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Outcomes and mortality in parturient and non-parturient patients with peripartum cardiomyopathy: A national readmission database study

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ABSTRACT

Background: Peripartum cardiomyopathy (PPCM) affects young females and mortality occurs after the peripartum period. Hospital readmissions for patients discharged with PPCM are poorly understood. The aim of this study was to evaluate differences in readmission rates, risk factors, and mortality in women with PPCM.

Methods: We conducted a retrospective cohort analysis using the Healthcare Cost and Utilization Project 2013 National Readmissions Database. From the database, we selected patients with PPCM to include patients discharged between January and November 2013. Readmission rate, mortality rate and risk factors were analyzed. In our cohort of 3800 patients, we found a readmission rate of 15.1% and a mortality rate of 1.6%. Comorbidities associated with readmission were pulmonary hypertension, obesity, renal failure, and drug abuse. Mortality on initial admission was associated with coagulation disorders and respiratory failure. Women who delivered on initial admission had a statistically lower rate of readmission than women who did not deliver on initial admission.

Conclusions: In a large retrospective nationwide analysis of PPCM patients, we found associated conditions that may help predict which patients will have a higher risk for readmission and mortality.

1. Introduction

Peripartum cardiomyopathy (PPCM) is defined as systolic heart failure developing in the third trimester of pregnancy and up to 6 months postpartum [1]. PPCM affects young women with a mean age of 27–33 years in the United States and is associated with considerable morbidity and mortality [2]. Although the mechanisms underlying the development of PPCM are unknown, predisposing factors include: multiparity [3], smoking [3], diabetes [3], hypertension [3], pre-eclampsia [3] African descent [4], advanced maternal age [5], and cocaine use [6]. PPCM associated mortality occurs most commonly because of progressive heart failure [7], sudden death [8], or thromboembolic events [7]. Considerable mortality may occur after the immediate 42-day postpartum period, as observed in one 2015 study [9].

Hospital readmissions for patients discharged with PPCM remain incompletely understood. In patients with heart failure from other causes, the 30-day period immediately following discharge is a period of increased risk for readmission [10,11]. Addressing diagnoses and risk factors associated with readmission for PPCM may thus improve post-PPCM management, reduce readmissions, and facilitate recovery.

To better understand the epidemiology of hospital readmission and mortality in PPCM patients, we retrospectively analyzed a national inpatient readmission dataset from 2013. Using woman with a PPCM diagnosis at initial hospitalization as our cohort, we studied in-hospital readmissions within 30 days of discharge and mortality We hypothesized that PPCM patients would have specific comorbidities affecting both. We also compared these outcomes between parturient and non-parturients.

Abbreviations: PPCM, Peripartum cardiomyopathy; HCUP, Healthcare Cost and Utilization Project; NRD, National Readmissions Database.

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2. Materials and methods

2.1. Data source and definitions

We conducted a retrospective cohort analysis using the Healthcare Cost and Utilization Project (HCUP) 2013 National Readmissions Database (NRD). NRD 2013 is an all-payer discharge level file containing the combined inpatient databases of 21 participating states. These states represent 49.3% of the resident population and 49.1% of all hospitalizations in the United States [12]. The data are weighted to provide estimates of national trends. Unweighted, the NRD 2013 consists of approximately 14 million discharges in 2013. The weighted database represents approximately 26 million discharges nationwide. Each patient is assigned a unique de-identified linkage number to track discharges from initial admission and subsequent admissions.

2.2. Data elements in national readmissions database (NRD)

NRD 2013 has data elements in the following categories: patient demographics, hospital demographics, patient disposition (died, discharged alive, same day readmission, discharge to rehabilitation facilities), patient diagnoses and procedure codes, comorbidities, and discharge weights.

We also collected hospital characteristics such as bed size, location, teaching status, hospital state same as patient residency, and hospital control as defined by the American Health Association Annual Survey of Hospitals.

2.3. Study population

From the database, we selected patients who were 18 years or older and discharged between January and November 2013 with a primary or secondary diagnosis code of PPCM (diagnosis code 674.5 of the International Classification of Diseases, 9th Revision, Clinical Modification). As the NRD does not collect information on readmissions from rehabilitation facilities, we excluded patients who were discharged to these facilities. Records with missing readmission information were also excluded.

Patients discharged alive were considered for readmission analysis.

2.4. Identification of cohort

All admissions occurring within 30-days after first discharge were identified. Only first readmissions were considered for this study.

We used ICD-9 procedure and diagnosis codes to identify live births based on the previously validated algorithm by Kuklina et al. [13].

2.5. Outcomes

Outcomes were assessed for entire cohort. Two *a priori* subgroups were analyzed: PPCM patients with delivery on initial admission and PPCM patients without delivery on initial admission.

The primary outcome was 30-day first hospital readmission among PPCM patients in 2013. We also examined risk factors for death and readmission in PPCM patients discharged after delivery versus those with PPCM who were discharged for nonobstetric reasons.

2.6. Statistical analysis

Analyses were performed using SAS 9.4 (SAS Institute, Cary, NC) and SUDAAN 11.1 (Research Triangle Institute, Research Triangle Park, NC). Weighted estimates were utilized to adjust for design effects of the sampling. For comparing various groups (survivors vs. non-survivors, readmitted vs. non-readmitted patients, parturients vs. non parturients), p-values were generated with a Wald test. All tests were 2-sided and p-values below 0.05 were considered statistically significant. Covariates were selected based upon known risk factors for heart failure readmission and mortality. If the p-value was below 0.1 for any variable, it was placed into a generalized estimation equation model with robust standard error and exchangeable correlation to calculate odds ratios and 95% confidence intervals. The model with the lowest quasi-likelihood criterion was chosen and utilized for all variables.

Mortality rates were calculated using the initial admission PPCM cohort. For association with death on first admission, we also compared associated diagnoses and demographics, generating a p-value with the Wald test. Variables were placed into a generalized equation model and odds ratios with 95% confidence intervals were calculated.

3. Results

Among 35,580,348 weighted discharges, we identified 3800 patients with a PPCM diagnosis on their first discharge record.

3.1. Mortality rates and risk factors

In the PPCM cohort, 62 of 3800 patients did not survive to hospital discharge (1.6% mortality). The mean age was 32.1 years (SD ± 11.2) and mean length of stay was 11.1 days (SD ± 37).

The most common causes of death were acute on chronic systolic heart failure, intracerebral bleed, septicemia, arrhythmia, anoxic brain damage and sepsis. Both respiratory failure and coag-

Table 1
Demographics and associated diagnoses in PPCM patients that were readmitted and PPCM patients who were not readmitted.

Weighted N			
Variables	PPCM, not readmitted (%)	PPCM, readmitted (%)	p-value
Age (years)			
18–25	798 (25.2)	151 (26.8)	0.91
26–35	1510 (47.6)	269 (47.7)	
36–45	810 (25.5)	132 (23.3)	
Over 45	56 (1.8)	12 (2.2)	
Associated diagnoses			
Congestive heart failure	1680 (52.9)	298 (52.8)	0.02
Pulmonary hypertension	201 (6.3)	62 (11.0)	0.02
Diabetes mellitus, with chronic complications	51 (1.6)	33 (5.8)	0.01
Renal failure	103 (3.2)	60 (10.7)	0.003
Obesity	683 (21.5)	166 (29.5)	0.03
Chronic blood loss anemia	880 (27.7)	110 (19.6)	0.03
Hypertension	1210 (38.1)	229 (40.6)	0.4
Cardiac valvular disease	455 (14.3)	83 (14.7)	0.11
Diabetes mellitus, uncomplicated	233 (7.3)	50 (8.9)	0.46
Weight loss	73 (2.3)	19 (3.4)	0.39
Deficiency anemias	869 (27.4)	160 (28.3)	0.8
Drug abuse	164 (5.2)	50 (8.9)	0.07
Psychoses	108 (3.4)	32 (5.8)	0.35
Depression	251 (7.9)	56 (10.0)	0.33
Coagulation disorder	146 (4.6)	31 (5.5)	0.56
Fluid and electrolyte disorders	855 (27.0)	177 (31.3)	0.22

ulation disorders were associated with mortality on initial admission (Tables 2 and 4).

3.2. PPCM and risk factors for readmission

3738 PPCM patients survived to initial discharge. Of those, 561 were readmitted within 30 days (15.1%). The mean time from initial discharge to readmission was 11.2 days (SD ± 13.2), and 68% of readmissions occurred within first 15 days. The most common reasons for readmission were acute on chronic systolic heart failure, pulmonary embolism and arrhythmia.

When compared to women with PPCM who were not readmitted, women with PPCM who were readmitted were more likely to have pulmonary hypertension, obesity, renal failure, and drug abuse (Table 1). Of these risk factors, renal failure had the highest odds ratio for readmission (Table 3).

3.3. Women with PPCM who delivered on initial admission

Among 3800 patients, 854 patients (22.4%) had a delivery during initial admission. 18 of these patients (2.1%) did not survive to hospital discharge. The mean age for these 18 patients was 28.2 years (SD ± 8.6) and the average length of stay was 19.6 days (SD ± 65.4). The most common causes of death were obstetrical complications (59.1%) including surgical complications, postpartum hemorrhage, breech presentation, fetopelvic disproportion, post-term pregnancy, premature rupture of membranes and postpartum disorder not otherwise specified. The second most common cause of death was pre-eclampsia (15.7%).

3.4. Readmission rates and risk factors among women with PPCM who delivered during their initial admission

Amongst 836 patients who delivered on initial admission and survived to initial discharge, the readmission rate was 12.2%. The vast majority (92%) of readmissions occurred in the first 15 days with the mean time to readmission being 6.7 days (SD ± 8.55). Common causes for readmission among women in this cohort included cardiac conditions (acute on chronic systolic heart failure, arrhythmias and cardiac device failure), and obstetrical complications (Fig. 1).

Table 2
Demographics and associated diagnoses in surviving and non-surviving PPCM patients on index admission.

Weighted N			
Variables	PPCM, survivors (%)	PPCM, non survivors (%)	p-value
Age (years)			
18–25	950 (25.4)	12 (19.5)	0.81
26–35	1779 (47.6)	33 (53.2)	
36–45	941 (25.2)	15 (23.6)	
Over 45	68 (1.8)	2 (3.6)	
Associated Diagnoses			
Respiratory failure	620 (16.5)	43 (69.2)	0.0001
Coagulation disorder	177 (4.7)	28 (45.7)	0.01
Fluid and electrolyte disorders	1032 (27.2)	41 (65.7)	0.002
Congestive heart failure	1978 (52.9)	28 (44.9)	0.16
Hypertension	1440 (38.5)	16 (25.3)	0.11
Pulmonary hypertension	263 (7.0)	12 (19.1)	0.25
Cardiac valvular disease	538 (14.4)	12 (19.2)	0.61
Renal failure	163 (4.4)	6 (9.8)	0.34
Liver disease	34 (1.0)	5 (7.6)	0.38
Diabetes mellitus, uncomplicated	283 (7.6)	5 (7.4)	0.96
Diabetes mellitus, with chronic complications	84 (2.2)	2 (2.4)	0.96
Obesity	849 (22.7)	11 (18.2)	0.57
Weight loss	92 (2.5)	7 (10.8)	0.19
Chronic blood loss anemia	999 (26.5)	15 (24.9)	0.84
Deficiency anemias	1029 (27.5)	18 (29.1)	0.88

Table 3
Regression Model Results for Readmission Variables.

Regression Model Readmission Odds Ratios	
Associated diagnoses	Odds Ratio (95% CI)
Pulmonary hypertension	1.63 (1.03–2.57)
Renal failure	2.57 (1.36–4.84)
Obesity	1.52 (1.07–2.17)
Drug abuse	1.83 (1.05–3.18)
Congestive heart failure	1.33 (0.95–1.87)
Diabetes mellitus with chronic complications	2.20 (0.95–5.08)
Chronic blood loss anemia	0.75 (0.50–1.11)
Valvular disease	1.21 (0.81–1.81)

Table 4
Regression Model Results for Mortality Variables.

Regression Model Mortality Odds Ratios	
Variable	Odds Ratio (95% CI)
Coagulation disorder	6.00 (2.30–15.64)
Respiratory failure	6.50 (2.50–16.91)
Fluid and electrolyte disorders	2.73 (0.99–7.56)

3.5. Mortality, readmission rates and risk factors among women with PPCM who did not deliver during their initial admission

2946 of 3800 patients (77.6%) did not have a delivery code associated with the initial admission and survived to discharge 44 of 2946 patients (1.5%) died during the initial admission without delivering. The mean age among those patients was 33.7 years (SD ± 11.4) and length of stay was 7.7 days (SD ± 12.2). The most frequent cause of death for PPCM patients that did not deliver on initial admission was cardiac (42.0%).

Amongst the 2902 women with PPCM who did not deliver and survived to hospital discharge, the readmission rate was 15.9%. The mean time to readmission was 13.0 days (SD ± 13.5) and 63% of readmissions occurred in the first 15 days. The most common readmission diagnosis was secondary to a cardiac condition as shown in Fig. 1.

3.6. Comparison between delivery on initial admission and no delivery at initial admission subgroups

The mortality rate did not differ between PPCM patients who delivered or did not deliver on their initial admission ($p = 0.44$). Women who delivered on initial admission had a statistically lower rate of readmission than women who did not ($p = 0.003$).

4. Discussion

In a retrospective large database analysis, we found a 1.6% mortality rate and 15.1% 30-day readmission rate for patients discharged with a diagnosis of PPCM. In our nationwide cohort of PPCM patients, we found a 1.6% in-hospital mortality rate which is consistent with the 1.8% mortality rate observed in 2011 using the HCUP National Inpatient Sample database [14].

Factors associated with readmission included pulmonary hypertension, obesity, renal failure, and drug abuse all of which may contribute to cardiac origin being the most common cause for readmission. Mortality on initial admission was associated with coagulation disorders and respiratory failure which also may lead

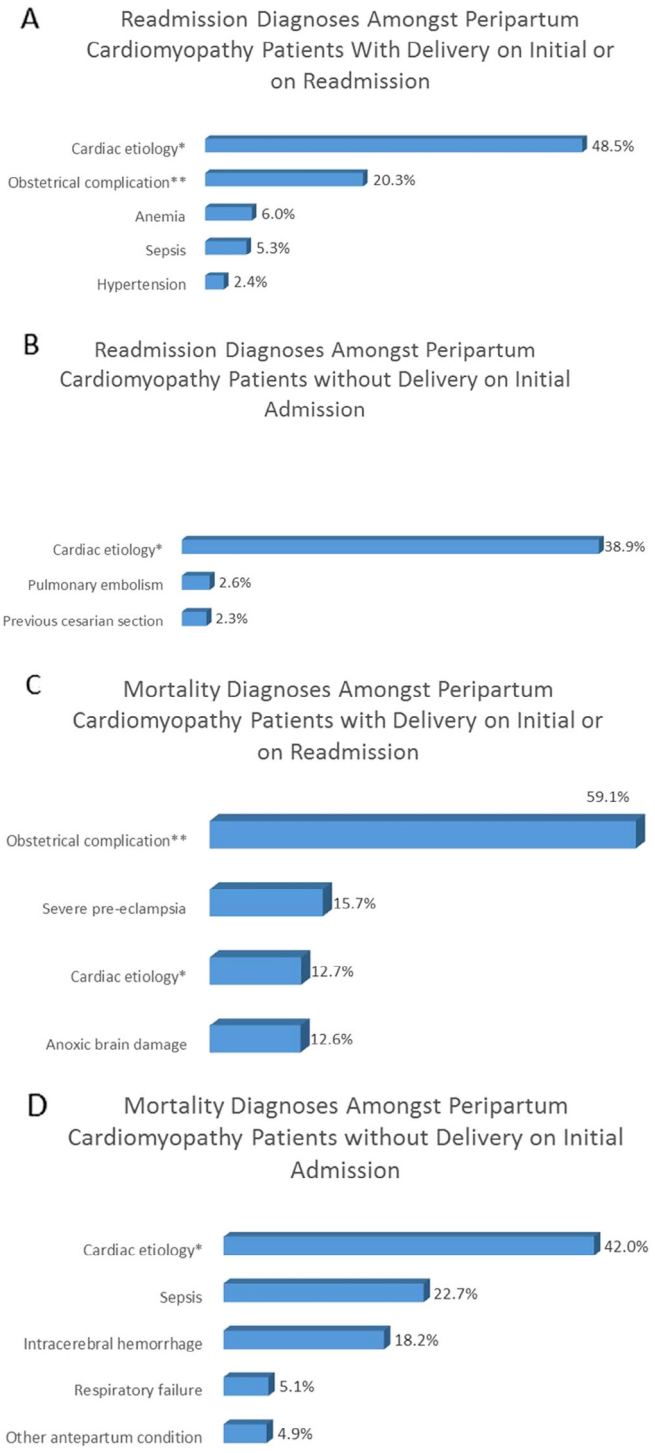

Fig. 1. Top Diagnoses upon readmission among patients with PPCM who were delivered on initial or on readmission (A) and who did not delivery on either admission (B). Top diagnoses amongst non-survivors with PPCM who were delivered on admission (C) and PPCM patients that did not deliver (D). Cardiac etiologies included: PPCM, acute on chronic systolic heart failure, arrhyth-mias and cardiac device failure; obstetric complications include surgical complication, postpar-tum hemorrhage, breech presentation, fetopelvic disproportion, post-term pregnancy, prema-ture rupture of membranes, postpartum disorder not otherwise specified.

to worsening obstetrical complications or cardiac issues which we found to be the most common causes for mortality.

No previous studies have evaluated hospital readmission in patients with PPCM. In a 2010 review, the Heart Failure Society of America found that heart failure patients with renal insufficiency, low cardiac output and diabetes were at higher risk for readmission [15]. Our data are consistent with that study.

We also found that pulmonary hypertension was associated with readmission. In a recent study identifying pregnant patients with pulmonary hypertension, seven out of eight deaths occurred within the first 3 weeks postpartum, highlighting the importance of close follow up for this patient population [16]. Although the mechanism underlying this association is unknown, pulmonary hypertension may be a consequence severe left ventricular failure, compromising right heart function and cardiac output which may lead to an increased likelihood of readmission in PPCM patients [17,18].

We also found that obesity among PPCM patients was a risk factor for readmission. This finding stands in contrast to a 2017 study which found that obesity reduced the risk for readmission with an OR of 0.84 (95% CI 0.82–0.86, $p < 0.001$) [11]. The reason for these paradoxical findings is unclear. Barasa et al. found that obesity was a risk factor for mortality in PPCM patients in Sweden [19]. Successfully managing obesity may reduce readmission rates in patients with PPCM but further investigation is warranted.

Patients with renal failure were significantly more likely to be readmitted within 30-days than those without. This finding is consistent with a 2016 investigation of over 2000 patients with heart failure that also found an association between renal failure and 30-day readmission [20]. A 2017 study evaluating risks for readmission in heart failure patients also identified renal failure to be a risk factor [11]. Although a plausible mechanism of decreased forward flow and renal perfusion due to worsening PPCM may explain the association between renal failure and readmission, further studies are needed to better understand how to prevent renal failure related readmissions.

In our cohort, drug abuse patients with PPCM may be associated with an increased risk of 30-day readmission. Such an association diverges from published data in a nonsurgical population finding that substance abuse did not increase 30-day readmission but slightly lowered the risk [21]. In that 2013 single center study, a multidisciplinary team ensured patient follow up and resources were available [21]. We could not assess access to such a team in our PPCM cohort. In pregnant women, a high level of drug abstinence and postpartum relapse rate may explain our results [22,23]. Relapse has been identified as a cause of readmission in other patient populations. For example, a relapse in methamphetamine use was found to worsen heart failure [24] and contribute a higher readmission rate.

Our study found that the risk of in-hospital mortality in PPCM patients was dramatically increased with concurrent respiratory failure. Respiratory decompensation is the most common reason for readmission to the intensive care unit [25] and is associated with increased mortality [26]. We also found an association between discharge codes for coagulation disorders (including factor deficiencies and prothrombotic conditions) and mortality. While an association between coagulopathy disorders and mortality has not been observed in previous studies, a common cause of death in PPCM patients is thromboembolism [2]. Maternal hemorrhage was also part of obstetrical complications which we found to be one of the leading causes of mortality in PPCM patients who delivered. Further studies are indicated to determine the relationship between coagulation abnormalities and mortality in PPCM patients.

Mortality rates in our study did not significantly differ between PPCM patients that delivered during a hospital admission and PPCM patients who did not deliver during hospital admission. However, a 2015 study of cardiovascular pregnancy related deaths found that most cardiovascular deaths occurred after the peripartum period, indicating the potential need for closer monitoring

[9]. We found a significantly increased readmission rate for PPCM patients with delivery than those who did not deliver, indicating that chronicity may result from a different pathophysiology in longstanding PPCM, though the underlying cause is unknown. As the NRD only records preexisting diagnoses if they were present on a 2013 admission, it is difficult to assess the chronicity of a patient's PPCM diagnosis and its effect on readmission and mortality.

Our findings extend current knowledge regarding the clinical trajectory of PPCM patients. Although risk factors for mortality after PPCM have been studied previously, our study is unique in that to our knowledge, we are the first to report 30-day readmission rates, causes for readmission and was performed using a large nationwide database for patients with PPCM.

While we did not estimate the health care costs of patient readmission, unplanned readmissions are costly and the impact of such readmissions in 2004 was estimated at $17.4 billion dollars with a Medicare fee-for-service readmission rate of 19.6% [27].

Our study has limitations. Because data were retrospectively derived from an administrative database, missing or incorrect information may have skewed our findings. Our study population also consisted of younger patients of child-bearing age. As a result, the PPCM patient population has fewer preexisting medical conditions at baseline than elderly patient groups. We were also unable to assess risk factors for readmission related to hospital care including adverse drug events, optimal management of heart failure, or poor patient handoffs [28]. Although some authors note that patients of African descent are at higher risk for developing PPCM [4], we did not assess the effect of race on the risk for readmission of mortality as this information was not collected by the NRD.

The NRD also has inherent limitations. It does not count readmissions during the previous calendar year or in a different state from initial admission. It is thus possible that some of our patients had a readmission that was misidentified as an initial admission. However, HCUP-generated sensitivity analyses suggest that condition-specific readmission rates (including PPCM) were less than 5% higher if a patient could be tracked across all states. As a result, our readmission rate of 15% may have underestimated the true rate by a small amount. In addition, the NRD does not include data from rehabilitation facilities, actual readmission rate may be slightly higher.

In summary, our analysis of the NRD identified obesity, renal failure, and pulmonary hypertension as factors associated with 30-day readmission in patients with PPCM. Our data raise the possibility that better management of these associated conditions may lead to fewer readmissions. In addition, our observations that PPCM patients with coagulation disorders and respiratory failure were more likely to die suggest that identification and treatment of those conditions may improve mortality rates. Further studies are needed to better understand comorbidities associated with readmission and risk factors for mortality in this young patient population.

5. Conclusions

In a large national inpatient database analysis, we found that PPCM patients with pulmonary hypertension, obesity, renal failure, and drug abuse have an increased risk of readmission. Women with coagulation and respiratory failure had increased risk of in-hospital mortality.

Conflict of interest

Conducted in Chicago, IL. The authors report no conflict of interest.

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