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Original Article

Association Between Right Ventricular Dysfunction and Adverse Outcomes in Peripartum Cardiomyopathy: Insights From the BRO-HF Quebec Cohort Study

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ABSTRACT

Background: Peripartum cardiomyopathy (PPCM) is associated with severe morbidity and mortality, and the significance of right ventricular (RV) involvement is unclear. We sought to determine whether RV systolic dysfunction or dilatation is associated with adverse clinical outcomes in women with PPCM.

Methods: We conducted a multicentre retrospective cohort study examining the association between echocardiographic RV systolic dysfunction or dilatation at the time of PPCM diagnosis and clinical outcomes. Clinical endpoints of interest were the need for mechanical

RÉSUMÉ

Introduction : La cardiomyopathie du péripartum (CMP-PP) est associée à la morbidité grave et à la mortalité, mais on ignore l'importance de l'atteinte ventriculaire droite (VD). Nous avons cherché à déterminer si la dysfonction systolique ou la dilatation VD sont associées aux résultats cliniques défavorables chez les femmes atteintes de CMP-PP.

Méthodes : Nous avons mené une étude de cohorte rétrospective multicentrique sur l'association entre la dysfonction systolique ou la dilatation VD à l'échographie au moment du diagnostic de CMP-PP et

Peripartum cardiomyopathy (PPCM) is a condition affecting young, previously healthy women.[1] Several etiologic pathways have been proposed, including oxidative injury mediated by cleavage of the lactation hormone prolactin.[2] Symptoms develop toward the end of pregnancy, or in the first months postpartum,[3] and can vary from dyspnea to cardiogenic shock[4] requiring ventricular assistance or transplantation.[5,6] Despite advances in heart failure (HF) therapies, PPCM continues to carry a significant morbidity and mortality burden, including transplantation and death at rates ranging from 13% to 41% at 1-year follow-up.[7,8] Although several predictors of adverse outcomes have been identified,[8-11] the current burden of severe levels of morbidity and mortality of this disease underscores the importance of identifying additional markers to improve risk stratification and treatment.

Right ventricular (RV) dysfunction is identified in nearly half of women with PPCM,[12] and it is a strong predictor of adverse outcomes in HF outside of pregnancy.[13-18] Indeed, several reports suggest that biventricular dysfunction, in the

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Ethics Statement: Multicentric approval was granted by the Montreal Heart Institute Ethics Review Board; as this was a retrospective analysis conducted per institutional guidelines for data security and privacy, a waiver of consent was granted. The study was initiated, designed, and conducted by cardiology fellows under the close supervision of attendings with clinical research experience, in compliance with the collectively-operated fellow-initiated research principles. The authors had full access to data and take full responsibility for the integrity of the article content.

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support, recovery of left ventricular ejection fraction at follow-up, and a combined endpoint of hospitalization for heart failure, cardiac transplant, or death.

Results: A total of 67 women, median age 30 years (interquartile range: 7), were diagnosed with PPCM between 1994 and 2015 in 17 participating centres. Twin pregnancies occurred in 11%; 62% of women were multiparous; and 24% had preeclampsia. RV systolic function was impaired in 18 (27%) and dilated in 8 (12%). Seven women required ventricular assistance, and 8 experienced the composite outcome during follow-up (25 [interquartile range 61] months). RV dysfunction was associated with the need for mechanical support (odds ratio 10.10 (95% confidence interval: 1.86-54.81), $P = 0.007$), but neither RV dysfunction nor dilatation was associated with left ventricular ejection fraction recovery, the need for cardiac transplant, heart failure hospitalization, or death.

Conclusions: RV dysfunction is associated with the need for mechanical support in women with PPCM. These findings may improve risk stratification of complications and clinical management.

les résultats cliniques. Les critères cliniques d'intérêt étaient la nécessité d'une assistance mécanique, la récupération de la fraction d'éjection ventriculaire gauche (FEVG) au suivi et un critère combiné d'hospitalisation liée à l'insuffisance cardiaque (IC), la transplantation cardiaque ou la mort.

Résultats : Un total de 67 femmes, dont l'âge médian était de 30 ans (écart interquartile [EI] : 7), ont reçu un diagnostic de CMP-PP entre 1994 et 2015 dans 17 centres participants. Les grossesses gémellaires sont survenues chez 11 % ; 62 % de femmes étaient multipares ; et 24 % souffraient de prééclampsie. La fonction systolique VD était compromise chez 18 (27 %) femmes et le VD, dilaté, chez huit (12 %) femmes. Sept femmes ont eu besoin d'une assistance ventriculaire, et huit ont subi le critère composite durant le suivi (25 [EI : 61] mois). La dysfonction VD a été associée à la nécessité d'une assistance mécanique (rapport de cotes 10,10 [intervalle de confiance à 95 % : 1,86-54,81], $P = 0,007$), mais ni la dysfonction ni la dilatation VD n'ont été associées à la récupération de la FEVG, à la nécessité d'une transplantation cardiaque, à une hospitalisation liée à l'IC ou à la mort.

Conclusions : La dysfonction VD est associée à la nécessité d'une assistance mécanique chez les femmes atteintes de CMP-PP. Ces conclusions peuvent permettre d'améliorer la stratification des risques de complications et la prise en charge clinique.

setting of certain acute cardiomyopathies, is associated with a fulminant initial clinical course.[19-21] However, worse New York Heart Association class and biventricular failure, interestingly, have been associated with later improvement in left ventricular ejection fraction (LVEF)[22] in PPCM[23] and transplant-free survival.[20,21] RV dysfunction or dilatation specifically may predict worse LVEF recovery[11,24] and event-free survival[24,25] in PPCM, but some data suggest that no such association holds.[26] Therefore, what remains unclear, particularly in Canadian women diagnosed with PPCM, is whether RV dysfunction or dilatation at diagnosis is associated with a fulminant presentation, a chronic condition, or adverse events, an issue that has major implications for clinical management, prognosis, and risk stratification.

This study aimed to assess whether RV dysfunction or RV dilatation, at initial presentation, were associated with poor outcomes during short-term and/or long-term follow-up in this population.

Methods

Study population

We conducted a retrospective cohort study within previously collected retrospective data for the **Bro**mocriptine in **H**eart **F**ailure (BRO-HF) network from 17 hospitals in Quebec, Canada. Methodology has been described previously.[23] Briefly, possible cases of PPCM were identified from women hospitalized between January 1st, 1994 and December 31st, 2015 who displayed the International Classification of Diseases (ICD) 9 and 10 codes for [peripartum cardiomyopathy (674.5-O90.3)] or [diseases of the circulatory system (390-459−100-199) + pregnancy, childbirth and the puerperium (630-679−O00-O9A)] in their discharge summary. Peripartum cardiomyopathy was defined per current guideline definitions[1,3] as follows: (i) HF secondary to LV systolic dysfunction toward the end of pregnancy or in the months following delivery; (2) when no other cause of HF is found, in which case ejection fraction is nearly always reduced $< 45\%$. Baseline characteristics were abstracted from medical records in a standardized electronic database. Data collected included ethnicity, which was specified in medical records only if not Caucasian, obstetrical data (number of gestations, pre- or post-delivery PPCM diagnosis, complications of pregnancy), clinical (past medical history, vital signs) and laboratory results, and medication at discharge.

Echocardiographic data

The following echocardiographic parameters were abstracted from echocardiogram reports: degree of RV dysfunction (none, mild, moderate, or severe—as reported on the diagnostic echocardiogram report by the original performing physician, based on at least one abnormal value of either tricuspid annular plane systolic excursion [TAPSE], fractional area change [FAC], Doppler tissue imaging-derived tricuspid annular systolic velocity [S']), or degree of RV dilatation (none, mild, moderate, or severe—as reported on the diagnostic echocardiogram report by the original performing physician). Baseline characteristics in women were compared according to the presence or absence of reported RV dysfunction (normal vs mild, moderate, or severe dysfunction). Baseline characteristics also were compared according to the presence or absence of some degree of reported RV dilatation (Supplemental Table S1). LVEF, left ventricular end diastolic diameter (LVEDD), systolic pulmonary arterial pressure, and degree of mitral regurgitation (none, mild, moderate, severe) were abstracted from echocardiogram reports.

Quality assessment

Echocardiograms at diagnosis available in a digital format were reinterpreted in our echocardiography laboratory using an offline workstation (Echopac system, BT 12, General

Electric, Boston, MA) by one investigator (C.P.), who was blinded to clinical assessment. RV function parameters obtained on our assessment and reinterpretation were then compared to RV function as abstracted from clinical reports. Intraobserver variability was assessed through the reinterpretation, by C.P., of 10 randomly selected echocardiograms. A second investigator (M.T.G.) blindly reinterpreted 10 randomly chosen echocardiograms to estimate calibration and interobserver variability. RV size was assessed by linear dimensions. RV end-systolic area (ESA) and end-diastolic area (EDA; non-indexed) were used to calculate FAC. The RV base was measured in the apical 4-chamber view ($N < 42$ mm).[27] RV function was assessed using FAC, calculated using the formula[27] (FAC(%) = ((EDA− ESA)/EDA) x 100), $N > 34\%$), S' ($N > 9.5$ cm/s), and measurement of TAPSE using M-Mode ($N > 16$ mm). Systolic pulmonary arterial pressure was estimated by adding the pressure gradient measured between the RV and the right atrium to estimated central venous pressure, with the assumption of no pathology of the pulmonary valve. LVEDD and LVEF were assessed using the biplane Simpson method (without contrast).

Clinical endpoints

Clinical endpoints of interest included the following: (i) the need for ventricular assist devices; (ii) an LVEF at follow-up of $\geq$ 50%; and (iii) a combined clinical endpoint of hospitalization for HF, need for cardiac transplant, or death at longest available follow-up. The need for ventricular assist devices was defined as the implantation of an intra-aortic balloon pump, use of extracorporeal membrane oxygenation, or use of a left ventricular assist device (LVAD). HF events were defined per the 2014 American College of Cardiology/American Heart Association Key Data Elements and Definitions for Cardiovascular Endpoint Events in Clinical Trials.[28] Any hospital admission primarily for HF was considered an endpoint if the patient exhibited clear symptoms, the patient had objective evidence of HF, and treatment was intensified.

LVEF at follow-up was abstracted from clinical reports 6 ± 3 months following diagnosis and up until the last available echocardiograms thereafter. Patients were followed through medical records until the last available follow-up. Duplicate and parallel medical records, in the case of transfer between institutions, were reconciled using the unique health identification number, as provided by the Régie de l'Assurance Maladie du Québec (RAMQ).

Statistical analysis

A D'Agostino−Pearson test was used to assess the normality of distribution. Data are reported as mean and standard deviation, or median (interquartile range). Categorical variables are reported as absolute numbers (%). Continuous variables were compared using a paired *t*-test, a Wilcoxon signed-rank test, or a Kruskal-Wallis test. Categorical variables were compared with the χ^2 or Fisher's exact test, or with the McNemar test, as appropriate. Statistical significance was determined at the 2-sided $\alpha = 0.05$. Intraobserver variability was assessed using intraclass correlation coefficients. Univariate logistic regression analyses were performed to identify clinical and echocardiographic characteristics associated with the following: (i) the need of cardiac assist devices in our study group; and (ii) an LVEF $\geq$ 50% at follow-up. Receiver operating characteristics curve analysis was performed to identify optimal cutoff values of variables predicting a LVEF $\geq$ 50% at follow-up. Univariate analyses using χ^2 tests were also performed to test the association between LV recovery and medications at discharge. Univariate Cox proportional hazards models were used to assess the association between the combined endpoint and the following variables: age, ethnicity, RV dysfunction and dilatation, and LV dysfunction and dilatation. Kaplan−Meier survival analysis was conducted according to identified univariate predictors of the combined endpoint. No data imputation was performed. Patients with missing information concerning RV dysfunction and dilatation were omitted from analyses reported in this article. No correction for multiple comparisons was performed, as all analyses are considered exploratory. Statistical analyses were performed using MedCalc for Windows, version 18 (MedCalc Software, Mariakerke, Belgium). The authors had full access to data and take full responsibility for the integrity of the article content.

Multicentric approval was granted by the Montreal Heart Institute Ethics Review Board: as this was a retrospective analysis conducted per institutional guidelines for data security and privacy, a waiver of consent was granted. The study was initiated, designed, and conducted by cardiology fellows under the close supervision of attendings with clinical research experience, in compliance with the collectively-operated fellow-initiated research principles.[29]

Results

Study population

A total of 76 women fulfilled PPCM diagnostic criteria. RV data were available for 67 of them, constituting our study population (Table 1). Most were Caucasian (68%), whereas 26% were African American, and 5% were Native American. Twin pregnancies occurred in 11%; 62% of patients were multiparous. Among the 67 patients, 18 (27%) had an impaired RV function at diagnosis. Among those, the RV function was described as mildly impaired in 7 patients (11%), moderately impaired in 10 patients (15%), and severely impaired in 1 patient (2%). RV dilatation was reported in 8 of the patients (12%). The dilatation was mild in 5 women (8%), moderate in 2 (3%), and severe in 1 patient (2%). Bromocriptine was used in 8 women (12%), more frequently in those with RV dysfunction ($P = 0.02$). Women with RV dysfunction had higher creatinine levels ($P = 0.02$), although their creatinine levels were still within normal range. Initial LVEF was lower in these women ($P < 0.001$). More women with RV dysfunction had at least moderate mitral regurgitation ($P = 0.02$) and were more likely to be discharged on mineralocorticoid receptor antagonists ($P = 0.02$).

Accuracy of the echocardiography report assessments

Echocardiograms were available for review in 29 patients. Median measured FAC and TAPSE were 37% (range: 28%-45%) and 18 mm (range: 16-21 mm), respectively. For both

Table 1. Patients' baseline characteristics according to right ventricular (RV) function

Characteristics	All patients (n = 67)	Preserved RV function (n = 49)	Impaired RV function (n = 18)	*P*
Demographics				
Age, y, median (IQR)	30 (7)	31 (6)	30 (10)	0.45
Ethnicity				
Caucasian	43(68)	33 (71)	10 (59)	0.25
African American	17 (26)	12 (26)	5 (29)	
Native American	3 (5)	1 (2)	2 (12)	
Index pregnancy details				
Postpartum presentation	62 (93)	45 (92)	17 (94)	0.72
Twin pregnancy	6 (11)	5 (14)	1 (6)	0.24
Multiparity	38 (62)	30 (67)	8 (50)	0.24
Preeclampsia	16 (24)	12 (25)	4 (22)	0.85
Medical history				
Pre-existing hypertension	10 (15)	6 (12)	4 (22)	0.31
Pre-existing diabetes	8 (12)	6 (12)	2 (11)	0.90
Hyperlipidemia	2 (3)	2 (4)	0	—
Tobacco use	16 (25)	12 (24)	4 (27)	0.86
Clinical characteristics, median (IQR)				
NYHA functional class at diagnosis	4 (1)	3 (2)	4 (0)	0.08
SBP, mm Hg	126 (30)	129 (33)	120 (38)	0.20
Heart rate, bpm	115 (35)	110 (35)	118 (29)	0.43
Creatinine, mmol/L	68 (27)	65 (21)	78 (31)	**0.02**
Hemoglobin, g/L	117 (28)	117 (24)	110 (31)	0.90
Echocardiographic findings at diagnosis				
LVEF, %, median (IQR)	25 (20)	33 (19)	21 (10)	**0.001**
LVEDD, %, median (IQR)	58 (9)	59 (9)	56 (11)	0.95
SPAP, %, median (IQR)	44 (18)	45 (20)	43 (12)	0.64
At least moderate MR	36 (54)	22 (45)	14 (78)	**0.02**
Medication at discharge				
Beta-blockers	54 (81)	39 (81)	15 (83)	0.84
ACEIs/ARBs	56 (85)	41 (85)	15 (83)	0.83
MRA	8 (12)	3 (6)	5 (28)	**0.02**
Loop diuretics	40 (61)	28 (58)	12 (67)	0.54
Oral anticoagulation	18 (27)	11 (23)	7 (39)	0.19
Digoxin	12 (18)	6 (13)	6 (33)	0.05
Bromocriptine	8 (12)	3 (6)	5 (28)	**0.02**
CRT	2 (3)	1 (2)	1 (6)	0.45
ICD	8 (12)	5 (10)	3 (17)	0.47

Values are n (%), unless otherwise indicated. Bold font = $P < 0.05$.

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CRT, cardiac resynchronization therapy; ICD, implantable cardiac defibrillator; IQR, interquartile range; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; MRA, mineralocorticoid receptor antagonists; NYHA, New York Heart Association; SBP, systolic blood pressure; SPAP, systolic pulmonary arterial pressure.

FAC and TAPSE, the intraobserver intraclass correlation coefficient (ICC) was 0.95 ($P < 0.01$), suggesting excellent reliability (Supplemental Table S2). Interobserver ICC for FAC and TAPSE was 0.81 ($P < 0.01$) and 0.96 ($P < 0.01$), respectively, suggesting good reliability (Supplemental Table S3). FAC was considered abnormal in 13 patients (45%), and TAPSE in 10 (35%). A significant association was found between measured FAC and reported RV function (Fig. 1), confirming that the estimated grades of RV dysfunction had some accuracy. Median measured FAC was 43% (range: 34%-47%) in women with reported normal function, 32% (range: 26%-36%) in women with reported mild dysfunction, and 30% (range: 21%-36%) in those with reported moderate dysfunction ($P = 0.04$). Similar findings were observed with measured TAPSE, but with less statistical significance ($P = 0.05$). Measured RV basal diameter was significantly smaller in patients with no reported dilatation than in those with reported dilatation ($P = 0.03$). Finally, a strong correlation was seen between both measured and reported LVEF ($R^2 = 0.79$, $P < 0.001$) and LVEDD ($R^2 = 0.83$, $P < 0.001$; Supplemental Fig. S1).

Outcomes of interest in women with PPCM

Seven women required mechanical circulatory support in the early onset of PPCM (6 required intra-aortic balloon pumps, 1 required an LVAD, and none required extracorporeal membrane oxygenation) (Fig. 2). Univariate logistic

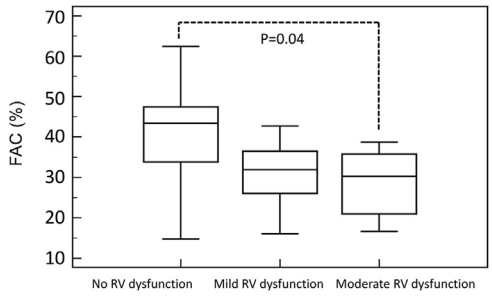

Figure 1. Association between the measured fractional area change (FAC) and the degree of right ventricular (RV) dysfunction abstracted from the echocardiogram reports.

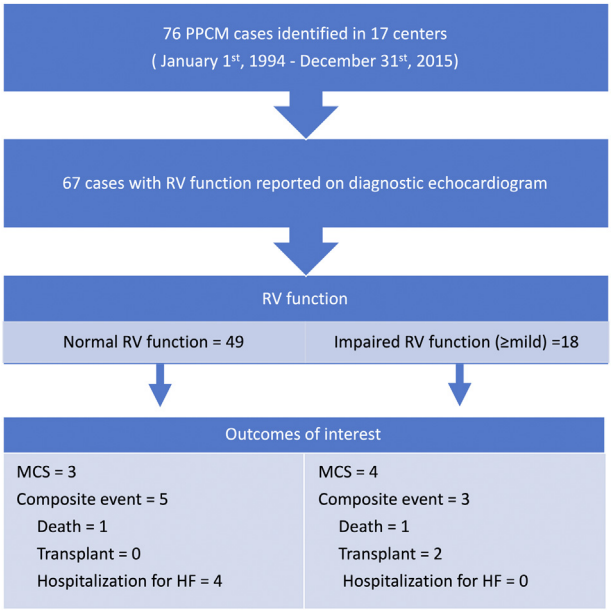

Figure 2. Events according to right ventricular (RV) function. HF, heart failure; MCS, mechanical circulatory support; PPCM, peripartum cardiomyopathy.

regression analysis for factors associated with mechanical circulatory support is shown in Table 2 (excluding LVEF because of collinearity). Only RV dysfunction (moderate or more), and not RV dilatation, LVEDD, mitral regurgitation, or systolic pulmonary arterial pressure, was found to be associated with the need of cardiac assist devices (odds ratio [OR] 10.10, confidence interval [CI] 1.86- 54.81, $P = 0.007$; Table 2).

The result of an echocardiogram performed 3-9 months after diagnosis was available in 35 of 67 patients (52%; median echo follow-up 5.7 [range: 4.6-7.0] months). In this subgroup of patients, the median LVEF improved (from 25% [range: 20%-39%] to 54% [range: 42%-60%], $P < 0.001$). LVEDD was the only variable associated with an LVEF $\geq$ 50% at follow-up (OR 0.82 [CI 0.69-0.96], $P = 0.02$; Supplemental Table S4). For LVEDD, a value of $\leq$58 mm was predictive of an LVEF $\geq$ 50% at follow-up, with a sensitivity of 78% and a specificity of 64% (area under the curve, 0.74; (CI 0.55-0.88); $P = 0.008$; see Supplemental Fig. S2). Similarly, univariate analyses using χ^2 tests also were

Table 2. Univariate analysis for factors associated with the need for ventricular assist devices during index hospitalization

Parameter	Univariate analysis, n = 67 OR (95% CI); *P*
RV dysfunction (≥ moderate)	10.10 (1.86−54.81); **0.007**
RV dilatation (≥ mild)	3.60 (0.57−22.76); 0.17
LVEDD	0.99 (0.89−1.11); 0.91
Mitral regurgitation (≥ moderate)	2.34 (0.42−13.01); 0.33
SPAP	1.03 (0.96−1.11); 0.38

Bold font = $P < 0.05$.

CI, confidence interval; LVEDD, left ventricular end diastolic diameter; OR, odds ratio; RV, right ventricular; SPAP, systolic pulmonary arterial pressure.

Table 3. Univariate analysis for predictors of heart failure, cardiac transplant, or death

Parameter	Univariate analysis, n = 67 HR (95% CI); *P*
Age	0.90 (0.78−1.05); 0.17
African American women	0.69 (0.08−5.82); 0.73
Use of bromocriptine	0.91 (0.11−7.39); 0.93
RV dysfunction (moderate and more)	2.06 (0.41−10.27); 0.38
RV dilatation (mild and more)	2.38 (0.48−11.84); 0.29
LVEDD at diagnosis	1.16 (1.06−1.26); **0.002**
LVEF at diagnosis	0.93 (0.86−1.01); 0.10

Bold font = $P < 0.05$.

CI, confidence interval; HR, hazard ratio; LVEDD, left ventricular end diastolic diameter; LVEF, left ventricular ejection fraction; RV, right ventricular.

performed to test the association between LV recovery and the following medications: beta-blockers (n = 31, $P = 0.48$), mineralocorticoid receptor antagonists (n = 3, $P = 0.58$), an angiotensin-converting enzyme inhibitor or an angiotensin II receptor blocker (n = 32, $P = 0.75$), and bromocriptine (n = 7, $P = 0.09$).

Eight patients (12%) reached the composite outcome of admission for HF, cardiac transplant, or death. Using univariate analysis, baseline LVEDD appeared to be the only significant predictor of adverse events (Table 3, hazard ratio 1.16 [CI 1.06-1.26], $P < 0.01$). Using the cutoff of 58 mm for LVEDD, as defined by the receiver operating characteristics analysis (Supplemental Fig. S2), revealed a trend for a higher event-free survival in patients with an LVEDD $\leq$58 mm ($P = 0.07$; Fig. 3).

Discussion

This is the first report of echocardiographic RV evaluation in Canadian women diagnosed with PPCM, and the second-largest cohort examining the association between RV function and size and adverse clinical outcomes. To our knowledge, our study is also the first to examine the correlation between qualitative evaluation and quantitative echocardiographic parameters of RV size and function in women with PPCM. In 67

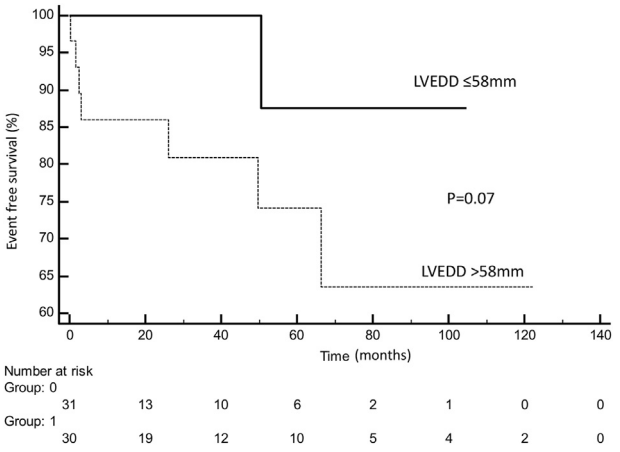

Figure 3. Kaplan-Meier curves for event-free survival according to left ventricular end-diastolic diameter (LVEDD).

women diagnosed with PPCM in this cohort, RV systolic function was impaired in 27%, and the RV was dilated in 12%. RV dysfunction predicted the need for mechanical support, but neither RV dysfunction nor dilatation was predictive of an LVEF $\geq$ 50% at follow-up, or the combined clinical endpoint of hospitalization for HF, cardiac transplant, or death.

One in 4 women presented with RV dysfunction in our population, similar to findings in most previously reported PPCM cohorts,[11,24,26,30] except for the international PPCM registry,[12] in which some degree of RV dysfunction was reported in 47% of women. RV dilatation was described in 12% of women in our cohort, compared to 56% in previous reports.[24] These differences may be due to heterogeneous methodology and classification of RV size and function, or potential regional phenotypical differences. At-least-moderate RV dysfunction was the only predictor for the need for mechanical circulatory support, identifying a subgroup of patients at higher risk of cardiogenic shock requiring LVADs. Three retrospective studies have previously examined RV dysfunction and adverse outcomes in PPCM. A study of 45 PPCM patients in Nigeria found that TAPSE $\leq$ 16 mm was not associated with 1-year mortality.[26] Another study identified moderate-to-severe RV dysfunction as the only independent predictor of adverse clinical events in 53 women, 11 of whom required cardiac transplantation.[25] Women in this cohort with worse RV dysfunction had an median LVEF of 12.5% vs 32.5% (compared to an LVEF of 33% vs 21% in our cohort)[25]; thus, they likely represented a distinct phenotype of PPCM, given the much higher incidence of cardiac transplantation than that in both our cohort and a prospective study examining RV dysfunction in 84 women with PPCM.[24] This prospective study identified FAC $<$ 30% as a predictor of a combined outcome, in which 4 of 6 events were LVAD implantation.[24] Our findings support those previously in the literature suggesting that significant RV dysfunction likely portends more extensive acute myocardial stunning and damage in the acute phase of PPCM,[31] and predicts the need for aggressive management including temporary mechanical assistance. These echocardiographic findings identify women at higher risk of potential complications who require heightened clinical surveillance, and earlier consideration for mechanical support interventions.

RV dysfunction was not associated with the composite outcome of hospitalization for HF, cardiac transplant, and death in our cohort. It may not carry the same long-term prognostic significance in PPCM, in which LV recovery occurs more frequently than it does in other types of nonischemic cardiomyopathy.[22,32]TAPSE has been found to be significantly lower in PPCM patients, compared to the level in those diagnosed with dilated nonischemic cardiomyopathies,[30] despite a well-established poorer prognosis in the latter.[22,32] PPCM-related RV dysfunction, therefore, is likely indicative of a more severe clinical phenotype, characterized by acute biventricular dysfunction, lower LVEF at diagnosis, more severely decompensated HF, and cardiogenic shock often requiring urgent intervention, whereas LV dilatation, likely a surrogate for irreversible structural remodelling, fibrosis,[33] and permanent myocardial injury, identifies women at higher risk for persistent LV dysfunction and long-term adverse clinical outcomes.

RV dysfunction was not associated with worse LVEF recovery in our cohort. These results are in contrast to those in previous reports in the literature, which have suggested that RV dysfunction on cardiac magnetic resonance imaging is associated with poor LV recovery.[11] A recent study examining RV dysfunction as assessed by cardiac magnetic resonance imaging in 40 women with PPCM found that those with reduced RVEF at baseline had significantly lower rates of LVEF recovery ($\geq$ 50%) at 6 months, with all women receiving either a 1-week or an 8-week course of bromocriptine.[34] Possible explanations for our contrasting findings include differences in sample size, the limited number of follow-up echocardiograms performed in our cohort, regional phenotypical differences, and unknown residual confounders. LVEDD $\geq$ 58 mm was a useful discriminator in identifying women with poor LVEF recovery and was the only echocardiographic parameter associated with transplantation or death. LV dilatation has been previously associated with poor LV recovery or adverse outcomes in several cardiomyopathies, including PPCM.[8,10,35,36]

African American women comprised 26% of this cohort, similar to the proportion in the international PPCM registry, but higher than that in European countries, where they only represent 5.1% of cases.[12] In our cohort, African American women had proportions of RV dysfunction and dilatation similar to those among other women. In contrast with previous reports, we found that ethnicity was not a predictor for an LVEF recovery or adverse outcomes.[8,24] This finding may be due to environmental and socioeconomic factors differing in the Canadian context, as well as the small size of our study population.

On quality analysis, RV function and size as assessed on initial diagnosis by the original echocardiographer correlated with precise RV function and size parameters on reinterpretation of echocardiograms obtained. We found that both FAC and TAPSE and RV basal diameter measurements correlated significantly with qualitatively assessed reported RV function and size, respectively. The global assessment of RV function in everyday practice is determined after consideration of one or more of these parameters, as recommended by current guidelines.[27] Previous studies have described a similar correlation between qualitative assessment of RV function using echocardiography and right heart catherization findings indicative of worse RV function in the PPCM population.[25]

Our study has several limitations. As a retrospective trial, it has potential bias and confounders inherent to this type of study. The sample size is relatively small, albeit similar to that of other PPCM cohorts.[8,24,26,36] Reporting of ethnicity was incomplete in medical records, limiting analysis and interpretation of findings. Quantification of RV function was not uniformly performed using a single parameter, and RV dysfunction may have been underdiagnosed, as suggested by the higher proportion of RV dysfunction found in revised echocardiograms; however, correlation between our laboratory reinterpretation of the echocardiogram and the original echocardiographic report suggests adequate assessment of RV function by the initial reader. Given that reported RV size did not correlate with all measured parameters of RV size on echocardiogram reinterpretation, misclassification of RV dilatation in this cohort is possible. Guideline recommendations for RV size measurements also changed over the time

period covered by our study. Our study employed frequently obtained measurements, such as FAC, TAPSE, and S', which are simple to perform and are reproducible.[27,37] Echocardiograms performed between 3 and 9 months following diagnosis were not available in all women, as follow-up echocardiograms were ordered clinically according to treating physician, introducing loss to follow-up and thus limiting interpretation of findings concerning LVEF recovery.

Conclusions

Peripartum cardiomyopathy carries significant morbidity risk in both the acute and chronic phase of its clinical course. Women requiring advanced HF therapies in the acute phase of PPCM must be appropriately identified using clinical and paraclinical parameters, including echocardiographic data. Findings in this retrospective cohort are hypothesis-generating, but they suggest that women with PPCM and RV dysfunction are at higher risk of acute morbidity. These findings, if confirmed in larger prospective studies, may help improve appropriate and timely referral of women with PPCM for advanced therapies, improving risk stratification and clinical management.

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Supplementary Material

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