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) © 2021 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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 VO₂), is prognostic in patients with heart failure (4), and impairment of peak VO₂ has been reported late after PPCM (5).

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...
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 VO2 (% predicted VO2 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 VO2 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 VO2 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** | **Age at pregnancy (y)** | **Race** | **Gravity (G) and parity (P)** | **Timing of presentation** | **Complications of pregnancy** | **Cardiovascular comorbidities** | **LVEF nadir** | **LVEF recovery to >50%** | **Time to LVEF recovery** | **Resting global LV strain at the time of CPET** | **Resting RV function at diagnosis** | **GDMT at the time of CPET** |
|-------------|--------------------------|---------|-------------------------------|--------------------------|-----------------------------|-------------------------------|----------------|--------------------------|---------------------------|--------------------------------|-----------------------------|-----------------------------|
| 1           | 33                       | Caucasian | G1:1 | Immediate postpartum | Preeclampsia | Obesity | 35% | Yes | 2 months | -25.1 | Mildly impaired | Metoprolol succinate |
| 2           | 22                       | African American | G1:1 | 36 weeks gestation | Gestational hypertension | Obesity | 32% | Yes | 12 months | -23.7 | Normal | Metoprolol succinate |
| 3           | 32                       | Caucasian | G1:1 | Immediate postpartum | Preeclampsia | Obesity | 42% | Yes | 2 months | -20.5 | Normal | None |
| 4           | 53                       | Caucasian | G1:1 | 38 weeks gestation | Gestational hypertension | None | 35% | Yes | 18 months | -26.1 | Normal | Losartan, metoprolol succinate |
| 5           | 30                       | Asian | G4:1 | 6 weeks postpartum | Gestational diabetes | None | 20% | Yes | 12 months | -24.3 | Unknown | None |
| 6           | 29                       | Caucasian | G4P3 | Immediate postpartum | Gestational hypertension | Obesity | 45% | Yes | 4 months | -20.1 | Normal | 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    | Impaired  | Normal    | 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 VO2 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 VO2 is prognostic in patients with chronic systolic heart failure (4,8). Some evidence suggests that women with PPCM will have reduced peak VO2 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 VO2 represents multiorgan function and is not specific to cardiac capacity; however, it is plausible that women with lower peak VO2 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 contractile reserve in a single test. Of note, RNV measures of cardiorespiratory fitness and ventricular contractile reserve in a single test. Of note, RNV measures of cardiorespiratory fitness; however, it is plausible that women with lower peak VO2 might be more prone to decompensation when exposed to recurrent pregnancy.

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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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