Frequency of Peripartum Cardiomyopathy

Lisa M. Mielniczuk, MD[a,*], Kathryn Williams, MS[b], Darryl R. Davis, MD[b], Anthony S.L. Tang, MD[b], Robert Lemery, MD[b], Martin S. Green, MD[b], Michael H. Gollob, MD[b], Haissam Haddad, MD[b], and David H. Birnie, MD[b]

Reports from case series have estimated the incidence of peripartum cardiomyopathy (PC) at 1 case/1,485 live births to 1 case/15,000 live births and probable mortality rates of 7% to 60%. The objective of this study was to produce the first population-based study of the incidence, mortality, and risk factors for PC. The National Hospital Discharge Survey was used. Discharge information was available for 3.6 million patient discharges from 1990 to 2002. There were an estimated 16,296 cases of PC from 1990 to 2002. During this period, there were 51,966,560 live births in the United States. Thus, the incidence of PC was 1 case/3,189 live births. There was a trend toward an increase in PC incidence during the study period, with an estimate for the years 2000 to 2002 of 1 case/2,289 live births. The in-hospital mortality rate was 1.36% (95% confidence interval 0% to 10.2%). The total mortality rate was 2.05% (95% confidence interval 0.29% to 10.8%). Patients with PC were older (mean age 29.7 vs 26.9 years), were more likely to be black (32.2% vs 15.7%), and had a higher incidence of pregnancy associated hypertensive disorders (22.5% vs 5.87%) compared with national data. In conclusion, the incidence of PC is relatively uncommon, occurring at an average frequency of 1 case/3,189 live births from 1990 to 2002. The estimated mortality of 1.36% to 2.05% (95% confidence interval 0.29% to 10.8%) is less than previously reported from most case series. **(Am J Cardiol 2006;97:1765–1768)**

Peripartum cardiomyopathy (PC) is a cardiomyopathy of unknown cause that occurs in the peripartum period in women without preexisting heart disease. The condition is defined on the basis of 4 criteria adapted from the work of Demakis et al[1,2] and agreed at a National Heart, Lung, and Blood Institute workshop in 1997.[3] The incidence of PC is unknown, because there have been no population-based studies to date.[3] Reports from case series have produced incidence estimates of 1 case/1,485 live births[4] to 1 case/15,000 live births.[5] In the absence of population studies, the true mortality of the condition is unknown; small case series have suggested that mortality rates range from 7% to 60% (see Table 1).[1,6–12]

The objective of this study was to produce the first population-based study of the incidence, mortality, and risk factors for PC.

Methods

Database: The National Hospital Discharge Survey (NHDS) has been conducted continuously by the National Center for Health Statistics since 1965.[13] The National Center for Health Statistics obtains a nationally representative sample of discharge records from hospitals in the United States. On average, 464 hospitals are selected, and 265,000 to 270,000 records are abstracted annually, representing about 1% of all discharges from nonfederal, short-stay hospitals in the United States. A 3-stage probability design is used that involves sampling within geographic areas, then hospitals within areas, and then discharges within hospitals. Data on birth, gender, race, marital status, expected source of payment for hospitalization, and characteristics of the hospitals are abstracted. In addition, up to 7 discharge diagnoses and 4 operative procedures are abstracted. The diagnoses and procedures are then coded according to the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM).

Because of the NHDS's complex, multistage design, the survey data must be inflated or weighted to produce national estimates. The estimation procedure produces essentially unbiased national estimates. Estimates of the sampling variability that occurs by chance are provided by approximate relative SEs. Technical details of the calculation of the estimates are provided elsewhere.[14] There is an ongoing quality control program in which 5% to 10% of the abstracts are independently recoded by an NHDS coder, with discrepancies resolved by the chief coder. In 2002, there was an overall error rate for medical coding and other data entry of $<0.1\%$.[13] In addition, the quality of the NHDS data has been shown to be very good in independent validation studies.[15–17] The NHDS data have been used in multiple publications.[18–22]

[a]Cardiovascular Division, Brigham and Women's Hospital, Boston, Massachusetts; and [b]University of Ottawa Heart Institute, Ottawa, Ontario, Canada. Manuscript received October 10, 2005; revised manuscript received and accepted January 9, 2006.

* Corresponding author: Tel: 617-732-6660 ext. 35415; fax: 617-582-6027.

E-mail address: lmielniczuk@partners.org (L.M. Mielniczuk).

0002-9149/06/$ – see front matter
doi:10.1016/j.amjcard.2006.01.039

Table 1
Previous mortality reports

Source	Period	Country	n	Follow-Up (yrs)	Mortality	Transplantation
Elkayam et al[7]	1997–1998	United States	100	2	9%	4%
Felker et al[8]	1983–1998	United States	42	8.6	7%	7%
Sliwa et al[11]	1996–1997	South Africa	29	0.5	27.6%	
Witlin et al[12]	1986–1994	United States	28	N/A	18%	11%
Carvalho et al[6]	1983–1988	Brazil	19	1.7	16%	5.2%
Demakis et al[1]	1947–1967	United States	27	10.7	41%	
McDonald et al[26]	1953–1957	United States	15	1.2	60%	
Seftel and Susser[10]	1953–1957	South Africa	23	N/A	23%	
Meadows[9]	1945–1957	United States	15	5–9	27%	

All reports are single-center case series except for the report of Elkayam et al.[7] Their series was mostly obtained from a survey (with a response rate of 2.7%) of members of the American College of Cardiology.

Data extraction: The ICD-9-CM code for PC is 674.8. This code also covers subinvolution of the uterus and hepatorenal syndrome in pregnancy. Hence, to discriminate among these 3 diagnoses within code 674.8, a case had to have an additional cardiac code to be classified as a case of PC. That is, a case had to have a cross-diagnosis of ≥1 of the following: pulmonary edema (code 514), heart failure (code 428), cardiomyopathy (code 425.4), or cardiovascular complications in pregnancy (code 648.64). Data were collected from 1990 to 2002. Each possible case of PC was reviewed in detail by 2 independent investigators to determine its appropriateness for inclusion. Cases in which there was consensus between the 2 investigators were included for analysis.

PC incidence and mortality calculation: Population data on total annual birthrate, maternal age, and race were obtained from the National Vital Statistics System reports. Population estimates were obtained through the summation of individual sample case weights published by the NHDS. In addition, NHDS relative SE tables were used to produce 95% confidence intervals (CIs) for the estimates.

Mortality was calculated in 2 ways: initially with the sole use of NHDS data and then with the incorporation of data obtained from the Pregnancy Mortality Surveillance System, as published recently by Whitehead et al,[23] who examined pregnancy-related deaths due to cardiomyopathy from 1991 to 1997. They reviewed all available information on all deaths occurring during pregnancy or <1 year after delivery in the entire United States. This information included death certificates, handwritten notes, and American College of Obstetricians and Gynecology system data. Strict criteria were used to classify deaths due to PC or other cardiomyopathy, and a total of 245 pregnancy-related cardiomyopathy deaths (70% due to PC) were identified.

PC risk factor assessment: Each case of PC was evaluated for the postulated risk factors: maternal age, parity, race, the incidence of multifetality, and hypertensive disorders in pregnancy. The data on maternal age and race were compared with those for a population obtained from the National Vital Statistics System reports. The data on hypertensive disorders in pregnancy were compared with previously published national data also extracted from the NHDS.[22]

Table 2
Incidence of peripartum cardiomyopathy during the study

Period	Live Births	Cases of PC	PC Incidence (no. of live births/1 case)
2000–2002	12,106,473	5,432	2,229
1996–1998	11,781,864	3,508	3,359
1994–1996	11,743,850	3,601	3,261
1990–1993	16,334,373	3,755	4,350
Total	51,966,560	16,296	3,189

Results

Number of records abstracted: Discharge information was available for 3.6 million patient discharges for the years 1990 to 2002 inclusive. One thousand five hundred twenty-seven of these 3.6 million discharges had a discharge diagnostic code of 674.8. Each of these cases was evaluated in detail according to the strict criteria detailed previously, and a total of 171 sample cases of PC were included for the analysis.

PC incidence estimates: Incorporating the individual sample case weights resulted in an estimate of 16,296 cases of PC from 1990 to 2002 (95% CI 0 to 83,117). During this period, there were a total of 51,966,560 live births in the United States. Hence, the estimated incidence of PC was 1 case/3,189 live births. When the data were evaluated in 4-year time periods, there was a nonsignificant trend for an increase in PC incidence over time, from 1 case/4,350 live births from 1990 to 1993 to 1 case/2,229 live births from 2000 to 2002 (see Table 2).

PC mortality estimates: The discharge status of 15,742 of patients (96.6%) was known. Mortality from PC was calculated in 2 ways. First, using only the NHDS data and incorporating the individual sample case weights resulted in an estimate of 314 deaths in 15,742 cases of PC. This corresponds to an in-hospital mortality rate of 1.36% (95% CI 0% to 10.2%). Second, we used data from Whitehead et al's[23] work. They identified 171 deaths from PC from 1991 to 1997. The NHDS data showed an estimated 8,326 cases of PC during this time, and together, the data indicate a total mortality from PC from 1991 to 1997 of 2.05% (95% CI 0.29% to 10.8%).

Table 3
Distribution of cases of peripartum cardiomyopathy by race with comparison with national data

Race	PC Cases	Percentage of all PC Cases	National Data
Caucasian	6,828	41.9%	79%
African-American	5,248	32.2%	15.7%
All other	402	2.5%	5.3%
Not stated	3,818	23.4%	0%

Table 4
Incidence of hypertensive disorders in peripartum cardiomyopathy sample compared with national pregnancy data

Type	ICD-9-CM Code	National Data	PC
Chronic hypertension	642.0–642.2	0.61%	0.62%
Transient hypertension	642.3	0.77%	1.50%
Preeclampsia	642.5	2.58%	9.49%
Eclampsia	642.6	0.10%	0.83%
Preeclampsia/eclampsia superimposed on chronic hypertension	642.7	0.18%	2.90%
Unspecified hypertension	642.9	0.63%	7.17%
Overall hypertension		5.87%	22.50%

PC risk factor assessment: The mean age of the mothers in our series was 29.7 years (range 14 to 49). This compares with data from the National Vital Statistics System, showing that the mean age of all mothers in the United States from 1990 to 2002 was 26.9 years. The mean age of all mothers increased from 26.4 in 1990 to 27.2 in 2002. The NHDS does not record data on maternal parity; the incidence of multiparity is also not consistently recorded by the NHDS.

Details about race were available for 76.6% of the women in our PC sample (see Table 3 for details). Over the 13 years of study, an estimated 5,248 patients with PC (32.2%) were identified as African-American. This is greater than the percentage of all African-American mothers (15.7%) in the same period.

Zhang et al[22] reported a previous analysis of the incidence of hypertensive disorders in pregnancy. Using NHDS data for 1988 to 1997 inclusive, they calculated an overall incidence of hypertensive disorders in pregnancy of 5.87%. There was a greater incidence of hypertensive disorders in our sample, occurring in 22.5% of all patients with PC. Specifically, the occurrence of preeclampsia, eclampsia, and unspecified hypertension were more prevalent in patients with PC (see Table 4).

Discussion

PC is defined as the development of heart failure in the last month of pregnancy or the first 5 months after delivery. Additional diagnostic criteria have been suggested to increase the specificity of this disorder. These include the absence of an identifiable cause of heart failure, no known previous cardiac disease, and objective evidence of left ventricular systolic dysfunction.[3] Little is known about the epidemiology and prognosis of PC. We believe that this is the first population-based study of PC. Discharge information was available for 3.6 million patient discharges from 1990 to 2002 inclusive. Incorporating the individual sample case weights resulted in an estimate of 16,296 cases of PC in the United States during the 13 years of the study. During this time, there were a total of 51,966,560 live births. Hence, the incidence of PC was 1 case/3,189 live births. This estimate of incidence is within the range of previously published estimates of incidence, from 1 case/1,485 live births to 1 case/15,000 live births.[23] Previous estimates were drawn from case series and were not population based; hence, it is probable that our estimate more closely approaches a true population incidence. There was a trend toward an increase in PC incidence over the study period, with an estimate for the years 2000 to 2002 of 1 case/2,289 live births. It is possible that the actual incidence of this condition has increased over time, and this may be related to increasing maternal age and rates of multiple births.[24] However, our data may also be explained, at least in part, by increasing recognition and diagnosis of the condition.

We found mortality due to PC to be less than reported previously. Using hospital discharge data alone, the estimate for in-hospital mortality was 1.36% (95% CI 0% to 10.2%). We also estimated mortality using data obtained from the Pregnancy Mortality Surveillance System previously published by Whitehead et al.[23] Applying this data set resulted in an estimate of mortality from PC of 2.05% (95% CI 0.29% to 10.8%) from 1991 to 1997. There is an important distinction between the 2 methods of estimating mortality. The first method estimates only in-hospital mortality, whereas the second method estimates mortality in and out of the hospital. The consistency of the results from the 2 methods suggests that they are credible estimates.

These estimates of mortality are less than those of previous reports, and there are a number of possible explanations for this discrepancy. First, the difference may be related to the later time period of our study compared with most of the case series. The most closely chronologically related case series, from Felker et al[8] (1983 to 1998), reported a 7% mortality. Earlier diagnosis coupled with modern heart failure management likely has an important influence on this disease. Second, it is known that in some of the earlier series, PC was misdiagnosed in some patients, and it is possible that this misdiagnosis led to an exaggerated mortality.[4] Third, some estimates of mortality may have been confounded by referral bias of the sickest patients to tertiary care centers. Fourth, the increased recognition of less severe cases of PC would have an important influence on mortality rates. Regardless of the likely multiple reasons for the discrepant mortality figures, our data indicate a better contemporary prognosis from the condition than had previously been reported.

The mortality and incidence rates estimated in this study

differ significantly from regional studies in South Africa and Haiti. In these regions, estimates of PC are as high as 1 case/100 live births. There are many reasons for this discrepancy. It is known that in Nigeria, a postpartum tradition of ingesting dried lake salt, kanwa, was responsible for many cases of volume overload ascribed to PC.[25] However, it is also possible that regional variations in genetics, diagnosis, and management options may all contribute to the escalated mortality reported in these areas.

Several limitations exist when using epidemiologic data from the NHDS. First, the quality of the data can only be as good as that on the summary of patient discharges. Internal auditing and previous validation studies have demonstrated good correlation to the actual medical record.[15–17] However, it is possible that some cases of PC were misdiagnosed, and patients actually had alternative, preexisting cardiac conditions. In the present study, there was no way to verify if the strict diagnostic criteria for PC were followed. This limitation has also been recognized in previous publications on PC.[4] Second, our study may have underestimated the incidence of PC, because the database records only cases either diagnosed at the time of inpatient delivery or severe enough to require hospital admission. Third, the National Center for Health Statistics requires a conservative statistical approach in view of the complex sampling design. This is especially true for rare conditions such as PC. For multiyear studies, the National Center for Health Statistics advises the use of the largest annual relative SEs, which results in wide CIs for rare conditions. In addition, the NHDS files do not contain sufficient information on the sampling variability of this complex, multistage design to allow logistic regression modeling. These latter 2 points explain the limited statistical analysis that was possible in this study. Long-term prognosis and follow-up are not possible through NHDS data extraction. Each patient visit is coded by a unique identifier, such that subsequent readmissions or deaths would not be possible to track over time. This is done to ensure complete patient confidentiality, because these are all public-access records. A final limitation of this study is the comparison of NHDS data with those from other databases (National Vital Statistics System, Pregnancy Mortality Surveillance System) to develop incidence and mortality rate data. Although these records represent the most complete data on birth rate and mortality, it is possible that errors or omissions in data reporting from these records could create additional error in the calculation of case rate incidence and mortality. Despite these limitations, this study provides the first population-based estimates of the incidence and mortality of PC.

1. Demakis JG, Rahimtoola SH, Sutton GC, Meadows WR, Szanto PB, Tobin JR, Gunnar RM. Natural course of peripartum cardiomyopathy. *Circulation* 1971;44:1053–1061.
2. Demakis JG, Rahimtoola SH. Peripartum cardiomyopathy. *Circulation* 1971;44:964–968.
3. Pearson GD, Veille JC, Rahimtoola S, Hsia J, Oakley CM, Hosenpud JD, Ansari A, Baughman KL. Peripartum cardiomyopathy: National Heart, Lung, and Blood Institute and Office of Rare Diseases (National Institutes of Health) workshop recommendations and review. *JAMA* 2000;283:1183–1188.
4. Lampert MB, Lang RM. Peripartum cardiomyopathy. *Am Heart J* 1995;130:860–870.
5. Cunningham FG, Pritchard JA, Hankins GD, Anderson PL, Lucas MJ, Armstrong KF. Peripartum heart failure: idiopathic cardiomyopathy or compounding cardiovascular events? *Obstet Gynecol* 1986;67:157–168.
6. Carvalho A, Brandao A, Martinez EE, Alexopoulos D, Lima VC, Andrade JL, Ambrose JA. Prognosis in peripartum cardiomyopathy. *Am J Cardiol* 1989;64:540–542.
7. Elkayam U, Akhter MW, Singh H, Khan S, Bitar F, Hameed A, Shotan A. Pregnancy-associated cardiomyopathy: clinical characteristics and a comparison between early and late presentation. *Circulation* 2005; 111:2050–2055.
8. Felker GM, Jaeger CJ, Klodas E, Thiemann DR, Hare JM, Hruban RH, Kasper EK, Baughman KL. Myocarditis and long-term survival in peripartum cardiomyopathy. *Am Heart J* 2000;140:785–791.
9. Meadows WR. Idiopathic myocardial failure in the last trimester of pregnancy and the puerperium. *Circulation* 1957;15:903–914.
10. Seftel H, Susser M. Maternity and myocardial failure in African women. *Br Heart J* 1961;23:43–52.
11. Sliwa K, Skudicky D, Bergemann A, Candy G, Puren A, Sareli P. Peripartum cardiomyopathy: analysis of clinical outcome, left ventricular function, plasma levels of cytokines and Fas/APO-1. *J Am Coll Cardiol* 2000;35:701–705.
12. Witlin AG, Mabie WC, Sibai BM. Peripartum cardiomyopathy: an ominous diagnosis. *Am J Obstet Gynecol* 1997;176:182–188.
13. National Center for Health Statistics. National hospital discharge and ambulatory surgery data. Available at: *http://www.cdc.gov/nchs/about/major/hdasd/listpubs.htm*. Accessed on March 14, 2004.
14. Dennison C, Pokras R. Design and operation of the National Hospital Discharge Survey: 1988 redesign. *Vital Health Stat* 2000;1:1–42.
15. National Center for Health Statistics. Age adjustment. Available at: *http://www.cdc.gov/nchs/datawh/nchsdefs/ageadjustment.htm*. Accessed on March 18, 2004.
16. Hsia DC, Krushat WM, Fagan AB, Tebbutt JA, Kusserow RP. Accuracy of diagnostic coding for Medicare patients under the prospective-payment system. *N Engl J Med* 1988;318:352–355.
17. Romano PS, Mark DH. Bias in the coding of hospital discharge data and its implications for quality assessment. *Med Care* 1994;32:81–90.
18. Koelling TM, Chen RS, Lubwama RN, L'Italien GJ, Eagle KA. The expanding national burden of heart failure in the United States: the influence of heart failure in women. *Am Heart J* 2004;147:74–78.
19. Stein PD, Kayali F, Olson RE. Twenty-one-year trends in the use of inferior vena cava filters. *Arch Intern Med* 2004;164:1541–1545.
20. Thompson WW, Shay DK, Weintraub E, Brammer L, Bridges CB, Cox NJ, Fukuda K. Influenza-associated hospitalizations in the United States. *JAMA* 2004;292:1333–1340.
21. Voigt A, Ezzeddine R, Barrington W, Obiaha-Ngwu O, Ganz LI, London B, Saba S. Utilization of implantable cardioverter-defibrillators in survivors of cardiac arrest in the United States from 1996 to 2001. *J Am Coll Cardiol* 2004;44:855–858.
22. Zhang J, Meikle S, Trumble A. Severe maternal morbidity associated with hypertensive disorders in pregnancy in the United States. *Hypertens Pregnancy* 2003;22:203–212.
23. Whitehead SJ, Berg CJ, Chang J. Pregnancy-related mortality due to cardiomyopathy: United States, 1991-1997. *Obstet Gynecol* 2003;102: 1326–1331.
24. Reynolds MA, Schieve LA, Martin JA, Jeng G, Macaluso M. Trends in multiple births conceived using assisted reproductive technology, United States, 1997-2000. *Pediatrics* 2003;111:1159–1162.
25. Davidson NM, Perry EH. Peripartum cardiomyopathy: a comprehensive review. *Am J Obstet Gynecol* 1978;178:409–414.
26. McDonald CD, Burch GE, Walsh JJ. The effect of prolonged bed rest on postpartal cardiomyopathy. *Am Heart J* 1971;74:681–691.