

Brief Communication: Outcomes of Subsequent Pregnancy after Peripartum Cardiomyopathy: A Case Series from Haiti

James D. Fett, MD; Len G. Christie, MD; and Joseph G. Murphy, MD

Background: Maternal risks with pregnancies after an index diagnosis of peripartum cardiomyopathy (PPCM) are inadequately understood.

Objective: To describe the clinical outcomes of subsequent pregnancy in Haitian women with PPCM.

Design: Prospectively identified cases from a defined population base, 2000–2005.

Setting: Hôpital Albert Schweitzer, Deschapelles, Haiti.

Patients: 15 patients with PPCM and subsequent pregnancies among 99 prospectively identified patients with PPCM.

Measurements: Clinical and echocardiographic parameters.

Results: Fifteen women with PPCM had 16 subsequent pregnancies after the index pregnancies. Eight of these patients experienced

worsening heart failure; of these, 1 died and 1 regained normal left ventricular systolic function. Seven patients tolerated pregnancy without worsening heart failure, and ventricular function recovered in these patients within 30 months after the subsequent pregnancy.

Limitations: The results may not apply to non-Haitian women, and power was insufficient to identify factors that might predict recovery ($n = 15$).

Conclusions: Half of the women with subsequent pregnancy after PPCM experienced worsening heart failure and long-term systolic dysfunction, while the other half experienced no deterioration and regained normal left ventricular systolic function.

Ann Intern Med. 2006;145:30-34.

For author affiliations, see end of text.

www.annals.org

Peripartum cardiomyopathy (PPCM) is a poorly characterized cause of heart failure in previously healthy women, with onset in late pregnancy or early in the postpartum period. We have reported (1–3) the high incidence of PPCM in the Hôpital Albert Schweitzer (4) district of Haiti: 1 case per 300 live births (10 times the incidence in the United States). Other outcome features reported in this population (3) include a mortality rate of 15.3% over a 5-year observational period for 98 prospectively identified patients and a left ventricular systolic function recovery rate of 28% in 92 patients who were observed for at least 6 months after diagnosis. Important additional concerns of clinical research in PPCM are maternal survival and tolerance of future pregnancies. In 1 of few articles that examine this, Elkayam and colleagues (5) reported a retrospective multicenter case study from the United States that underlined the high level of risk in subsequent pregnancies. We report the outcome of subsequent pregnancies in a case-series study from Haiti, an island nation that is burdened by poverty, political instability, and massive health problems.

METHODS

Our study focuses on women with subsequent pregnancies among 99 prospectively identified patients with PPCM who were enrolled in the Hôpital Albert Schweitzer Peripartum Cardiomyopathy Registry from 1 February 2000 to 31 January 2005. We included patients if their disease met accepted definition criteria (6–8) for PPCM: 1) the onset of heart failure in the month before delivery to 5 months after delivery, 2) no preexisting heart disease, 3) no other cause identified for the heart failure, and 4) echo-

cardiographic evidence of left ventricular systolic dysfunction with ejection fraction less than 0.45. We confined the study to HIV-negative patients.

We defined the pregnancy associated with the initial diagnosis of PPCM as the index pregnancy, and we defined all later pregnancies as the subsequent pregnancies. We use the term *worsening heart failure* throughout the paper to denote 1) the reappearance of clinical signs of heart failure or progression to New York Heart Association (NYHA) (9) functional class II or greater and 2) a decrease in left ventricular ejection fraction by at least 0.10 points during or within 5 months after the subsequent pregnancy. We defined recovery of cardiac function as 1) NYHA functional class I, 2) no clinical signs of heart failure, and 3) left ventricular ejection fraction greater than 0.50.

Patients had a clinical and echocardiographic examination at least every 6 months and were also counseled to avoid pregnancy until ventricular function returned to normal. We reviewed family-planning measures and made them available to patients at no cost during each patient visit. Standard treatment goals included an angiotensin-converting enzyme inhibitor during the postpartum period, replaced by nitrates plus hydralazine during pregnancy; diuretics for clinical fluid overload and digoxin for

See also:

Print

Editors' Notes 31

Web-Only

Conversion of figure and tables into slides

patients who were not improving with initial treatment (withdrawn if they achieved NYHA functional class I); prophylactic heparin for all hospitalized patients; warfarin for selected nonpregnant outpatients on the basis of clinician assessment of risk and benefit and adherence; and β -blockers (limited to atenolol) on the basis of clinician preference and availability.

We are volunteer medical staff of the Hôpital Albert Schweitzer, and our study was part of the Peripartum Cardiomyopathy Research Project, conducted with the approval of the Hôpital Albert Schweitzer Ethics Committee.

Statistical Analysis

We performed statistical analyses with Epi Info 2000 software (U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, Atlanta, Georgia). We considered a *P* value (Mann–Whitney test, Wilcoxon 2-sample test, mid-*P* exact test, and Fisher exact test) of 0.05 or less to be statistically significant.

Role of the Funding Source

The study was funded by charitable contributions (Pierre Paulette Peripartum Cardiomyopathy Fund) that are separate from the operating budget of the Hôpital Albert Schweitzer. The funding source had no role in the design, conduct, or reporting of the study or in the decision to submit the manuscript for publication.

RESULTS

We identified 16 subsequent pregnancies in 15 patients with PPCM who had had an index pregnancy with a diagnosis of PPCM. Mean interval between delivery of index pregnancy and delivery of subsequent pregnancy was 26.7 months (range, 16 to 37 months). Mean follow-up after the delivery of the subsequent pregnancy was 20.1 months (range, 6 to 30 months). All but 1 patient with

Context

Peripartum cardiomyopathy occurs once in every 300 live births in Haiti. The outcome of subsequent pregnancies in this impoverished population is not known.

Contribution

The authors prospectively identified 99 cases and followed them clinically and with echocardiography. Fifteen patients became pregnant again; only 1 had already recovered normal ventricular function. Eight experienced worsening heart failure during the subsequent pregnancy; only 1 regained normal ventricular function. The remaining 7 regained normal ventricular function after the pregnancy.

Cautions

The study was too small to reliably identify predictors of worsening heart failure during a subsequent pregnancy.

Implications

Some women in heart failure from peripartum cardiomyopathy tolerate subsequent pregnancy, but many get worse.

—The Editors

subsequent pregnancy became pregnant before full recovery of left ventricular systolic function and against medical advice.

Eight of 15 patients (53%) had worsening heart failure during subsequent pregnancy, and only 1 of these patients regained normal left ventricular systolic function after the subsequent pregnancy. One patient died of severe heart failure 10 months after the subsequent pregnancy. Seven patients (47%) showed no worsening heart failure with subsequent pregnancy, and they recovered normal left ven-

Table 1. Baseline Characteristics*

Characteristic	Patients with Subsequent Pregnancy (n = 15)		Patients without Subsequent Pregnancy (n = 84)
	Patients with Worsening Heart Failure (n = 8)	Patients without Worsening Heart Failure (n = 7)	
Mean age at diagnosis (range), y	34 (21–37)	32.3 (21–41)	32.7 (17–45)
Median parity (range)	5 (2–9)	5 (2–7)	4 (1–11)
Mean interval between index and subsequent pregnancies (range), mo	17.6 (7–32)	20.3 (14–37)	NA
Median NYHA functional class at diagnosis (range)	IV (II–IV)	IV (II–IV)	IV (II–IV)
Eventual recovery of LV systolic function, n (%)	1 (11.1)	7 (100)	22 (26.1)
Survival, n (%)	7 (87.5)	7 (100)	70 (83.3)
Fetal loss in subsequent pregnancy, all spontaneous abortions, n (%)	2 (25)	1 (14)	NA
Toxemia of pregnancy, n (%)	0	0	11 (13.1)
Obstetric delivery, n (%)			
Home	7 (87.5)	5 (71.4)	59 (70.2)
Hospital	1 (11.1)	2 (28.6)	21 (25)
No formal schooling, as measure of resources, n (%)	3 (37.5)	4 (57.1)	49 (58.3)

* Last point of data collection was 27 January 2006. LV = left ventricular; NA = not applicable; NYHA = New York Heart Association.

tricular systolic function during or after the subsequent pregnancy. One patient had 2 subsequent pregnancies after the index pregnancy, with worsening heart failure occurring after the second subsequent pregnancy but not after the first subsequent pregnancy.

We could not identify any characteristic that distinguished the group with subsequent pregnancy ($n = 15$) from the group without subsequent pregnancy ($n = 84$) (Table 1). Also, except for recovery of left ventricular systolic function, we could not find a distinguishing feature between the group that fully recovered ($n = 8$) and the group that continued to have abnormal heart function ($n = 7$). The Figure shows the mean echocardiographic left ventricular ejection fractions over time. Table 2 shows the treatment regimens for the 15 patients with PPCM and subsequent pregnancy.

Approximately 75% of the 99 patients with PPCM accepted family-planning measures and did not become pregnant again. Among the 25 patients who did not use family-planning measures, 14 became pregnant again. One patient became pregnant again despite having an intrauterine device.

DISCUSSION

Our observational study of subsequent pregnancies in women with well-documented PPCM reports several new important findings. First, approximately half of the case-patients experienced worsening heart failure associated

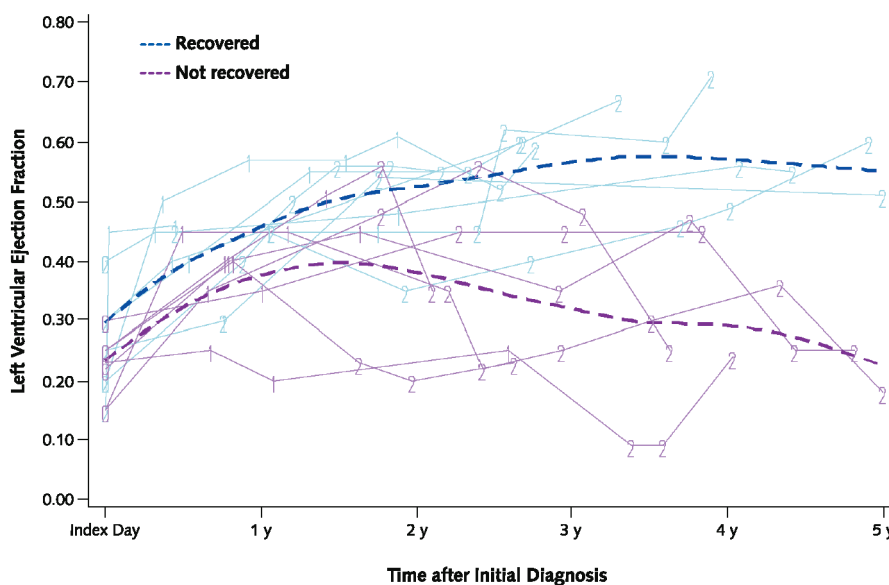
with the subsequent pregnancy; only 1 case-patient regained normal clinical or echocardiographic cardiac function during the 6- to 30-month follow-up after the subsequent pregnancy. Further observations are necessary to determine whether their ventricular dysfunction will be permanent.

Second, the 7 patients who did not experience worsening heart failure associated with the subsequent pregnancy regained normal left ventricular function. They not only showed improvement after the index pregnancy but also continued improvement during and after the subsequent pregnancy. Only 1 of these patients was still receiving heart failure medication during the postpartum period of the subsequent pregnancy (Table 2).

Third, improvement in ventricular systolic function is not limited to the first 6 to 12 months after diagnosis, as is commonly believed, but may continue for several years after a diagnosis of PPCM in Haiti. The extended observation period up to 30 months postpartum for the subsequent pregnancy allowed us to identify both late recovery and late deterioration.

Fourth, toxemia of pregnancy, twin pregnancy, and the use of tocolytics, which are all previously cited as risk factors for PPCM, did not occur in any of the 15 patients with PPCM and subsequent pregnancy. Toxemia of pregnancy and PPCM are both common in Haiti, but the absence of toxemia in the 15 patients and its low incidence in the other 84 patients suggest that toxemia is not a major

Figure. Left ventricular ejection fraction in 15 patients with peripartum cardiomyopathy (PPCM) who experienced a subsequent pregnancy with ($n = 8$) or without ($n = 7$) recovery during follow-up.



0 = at diagnosis, PPCM index pregnancy; 1 = postpartum to index pregnancy; 2 = postpartum to subsequent pregnancy. Solid lines connect individual patients' left ventricular ejection fractions. Dashed lines are smooth mean estimates from cubic smoothing splines. Last point of data collection was 27 January 2006.

Table 2. Treatment of Heart Failure for 15 Patients with Peripartum Cardiomyopathy and Subsequent Pregnancy*

Patient	Postpartum to Initial Diagnosis†	During Subsequent Pregnancy	Postpartum to Subsequent Pregnancy
Group 1‡			
1	Furosemide, hydralazine, nitrates	Furosemide, hydralazine, nitrates	Furosemide, captopril
2	Furosemide, captopril	Furosemide, hydralazine, nitrates	Captopril
3	Furosemide, captopril, digoxin	None	Furosemide, captopril
4	Furosemide, captopril, digoxin	Furosemide, hydralazine, nitrates	Captopril, atenolol
5	Furosemide, captopril, digoxin	Furosemide, atenolol	None
6	Furosemide, captopril, digoxin	None	Furosemide, captopril
7	Furosemide, captopril, digoxin	Furosemide, hydralazine	Furosemide, captopril, hydralazine, digoxin
8	Furosemide, captopril, digoxin	None	Furosemide, captopril
Group 2‡			
1	Furosemide, captopril, digoxin	None	None
2	Furosemide, captopril, digoxin	None	None
3	Captopril	Hydralazine, nitrates	None
4	Furosemide, captopril, digoxin	None	None
5	Furosemide, captopril, digoxin	Atenolol	None
6	Furosemide, captopril	Furosemide, atenolol	Atenolol
7	Furosemide, captopril, digoxin	None	None

* Last point of data collection was 27 January 2006.

† All patients received initial diagnosis during the postpartum period.

‡ Group 1: worsening heart failure associated with subsequent pregnancy; group 2: no worsening heart failure associated with subsequent pregnancy.

risk factor in the development of PPCM in this population.

Elkayam and colleagues (5), in a multicenter U.S. study, retrospectively analyzed 44 patients with PPCM and subsequent pregnancy and identified 2 groups of patients: those who began the subsequent pregnancy with normal left ventricular function and those who began the subsequent pregnancy with persistent left ventricular dysfunction. Heart failure occurred in 21% of the former patients and 44% of the latter patients. All deaths (3 deaths [7%] in 44 patients) occurred in patients with abnormal baseline left ventricular function.

Sliwa and colleagues (10) reported that 5 of 6 patients with PPCM in Soweto, South Africa, had deterioration of left ventricular systolic function with subsequent pregnancy, and 2 patients (33%) died of heart failure within 8 weeks postpartum. All patients began the subsequent pregnancy with impaired left ventricular systolic function.

In the 15 Haitian patients with PPCM and subsequent pregnancy, the distribution of echocardiographic measures at initial diagnosis and before the subsequent pregnancy was similar between the 8 patients with and the 7 patients without worsening heart failure. This has implications for counseling in that clinicians may find it difficult to predict which patients will and will not recover, as well as which patients will and will not experience worsening heart failure, before the subsequent pregnancy.

Our results may not apply to non-Haitian patients with PPCM. Since only 1 of the 15 patients had regained normal ventricular function before the subsequent pregnancy, results may not apply to patients with PPCM who have recovered normal heart function. Our case series does not permit identification of factors that might predict left ventricular recovery. Although anecdotal evidence suggests a high incidence of PPCM in other regions of Haiti, no

published studies have confirmed this observation. We do not know the reason for the high incidence of PPCM in Haiti, and we cannot yet explain the reasons for these different responses in subsequent pregnancies. Some women with subsequent pregnancy after PPCM experienced worsening heart failure and subsequent abnormal heart function, while others experienced no deterioration and regained normal left ventricular systolic function.

From Hôpital Albert Schweitzer, Deschappelles, Haiti; Oregon Health Sciences University, Portland, Oregon; and Mayo Clinic, Rochester, Minnesota.

Acknowledgments: The authors thank the patients, volunteers, and staff at Hôpital Albert Schweitzer.

Grant Support: No grants were received. Funding was provided through charitable contributions (Pierre Paulette Peripartum Cardiomyopathy Fund) that are separate from the operating budget of the Hôpital Albert Schweitzer.

Potential Financial Conflicts of Interest: None disclosed.

Requests for Single Reprints: Joseph G. Murphy, MD, Division of Cardiovascular Diseases, Mayo Clinic, 200 First Street SW, Rochester, MN 55905; e-mail, murphy.joseph@mayo.edu.

Current author addresses and author contributions are available at www.annals.org.

References

- Fett JD, Carraway RD, Dowell DL, King ME, Pierre R. Peripartum cardiomyopathy in the Hospital Albert Schweitzer District of Haiti. *Am J Obstet Gynecol*. 2002;186:1005-10. [PMID: 12015528]
- Fett JD, Carraway RD, Perry H, Dowell DL. Emerging insights into peripartum cardiomyopathy. *J Health Popul Nutr*. 2003;21:1-7. [PMID: 12751668]
- Fett JD, Christie LG, Carraway RD, Murphy JG. Five-year prospective study of the incidence and prognosis of peripartum cardiomyopathy at a single institu-

tion. *Mayo Clin Proc.* 2005;80:1602-6. [PMID: 16342653]

4. Barry M, Stansfield SK, Bia FJ. Haiti and the Hôpital Albert Schweitzer. *Ann Intern Med.* 1983;98:1018-20. [PMID: 6344707]

5. Elkayam U, Tummala PP, Rao K, Akhter MW, Karaalp IS, Wani OR, et al. Maternal and fetal outcomes of subsequent pregnancies in women with peripartum cardiomyopathy. *N Engl J Med.* 2001;344:1567-71. [PMID: 11372007]

6. Pearson GD, Veille JC, Rahimtoola S, Hsia J, Oakley CM, Hosenpud JD, et al. Peripartum cardiomyopathy: National Heart, Lung, and Blood Institute and Office of Rare Diseases (National Institutes of Health) workshop recommendations and review. *JAMA.* 2000;283:1183-8. [PMID: 10703781]

7. Demakis JG, Rahimtoola SH. Peripartum cardiomyopathy. *Circulation.*

1971;44:964-8. [PMID: 4255967]

8. Hibbard JU, Lindheimer M, Lang RM. A modified definition for peripartum cardiomyopathy and prognosis based on echocardiography. *Obstet Gynecol.* 1999;94:311-6. [PMID: 10432149]

9. Konstam MA, Dracup K, Baker DW, Bortorff MB, Brooks NH, Dacey RA, et al. Heart Failure: Evaluation and Care of Patients with Left-Ventricular Systolic Dysfunction. Clinical Practice Guideline no. 11. Rockville, MD: Agency for Health Care Policy and Research; 1994. AHCPR publication no. 94-0612.

10. Sliwa K, Forster O, Zhanje F, Candy G, Kachope J, Essop R. Outcome of subsequent pregnancy in patients with documented peripartum cardiomyopathy. *Am J Cardiol.* 2004;93:1441-3, A10. [PMID: 15165937]

DOWNLOAD IMPORTANT REFERENCES TO CITATION MANAGERS

At www.annals.org, article citations may be directly downloaded to any of the following formats: EndNote, Reference Manager, ProCite, BibTeX, or Medlar.