropriate Doppler aortic or pulmonary time velocity contour measurements.\textsuperscript{29} An appropriate echo-Doppler study can also estimate pulmonary artery pressures and may indicate the presence of pulmonary embolus.

**Monitoring of patients in AHF**

Monitoring of the patient with AHF should be initiated as soon as diagnosis is established. The types and level of monitoring required for any individual patient vary widely depending on the severity of cardiac decompensation and the response to initial therapy.\textsuperscript{29}

Echocardiography is an essential tool for the evaluation of the functional and structural changes underlying or associated with AHF.

### Non-invasive monitoring:

In all critically ill patients, measurements of BP, temperature, respiratory rate, heart rate and ECG are mandatory. Some laboratory tests like electrolytes, creatinine, glucose, markers for infection or other metabolic disorders should be done at regular time intervals. Hypo- or hyperkalaemia must be controlled. Maintenance of normal blood pressure is critical and should be measured regularly until the dosage of vasodilators, diuretics or inotropes has been stabilised. A pulse oximeter should be used on any patient receiving oxygen. Cardiac output and preload can be monitored non-invasively by Doppler echocardiography as described before.\textsuperscript{29}

**Invasive monitoring:** Indications for the insertion of an indwelling arterial catheter are dictated by the need for either continuous beat-to-beat analysis of arterial blood pressure due to haemodynamic instability or the requirement for multiple arterial blood analyses. A central venous line is useful for delivery of fluids and drugs and can be used to monitor CVP and venous oxygen saturation.\textsuperscript{28}

**Present approaches towards treatment of heart failure in PPCM**

Treatment of acute heart failure in PPCM

In the absence of systematic studies comparing therapeutic approaches in PPCM, standard heart failure therapy should be initiated. In pregnant mothers careful attention must be paid to foetal safety and to excretion of drug or drug metabolites during breastfeeding after delivery. Collaboration among medical specialists, including obstetricians and cardiologists is essential.\textsuperscript{3} Treatment is directed toward symptomatic relief and improvement of cardiac function and similar to other forms of congestive heart failure. The maintenance of \( \text{SaO}_2 \) within the normal range (95-98\%) is important to maximise oxygen delivery to the tissues and tissue oxygenation, thus helping to prevent end-organ dysfunction and multiple organ failure. This is best achieved by first ensuring that there is a patent airway and then by administration of an increased \( \text{FiO}_2 \). Endotracheal intubation is indicated if these measures fail to improve tissue oxygenation. The use of CPAP and NIPPV in acute cardiogenic pulmonary oedema is associated with a significant reduction in the need for tracheal intubation and mechanical ventilation. Respiratory muscle fatigue is the most frequent reason for endotracheal intubation and mechanical ventilation in AHF. It may be diagnosed by decreased respiratory rate associated with hypercapnia and a confused state of mind. Invasive mechanical ventilation should only be used if acute respiratory failure does not respond to vasodilators, oxygen therapy and/or CPAP or NIPPV.\textsuperscript{29}

The administration of morphine is indicated during the early stage of treatment of patients with severe AHF, especially if associated with restlessness and dyspnoea. Morphine induces venodilation, mild arterial dilatation and a reduction in heart rate. Anticoagulation should be initiated unless contraindicated to avoid both venous and arterial thromboembolic events. Careful monitoring of INR and PTT is advised since auto-anticoagulation due to hepatic congestion may be present.

Vasodilators are indicated as first line therapy if hypoperfusion is associated with an adequate blood pressure and signs of congestion with low diuresis, in order to open the peripheral circulation and to lower pre-load. Angiotensin converting enzyme (ACE)-inhibitors are not indicated in the early stabilisation of patients with HF. Administration of diuretics is indicated in the presence of symptoms secondary to fluid retention. There has been no study to date with beta-blocker therapy in AHF targeted to acutely improve the condition. On the contrary such beta-blocker therapy is generally contraindicated in patients with AHF.

It is important to note that management will differ in women who are still pregnant since the threshold to perform X-rays or a CT scan will be much higher. Before the administration of drugs, contraindications during pregnancy need to be observed.
In patients with chronic heart failure, beta-blockers should be initiated when the patient has stabilised after the acute episode (usually after 4 days). Inotropic agents are indicated in the presence of peripheral hypoperfusion (hypotension, decreased renal function) with or without congestion or pulmonary oedema refractory to diuretics and vasodilators. In clinical experience, PPCM often shows remarkable spontaneous improvement. The decision for heart transplantation should therefore only be made very carefully, after all other options have been exhausted and sufficient time for recovery has been allowed.

Cardiac transplantation has been performed successfully in PPCM patients. Favourable outcomes have been attributed to the young age of the recipients and to the recent onset of heart failure, resulting in minimal end-organ damage. In view of the success that has been achieved by transplantation in these young and otherwise healthy mothers, aggressive measures such as temporary life support in form of cardiopulmonary bypass or a left ventricular assist device until availability of transplant have been advocated.

**Treatment of chronic heart failure in PPCM**

Angiotensin-converting enzyme-inhibitors are recommended as first-line therapy in patients with a reduced left ventricular systolic function less than 40–45% with or without symptoms, but are contraindicated during pregnancy because of teratogenicity. Vasodilator therapy reduces afterload and improves cardiac output, resulting in a reduction in left ventricular end-diastolic pressure and a decrease in pulmonary and systemic vascular resistances. Godsel et al viewed an ACE-inhibitor as the most valuable medication, not only because of its direct beneficial effects on the heart but also because of its potential benefit to interrupt the chain of events in the pathobiology of PPCM. ACE-inhibitors should be uptitrated to dosages shown to be effective in the large controlled trials in heart failure and not on symptomatic improvement alone.

Diuretics are essential for symptomatic treatment when fluid overload is present and manifest as pulmonary congestion or peripheral oedema, but their use should be carefully considered during pregnancy. In patients with chronic heart failure, diuretics should be administered in combination with ACE-inhibitors and beta-blockers if tolerated.

Beta-blockers should be considered for treatment of all patients with stable, mild, moderate and severe heart failure, unless there is a contraindication. Beta-blocker therapy reduces hospitalisations, improves the NYHA functional class and leads to decreased worsening of heart failure. The initial dose should be low and increased slowly and progressively to the target dose used in the large clinical trials. Carvedilol reduces the risk of death as well as the risk of hospitalisation for cardiovascular causes in patients with heart failure. Vasodilating beta-blockers such as carvedilol also reduce afterload through alpha-1 adrenergic blockade. Lowes et al reported functional improvement in IDCM patients related to treatment with beta-blockers and an association with changes in myocardial gene expression.

Beta-blocker treated patients who improved left ventricular ejection fraction had an increase in sarcoplasmatic reticulum calcium ATPase mRNA and alpha-myosin heavy chain mRNA and a decrease in beta-myosin heavy chain mRNA. Uptitration should be adapted to individual responses. Aldosterone receptor antagonists are recommended in addition to ACE-inhibitors, beta-blockers and diuretics in advanced heart failure (NYHA III–VI) with systolic dysfunction to improve survival and morbidity. In the RALES study, low doses of aldactone, added to standard of care for severe heart failure, improved survival by 30% and lowered hospitalisation by 35%. Angiotensin II receptor blockers (ARB) can be used as an alternative to ACE-inhibition in symptomatic patients intolerant to ACE-inhibitors to improve morbidity and mortality, but are also contraindicated during pregnancy.

Digoxin therapy is associated with an increased risk of death from any cause among women with heart failure and depressed left ventricular systolic function. Retrospective analysis of data from the DIG trial indicates a beneficial effect of digoxin on morbidity and no excess mortality in women at serum concentrations from 0.5 to 0.9 ng/ml, whereas serum concentrations > or =1.2 ng/ml seem harmful. The use of digoxin has not been studied in pregnant women and it is categorised as a class C drug. Digoxin is considered relatively safe to the foetus. However, peripartum monitoring of serum levels is advised.

While ACE-inhibitors and ARBs are contraindicated during pregnancy, hydralazine might be the vasodilator of choice although controversy exists. Among the vasodilators, nitrates are another alternative during pregnancy. It is important to note that various therapeutic modalities mentioned in the article have never been studied specifically in PPCM patients but in DCM patients.

Thromboembolic phenomena have been reported in PPCM patients. Pregnant patients are at an increased risk of thromboembolic complications due to the hypercoagulable state of late pregnancy that may persist up to six weeks postpartum. Left ventricular systolic dysfunction resulting in blood stasis, additionally predisposes patients to develop left ventricular, pulmonary and cerebral thromboemboli. The decision for anticoagulation should be made after careful consideration, that should include dilated left ventricular dimensions and low ejection fraction. It is important to stress that not all PPCM patients need to be anticoagulated. During the last weeks of pregnancy low-molecular heparin is the agent of choice while warfarin is preferred postpartum.

Maisch et al recommend heart catheterisation with the procurement of an endomyocardial biopsy to allow for a more precise diagnosis of the underlying cardiac process (inflammatory and/or viral vs autoreactive myocarditis or non-inflammatory or non-viral forms). But this is not an established routine procedure. Until a link between immunosuppressive therapy and resolution of myocarditis can be established in PPCM patients, the use of these agents is not recommended. In fact the benefit of immunosuppressive and antiviral therapy continues to be a debated issue.
Recommendations for delivery: If possible, pregnancy should be permitted to continue to term in PPCM patients diagnosed during the last month of gestation. A possible need for early delivery and the mode of delivery should be assessed in collaboration with obstetricians, cardiologists, and anaesthesiologists. Urgent delivery of the foetus may be considered for patients who present with advanced heart failure with haemodynamic instability. Patients with adequate cardiac output may tolerate induction and vaginal delivery. Critically ill patients who require inotropic therapy or mechanical support should undergo Caesarean delivery.  

Prognosis

Echocardiography is an important diagnostic tool in PPCM and may provide significant prognostic information with regards to recovery of cardiac function. End diastolic dimensions of 6 cm or greater at the time of diagnosis were associated with a more than three-fold higher risk for persistent left ventricular dysfunction.  

In a study from Haiti, Dorbala et al studied the left ventricular contractile reserve in seven PPCM patients duringdobutamine stress echocardiography and documented a correlation (r=0.79) with subsequent recovery of LV function.  

In a cohort of 100 patients from South Africa, Sliwa et al reported a mortality of 15% within a six months period. Baseline plasma levels of Fas/Apo-1 (OR=1.30, CI 95%=1.11-1.54) and NYHA FC (OR=2.88, CI 95%=1.10-7.53) were identified as independent predictors of death.  

In a study from the US, Elkayam et al reported that heart transplantation was performed in 4% of the PPCM patients. Maternal mortality of the PPCM patients was 9% within a period of 2.2 years and was described as sudden in four patients and as a result of complications from heart transplantation in two patients. Three per cent of the patients required implantation of an automatic implantable cardioverter-defibrillator, and 2% required implantation of a permanent pacemaker during the follow-up period. LVEF at the time of diagnosis was 29±11% and improved to 46±14% (P< or =0.0001) at follow-up. Normalisation of LVEF occurred in 54% and was more likely in patients with LVEF >30% at diagnosis.  

Felker et al found better survival rates in 51 PPCM patients than in patients with other causes of cardiomyopathy (n=1230) (adjusted hazard ratio for death, 0.31; 95% confidence interval, 0.09 to 0.98).  

In a study from Haiti, the ratio of PPCM deaths for the 5-year period was 47.1 per 100 000 births compared with the US ratio of 0.62 per 100 000 births. The mortality rate was 15.3% during a mean follow-up period of 2.2 years. Of the PPCM patients who were observed for at least 6 months, 28% regained normal left ventricular function. The difference in left ventricular echocardiographic features at diagnosis between deceased patients and survivors was not statistically significant, but a statistically significant difference occurred at diagnosis between the recovered and the non-recovered group for mean ejection fraction (28% vs. 23%; P<0.001) and fractional shortening (17% vs. 14%; P=0.004).  

Subsequent pregnancy  

One of the most common issues for women surviving an episode of PPCM is whether it is safe to become pregnant again. Appropriate birth-control measures are recommended. Oral contraceptives should be avoided due to the increased incidence of thromboembolism. However, the use of quarterly injections of depot hormone or other methods of preventive family planning need to be encouraged.  

If a subsequent pregnancy occurs, it should be managed in close collaboration between an obstetrician and a cardiologist. Most investigators agree that patients with PPCM and persistent left ventricular dilatation and dysfunction are at high risk for complications and death should they become pregnant again. Sliwa et al reported on six patients with a subsequent pregnancy in previous PPCM in a single centre study, resulting in reduction of ejection fraction by >10% in five patients at one month postpartum. Two patients with impaired ejection fraction and dilated left ventricular dimensions at onset of subsequent pregnancy died three months postpartum due to heart failure despite optimal medical therapy.  

In contrast, the issue of whether patients with PPCM and recovered left ventricular function can safely undergo a subsequent pregnancy remains controversial. Elkayam et al conducted a record review among members of the American College of Cardiology in the United States and one hospital in South Africa and described the outcome of 60 subsequent pregnancies in 44 women with a history of PPCM. Among the first subsequent pregnancies in the 44 women, 28 occurred among women, in whom left ventricular function had returned to normal (group 1) and 16 occurred in women with persistent left ventricular dysfunction (group 2). The pregnancies were associated with a reduction in mean left ventricular ejection fraction in each group (from 56 ±7% to 49 ±10% in group 1, p=0.002 and from 36±9% to 32±11% in group 2, p=0.08). During these pregnancies, a decrease of more than 20% in left ventricular ejection fraction occurred in 21% of women in group 1 and 25% of those in group 2, and symptoms of heart failure occurred in 21% of women in group 1 and 44% of those in group 2. The mortality rate was 0% in group 1 and 19% in group 2 (p=0.06). The likelihood of maternal death seems to be very low in women who recover their left ventricular function before a subsequent pregnancy.  

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**The South African Heart Association Travel Scholarship**

The travel scholarship is available to all SA Heart Association members and associate members. It is primarily intended to assist junior colleagues to ensure continued participation in local or international scientific meetings or workshops.

**Requirements**
- Applicants must be fully paid up members/associate members in good standing for at least two years.
- Applications must include:
  - full details of the meeting/workshop
  - an abbreviated CV of the applicant
  - a breakdown of the expected expenses
- Applications must reach the Association a minimum of three months before the event to be attended.

**Recommendations**
- Acceptance of an abstract at the scientific meeting to be attended
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- Publications in a peer-reviewed journal in the preceding year
- Applicants from a previously disadvantaged community
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