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CASE REPORT

INTERMEDIATE

CLINICAL CASE SERIES

Exercise Ventricular Reserve Among Women With a History of Peripartum Cardiomyopathy

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ABSTRACT

Peripartum cardiomyopathy (PPCM) is associated with highly variable clinical outcomes. Small series suggest postpartum variation in exercise capacity and ventricular reserve. We describe limitations in exercise capacity and/or ventricular reserve in asymptomatic women who had recovered from PPCM and underwent a detailed physiologic assessment by cardiopulmonary exercise testing. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2021;3:1649–1653)

Peripartum cardiomyopathy (PPCM) is an uncommon complication of pregnancy characterized by new-onset left ventricular (LV) dysfunction (1). The majority of affected women will demonstrate recovery of resting LV function (LVEF) (1); however, even among women who recover there is a significant risk of recurrence during subsequent pregnancies (SSP) (2). Ventricular contractile reserve is predictive of outcome in a range of cardiomyopathies (3) and is incompletely understood in women with PPCM. Additionally, exercise capacity, measured by peak oxygen uptake (peak VO_2), is prognostic in patients with heart failure (4), and impairment of peak VO_2 has been reported late after PPCM (5).

LEARNING OBJECTIVES

- To demonstrate the variable pattern of exercise capacity in woman after PPCM.
- To demonstrate the variable pattern of ventricular reserve in women after PPCM

Cardiopulmonary exercise testing (CPET) with first-pass radionuclide ventriculography (FP-RNV) can be used to understand exercise capacity and biventricular contractile reserve and may be helpful in risk stratifying women with a history of PPCM. We report on the variability of exercise capacity and ventricular contractile reserve in 6 women with a history of PPCM who underwent subsequent clinical CPET with FP-RNV imaging.

PATIENT CHARACTERISTICS AND OUTCOMES

Patients were identified from our institutional database of women with a diagnosis of PPCM. We identified 6 women who had been referred for subsequent CPET with FP-RNV to assess their exercise capacity and ventricular reserve. **Table 1** outlines the clinical and transthoracic echocardiographic (TTE) characteristics of the PPCM presentation and status before CPET. One patient was 53 years old, and others' ages ranged from 22 to 33 years at presentation. Four out of 6 women experienced hypertensive disorder of

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ABBREVIATIONS AND ACRONYMS

CPET = cardiopulmonary exercise testing

FP-RNV = first pass radionuclide ventriculography

GDMT = guideline-directed medical therapy

LV = left ventricle

LVEF = left ventricular ejection fraction

PPCM = peripartum cardiomyopathy

RV = right ventricle

RVEF = right ventricular ejection fraction

SSP = subsequent pregnancy

pregnancy. LVEF nadir range was 20% to 45% by TTE. The majority (4/6) presented in the early postpartum period with symptomatic heart failure. By TTE, LVEF recovered to >50% in all patients over 2 to 18 months. Right ventricular function (RVEF) was mildly impaired in 1 patient at diagnosis and normalized at follow-up. At the time of the CPET, all patients were asymptomatic, and guideline-directed medical therapy (GDMT) for heart failure had been discontinued in 3 patients after sustained normalization of LVEF. Left (−23.3 ± 2.4) and right (−28.3 ± 4.3) ventricular global longitudinal strain and diastolic function were normal in all patients at the time of CPET.

CARDIOPULMONARY EXERCISE TESTING WITH FIRST-PASS RADIONUCLIDE VENTRICULOGRAPHY RESULTS

CPET with FP-RNV testing was conducted between 1 and 5 years after affected pregnancy by our institution's standard protocol. LV contractile reserve was defined as an increase in LVEF ≥5% with exercise. Right ventricular (RV) contractile reserve was defined as a peak exercise RVEF to above 45% and augmentation of >5% from rest or exercise RVEF >50% (6). Detailed findings are described in **Table 2**. Five women had mild or moderate impairment of exercise capacity based on peak VO_2 (% predicted VO_2 peak = 52% to 74%, n = 5), and achieved metabolic equivalents (METS) were relatively low (4.3-5.9). Three women showed evidence of impaired ventricular reserve (1 LV and 2 RV) and all had normal resting biventricular systolic function based on TTE.

SUBSEQUENT PREGNANCIES

Two women had subsequent pregnancies (SSP) during follow-up (Patients 2 and 3). The first had normal exercise capacity, normal peak VO_2 max, and mild impairment of RV contractile reserve on CPET. Her LVEF remained normal throughout pregnancy and the postpartum period. The second had impaired RV reserve and demonstrated moderately reduced exercise capacity by peak VO_2 max (**Figure 1**). Her pregnancy and delivery were uncomplicated. In the early postpartum period, she experienced recurrent heart failure symptoms with reduction in LVEF to 34% and associated elevation in NT-proBNP (559 pg/mL). She experienced persistent severe reduction in LVEF to 30% out to 9 months of postpartum follow-up despite reintroduction of GDMT.

DISCUSSION

We describe the variable pattern of exercise capacity and ventricular contractile reserve in women with a history of recovered PPCM. Notably, impaired exercise capacity and impaired LV or RV contractile reserve were observed among women with echocardiographically normal resting biventricular systolic function without evidence of subclinical ventricular dysfunction at rest, based on strain echocardiography.

Ventricular contractile reserve is prognostic in many populations (3,6) and has been considered a

TABLE 1 Characteristics of PPCM and Subsequent Ventricular Function

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age at pregnancy (y)	33	22	32	53	30	29
Race	Caucasian	African American	Caucasian	Caucasian	Asian	Caucasian
Gravity (G) and parity (P)	G1:P1	G1:P1	G1:P1	G4:P1	G1 P1+1	G4P3
Timing of presentation	Immediate postpartum	36 weeks gestation	Immediate postpartum	38 weeks gestation	6 weeks postpartum	Immediate postpartum
Complications of pregnancy	Preeclampsia		Gestational hypertension	Preeclampsia	Gestational diabetes	Gestational hypertension
Cardiovascular comorbidities	Obesity	Obesity	Obesity	None	None	Obesity
LVF nadir	35%	32%	42%	35%	20%	45%
LVEF recovery to >50%	Yes	Yes	Yes	Yes	Yes	Yes
Time to LVEF recovery	2 months	12 months	2 months	18 months	12 months	4 months
Resting global LV strain at the time of CPET	-25.1	-23.7	-20.5	-26.1	-24.3	-20.1
Resting RV function at diagnosis	Mildly impaired	Normal	Normal	Normal	Unknown	Normal
GDMT at the time of CPET	Metoprolol succinate	Metoprolol succinate	None	Losartan, metoprolol succinate	None	None

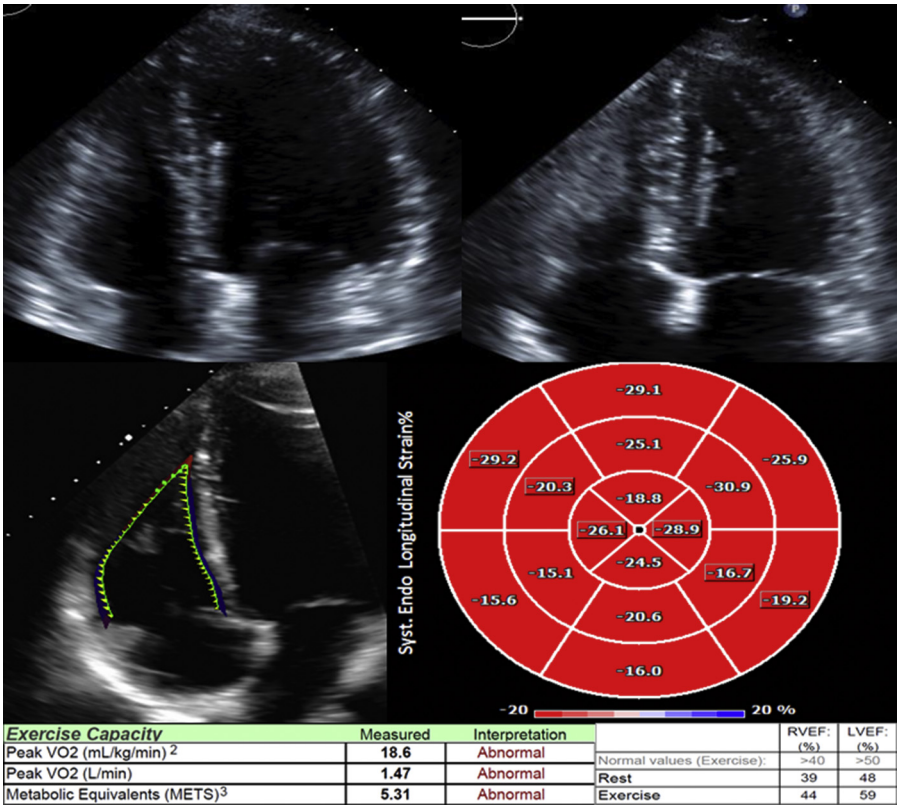
CPET = cardiopulmonary exercise testing, LV = left ventricle, LVEF = left ventricular ejection fraction, PPCM = peripartum cardiomyopathy, RV = right ventricle.

TABLE 2 Detailed CPET Results

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Time from PPCM to CPET (y)	1.7	1.1	1.2	2.9	3.0	4.8
Peak VO_2 (ml/kg/min)	17.1	18.6	18.4	15	18	20.6
% Age predicted VO_2	74	64	96	81	65	52
Peak heart rate (beats/min)	151	159	177	166	171	168
% Predicted peak HR	82	81	95	102	91	90
METs	4.9	5.3	5.3	4.3	5.1	5.9
Peak SBP (mm Hg)	148	135	140	174	178	142
O_2 pulse peak (ml/beat)	8.0	9.2	10.7	8.3	8.6	7.0
VE/VCO_2 slope	23.9	29.6	21.7	32.1	30.6	28.9
Resting LVEF by FP-RNV (%)	56	48	67	48	56	53
Exercise LVEF by FP-RNV (%)	69	59	74	56	58	62
LV reserve	Normal	Normal	Normal	Normal	Impaired	Normal
Resting RVEF by FP-RNV (%)	50	39	46	42	51	51
Exercise RVEF by FP-RNV (%)	51	44	50	49	56	53
RV reserve	Normal	Impaired	Impaired	Normal	Normal	Normal

CPET = cardiopulmonary exercise testing, FP-RNV = first pass radionuclide ventriculography, HR = heart rate, METs = metabolic equivalents, O_2 pulse peak = VO_2/HR, Peak VO_2 = maximum rate of oxygen consumption at peak exercise, SBP = systolic blood pressure, VE/VCO_2 = minute ventilation/carbon dioxide production (normal = <33).

FIGURE 1 Normal Biventricular Function and Strain in a Patient With Absence of Right Ventricular Reserve and Subsequent Recurrent PPCM



These images demonstrate the normal resting right ventricular (RV) and left ventricular systolic function and strain in a patient recovered from peripartum cardiomyopathy (PPCM). This patient exhibited impaired RV reserve on cardiopulmonary exercise testing with a moderate reduction in exercise capacity and experienced recurrent PPCM in a subsequent pregnancy. VO_2 = peak oxygen uptake.

potential mechanism of predicting recurrence of PPCM. A small case series evaluating the relapse risk in pregnancy after PPCM reported no evidence of recurrence in 9 women who underwent pre-pregnancy exercise echocardiography with evidence of normal contractile reserve (7) The 2 patients in our series who underwent SSP both had evidence of impaired RV reserve, although they differed in the patterns of their RV impairment and exercise capacity by VO_2 max. Interestingly, all patients had normal echocardiographically derived LVEF and left and right ventricular longitudinal strain at the time of CPET testing, suggesting that exercise testing unmasked abnormalities that could not be identified at rest. Although data are very limited, we consider evidence of intact ventricular contractile reserve on CPET with FP-RNV reassuring when a woman with PPCM is contemplating SSP. Lack of contractile reserve may also identify a population in whom consideration should be given to the long-term continuation of GDMT.

In this young asymptomatic population, impaired exercise capacity was seen in the majority of women, and the METS achieved was modest. Exercise capacity measured by peak VO_2 is prognostic in patients with chronic systolic heart failure (4,8). Some evidence suggests that women with PPCM will have reduced peak VO_2 at long-term follow-up independently of the presence of coexisting hypertensive disorders of pregnancy (5). We have demonstrated similar findings even among women in clinically stable condition with recovered LVEF. Peak VO_2 represents multiorgan function and is not specific to cardiac capacity; however, it is plausible that women with lower peak VO_2 might be more prone to decompensation when exposed to recurrent pregnancy.

CPET with FP-RNV is unique in providing overall measures of cardiorespiratory fitness and ventricular contractile reserve in a single test. Of note, RNV carries a small risk of radiation exposure, and frequent serial testing is not recommended. FP-RNV may also underestimate LVEF when compared with other modalities and therefore was not used as the sole determinant of ventricular recovery in this series (9). Although the current series is insufficiently powered to evaluate the interaction of exercise tolerance and ventricular reserve on prognosis and future risk, it seems reasonable that such detailed assessment will provide additive information to stress testing or VO_2 max testing alone. This series demonstrates that the impaired exercise capacity as assessed by peak VO_2 as well as abnormal LV or RV reserve may be present even among asymptomatic women with recovered resting ventricular function, suggesting that ongoing abnormalities in myocardial contractility may exist even years after resting function recovers.

CONCLUSIONS

A subset of asymptomatic women with a history of PPCM and normalized LVEF and strain patterns demonstrate exercise limitation and loss of ventricular reserve on CPET with FP-RNV. Objective measures of exercise capacity and ventricular reserve may provide additive information for clinicians in estimating the risk of recurrence in future pregnancies in this population and the need for long-term medical therapy.

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