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Reversing Heart Failure With a Ventricular Anchoring Device: Another Hope for Myopathic Mitral Regurgitation.

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EDITORIAL COMMENT

Reversing Heart Failure With a Ventricular Anchoring Device

Another Hope for Myopathic Mitral Regurgitation*

J. Eduardo Rame, MD

Heart failure due to left ventricular (LV) systolic dysfunction remains highly prevalent, progressive in natural history, and problematic for patients hoping to survive with a good quality of life. The anatomic and physiologic adaptations in response to myocardial injury with ensuing LV dysfunction include neurohumoral activation of sympathetic and renin-angiotensin-aldosterone systems, along with counter-regulatory response of natriuretic peptide systems; metabolic shifts adapting to increasing energetic demand; and LV chamber dilatation. We evolved to incorporate these adaptations to facilitate survival in the critical period of acute exposure to risk. However, at least 2 of these adaptations—neurohumoral activation and LV dilatation—become maladaptive over the longer term. Indeed, we are confident from the positive results of many randomized clinical trials that blockade of neurohumoral pathways improves heart failure, in some instances achieving a high degree of myocardial reverse remodeling, returning the LV cavity to near normal end-systolic and end-diastolic dimensions.

Increasing end-systolic and end-diastolic LV dimensions is a hallmark of progressive, cardiomyopathic failure, which is often accompanied by secondary mitral regurgitation (MR). The increase in LV volumes allows for maintenance of stroke volume and, depending on the changes in myocardial stiffness, could also maintain lower LV filling pressures. However, LV dilatation comes with the bioenergetic cost of increasing wall stress and myocardial oxygen consumption, along with the increasing risk of pulmonary venous congestion due to secondary MR of myopathic origin. In the current era, device therapy for heart failure due to cardiomyopathic LV systolic dysfunction incorporates paradigms of resynchronization (cardiac resynchronization therapy), mechanical unloading with ventricular assist devices, and aortic counterpulsation. All of these have been demonstrated to induce reverse remodeling of the LV via multifaceted mechanisms, especially in the patients with a good clinical response (1–3).

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In this issue of *JACC: Basic to Translational Science*, it is in this context that the work by Saeed et al. (4) should be considered. The soft robotic ventricular assist device (SRVAD) is a free wall to septal brace that effectively anchors the LV dimension while actuating through an extrinsic force an increase in LV ejection. By applying synchronized cyclic force transmitted from the LV free wall to the interventricular septum, the device provides dynamic external compression and diastolic phase recoil back to the "relaxed" curved configuration.

The preclinical data to investigate the effect of the SRVAD using an adult swine model of acute LV systolic dysfunction with secondary MR induced by intracoronary microsphere injections has demonstrated elimination of the MR with significant increase in LV fractional shortening at 5 and 30 min, an increase in the median ejected stroke volume of 50%,

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and an increase in the LV developed pressure. With the increased stroke volume, there is a significant decrease in LV end-diastolic and left atrial pressure. Finally, the electrocardiography-synchronized augmentation of native pulsatile flow results in an increase in pulse pressure and surplus hemodynamic energy.

Although Saeed et al. (4) clearly demonstrate the successful augmentation of LV output with reduction of MR in this acute model, several questions remain. First, what happens to the structure and function of the LV, in the intermediate to long-term phase? Saeed et al. intend to incorporate built-in pressure sensors and test the device in a chronic animal model, but the fundamental question of what physiologic changes will result from sustained actuation of a ventricular anchoring and compression device remains prescient. Second, what are the longitudinal changes in neurohumoral activation within the acute, intermediate, and long-term phases of this form of ventricular support? If we expect, as is the case with pericardial constriction, to have a net decrease in the myocardial production and circulating levels of natriuretic peptides, what should constitute the optimal neurohormonal antagonist therapy to work synergistically with this mechanical paradigm of circulatory support? Third, what are the acute and chronic changes in right ventricular (RV) size and function, and the effects on tricuspid regurgitation? Although we expect that a decrease in MR and left atrial pressure will impact RV afterload favorably, a critical question is: what effect, if any, will the actuation of the device have on the RV free wall to septal dimension? We know from studying the effects of direct mechanical unloading with LV assist devices that RV mechanics are affected with at times a deleterious impact on RV function. Fourth, in dyssynchronous heart failure, often accompanied by clinically significant MR, can this device remain effective, and what timing algorithms should be considered to offset the septal to free wall delay? Fifth, what is the potential for myocardial recovery with adjunctive heart failure therapies of this mechanical platform? If the device can safely be maintained in low-support or nonactuated mode, can future investigations demonstrate improved contractility? Last, to target both clinical effectiveness and maximize myocardial recovery, is there a range for LV end-diastolic dimension and the degree of MR that could be used to identify the patients who could benefit the most after implantation of this cardiac support device? We know from the ACORN trial (5) that the CorCap fabric mesh device (Acorn Cardiovascular, St. Paul, Minnesota) that was surgically implanted for circumferential diastolic support benefited patients the most who had a LV end-diastolic dimension index in the range of 30 to 40 mm/m^2. If the chronic preclinical models provide variability in the degree of LV remodeling after myocardial injury, it would be important to look for this phenotype of maximal treatment response to the SRVAD before translation toward clinical delivery.

Despite the need for clarity on these questions, which will enhance our grasp of the physiology relevant to this form of mechanically assisted heart failure, the work by Saeed et al. (4) has undoubtedly introduced the question whether a single device paradigm can reverse myopathic MR while sustaining ventricular output. Stay tuned. We can only hope.

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REFERENCES

1. St. John Sutton M, Keane MG. Reverse remodelling in heart failure with cardiac resynchronisation therapy. Heart 2007;93:167–71.

2. Birks EJ. Molecular changes after left ventricular assist device support for heart failure. Circ Res 2013;113:777–91.

3. Kontogiannis CD, Malliaras K, Kapelios CJ, Mason JW, Nanas JN. Continuous internal counterpulsation as a bridge to recovery in acute and chronic heart failure. World J Transplant 2016;6:115–24.

4. Saeed MY, Van Story D, Payne CJ, et al. Dynamic augmentation of left ventricle and mitral valve function with an implantable soft robotic device. J Am Coll Cardiol Basic Trans Science 2020;5:229–42.

5. Mann DL, Acker MA, Jessup M, Sabbah HN, Starling RC, Kubo SH. Clinical evaluation of the CorCap cardiac support device in patients with dilated cardiomyopathy. Ann Thorac Surg 2007;84:1226–35.

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