Clinical Characteristics of Heart Failure With Preserved Ejection Fraction in Children

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In this issue of the Journal, Masutani et al report on their study of pediatric patients with HFpEF through a retrospective review of 3,907 patients in their institute, and they describe certain clinical characteristics of this condition. The mean age of the patients with HFpEF was 1.12±0.8 years, which was significantly lower than that of the patients with heart failure and reduced EF (HFrEF). Growth retardation was more severe in patients with HFpEF than in those with HFrEF. Moreover, HFpEF primarily developed during the postoperative course of congenital heart disease (CHD) that was associated with a potentially underloaded LV, including tetralogy of Fallot (TOF), total anomalous pulmonary venous connection (TAPVC) and coarctation/interruption of the aorta (CoA/IAA). 5-8 Concentric hypertrophy with normal LV size and high systolic blood pressure were commonly observed in HFpEF patients. Serum aldosterone levels were elevated to a significantly greater extent in patients with HFpEF than in those with HFrEF; however, the plasma brain natriuretic peptide (BNP) levels were significantly lower in patients with HFpEF than in those with HFrEF, although these levels were elevated in both groups. The patients with HFpEF showed amelioration of HF symptoms during the follow-up period, and the HF mortality rate was significantly lower in patients with HFpEF than in those with HFrEF. This is the first report of the incidence and clinical features of HFpEF in the pediatric population.

The most important and valuable finding in this report is the hormonal characteristics and differences between HFpEF and HFrEF. The significantly elevated serum aldosterone levels were specific to HFpEF and could help differentiate between HFpEF and the systolic HF that is usually associated with significantly high levels of plasma BNP. A high ratio of aldosterone/BNP levels may be helpful in diagnosing HFpEF. As speculated by the authors, the arterial stiffness and ventricular diastolic dysfunction associated with concentric hypertrophy and fibrosis, which appear to be caused by hyperaldosteronemia, may be involved in the pathogenic mechanism of HFpEF, even in children.

The second clinical interest is that HFpEF is usually transient and spontaneously improves during the follow-up period in children. This finding is contrary to the high mortality rate among adult HFpEF patients. 9, 10 According to the present study, HFpEF was commonly observed in young infants of approximately 1 year of age and during the postoperative course, and these patients experienced severe growth retardation, which appeared to be mainly caused by milk intake restriction and subsequent poor nutrition. A recent study showed that the nutritional risk index calculated using serum albumin level and body mass index value is useful for predicting functional dependency and mortality in elderly patients with HFpEF, 11 suggesting that malnutrition is highly related to the pathology of HFpEF. This may also be the case with pediatric patients. A young infant with malnutrition and an unloaded LV might exhibit HFpEF when surgical repair of CHD acutely normalizes cardiac function, thereby increasing the volume load to the unloaded LV and subsequently inducing concentric hypertrophy, fibrosis and low compliance of the LV. 12-14 However, increased milk intake and improved nutrition after surgery would accelerate physical growth and exercise capacity. A systematic review conducted by Taylor et al showed that exercise training for patients with HFpEF was beneficial in terms of enhanced exercise capacity and health-related quality of life. 15 Therefore, improvements in both nutrition and exercise capacity may contribute to spontaneous improvement of HFpEF.

Although the report by Masutani et al provides some useful clinical information on the diagnosis and treatment of pediatric patients with HFpEF, some important clinical problems remain unsolved. The first is why some patients with CHD, such as TOF, TAPVC or CoA/IAA, develop HFpEF and others do not. As discussed, the patient’s nutritional state may be highly related to the occurrence of HFpEF. A more precise nutritional evaluation before surgery could provide the answer to this question.

Another important question is whether anti-aldosterone...
agents would be effective in treating HFpEF. In other words, the reason for the elevation of serum aldosterone levels in patients with HFpEF is still not precisely known. Furthermore, it is also unclear whether the hyperaldosteronemia and histopathologic changes, including fibrosis, will be reversible when HFpEF spontaneously improves. In order to provide a therapeutic strategy for HFpEF, a physiological or biochemical approach and consideration of these questions are essential. Future prospective studies to clarify the clinical effects of anti-aldosterone agents on HFpEF would provide the answer to these questions.

The clinical recognition and understanding of HFpEF in children have just started. Thus, correct diagnosis and careful observation of pediatric patients with this condition will provide more precise clinical information about this type of HF.

Disclosure
The author has no conflict of interest to disclose.

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