Can Echocardiographic Assessment of Pathophysiology in Gestational Hypertension Give a Clue for Diagnosing Peripartum Cardiomyopathy?

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Hemodynamic changes during pregnancy are profound and begin even early in the first trimester. The plasma volume begins to increase in the 6th week of pregnancy, and by the second trimester is approaches approximately 50% above baseline volume, but then plateaus until delivery. The heart rate also increases to about 20% above baseline, resulting in an increase in cardiac output by 30% at the end of the second trimester. Uterine blood flow increases with placental growth, and there is a fall in peripheral resistance, which may result in a slight fall in blood pressure (BP), also beginning in the first trimester. On the other hand, venous pressure in the lower extremities increases and leads to the common pedal edema that can develop in any healthy pregnant woman. Importantly, these dramatic changes only occur during a limited period of time.

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Gestational hypertension (GH) is defined as newly diagnosed hypertension with BP >140/90 mmHg without proteinuria, arising de novo after the 20th week of pregnancy.¹ GH is one of the several causes of hypertension in pregnant woman and occurs in approximately 6% of pregnancies.² However, GH is a temporary diagnosis, and the subsequent definitive diagnosis includes the following: preeclampsia, if proteinuria develops; chronic hypertension, if BP elevation persists more than 12 weeks postpartum; and transient hypertension of pregnancy, if BP returns to normal by 12 weeks postpartum. Accordingly, reassessment up to 12 weeks postpartum is necessary to establish a final definitive diagnosis of GH.

In this issue of the Journal, Cho et al interestingly demonstrate that GH aggravated left ventricular (LV) function and induced a characteristic geometric pattern.³ GH induced LVH as indicated by the increased LV mass index and relative wall thickness. The authors found that 62% of GH women showed an abnormal geometry pattern, of which 40% were eccentric hypertrophy, 17% were concentric remodeling and 5% were concentric hypertrophy. Despite the limited period of hypertensive status in GH women, their LV geometric patterns were actually very similar to those reported in patients with essential hypertension.⁴ LV functional deterioration was indicated by longer isovolumetric relaxation time, lower E/A, higher Tei index and lower global longitudinal LV

strains in GH women. These findings in women with GH were again similar to those observed in patients with essential hypertension. Accordingly, echocardiographic assessments of LV function as well as geometry should be performed in women with GH. Why do these geometric LV alterations occur in such a limited period of time? Although the precise mechanisms of these interesting phenomena are not yet clarified, one can hypothesize that both the volume overload during pregnancy and neurohumoral activation may play a significant role in concert.

The follow-up study in 37 women with GH revealed that a substantial percentage of these patients developed preeclampsia (10 patients). Furthermore, 5 patients with preeclampsia did develop peripartum cardiomyopathy. Importantly, all patients with preeclampsia who developed peripartum cardiomyopathy later showed abnormal LV geometric patterns; 2 patients showed eccentric hypertrophy and 3 showed concentric remodeling. Therefore, echocardiographic LV assessment can provide a clue to the early diagnosis of peripartum cardiomyopathy. GH patients with LV dysfunction and/or abnormal LV geometric patterns should undergo repeated echocardiography. In addition, measurement of B-type natriuretic peptide (BNP) levels and cardiac troponin levels may be helpful. BNP may be viewed as a marker of cardiac load and neurohumoral crosstalk, whereas cardiac troponin is a marker of ongoing myocyte damage.⁵

The exact definition of LV afterload is the LV wall stress during ejection. Although it may be an oversimplification, Laplace's law emphasizes the following points. First, the bigger the LV cavity and the greater its radius, the greater the wall stress. Second, at any LV cavity size, the greater the pressure developed by LV, the greater the wall stress. Considering these 2 points, the LV wall stress in patients with GH should be increased substantially, especially in patients with eccentric hypertrophy. Because LV volume overload occurs even in normal pregnant women, the coexistence of volume overload and pressure overload in patients with GH may have a greater ability to enhance LV wall stress as compared with essential hypertension alone. An increase in LV wall stress elevates myocardial oxygen demand, potentially leading to endocardial ischemia in concert with neurohumoral activation. The renin-angiotensin-aldosterone system can be activated in pregnant women, because angiotensin-II may

The opinions expressed in this article are not necessarily those of the editors or of the Japanese Circulation Society.

Received March 17, 2011; accepted March 17, 2011; released online April 5, 2011

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ISSN-1346-9843 doi:10.1253/circj.CJ-11-0302

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play a substantial role in the angiogenesis of the placenta.

The reported incidence of peripartum cardiomyopathy varies throughout the world, with reported incidences of 1:15,000 deliveries in the US, 1:1,000 in South Africa, and 1:100 in Zaria Nigeria. The wide range of reported incidence may reflect an overestimation in the African studies, which were determined mainly on clinical criteria. However, the very high incidence in Nigeria may stem from a local Hausa custom of eating kanwa, a dry-lake salt for 40 days after delivery. Therefore, it has been suggested that the development of peripartum cardiomyopathy in these Africans may be related, at least in part, to hypervolemia and possible hypertension.⁶ Considering the high incidence of peripartum cardiomyopathy in Africans who have the unique custom of postpartum salt eating and the results of Cho et al together, early initiation of reasonable treatment for GH should be established. Although available data are insufficient to establish the effectiveness of bromocriptine to treat peripartum cardiomyopathy, a small randomized pilot study and several case reports have suggested a beneficial response to this treatment.^{7,8} Bromocriptine might be a promising and favorable drug for peripartum cardiomyopathy, however, it is the first essential to prevent the development of peripartum cardiomyopathy by successful treatment of GH.

Angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers have been extensively used for treatment of not only hypertension but also heart failure. Unfortunately, both drugs are contraindicated at any time during pregnancy due to a profound risk of adverse fetal effects. Medical agents for women with GH include methyldopa, labetalol, nifedipine, hydralazine and diuretics in the US. Because β -adrenergic activation is well known to play a significant role in the pathogenesis of cardiomyopathy, the use of β -blockers is reasonable for the treatment of GH to prevent the development of peripartum cardiomyopathy. Accordingly, labetalol, commonly used for safe treatment of GH in the US, may be a good drug of choice in all patients with GH. Unfortunately,

labetalol is hard to obtain in Japan. However, both carvedilol and bisoprolol have been successfully used in patients with heart failure.⁹ We strongly believe that both β -blockers should also be challenged in patients with GH.

Cho et al provide the underlying echocardiographic data in patients with GH. Careful repeated assessment of LV function by echocardiography may predict the onset of peripartum cardiomyopathy, especially in patients with preeclampsia. The pathophysiological mystery of peripartum cardiomyopathy may be solved gradually over time and with future clinical studies.

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