Cardiac Function in Women With Peripartum Cardiomyopathy
The Tip of the Iceberg*

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Peripartum cardiomyopathy (PPCM) remains challenging to manage, particularly related to the variable recovery pattern. Although many women have full recovery, others have persistent cardiac dysfunction (1). Among those with normalization of the left ventricular ejection fraction (LVEF), the optimal duration of guideline-directed medical therapy (GDMT) is unknown. Additionally, many women with PPCM wish to have another pregnancy, but recurrent heart failure and cardiac dysfunction is a risk (2). Therefore, prediction of relapse after withdrawal of medications or with a subsequent pregnancy is clinically important.

Prior studies of PPCM have assessed subclinical myocardial dysfunction as measured by abnormal global left ventricular strain imaging, contractile reserve, and cardiac magnetic resonance imaging (3-5). Studies of contractile reserve and functional capacity in women with PPCM are lacking, and cardiopulmonary exercise testing (CPET) with first pass radionuclide ventriculography (FP-RNV) has not been well-studied in this population.

In this issue of JACC: Case Reports, Yucel et al. (6) present a case series of 6 women with PPCM and LVEF recovery to >50% who subsequently underwent CPET with FP-RNV to evaluate exercise capacity and biventricular contractile reserve. The patients in this series were ages 22 to 33 years, except for 1 patient who was 53 years of age. Four of the patients had prior hypertensive disorders of pregnancy (2 with preeclampsia, 2 with gestational hypertension) and 4 had obesity. The nadir LVEF ranged from 20%-45%. The time to recovery ranged from 2 to 18 months. The time from initial diagnosis to the time of assessment by CPET with FP-RNV ranged from 4.1-4.8 years. All patients had a LVEF >50% with a normal strain pattern and diastolic function at the time of testing. These patients were asymptomatic at the time of testing and had received GDMT, but medications had been discontinued in 50% of patients. Impairment in ventricular contractile reserve was seen in 50% of the participants (1 with impaired LV reserve and 2 with impaired right ventricular reserve).

An average of 5 metabolic equivalents were achieved by the participants (range of 4.3-5.9 metabolic equivalents), which is a low level of exercise capacity for such a young population. Five women demonstrated impaired exercise capacity as determined by peak VO2. This raises concern for other underlying issues, such as exercise-induced diastolic dysfunction or deconditioning, and is concerning given the physical demands of raising a young child. Whether exercise programs could be useful, as shown with other forms of cardiomyopathy (7), has not been studied in PPCM.

In total, 2 women had subsequent pregnancies. One patient with only mildly impaired RV reserve, normal exercise capacity, and normal peak VO2 had an uneventful clinical course. The other patient with impaired RV reserve and reduced exercise capacity developed a persistently reduced LVEF in the postpartum period that did not recover despite medical therapy. Because an estimated 30% of women with...
LVEF >50% may relapse during a subsequent pregnancy (2), this adds anecdotal evidence that perhaps impairment in RV reserve (as shown by FP-RNV) and/or decreased exercise capacity (as measured quantitatively by CPET) could prove useful in providing additional risk stratification prior to a subsequent pregnancy.

The high proportion of obesity in this group of women may partially explain the decreased exercise capacity, impaired ventricular contractile reserve on FP-RNV, and LV systolic and diastolic dysfunction (8,9). Additional coexisting variables may also contribute to suboptimal CPET performance and warrant further study.

The use of FP-RNV demonstrated biventricular contractile reserve, but how the sensitivity and specificity would compare to stress echocardiography in this patient population should be further explored. Echocardiography has the added advantage of being free of radio-isotope exposure allowing for safer serial imaging, and it is more readily available and less expensive, making it a modality more easily accessible in resource-limited communities. Notably, an LVEF >50% rather than >55% was used to define LV recovery. An LVEF >55% may be associated with lower rates of heart failure relapse in women with PPCM and is more consistent with the American Society of Echocardiography’s definition for normal LVEF in women (10).

Many unanswered questions remain in our understanding of PPCM. The association of hypertensive disorders of pregnancy with adverse myocardial remodeling, decreased exercise capacity, and subsequent pregnancy outcomes are unknown. Future studies also need to include a racially diverse group, particularly because black women have a higher burden of PPCM with worse outcomes (1).

Long-term management of women with PPCM remains challenging with unanswered questions about the risks of relapse with a subsequent pregnancy or following discontinuation of GDMT. As the authors of this case series have elegantly demonstrated, CPET with FP-RNV may reveal significant limitations in exercise capacity and inadequate biventricular contractile reserve, despite LVEF >50%. Significantly more research is needed to determine the optimal cardiovascular assessment in women with PPCM. Indeed, reliance on echocardiographic LVEF as the sole measure of recovered myocardial function is really only the tip of the iceberg.

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REFERENCES

1. Davis MB, Arany Z, McNamara DM, Goland S, Elkayam U. Peripartum cardiomyopathy: JACC state-of-the-art review. J Am Coll Cardiol. 2020;75:207–221.
2. Joseph MS, Davis MB. Counseling women with peripartum cardiomyopathy about subsequent pregnancies. Curr Treat Options Cardio Med. 2021;23:1. https://doi.org/10.1007/s11936-021-00915-4
3. Sugahara M, Kajiyama N, Hasselberg NE, et al. Global left ventricular strain at presentation is associated with subsequent recovery in patients with peripartum cardiomyopathy. J Am Soc Echocardiogr. 2019;32:1565–1573.
4. Goland S, Weinstein JM, Zalik A, et al. Angiogenic imbalance and residual myocardial injury in recovered peripartum cardiomyopathy patients. Circ Heart Fail. 2016;9(11):e003349.
5. Ersbøll AS, Bojer AS, Hauge MG, et al. Long-term cardiac function after peripartum cardiomyopathy and preeclampsia: a Danish nationwide, clinical follow-up study using maximal exercise testing and cardiac magnetic resonance imaging. J Am Heart Assoc. 2018;7:e008991.
6. Yucei E, Davis EF, Scott N, Lewis GD, DeFaria Yeh D. Exercise ventricular reserve among women with a history of peripartum cardiomyopathy. J Am Coll Cardiol Case Rep. 2021;3:1649–1653.
7. Saberi S, Wheeler M, Bragg-Gresham J, et al. Effect of moderate-intensity exercise training on peak oxygen consumption in patients with hypertrophic cardiomyopathy: a randomized clinical trial. JAMA. 2017;317:1349–1357.
8. Licata G, Scaglione R, Barbagallo M, et al. Effect of obesity on left ventricular function studied by radionuclide angiocardiography. Int J Obes. 1991;15:295–302.
9. Powell-Wiley TM, Poirier P, Burke LE, et al. Obesity and cardiovascular disease: a scientific statement from the American Heart Association. Circulation. 2021;143:e984–e1010.
10. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2015;16:233–270.

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