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Editorial

Editorial: Baroreflex activation is a novel therapy for heart failure independent of left ventricular systolic function

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It is known that abnormal sympathoexcitation is involved in the pathogenesis of chronic heart failure, and the sympathetic nerve activity is mainly and quickly regulated by baroreflex [1]. Interestingly, the arterial baroreflex is impaired both in heart failure with reduced left ventricular ejection fraction (HFrEF) and with preserved left ventricular ejection fraction (HFpEF) [1–5]. The arterial baroreflex system is an important and powerful regulator of the stressed blood volume and systemic blood pressure [6–8]. The benefits of baroreflex activation therapy (BAT) in the treatment of heart failure have been already demonstrated in animals and humans [3,5,9–11].

In this issue of the *Journal of Cardiology Cases*, Brambilla et al. [12] report that BAT substantially improved the clinical course of a post-myocardial infarction HFrEF patient with recent, repeated, and lengthy hospitalizations for worsening heart failure. They implanted the Barostim^{TM} neo system (CVRx, Inc., Minneapolis, MN, USA) to a severe [New York Heart Association (NYHA) class III] 69-year-old male with left ventricular systolic dysfunction, signs of right ventricular failure, stage 3 chronic kidney disease, and insulin-dependent diabetes. In the acute phase, cardiac output increased with pulmonary artery systolic pressure and wedge pressure dropping. Moreover, in the chronic phase, muscle sympathetic nerve activity was chronically reduced through 6 months, and the 6-min hall walk distance, NYHA class, and serum brain natriuretic peptide improved. Does this case shed additional light on the clinical implications for severe heart failure? It likely does. In particular, the present case highlights the potential of systemic neuromodulation by BAT as a powerful new approach for advanced HFrEF.

We should discuss whether BAT could have benefits for only HFrEF. How about HFpEF? A recent study indicated that baroreflex activation could be a novel therapeutic strategy for patients with diastolic heart failure [3,11]. Recently, we have reported the role of baroreflex failure in HFpEF [13]. Left ventricular diastolic dysfunction is induced by arterial baroreflex failure [2]. We examined whether baroreflex failure (FAIL) mimicked by constant carotid sinus pressure (CSP) causes a striking increase in left atrial pressure (LAP) and systemic arterial pressure (AP) by volume loading in rats with normal left ventricular function. We mimicked the normal baroreflex by matching CSP to instantaneous AP and FAIL by maintaining CSP at a constant value regardless of AP. We infused dextran stepwise [infused volume (Vi)] until LAP reached 15 mmHg and obtained the LAP-Vi relationship. We estimated the critical Vi as the Vi at which LAP reached 20 mmHg. In FAIL, critical Vi decreased markedly, while AP at the critical Vi increased. Moreover, we demonstrated that an artificial baroreflex system we recently developed could fully restore the physiological volume intolerance in the absence of native arterial baroreflex. Our results strongly indicated that baroreflex failure induces striking volume intolerance in the absence of left ventricular dysfunction and may play an important role in the pathogenesis of acute heart failure, especially in states of HFpEF. We also consider that the bionic arterial baroreflex system would be an attractive therapeutic tool in preventing the volume intolerance in acute decompensated heart failure.

As the authors readily acknowledge, the present paper is just one case report. Randomized, controlled trials are underway to validate the safety and efficacy of BAT in a broader HFrEF population. Nevertheless, the present case may have clinical implications regarding the importance of BAT in the treatment of HFrEF. In addition, we should consider that BAT also has benefit on HFpEF. Acute heart failure demonstrates an elevated filling pressure in response to increased circulatory volume in both HFrEF and HFpEF [14]. In this regard, BAT might have a potential to be a therapy for "heart failure notwithstanding left ventricular ejection fraction."

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