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Clinical Outcomes for Peripartum Cardiomyopathy in North America

Results of the IPAC Study (Investigations of Pregnancy-Associated Cardiomyopathy)

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ABSTRACT

BACKGROUND Peripartum cardiomyopathy (PPCM) remains a major cause of maternal morbidity and mortality.

OBJECTIVES This study sought to prospectively evaluate recovery of the left ventricular ejection fraction (LVEF) and clinical outcomes in the multicenter IPAC (Investigations of Pregnancy Associated Cardiomyopathy) study.

METHODS We enrolled and followed 100 women with PPCM through 1 year post-partum. The LVEF was assessed by echocardiography at baseline and at 2, 6, and 12 months post-partum. Survival free from major cardiovascular events (death, transplantation, or left ventricular [LV] assist device) was determined. Predictors of outcome, particularly race, parameters of LV dysfunction (LVEF), and remodeling (left ventricular end-diastolic diameter [LVEDD]) at presentation, were assessed by univariate and multivariate analyses.

RESULTS The cohort was 30% black, 65% white, 5% other; the mean patient age was 30 ± 6 years; and 88% were receiving beta-blockers and 81% angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. The LVEF at study entry was 0.35 ± 0.10, 0.51 ± 0.11 at 6 months, and 0.53 ± 0.10 at 12 months. By 1 year, 13% had experienced major events or had persistent severe cardiomyopathy with an LVEF <0.35, and 72% achieved an LVEF ≥0.50. An initial LVEF <0.30 ($p = 0.001$), an LVEDD ≥6.0 cm ($p < 0.001$), black race ($p = 0.001$), and presentation after 6 weeks post-partum ($p = 0.02$) were associated with a lower LVEF at 12 months. No subjects with both a baseline LVEF <0.30 and an LVEDD ≥6.0 cm recovered by 1 year post-partum, whereas 91% with both a baseline LVEF ≥0.30 and an LVEDD <6.0 cm recovered ($p < 0.00001$).

CONCLUSIONS In a prospective cohort with PPCM, most women recovered; however, 13% had major events or persistent severe cardiomyopathy. Black women had more LV dysfunction at presentation and at 6 and 12 months post-partum. Severe LV dysfunction and greater remodeling at study entry were associated with less recovery. (Investigations of Pregnancy Associated Cardiomyopathy [IPAC]; NCT01085955) (J Am Coll Cardiol 2015;66:905–14)

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ABBREVIATIONS AND ACRONYMS

BMI = body mass index

BP = blood pressure

LV = left ventricular

LVAD = left ventricular assist device

LVEDD = left ventricular end-diastolic diameter

LVEF = left ventricular ejection fraction

ΔLVEF = change in left ventricular ejection fraction

PPCM = peripartum cardiomyopathy

Peripartum cardiomyopathy (PPCM) is an uncommon complication of pregnancy that remains a major cause of maternal morbidity and mortality (1). Although older studies estimate its prevalence in the United States at 1 in 4,000 live births, with increased recognition, more recent studies place this estimate closer to 1 in 2,000 (2). PPCM is endemic in Haiti (3) and parts of Africa (4), and race remains a

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major risk factor for its development (5,6). The clinical presentation is similar to that of other forms of nonischemic cardiomyopathy, with the onset in the later part of pregnancy or the first few months post-partum (7). Although the etiology remains uncertain, an autoimmune inflammatory pathogenesis triggered by fetal or placental antigens has been suspected (8,9). More recently, both genetic (10,11) and vascular (12) etiologies have been postulated to play a significant role.

Outcomes of PPCM are markedly heterogeneous. Previous investigations have demonstrated that many women with PPCM recover left ventricular (LV) function completely; however, a substantial percentage is left with persistent dilated cardiomyopathy and chronic progressive heart failure (13). Given the low prevalence of the disorder, most single-center reports are limited in study number and being retrospective, and there is minimal prospective data on clinical outcomes of contemporary evidence-based therapy (14,15). The utility of demographics or clinical phenotype for predicting myocardial recovery has not been prospectively evaluated.

The Peripartum Cardiomyopathy Network was formed as a 30-center collaborative group to facilitate research on this disorder. The IPAC (Investigations of Pregnancy Associated Cardiomyopathy) study was initiated in 2009 as a National Heart, Lung, and Blood Institute-funded multicenter, prospective investigation of the demographic characteristics, inflammatory pathogenesis, treatment, and clinical predictors of outcomes for PPCM patients in North America. We now report the clinical characteristics of the IPAC cohort, the subsequent outcomes during the first year post-partum, and the clinical and demographic predictors of myocardial recovery.

METHODS

COHORT. Between December 2009 and September 2012, 100 women with newly diagnosed PPCM were enrolled within the first 13 weeks post-partum at 30 centers (Online Appendix). All women were at least 18 years of age and had no history of cardiac disease, an estimated clinical LV ejection fraction (LVEF) ≤0.45 at the time of enrollment, and an evaluation consistent with idiopathic nonischemic cardiomyopathy. Women with significant valvular disease, coronary disease (>50% stenosis of a major epicardial vessel or a positive noninvasive study), evidence of ongoing bacterial septicemia (positive blood cultures), ongoing drug or alcohol abuse, history of chemotherapy or chest radiation within 5 years of enrollment, or a history of cardiomyopathy were excluded.

PROTOCOL. The study protocol was approved by the institutional review boards at all participating centers, and informed consent was obtained from all subjects. At the time of enrollment, demographic information (including self-designated race), previous clinical evaluation, and current medical therapy were recorded. Women were followed until 1 year post-partum. All hospitalizations and major cardiac events, including death, cardiac transplantation, and implantation of a left ventricular assist device (LVAD), were recorded.

LV FUNCTION. All subjects had an echocardiogram to assess LVEF at the time of enrollment, which was repeated at 6 and 12 months post-partum. Women enrolled early (within 6 weeks post-partum, n = 66) had a repeat assessment of LV function at 2 months. Echocardiograms were reviewed by a core laboratory at the University of Pittsburgh for assessment of ventricular volumes and calculation of ejection fraction. LV volumes and LVEFs were assessed by biplane Simpson's rule using manual tracing of digital images. Left ventricular end-diastolic diameter (LVEDD) was assessed in the parasternal long-axis view. Due to format, a subset of echocardiograms were not available for assessment by the core laboratory (22 of 310, 7%); for these studies, the LVEF calculated locally was used.

STATISTICAL ANALYSIS. The Student *t* and Fisher exact tests were used to compare continuous and categorical variables by self-identified race ("black" vs. "white and other"). The Kaplan-Meier method was next used to estimate survival free from events (cardiac transplantation and need for mechanical circulatory support). Using the exact log-rank test, event-free survival was compared between racial subsets. For analysis of event rate by baseline LVEF, an initial LVEF <0.30 delineated approximately one-third of the cohort with the most severe LV dysfunction on presentation (initial LVEF <0.30, n = 30), and this subset was compared with those with moderate LV dysfunction (LVEF ≥0.30, n = 70).