JACC: CARDIOVASCULAR INTERVENTIONS
© 2018 PUBLISHED BY ELSEVIER ON BEHALF OF THE
AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION

VOL. 11, NO. 22, 2018

EDITORIAL COMMENT

# Atrial Shunting for Heart Failure

## Where Do We Need to Go?*

Paul Sorajja, MD, Michael A. Samara, MD, Peter M. Eckman, MD

The epidemic of heart failure is well known, with ≥5 million afflicted patients in the United States alone and a prevalence that will continue to increase because of advancements in detection and population aging (1). The dismal prognosis for these patients has spurred a number of methods to reduce congestion and improve survival. Ventricular unloading via guideline-directed medical therapy is the cornerstone, supplemented with devices (e.g., cardiac resynchronization, implantable monitors, ventricular assist devices, and transplantation) for some patients. Nonetheless, further evolution of heart failure therapy is needed to address the persistently high mortality (≥25% per year) and the remarkable rate of hospitalizations (>1 million per year) and also to lessen the disease burden related to debilitating ambulatory symptoms.

The creation of an atrial shunt is a novel approach for the management of heart failure. For many patients, a principal determinant of symptoms and impaired functional capacity is elevation in left atrial pressure, which may be considered a "final common pathway" for a variety of cardiac disease states. The theoretical benefit of the iatrogenic shunt was extrapolated from prior natural history studies of small atrial septal defects, with the potential to reduce left atrial pressure at rest and during exercise, without significantly compromising cardiac output or leading to right ventricular failure or pulmonary hypertension. Unloading of the left atrium could occur as needed, with the new shunt, in effect, serving as a regulator of pressure. Transcatheter techniques for creating such shunts have been known for decades, since the emergence of septostomy for the treatment of cyanosis in congenital heart disease and for palliation in patients with severe, refractory pulmonary hypertension.

There already are a number of technologies for the creation of atrial shunts for heart failure that are in rapid development. One leading device is the Interatrial Shunt Device System II (IASD II) implant (Corvia Medical, Tewksbury, Massachusetts), which is a self-expanding, double-disc metal cage that surrounds an 8-mm orifice. Early feasibility of the IASD II was demonstrated in open-label investigations, including a multicenter study in which therapy was successful in 64 of 68 treated patients with LVEF ≥40% and associated with reductions in pulmonary capillary wedge pressure at rest and during exercise, with sustained shunt patency ($Q_p/Q_s$ 1.27 [0.20]) at 6 months (2). A subsequent randomized clinical trial of 44 patients with sham control subjects demonstrated similar reductions in pulmonary capillary wedge pressure during exercise (3). Although the ability for shunt creation and safety (i.e., no adverse events periprocedurally or in follow-up) were demonstrated, these studies nevertheless were short in follow-up and limited in determining the effect on symptom status, hospitalization, and long-term outcomes.

SEE PAGE 2300

The present investigation by Rodés-Cabau et al. (4) in this issue of *JACC: Cardiovascular Intervention* is another venture into atrial shunting for heart failure. In this first-in-human report, Rodés-Cabau et al. (4) investigate the V-Wave shunt, which is an

*Editorials published in *JACC: Cardiovascular Interventions* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Interventions* or the American College of Cardiology.

From the Center for Valve and Structural Heart Disease, Minneapolis Heart Institute, Abbott Northwestern Hospital, Minneapolis, Minnesota. Dr. Sorajja has received consulting and speaking fees and research grants from Medtronic, Edwards Lifesciences, Boston Scientific, and Abbott Vascular; and has received consulting fees from and holds equity in Pipeline and Admedus. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ISSN 1936-8798/$36.00

https://doi.org/10.1016/j.jcin.2018.07.036

hourglass-shaped, self-expanding nitinol frame that contains a porcine trileaflet valve. The valve, with an internal diameter of 5.1 mm, is designed to be unidirectional, thereby inhibiting right-to-left shunting and theoretically reducing the risk for paradoxical embolism. Rodés-Cabau et al. (4) examined 38 patients (mean age 66 ± 9 years, 92% men) who had been treated with the V-Wave shunt at 6 centers as part of a single-arm, open-label cohort study. Nearly all had severe symptoms (97% New York Heart Association functional class III), and most had ischemic cardiomyopathy (79%). It is notable that the improvement in New York Heart Association functional class from 100% in class III or IV at baseline to 22% at 3 months almost exactly mirrors the 96%-to-25% change at 3 months observed in a trial of a ventricular assist device, a striking improvement in functional class for a passive device not designed to improve cardiac output (5). As in other studies of atrial shunting, device success was remarkable, occurring in 100%, without a single death or stroke. The only adverse events were an episode of cardiac tamponade and 1 vascular access complication.

The report of Rodés-Cabau et al. (4) is insightful not from the described feasibility, which has already been noted elsewhere, but as a consequence of the limitations noted with the current technological approach. Although there was initial device success, complete occlusion or severe stenosis of the V-Wave shunt occurred in 50% (18 of 36 treated patients) at 12-month follow-up. Although this finding certainly was disappointing, the outcome enabled a comparison of sorts for the potential treatment effect that might occur with atrial shunting in heart failure. Those patients in whom shunt patency was maintained (average $Q_p/Q_s$ 1.17 ± 0.12) had not only lower pulmonary capillary wedge pressure (18.0 ± 4.0 mm Hg vs. 23.3 ± 5.4 mm Hg) but also fewer adverse clinical events (i.e., death, left ventricular assist device placement, transplantation, and heart failure hospitalization). These lower rates of events occurred despite a worse profile for those with shunt patency (i.e., poorer baseline hemodynamic status, lower left ventricular ejection fraction) and were without evidence of pulmonary hypertension or right ventricular dysfunction.

Certainly, these observations are provocative, but they must be cautiously interpreted. Selection bias remains considerable from nonrandomized comparisons. The participants and observers were not blinded to the treatment effects. We do not know if the differences occurred from divergent clinical paths, with 1 group improving or 1 group worsening. The former path would reflect well on the potential effects of atrial shunting, while the latter could reflect either the burden of worsening heart failure or, albeit less likely, potential risk if loss of initial patency is a harmful event. Interestingly, there was an increase in heart failure hospitalization rates between the first and second years of follow-up for those who had lost shunt patency (0.65 per patient-year vs. 0.21 per patient-year).

As with any therapy, an ideal atrial shunt for heart failure would have durable benefits that are clinically meaningful and an excellent safety profile, supported by sound physiological principles that address the underlying pathology. The report by Rodés-Cabau et al. (4) in this issue reflects an early stage for the entire field of atrial shunting in heart failure, and this area is ripe for close scientific scrutiny. With common techniques, these shunts cannot be measured invasively, and echocardiography is subject to measurement errors given the intended small size of these defects. Moreover, the right ventricle is intended to be a permissive, passive reservoir for the shunted blood flow; this may be true, but methods that are not spatially limited and well established for accurate examination of the right ventricle (e.g., cardiac magnetic resonance imaging, computed tomography) should be used to document the lack of adverse remodeling in the long term. Although it is true that small atrial septal defects can be found in otherwise healthy adults without apparent deleterious effects, patients with heart failure with reduced ejection fraction and those with heart failure with preserved ejection fraction often have biventricular components to their cardiomyopathy and almost invariably have derangements in pulmonary arterial capacitance and some degree of pulmonary vascular remodeling, likely making them more vulnerable to even modest degrees of right ventricular volume overload.

Moreover, the major proposed benefit is relief of symptoms with exercise, and thus the hemodynamic effects must be assessed invasively with exercise, with assessments performed at baseline, immediately after implantation, and during follow-up. This is especially true for heart failure with preserved ejection fraction, in which invasive exercise testing is an essential component for diagnosis, and the benefit of any atrial shunt technology must be tested under such physiological conditions (6). We lack clarity on the optimal patient phenotype to benefit from a shunt, although this burgeoning area of study may present an opportunity to learn to individualize heart failure treatment from parameters other than left ventricular ejection fraction, such as hemodynamic status or exercise performance. For any given patient, there will be considerable heterogeneity in chamber

compliance, ventricular function, and load effects, thereby affecting the degree of shunting. One may envision the creation of smaller, larger, or multiple shunts, tailored to the patient's needs as determined by the hemodynamic response to treatment during exercise. Appropriate long-term medical therapy needs to be determined for risk mitigation in patients with right-to-left shunting, which has been noted in 15% of those who received the Corvia IASD II. Reduction in symptoms, improvements in quality of life, and reduction in hospitalization are minimal requirements, as has been demonstrated for other implantable devices in heart failure (7). Notably, despite therapy with V-Wave shunt, about one-third of the patients still had hospitalization for heart failure, and 10 of the 38 patients died during follow-up. More studies are needed to understand whether these shunts function only to mitigate the symptoms of left atrial hypertension or if they in fact confer benefits in neurohormonal regulation or reverse remodeling of the left ventricle. The present study suggests a modest but significant improvement in left ventricular ejection fraction (from $23 \pm 7\%$ to $26 \pm 8\%$; $p = 0.007$) in patients with maintained shunt patency. In patients with heart failure with preserved ejection fraction, these devices provide a much needed therapeutic option where none currently exist, but for patients the heart failure with reduced ejection fraction, it will be critical to understand optimal patient selection and also to avoid preventing the timely provision of advanced heart failure therapies such as transplantation and ventricular assist devices.

Rodés-Cabau et al. (4) are to be commended for providing remarkable insight into the rapidly emerging field of iatrogenic atrial shunting in heart failure. Early feasibility studies in humans are naturally optimistic, opportunistic, and provocative. Iteration in the field of atrial shunting in heart failure undoubtedly will occur, hopefully to the benefit of our patients with heart failure who continue to have significant unmet clinical needs.

**ADDRESS FOR CORRESPONDENCE:** Dr. Paul Sorajja, Valve Science Center, Minneapolis Heart Institute Foundation, Abbott Northwestern Hospital, 920 East 28th Street, Suite 200, Minneapolis, Minnesota 55407. E-mail: paul.sorajja@allina.com.

## REFERENCES

**1.** Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics—2013 update: a report from the American Heart Association. Circulation 2013;127:e6.

**2.** Hasenfuß G, Hayward C, Burkhoff D, et al. A transcatheter intracardiac shunt device for heart failure with preserved ejection fraction (REDUCE LAP-HF): a multicenter, open-label, single-arm, phase 1 trial. Lancet 2016;387:1298–304.

**3.** Feldman T, Mauri L, Kahwash R, et al. Transcatheter interatrial shunt device for the treatment of heart failure with preserved ejection fraction (REDUCE LAP-HF I [Reduce Elevated Left Atrial Pressure In Patients With Heart Failure]): a phase 2, randomized, sham-controlled trial. Circulation 2018;137:364–75.

**4.** Rodés-Cabau J, Bernier M, Amat-Santos IJ, et al. Interatrial shunting for heart failure: early and late results from the first-in-human experience with the V-wave system. J Am Coll Cardiol Intv 2018;11:2300–10.

**5.** Slaughter MS, Rogers JG, Milano CA, et al. Advanced heart failure treated with continuous-flow left ventricular assist device. N Engl J Med 2009;361:2241–51.

**6.** Obokata M, Kane GC, Reddy YN, et al. Role of diastolic stress testing in the evaluation for heart failure with preserved ejection fraction: a simultaneous invasive-echocardiographic study. Circulation 2017;135:825–38.

**7.** Adamson PB, Abraham WT, Stevenson LW, et al. Pulmonary artery pressure-guided heart failure management reduces 30-day readmissions. Circ Heart Fail 2016;9:e002600.

**KEY WORDS** device, heart failure, shunt