



Editorial

Peripartum Cardiomyopathy in 2015

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See article by Li et al., pages 362-368 of this issue.

Despite entering pregnancy with completely normal heart function, it is possible to develop pregnancy-associated cardiomyopathy with life-threatening heart failure toward the end of pregnancy or just after delivery. Peripartum cardiomyopathy (PPCM) can occur in women of any race or nationality.

New Era for PPCM

Fortunately, this is a new era for this devastating disease because important advances have been made.¹⁻⁶ Because PPCM ranks high worldwide as a cause of maternal mortality and morbidity, it has been given considerable attention (even if not enough) by clinicians and investigators, often expanding the boundaries of knowledge and understanding, helping to identify areas of greatest need in basic pathophysiology and therapeutics.

There is still much to learn, but among the greatest advances have been (1) an increased awareness of PPCM; and (2) the application of the combination treatment of β -blockers (BB) with angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin releasing hormone blockers (ARBs), as found in class I (“should”) recommendations of the American Heart Association and European Society of Cardiology Guidelines^{7,8} for treatment of heart failure with reduced left ventricular ejection fraction (LVEF). Making an earlier diagnosis and following these evidence-based guidelines make a large difference in outcomes with more “full recoveries” and a great reduction in those left with severe cardiomyopathy and/or the need for transplantation. Even if there is not yet uniform application of these therapeutic recommendations, there have been important gains in that direction.

New Retrospective Study

Additional information on PPCM is found in this issue of the *Canadian Journal of Cardiology*, with the helpful article

from Li, et al.,⁹ who add to our store of knowledge and understanding of PPCM in the Beijing region of China. Their report opens the door wider to better treatment for PPCM mothers and should help clinicians and investigators in many countries in the quest to solve the puzzle of PPCM.

The retrospective study of Li et al. on 71 PPCM subjects identified baseline LVEF < 0.34, left ventricular end-diastolic diameter (LVEDD) > 64 mm and serum B-type natriuretic peptide (BNP) > 1864 pg/mL as independent prognostic factors that characterize a lesser likelihood of recovery, defined as a final LVEF \geq 0.50 during the minimum follow-up period of 12 months after diagnosis. The authors indicate that some of their subjects were identified as early as 2004, when not so many received the combination treatment of BB with ACEIs/ARBs. Despite that, full recovery outcomes resulted for 56% of subjects.

The power of serum BNP as a predictor is a unique aspect of this study. BNP is believed to be protective of left ventricle (LV) function, with increasing levels reflecting stress on the LV, and elaboration of this hormone is seen as an adaptive effort to preserve systolic function. It is a biomarker that can be an indicator of cardiac skeleton stretch and adverse remodelling, not a causal agent.

Three other aspects of this study are particularly noteworthy. The high proportion of women with preeclampsia/eclampsia, the poor fetal outcomes, and many early deliveries. Although there were no maternal deaths during follow-up (mean 43 months), the severity of maternal cardiac dysfunction was apparent from adverse effects on the fetus/neonate with 4 stillbirths and 2 neonatal deaths from asphyxia within 12 hours of delivery. The cohort of Li et al included many with hypertension. Nine subjects had gestational hypertension, 24 had preeclampsia, and 5 had eclampsia. Their study highlights the need for additional investigation of the interrelationship of PPCM and preeclampsia and the importance of being alert for the development of PPCM in preeclampsia pregnancies.¹⁰ Certainly the presence of hypertension adds a serious additional stress to the failing heart of PPCM.

New Prospective Study

The recent report of the first prospective study of 100 PPCM patients from 30 medical centres in Canada and the

Received for publication August 18, 2015. Accepted August 18, 2015.

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See page 287 for disclosure information.

United States by McNamara et al.¹ identifies full recovery rates, also defined as LVEF of ≥ 0.50 at 12 months postpartum, in an impressive 72% of subjects. In this Investigations of Pregnancy Associated Cardiomyopathy (IPAC) cohort, treatment included a high percentage of BB with ACEI/ARB usage. Greater risk for nonrecovery was identified in patients with initial LVEF < 0.30 , LVEDD ≥ 60 mm, self-identified “black” race, and identification of PPCM > 6 weeks postpartum. Self-identified “black” women presented with a lower initial LVEF that persisted at 6 and 12 months postpartum ($P < 0.001$). Baseline LVEF had a much greater effect on 12-month LVEF in “black” women than it did in “white and all others” women.

The IPAC investigators found that a combination baseline echocardiographic LVEF and LVEDD helped in the prognostication of outcomes: no subjects with an LVEF < 0.30 and an LVEDD ≥ 6.0 cm reached recovery levels by 1 year postpartum, compared with 91% of subjects with full recovery when they had a baseline LVEF ≥ 0.30 and an LVEDD < 6.0 cm ($P < 0.00001$). This is a greater proportion of full recoveries reported than in any retrospective study to date.^{11,12} Event-free survival did not vary according to race.

Despite these encouraging outcomes in patients with favourable LV function and less adverse remodelling, IPAC’s reported outcomes remain unsatisfactory for 13%, with 4 deaths, 6 left ventricular assist devices, 1 transplant, and 6 with severe chronic cardiomyopathy (LVEF < 0.35) in the 1-year postpartum observation period. There were no fetal/neonatal deaths.

This first North American prospective study of PPCM patients has helped to identify clear risk factors for those of African heritage; namely, significantly more hypertension (preeclampsia, gestational and chronic) and significantly later postpartum identification of a PPCM diagnosis. Despite that, an encouraging 60% of self-declared “black” subjects reached full recovery by 1 year postpartum, compared with 77% of self-declared “white and all others” who reached full recovery. Unexpectedly, the latter with baseline LVEF < 0.30 were found to significantly more often regain full recovery levels by 1 year postpartum compared with “black” women. It is unknown why this happens; one can only speculate that (aside from genetics) it could be related to an earlier diagnosis and/or less hypertension in the “white and all others” group. These negative prognosticators for those of African heritage in North America seem to also hold true for women in Haiti,¹³ and for women in South Africa.¹²

Best Predictor of Poor Outcomes

These recent studies add to the growing body of evidence that echocardiography is currently the best predictor of poor outcomes; particularly presentation with very low LVEF (< 0.30) and large LVEDD (> 6 cm).^{4,9,14} Hopefully, this will help to set the stage for interventional trials for PPCM subjects who stand in greatest need of some additional treatment if they are to reach recovery levels.

New Intervention Trials?

We are not yet sure what might be worthy of new intervention trials in future research.^{2,3} Despite some early

promise, pentoxifylline benefit has not been duplicated in any trial as an add-on to standard heart failure treatment.^{15,16} Thus far, the same might be said for bromocriptine. Aside from efficacy, there are remaining issues of concern for the safety of the use of bromocriptine in the peripartum setting. Also, abrupt loss of breast milk has an immediate negative effect on infant nutrition, and particularly in situations where bottle formula milk is neither affordable nor available.

IPAC results in subjects for whom no bromocriptine had been used seem to be comparable with that of the German investigators’ PPCM patients who received bromocriptine in addition to standard evidence-based treatment.¹⁷ We await results of ongoing randomized trials in Germany and in Canada.¹⁵ Another study in China focused on cardiac auto-antibodies as a potential therapeutic target.¹⁸

What About a Subsequent Pregnancy?

Aside from survival and recovery in PPCM, most of these mothers wonder about the safety of ever having another pregnancy. Do you think a post-PPCM pregnancy is contraindicated and ill advised? It might come as a surprise to many health care providers that in actual fact outcomes of a subsequent pregnancy can be very good for PPCM subjects who have experienced full recovery—to the extent that we can measure that.^{19,20} It is important to closely monitor during pregnancy because even in women considered to be completely recovered, there remains a risk of recurrence during subsequent pregnancies because a relapse of heart failure can occur in up to 20%.²¹ We encourage and work toward a prospective study of post-PPCM pregnancies.

Conclusions

Although there are geographic, racial, genetic, and cultural differences in PPCM wherever it occurs in the world, there are also commonalities. These commonalities are becoming better understood; and as a consequence are leading to fewer maternal deaths, more complete cardiac recoveries, and a better life for PPCM mothers than ever before. Recent discoveries will help to guide future research, and hopefully result in newer intervention strategies with even better outcomes.

Disclosures

The author has no conflicts of interest to disclose.

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