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Commentary: Pumps for pEF

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There are a large number of patients with severe heart failure who have normal left ventricular (LV) systolic function with small, normal, or minimally dilated LV cavities: heart failure with preserved ejection fraction (HFpEF). This population is composed of heterogeneous groups of patients, all with limited therapeutic options.^{1,2} Very broadly, one HFpEF subgroup (group A) is characterized by severe diastolic dysfunction and includes patients with restrictive, amyloid, sarcoid, and other infiltrative cardiomyopathies. Another, larger subgroup (group B) includes patients with 1 or more comorbid conditions, most notably including hypertension, diabetes, renal dysfunction, anemia, and obesity. Although both groups have elevated left atrial (LA) pressures and enlarged LA chambers, they differ in other important aspects. Group A patients are characterized by very small volume, thick-walled LV chambers, normal-to-low blood pressure, and low cardiac output. Group B patients can have normal or elevated blood pressure and cardiac output at rest but are unable to increase cardiac output during exercise. Since, among both groups, there are patients with severe effort intolerance, frequent heart failure hospitalizations, and increased risk of mortality, it has been proposed that some patients with HFpEF might benefit from mechanical circulatory support (MCS) devices.

In this edition of the *Journal*, Fukamachi and colleagues³ describe a novel left atrial assist device (LAAD) for treating HFpEF. In contrast to typical MCS configurations, this device is intended to be placed in the mitral position and pump blood from the left atrium to the left ventricle. This approach is based on the premise that increasing mitral flow will simultaneously decompress the LA (also decreasing pulmonary venous pressure) and boost filling to increase cardiac performance. Several critical questions

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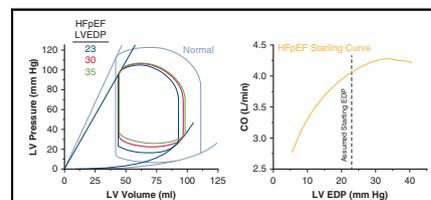
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Pressure–volume and Starling curves: large increases of LVEDP may not increase CO in HFpEF.

CENTRAL MESSAGE

General commentary is provided on the potential use of mechanical circulatory support for HFpEF patients and, more specifically, the pros and cons of a novel left atrial assist device for this purpose are reviewed.

arise regarding the use of MCS for HFpEF in general and regarding the proposed LAAD concept.

Relevant to Group A patients, there is already some clinical experience with traditional LV assist devices.⁴ Owing to the small LV chamber, inflow cannula insertion has been challenging and its position within the chamber has resulted in greater-than-usual rates of suction, arrhythmia, and pump thrombosis. Accordingly, a non-LV implant is ideal. We previously proposed pumping from the LA to the aorta with a small, partial support device, thus retaining aortic valve opening and arterial pulsatility.² Unfortunately, that pump did not reach clinical trial in HFpEF due to unsolvable problems with pump thrombosis, possibly due to the relatively long inflow cannula and outflow graft. The LAAD avoids the later problems. While decreasing LA pressure, the question related to LAAD is how the already pressure-overload diastolic LV would respond to forced, further increases in filling. The answer to this question is not likely answered by data from the mock loop used by Fukamachi and colleagues. The issue is that, by the time these patients would qualify for MCS, they already have relatively high left ventricular end-diastolic pressures (LVEDPs). Since the end-diastolic pressure–volume relationship of these hearts are very steep, dramatic increases in LVEDP are likely to be associated with little increase in filling volume (Central Figure, left panel). Furthermore, since likely operating on the flat portion of the Starling curve, increases in LVEDP would not likely increase cardiac output (Central Figure, right panel). Relating this

cellular physiology, even though the LV chamber is small, at high filling pressures, the sarcomeres are already stretched to (or near) their optimal lengths for force/pressure generation. None of these factors are accounted for in the artificial heart used in the mock loop, at least not based on the information provided, and effects on LVEDP were also not reported. It may be that effects demonstrated in Figures 3 through 5 of Fukamachi and colleagues overestimate effects that would be seen in the real-life setting of HFpEF.

In addition to these concerns, Group B patients typically have elevated blood pressures which, if cardiac output were increased, would be further increased by an LAAD. Elevated blood pressure has been identified as a risk factor for stroke during MCS with anticoagulation.^{5,6} One study showed that baseline HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly [>65 years], Drugs/alcohol concomitantly) score was predictive of bleeding events in patients with an LVAD⁷; since Group B patients are typically hypertensive and elderly, they have a minimum HAS-BLED score of 2, which was associated with 31% risk of bleeding events, one half of which included intracranial hemorrhage.

Additional questions relate to both groups. What are the implications of continuous-flow from the LA to LV regardless of the cardiac cycle phase and pins the mitral valve in an open state? What is the failure mode of this device; will a

device failure prohibit flow through the mitral valve, thus creating a catastrophic event? Assuming a nonfatal failure mode can be engineered, how difficult will it be to remove or replace a device if one fails?

There is a clear unmet need and rationale for the use of MCS in some patients with HFpEF, particularly group A patients. There is much to learn from additional theoretical modeling, experimental testing, and engineering on the path to developing “pumps for pEF.”

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