Editorials

Peripartum Cardiomyopathy

PERIPARTUM cardiomyopathy is a poorly understood condition whose incidence in the United States is 1 per 3000 to 4000 live births.[1] Previous descriptions of the disorder were based on a vague definition derived from a heterogeneous group of patients,[2] but in 1997, the participants in a National Heart, Lung, and Blood Institute (NHLBI) workshop agreed on a standardized definition.[3] Peripartum cardiomyopathy was defined clinically as the onset of cardiac failure with no identifiable cause in the last month of pregnancy or within five months after delivery, in the absence of heart disease before the last month of pregnancy. The finding of left ventricular systolic dysfunction by echocardiography is an important criterion for making the diagnosis. Stricter echocardiographic criteria have been recommended (a left ventricular ejection fraction of less than 45 percent, fractional shortening of less than 30 percent on an M-mode echocardiographic scan, or both, and a left ventricular end-diastolic dimension of more than 2.7 cm per square meter of body-surface area).[4]

The outcome of patients with peripartum cardiomyopathy is highly variable. In some patients, the clinical and echocardiographic status improves rapidly and returns to normal, and the initial severity of the left ventricular systolic dysfunction or dilatation is not necessarily predictive of the long-term functional outcome.[5] In contrast, some patients with this disorder deteriorate rapidly, do not have a response to medical therapy, and require cardiac transplantation[6] or die. Still others have persistent evidence of cardiac dysfunction, and a few have a slow return to normal cardiac function over several years.

In this issue of the *Journal,* the study by Elkayam et al.[7] attempts to answer important questions regarding the outcome of subsequent pregnancies in women with peripartum cardiomyopathy. The researchers sent questionnaires to members of the American College of Cardiology and others and, after obtaining consent, reviewed the medical records of women who had subsequent pregnancies after a diagnosis of peripartum cardiomyopathy. The authors concede that their data, obtained by a retrospective survey, may be incomplete and may be influenced by ascertainment bias and other forms of bias. Few cardiologists responded, and the authors reviewed the records of fewer than half of the identified patients. Except for a left ventricular ejection fraction of less than 40 percent, the criteria they used for the diagnosis of peripartum cardiomyopathy are broader than those that were recently recommended.[3] Their study included women with heart failure that developed during the last six months of pregnancy (not just the last month), and they did not exclude women who had had recognizable heart disease before the last month of pregnancy.

Nevertheless, some useful information emerged. Women with peripartum cardiomyopathy had a reduction in left ventricular systolic function during subsequent pregnancies, and this reduction was greater in the women with persistent left ventricular dysfunction at the start of these pregnancies. Furthermore, symptoms of heart failure developed in about 20 percent of the women whose systolic function was normal at the start of the subsequent pregnancy and in almost half the women who had persistent left ventricular dysfunction. The women who died were in the group with persistent cardiac dysfunction, and the frequency of premature birth was higher in this group.

The reason for the deterioration in systolic function in women with a history of peripartum cardiomyopathy who have subsequent pregnancies is unknown. During a normal pregnancy, cardiac output increases substantially, and there is a decrease in systemic vascular resistance, with a 5 to 10 percent increase in the ventricular ejection fraction.[8] There is also reversible cardiac remodeling that is associated with cardiovascular volume overload and that results in the gradual dilatation of all four cardiac chambers.[9] A clue to the cause of the observed deterioration in cardiac function may come from Lampert et al.,[10] who, with the use of dobutamine echocardiography, reported impaired contractile reserve in patients who had appeared to recover from peripartum cardiomyopathy and who had normal ventricular function at rest. Thus, the hemodynamic stress of a pregnancy may unmask impaired contractile reserve that is not apparent at rest.

Patients with peripartum cardiomyopathy are generally treated in the same way as other patients with heart failure. Salt restriction is recommended. Diuretics are used to decrease pulmonary congestion and volume overload. In patients with systolic dysfunction, afterload is usually reduced with vasodilating drugs. Because of the adverse effect of angiotensin-converting–enzyme (ACE) inhibitors in pregnancy, hydralazine is the vasodilator of choice for use before delivery. In the postpartum period, an ACE inhibitor is frequently given. Because of the association between impaired cardiac function and the prothrombotic state of pregnancy, patients with peripartum cardiomyopathy are at increased risk for thromboembolic events, and anticoagulant therapy is often indicated. After delivery, warfarin may be used. If anticoagulant therapy is needed before delivery or for short-term use, unfractionated heparin may be administered, and the dose may be adjusted according to the partial-thromboplastin time. Low-molecular-weight heparins have been used widely in pregnancy for the treatment of venous thrombosis and have the advantages of ease of dosing and reduced risks of thrombocytopenia and osteopenia.[11] It is likely that the use of low-molecular-

weight heparins will increase in patients with peripartum cardiomyopathy, although guidelines for their use have not yet been established. For patients with severe myocardial dysfunction, the use of an intraaortic balloon pump or a left ventricular assist device may be needed as a bridge until myocardial recovery occurs or cardiac transplantation is performed.

Felker et al.[12] reported that during long-term follow-up, women with peripartum cardiomyopathy appear to have a better survival rate (94 percent at five years) than patients with cardiomyopathy due to other causes. Neither their sex nor their younger age accounted for the better outcome. In this series,[12] a higher proportion of patients with peripartum cardiomyopathy had histologic evidence of myocarditis on endomyocardial biopsy (26 of 51 patients) than in other reports.

In women who have had peripartum cardiomyopathy, echocardiography should be repeated six months after the diagnosis was made to assess the extent of recovery of systolic function. There are currently no data to suggest that earlier echocardiographic imaging would contribute additional prognostic information or that earlier recovery of ventricular dysfunction diminishes the risk associated with a subsequent pregnancy. The persistence of cardiac dysfunction 6 to 12 months after the initial diagnosis of peripartum cardiomyopathy usually indicates an irreversible problem and almost always represents an absolute contraindication to a subsequent pregnancy. It is, however, a challenge to predict whether the health of an individual woman who has had peripartum cardiomyopathy will deteriorate during a subsequent pregnancy.

It is not currently possible to identify the small group of women in whom systolic ventricular function has returned to normal post partum who may tolerate a subsequent pregnancy without serious complications. Any such woman who becomes pregnant should be monitored with echocardiography, and an understanding should be reached that the pregnancy should be terminated if ventricular function deteriorates and increases the woman's risk to an unacceptable degree. It is possible that in the future the routine assessment of contractile reserve might allow clinicians to stratify women more accurately according to their risk. On the other hand, it is clear that patients with persistent left ventricular dysfunction have an unacceptably high risk of cardiac complications and death during subsequent pregnancies and should be counseled not to become pregnant.

We agree with the recommendations of the NHLBI working group[3] that an international registry should be established with the use of a strict definition of peripartum cardiomyopathy. This would allow prospective clinical documentation, the determination of risk factors and prognostic variables, the assessment of whether measurements of contractile reserve are useful, and the establishment of a serum and tissue bank to explore the pathogenesis of peripartum cardiomyopathy. The study by Elkayam et al. is a commendable attempt to systematize the knowledge available thus far and to draw reasoned and helpful conclusions that may aid in the treatment of patients with this rare and poorly understood but potentially fatal condition.

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THE POWERFUL PLACEBO AND THE WIZARD OF OZ

SOME myths really ought to be true. We react with surprise and pleasure when we encounter them and then believe them when they neatly and comfortably help to explain some confusing aspect of our world. Thereafter, evidence against them is unwelcome and not to be trusted. But some such myths are flawed and misleading.

John Snow has been widely credited with stopping a cholera epidemic in 1854. He noticed that the dis-