Peripartum cardiomyopathy

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Objective: To provide a review of the cardiac and obstetrical literature regarding the development of peripartum cardiomyopathy and, in particular, to examine risk factors, incidence, diagnosis, prognosis, and evidence-based treatment modalities.

Design: An extensive review of the current literature.

Results: Peripartum cardiomyopathy is a cardiomyopathy of unknown cause that occurs in pregnant females, most commonly in the early postpartum period. It shares many clinical characteristics with idiopathic dilated cardiomyopathy but occurs at a younger age and is associated with a better prognosis. Diagnosis is based upon the clinical presentation of congestive heart failure and objective evidence of left ventricular systolic dysfunction. Conventional pharmacologic therapy for congestive heart failure, such as diuretics, digoxin, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, and β-adrenergic blockers, are routinely used and are quite effective. For those patients who remain refractory to conventional pharmacologic therapy, cardiac transplantation and mechanical circulatory support are viable options.

Conclusion: Mortality rates in peripartum cardiomyopathy have decreased, and this is most likely related to advances over the past 5 yrs in medical therapy for heart failure. Aggressive use of implantable defibrillators has significantly reduced the risk of sudden death in these patients. For >50% of peripartum cardiomyopathy patients, left ventricular function normalizes with pharmacologic therapy. However, subsequent pregnancies almost always are associated with recurrence of left ventricular systolic dysfunction. (Crit Care Med 2005; 33[Suppl.]:S340–S346)

KEY WORDS: dilated cardiomyopathy; acute inflammatory myocarditis; endomyocardial biopsy; gestational hypertension; twin pregnancies; left ventricular systolic dysfunction; implantable defibrillators; angiotensin-converting enzyme inhibitors; mechanical circulatory support; cardiac transplantation

Cardiomyopathy associated with pregnancy was first described in 1937 (1). Peripartum cardiomyopathy is now defined as cardiomyopathy that develops in the last gestational month of pregnancy or in the first 5 months after delivery, with no identifiable cause for heart failure in the absence of heart disease (2). It occurs in 1 in 3,000 to 1 in 15,000 live deliveries in the United States, but its prevalence is much higher in Africa (1 in 3,000) and Haiti (1 in 350) (3–5). The natural history of peripartum cardiomyopathy is variable and its clinical presentation quite heterogeneous (6). It occurs more frequently in older women, obese females, and multiparous mothers having twin pregnancies (7). Other risk factors include preeclampsia and severe hypertension during pregnancy. Patients frequently present with systemic and pulmonary congestion, low cardiac output, cardiac arrhythmias, and systemic and pulmonary embolization (8).

Less frequently, cardiomyopathy can present for the first time earlier in pregnancy. There are, however, a few distinct clinical differences between patients with peripartum cardiomyopathy and those with cardiomyopathy diagnosed earlier in pregnancy. This includes a higher frequency of twin pregnancies and a shorter duration of pregnancy in patients who develop cardiomyopathy early in pregnancy. Left ventricular ejection fraction, though, improves similarly in the two groups (mean ± SE, 23 ± 28 months). In over half (54%) of these patients, normal left ventricular function (ejection >50%) is restored. The improvement in ejection fraction is significantly greater among patients with a left ventricular ejection fraction of >30% at the time of initial diagnosis. Maternal mortality is also similar in the two groups, although birth weight is significantly lower in the group diagnosed with cardiomyopathy earlier in pregnancy (Table 1) (9). It must be borne in mind that cardiomyopathy that occurs earlier in pregnancy may represent previously undiagnosed heart disease that is uncovered by the hemodynamic burden that occurs during pregnancy. A more likely hypothesis is that early presentation of symptoms represents a different spectrum of the same condition. It is important for clinicians to be aware of this so that unnecessary delays in diagnosis can be avoided and appropriate therapy can be prescribed in a timely fashion.

ETIOLOGY AND ASSOCIATED FACTORS

The etiology of peripartum cardiomyopathy is unknown. Many hypotheses have been suggested, including viral myocarditis, immune-mediated injury, selenium deficiency, and the hemodynamic stress of pregnancy (10–13). Acute inflammatory myocarditis has been reported to occur in peripartum cardiomyopathy, although the incidence of inflammation is variable. O'Connell et al. reported acute inflammatory myocarditis in 29% of patients with peripartum cardiomyopathy (10), whereas Midei noted this finding in 78% of patients (14). More recently, Rizeq noted acute inflammation in <10% of patients, which is similar to the rate seen among patients with idiopathic dilated cardiomyopathy (15).

This variability is mainly related to differences in the timing of endomyocar-

Table 1. Clinical characteristics of patients with peripartum cardiomyopathy and cardiomyopathy that develops early in pregnancy

Parameter	Patient Group Values		p Value
	Peripartum Cardiomyopathy (n = 100)	Cardiomyopathy Early in Pregnancy (n = 23)	
Mean age, yrs, ± SD	30.7 ± 6.4 (16–43)	30 ± 6 (20–44)	.67
Age >30 yrs, %	58	49	.36
White race, %	67	65	.8
Gravidity	2.6 ± 2.2	2.5 ± 1.7	.83
Parity	2.1 ± 1.7	1.9 ± 1.5	.64
Hypertension, %	43	30	.56
Twin pregnancy, %	13	26	.009
Tocolytic therapy	19	26	.5
Cesarean delivery, %	40	43	1.0
Duration of Pregnancy, wks	37.7 ± 3.5	32.4 ± 6.2	.00001
LVEF at diagnosis, %	28.8 ± 11.2	26.6 ± 10.5	.4
LVEF at last follow-up, %	46 ± 14.4	43.8 ± 15.6	.54
Birth weight, g	3092 ± 745	2238 ± 949	.0002
Maternal morbidity, %	9	13	.7

LVEF, left ventricular ejection fraction.
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dial biopsy (incidence of inflammation is higher in patients biopsied earlier after initial presentation) and whether strict criteria (Dallas criteria) were applied during histologic diagnosis. Furthermore, the presence or absence of inflammation has not been useful in predicting outcome of peripartum cardiomyopathy (16). During pregnancy, fetal cells cross the placenta into the maternal circulation. These are not destroyed because of the depressed immunologic state in the mother during pregnancy or because of the weak immunogenicity of the paternal haplotype of the chimeric antigen. The immunologic rebound that occurs during the terminal phase of gestation and the early postpartum period then attacks the chimeric cells in the myocardium (6). This immune reaction can be exacerbated by previous exposure to paternal major histocompatibility antigens through prior pregnancies.

Twin pregnancies are observed in 13% of patients with peripartum cardiomyopathy, which is significantly higher than the 1% to 2% rate noted among healthy women (17). Ansari et al. found high titers of autoantibodies against normal human cardiac tissue proteins in patients with peripartum cardiomyopathy that were not present in a comparable group with idiopathic dilated cardiomyopathy (11). Additional evidence for an immune hypothesis comes from the presence of antimyosin antibodies, adenine nucleotide translocator (ANT), and branched-chain α-ketoacid dehydrogenase in patients with peripartum cardiomyopathy,

in comparison with control subjects (18). All immunoglobulins of the G subclass are upregulated in peripartum cardiomyopathy. Immunoglobulin G3–positive patients have a higher New York Heart Association (NYHA) class and more advanced symptoms at initial presentation (19).

Peripartum cardiomyopathy can occur at any age but generally occurs in women over the age of 30 yrs. It is observed in all races, and even though multiparity is a risk factor, up to half the cases of peripartum cardiomyopathy are observed in association with the first pregnancy or the first two pregnancies (18). There is a strong association between peripartum cardiomyopathy and gestational hypertension. The incidence of gestational hypertension in peripartum cardiomyopathy is approximately 43%, which is substantially higher than the 8% to 10% incidence in the overall pregnant population. This observation raises the question of whether the hemodynamic stress of gestational hypertension may be the cause of heart failure that is seen in patients with peripartum cardiomyopathy. However, the fact that heart failure rarely develops in patients who develop hypertension associated with coarctation of aorta and that no alterations of left ventricular systolic function are generally observed in pregnant women with preeclampsia argues against this hypothesis (20).

Peripartum cardiomyopathy is associated with a higher incidence among patients who have received tocolytic ther-

apy (sympathetic agents). This association is probably a reflection of the increased incidence of premature labor that is seen in these patients (21). There is a high rate of cesarean delivery among patients with peripartum cardiomyopathy (40%), in comparison with the national rate of 22% and the rate of 29% for patients with known heart disease. Potential reasons include their high incidence of gestational hypertension, twin pregnancies, and older maternal age. These same reasons may also explain the higher observed rate of preterm delivery among peripartum cardiomyopathy patients than among healthy women (9).

DIAGNOSIS

The presentation of peripartum cardiomyopathy is similar to that of other types of dilated cardiomyopathies. Most patients present in NYHA class III or IV functional status (22). Patients who present early after delivery often have dramatic symptoms and signs of congestive heart failure. However, the diagnosis is frequently difficult and challenging during the late stages of pregnancy and early postpartum because of overlap with symptoms of pregnancy.

The presence of congestive heart failure should be considered in females who have dyspnea, orthopnea, persistent weight retention or weight gain, peripheral edema, nocturnal cough, and profound fatigue postpartum. Systemic and pulmonary embolization is seen more frequently in patients with peripartum

cardiomyopathy than in those with other forms of cardiomyopathies. The diagnostic workup should focus on ruling out other causes of cardiomyopathies. Evaluation of left ventricular size and left ventricular systolic function noninvasively with echocardiography, as well as hemodynamic assessment and evaluation of coronary anatomy by cardiac catheterization, is important. The role of routine endomyocardial biopsy in the diagnosis of peripartum cardiomyopathy is presently controversial and not standard practice (6).

O'Connell compared clinical characteristics of 14 patients with peripartum cardiomyopathy to those of 55 patients with primary dilated cardiomyopathy (10). The peripartum cardiomyopathy patients were younger, had a shorter duration of symptoms, a higher frequency of acute inflammatory myocarditis on endomyocardial biopsy, and a higher rate of improvement with medical therapy than did patients with primary dilated cardiomyopathy. No differences in left ventricular size, left ventricular ejection fraction, hemodynamics, incidence of arrhythmias, or mortality were noted between the two groups.

PROGNOSIS

The outcome of peripartum cardiomyopathy is variable. The maternal morbidity rate recently reported was 9%, with a 14% rate of death or cardiac transplantation (9). This is substantially lower than the 32% 6-month mortality reported by Sliwa et al., in their series from South Africa in 2000 (23). The decrease in this observed mortality might be related to improvements in medical therapy for heart failure over the past 5 yrs. Since over half the patients with peripartum cardiomyopathy die suddenly, the improvement in mortality might also be related to the aggressive use of implantable defibrillators for primary prevention against sudden death in this population.

In >50% of patients with peripartum cardiomyopathy the left ventricular ejection fraction normalizes, and this improvement generally occurs during the first 6 months of presentation. If the left ventricular ejection fraction is >30% at initial presentation, the probability of the left ventricular systolic function normalizing is high. Even among patients whose resting left ventricular systolic function normalizes, the contractile reserve of the left ventricle when challenged with do-

butamine frequently remains diminished (24). Among patients who do not demonstrate an increase in left ventricular ejection fraction by 6 months after delivery, the prognosis is poor, and mortality is 85% at 5 yrs. The factors that indicate a poor prognosis in peripartum cardiomyopathy include a lower left ventricular ejection fraction at 6 months after delivery, larger left ventricular end diastolic dimension, clinical presentation that is >2 wks postpartum, age >30 yrs, African-American descent, and multiparity.

Advice regarding subsequent pregnancies for patients who have complete recovery of left ventricular function is controversial (25). All females with peripartum cardiomyopathy, including those whose left ventricular function normalizes, experience a significant decrease (>10%) in left ventricular function during subsequent pregnancies (26). Patients who do not experience complete recovery of ventricular function should be counseled against subsequent pregnancies. Patients who recover normal resting function and have normal left ventricular contractile reserve after dobutamine challenge may undertake another pregnancy safely. However, patients who have normal resting left ventricular function but diminished contractile reserve should also be counseled against subsequent pregnancies (6).

TREATMENT

The treatment of peripartum cardiomyopathy is similar to the treatment of acute and chronic heart failure due to other causes of left ventricular systolic dysfunction. Patients who present with profound symptoms, acute respiratory failure, supraventricular or ventricular arrhythmias, syncope, or pulmonary or systemic emboli should be hospitalized. A careful bedside clinical assessment can frequently help identify the hemodynamic profile in most patients (Fig. 1). Signs of congestion that indicate high cardiac filling pressures include jugular venous distension, rales or pleural effusion, hepatic enlargement, ascites, and peripheral edema. Signs of diminished perfusion that indicate a low cardiac output include cool extremities, hypotension, decreased pulse pressure, renal and hepatic insufficiency, and mental status changes (27). Patients in cardiogenic shock will require invasive hemodynamic monitoring.
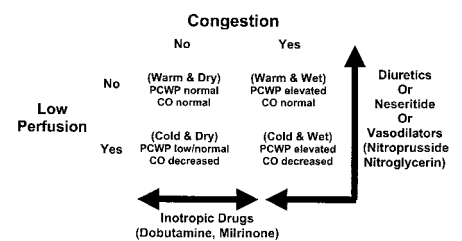

Figure 1. Bedside clinical assessment in acute heart failure (*PCWP*, pulmonary artery occlusion pressure; *CO*, cardiac output). Signs of low perfusion: cool extremities, hypotension, decreased pulse pressure, renal and hepatic insufficiency, and mental status changes. Signs of congestion: jugular venous distension, rales on auscultation, pleural effusion, hepatic enlargement, ascites, and peripheral edema.

MANAGEMENT OF ACUTE HEART FAILURE

Table 2 shows aspects of management of acute heart failure. Patients who are congested but have adequate perfusion will require treatment with intravenous diuretics alone or in combination with vasodilators such as nitroglycerin, nitroprusside, or neseritide (28–30). Patients with diminished perfusion will in addition require augmentation of their cardiac output with inotropic drugs such as intravenous dobutamine or milrinone (31, 32). Immediately following stabilization, patients should start treatment with an angiotensin-converting inhibitor if the diagnosis is made postpartum (33, 34). Angiotensin-converting enzyme inhibitors are contraindicated during pregnancy because of fetal anomalies that result in high fetal morbidity and even death (35). Patients intolerant of angiotensin-converting enzyme inhibitor due to cough could be treated with an angiotensin-receptor blocker (33). Patients who are intolerant of both these classes of drugs because of angioedema, hyperkalemia, or worsening renal function could be treated with a combination of hydralazine and isosorbide dinitrate (36). Once the patient is compensated and withdrawn from parenteral treatments, b-adrenergic blocker therapy should be initiated (33). If systemic or pulmonary emboli are documented, the patient should undergo anticoagulation.

The role of immune modulatory therapy in peripartum cardiomyopathy is not clear. Since an immune pathogenesis has been postulated, it is rational to consider immune modulation with immunoglob-

Table 2. Management of acute heart failure in peripartum cardiomyopathy

Pharmacologic therapy
  Diuretics
  Nitroglycerin
  Nitroprusside
  Neseritide
  Dobutamine
  Milrinone
  Heparin
Immune modulatory therapy
  Immunoglobulin (inconclusive evidence)
Mechanical circulatory support
  Intraaortic balloon counterpulsation
  Ventricular assist device
Cardiac transplantation

ulin, which has well-characterized anti-idiotype properties (37). The therapeutic effects of immunoglobulin therapy are well proven in immune thrombocytopenic purpura and Guillain-Barre syndrome (38). In a pilot trial, six women with peripartum cardiomyopathy were treated with intravenous immunoglobulin (2 g/kg), and their clinical outcomes were compared with those of 11 historical control patients who did not receive immune modulation (39). The two groups did not differ in age, parity, time from gestation to presentation, baseline left ventricular size, or ejection fraction. After a follow-up of 6.1 ± 2.9 months, it was noted that in the group that received immunoglobulin therapy the left ventricular ejection fraction improved significantly more than in the group not receiving immune modulation (increase of $26 \pm 8\%$ vs. $13 \pm 13\%$; $p = .042$).

These data have not been verified in a large, prospective clinical trial. Both immunosuppressive and immune modulatory therapies have not been shown to have consistent benefit in patients with acute cardiomyopathy and acute myocarditis. In a multicenter, randomized, controlled trial, intravenous immunoglobulin therapy did not significantly improve left ventricular ejection fraction or survival when compared with placebo in patients with acute cardiomyopathy (40). Likewise, immunosuppression with cyclosporine and prednisone failed to improve outcomes in comparison with standard therapy in a prospective, multicenter treatment trial in patients with acute myocarditis (41).

For patients who remain in shock despite aggressive medical therapy, additional therapies to maintain circulatory support and organ perfusion should be considered. Intra-aortic balloon counterpulsation is helpful acutely, although the

augmentation of cardiac output is seldom sustained. Long-term (>3 days) benefit of balloon counterpulsation is offset by the risk of line sepsis and limb ischemia. Surgical support with ventricular assist devices may be needed in appropriately selected patients. Frequently, both right and left ventricular assist device support is necessary because of biventricular dysfunction.

Cardiac transplantation should be considered for appropriate candidates (42, 43). In patients listed for transplantation, mechanical support may be necessary as a "bridge" until a suitable donor becomes available. Recovery of myocardial function can occur in some patients (approximately 15%) with peripartum cardiomyopathy on ventricular assist device support. In these patients, weaning from mechanical support is feasible and transplantation can be avoided. Assessments of ventricular function noninvasively with echocardiography and exercise tolerance testing and invasively with hemodynamic measurements should be made for device-supported patients to look for functional recovery.

If possible, pregnancy should be permitted to continue to term in patients with peripartum cardiomyopathy diagnosed in the last month of gestation. Urgent delivery of the fetus may be considered for patients who present with advanced heart failure with hemodynamic instability in the last month of gestation. The mode of delivery depends upon the hemodynamic status and obstetrical factors (22). Patients with adequate cardiac output may tolerate induction and vaginal delivery. However, patients who are critically ill and require inotropic therapy or mechanical support should undergo cesarean delivery.

MANAGEMENT OF CHRONIC HEART FAILURE

Table 3 shows aspects of management of chronic heart failure. Patients with peripartum cardiomyopathy who do not require hospitalization and those who are discharged home after treatment of their acute decompensation will require management similar to that for other patients with chronic heart failure. Dietary restrictions and lifestyle changes are important and complement appropriate pharmacologic therapy. Lifestyle modifications are often challenging and difficult because of anxiety related to the care of the newborn. Sodium restriction (2-g so-

Table 3. Management of chronic heart failure in peripartum cardiomyopathy

General measures
  Sodium and fluid restriction
  Smoking cessation
  Weight loss
  Exercise
Treatment of coexistent conditions
  Anemia
  Thyroid disease
  Diabetes
  Hypertension
  Nutritional deficiencies
Pharmacologic therapy
  Diuretics
  Digoxin
  Angiotensin-converting enzyme inhibitors
  Angiotensin-receptor blockers
  Hydralazine and isosorbide dinitrate
  β-Adrenergic blockers
  Aldosterone antagonists
  Pentoxifylline (inconclusive evidence)
  Warfarin
  Amiodarone
  Sotalol
Device therapy
  Implantable defibrillators
  Cardiac resynchronization therapy
Cardiac transplantation

dium diet) and fluid restriction (≤ 2 L in 24 hrs) are important, particularly in patients with NYHA class III and IV symptoms. Smoking cessation and avoidance of alcohol should be strongly emphasized. Weight loss if necessary and regular exercise are also important. Since many of the pharmacologic agents used in the management of chronic heart failure are secreted in the breast milk, breast-feeding of the newborn should be avoided. Optimal treatment of coexisting conditions such as anemia, thyroid disease, and diabetes is very important. Nutritional deficiencies such as selenium deficiency, if present, should be corrected appropriately.

Pharmacologic management of chronic heart failure should follow published evidence-based guidelines (33). Diuretics should be prescribed for symptom relief, if there are symptoms of systemic or pulmonary congestion. Generally, NYHA Class III and IV patients need chronic diuretic therapy. Careful monitoring of electrolyte balance and renal function is very important in all patients receiving chronic diuretic therapy. Loop diuretics should be used with caution in the last month of gestation.

Angiotensin-converting enzyme inhibitors are recommended for all patients. These drugs improve symptoms, functional class, ejection fraction, exer-

cise tolerance, and quality of life. They prevent progressive ventricular remodeling and hospitalizations and improve survival. Doses of angiotensin-converting enzyme inhibitors should be titrated as tolerated, as higher doses have greater hemodynamic benefit and can be particularly useful for blood pressure control in patients who also have gestational hypertension.

Patients who are intolerant of angiotensin-converting inhibitors because of cough should be prescribed angiotensin-receptor blockers. If there is intolerance of both angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers due to hyperkalemia, angioedema, hypotension, or renal insufficiency, the combination of hydralazine and isosorbide dinitrate is a useful alternative. Recently, the addition of hydralazine and isosorbide dinitrate to background angiotensin-converting enzyme inhibitor therapy was shown to further improve survival in African-American patients with chronic heart failure and NYHA class II and III symptoms (44).

Since chronic angiotensin-converting enzyme inhibitor therapy results in the "escape" of angiotensin II production through alternate pathways (chymases), it has been suggested that adding angiotensin-receptor blockers to the regimens of patients receiving chronic angiotensin-converting enzyme inhibitor therapy can result in sustained inhibition of the renin-angiotensin system. Indeed, the addition of angiotensin-receptor blockers to treatment regimens for patients of NYHA class II and III who are receiving angiotensin-converting enzyme inhibitors has been shown to improve outcomes.

Digoxin is recommended for patients with NYHA class II and III symptoms. It improves symptoms, exercise tolerance, and ejection fraction but has no effect on survival. Since it has a narrow therapeutic-to-toxic window, it must be used cautiously. Aldosterone antagonists are recommended for patients with NYHA class III and IV symptoms. These drugs improve survival but have limited effect on symptoms. In patients receiving angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers, the addition of aldosterone antagonists can result in dangerous hyperkalemia and renal insufficiency. Caution must therefore be exercised, and serum electrolytes and renal function should be monitored closely.

b-Adrenergic blockers are recommended for all patients with peripartum cardiomyopathy. These drugs improve symptoms, ejection fraction, and survival. They prevent progressive ventricular remodeling and hospitalization. Both the nonselective b-blocker carvedilol and the long-acting selective b-1-blocker metoprolol succinate are approved by the U.S. Food and Drug Administration for use in chronic heart failure in the United States. Approximately 15% of patients are intolerant of b-adrenergic blocker therapy. The doses of these drugs should be titrated cautiously, with careful scrutiny of blood pressure, heart rate, and signs of worsening heart failure.

Inhibitors of inflammatory cytokines may have a role in the treatment of patients with peripartum cardiomyopathy. Tumor necrosis factor-α levels are elevated in patients with peripartum cardiomyopathy. Pentoxifylline, a xanthine-derived inhibitor of tumor necrosis factor-α, has been evaluated in a prospective controlled trial in 59 peripartum cardiomyopathy patients (45). The group that received pentoxifylline, 400 mg three times a day, in addition to standard therapy had a significantly better clinical outcome than the group treated with standard therapy alone. Clinical outcome evaluated was a combined end point of death, failure of left ventricular ejection fraction to improve >10%, and persistent NYHA class III or IV symptoms during follow-up. Treatment with pentoxifylline was a significant independent predictor of outcome in this trial. For patients with other forms of cardiomyopathy, treatment with anticytokine agents has not been shown to improve clinical outcomes. Therefore, the role of pentoxifylline and other anticytokine agents in peripartum cardiomyopathy requires additional evaluation.

Anticoagulation is recommended if there is a documented history of systemic or pulmonary embolism or if the patient is in atrial fibrillation (6). Warfarin should not be prescribed during pregnancy, and its use should be monitored closely. Arrhythmias should be treated aggressively, particularly if they are associated with symptoms. b-adrenergic blockers are often adequate for treating supraventricular arrhythmias. Sometimes, calcium channel blockers such as diltiazem and class III anti-arrhythmic agents such as sotalol or amiodarone may be needed. Calcium channel blockers are negatively inotropic drugs and can decompensate a stable patient. Their chronic use is therefore not recommended. Sotalol and amiodarone have many systemic side effects during chronic use, and this should be carefully considered before they are prescribed.

In appropriate patients, electrical cardioversion may be necessary. Transesophageal echocardiography is often needed before electrical cardioversion to rule out the presence of a left atrial thrombus. Ventricular arrhythmias are frequently life-threatening and should be managed aggressively. The use of class I and class II antiarrhythmic agents is not recommended because these drugs are poorly tolerated and proarrhythmic. Again, class III antiarrhythmic drugs such as sotalol and amiodarone are useful options. Patients with symptomatic ventricular arrhythmias are candidates for defibrillator implantation (46). Also, patients who remain in persistent NYHA class III or IV heart failure despite optimal pharmacologic therapy for 6 months and who have a left ventricular ejection fraction of <30% may be candidates for defibrillator implantation for primary prevention against cardiac death.

If ventricular dys-synchrony is present, as manifested by a QRS duration that exceeds 130 milliseconds on a surface 12-lead electrocardiogram, consideration should also be given to implantation of a cardiac resynchronization therapy device. Cardiac resynchronization therapy improves symptoms, exercise tolerance, ejection fraction and survival in appropriate candidates. In addition, this therapy causes reverse remodeling of the left ventricle and improves survival. Chronic heart failure patients who remain in persistent NYHA class IV that is refractory to all medical therapy and have a severely depressed left ventricular systolic function may be candidates for cardiac transplantation. In this group of patients, implantation of a ventricular assist device should be considered as a "bridge" to cardiac transplantation, if deemed necessary. Generally, cardiac transplantation in patients with peripartum cardiomyopathy is associated with excellent survival (88% at 2 yrs and 78% at 5 yrs), similar to that for patients with idiopathic dilated cardiomyopathy. However, higher rates of rejection requiring augmentation of immunosuppression are seen early after transplantation in these patients. Infection risk is also higher because of the need to use aggressive immunosuppression protocols (43).

FOLLOW-UP

Follow-up of patients with peripartum cardiomyopathy is similar for patients with other forms of cardiomyopathy and left ventricular systolic dysfunction. Echocardiography should be repeated at 3 and 6 months after diagnosis to evaluate functional recovery. Subsequent serial assessments of left ventricular function at least annually are recommended. Measurement of inotropic contractile reserve during dobutamine-stress echocardiography has been shown to accurately correlate with subsequent recovery of left ventricular function (24). Patients with no recovery or incomplete recovery of ventricular function should be committed to life-long pharmacologic therapy for chronic heart failure. However, patients who recover completely and stay recovered for a year may have their drug therapy gradually withdrawn, with careful monitoring of their ventricular function by echocardiography.

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