Trends in Cardiovascular Medicine xxx (xxxx) xxx

Contents lists available at ScienceDirect

Trends in Cardiovascular Medicine

journal homepage: www.elsevier.com/locate/tcm

Interatrial shunt devices for the treatment of heart failure ☆

Sitaramesh Emani [a,*], Daniel Burkhoff [b], Scott M. Lilly [a]

[a] The Division of Cardiovascular Medicine, The Ohio State University Wexner Medical Center, Columbus, OH, USA
[b] Cardiovascular Research Foundation, New York, NY, USA

ARTICLE INFO

Keywords:
Atrial flow regulator
Heart failure
IASD
Interatrial shunt devices
V-Wave

ABSTRACT

Despite ongoing advances in the treatment of heart failure, overall symptom burden remains high. Underlying the primary symptom of dyspnea are often elevations in left atrial pressures, which occur across the spectrum of heart failure subgroups. Current therapies do not directly address improvements in left atrial pressures; however, passive left atrial decompression may offer a new avenue to treat heart failure. New technologies are currently being evaluated in clinical testing and may offer a novel therapeutic approach to heart failure.

Introduction

Heart failure (HF) as a clinical syndrome remains challenging to treat despite ongoing advancements in pharmacologic and device-based therapies. In fact, more than half of hospitalizations among those greater than age 65 are attributable to HF, and HF contributes significantly to the cost of healthcare in the US and Europe [1,2]. In the ambulatory setting, heart failure symptom burden is significant, with an estimation that more than 65% of patients experience some degree of limiting symptoms [3]. In most cases, the main symptom is exertional dyspnea, which is driven by elevations in left atrial pressure [4]. Currently, available therapies may result in reductions of left atrial pressure, but often do so secondarily by treating other aspects of HF such as reduction in preload and volume, or by changing left ventricular hemodynamics. Therapies aimed at directly improving left atrial pressures, however, are not yet considered standard of care, but represent a novel therapeutic target. Interatrial shunt devices represent a class of devices with a unique mechanism to directly reduce left atrial pressures, improve exercise tolerance and potentially improve clinical outcomes and heart failure.

Background

Heart failure classification schemes, including the NYHA Classification and ACC/AHA Stages, focus on clinical parameters such as functional status, risk factors, and the disease progression over time [5,6]. Practically, however, most heart failure patients are additionally characterized by their left ventricular systolic function, or ejection fraction (EF), with general groupings including heart failure with reduced ejection fraction (HFrEF, EF <40%), mid-range EF (HFmrEF, EF 40–50%), or preserved EF (HFpEF, EF ≥50%). These categorizations often correlate with differences in associated risk factors, pathophysiology, and clinical outcomes [5,7]. The vast majority of evidence-based therapies and guideline-recommended therapies for HF focus on the treatment of HFrEF, and the implementation of these therapies can result in marked improvements in patient outcomes [6].

Unfortunately, robust evidence-based therapies targeting the treatment of HFmrEF and HFpEF are lacking despite an increase in combined clinical burden that now exceeds that of HFrEF [8–10]. Recent investigations have failed to show significant impact on HFpEF outcomes using pharmacologic therapies. The use of mineralocorticoid antagonism did not reduce a combined primary endpoint of cardiovascular death, cardiac arrest, or heart failure hospitalizations when evaluated in the Spironolactone for Heart with Preserved Ejection Fraction (TOPCAT) trial [11]. Likewise, the use of sacubitril/valsartan also fell short of statistically significant benefit in reducing heart failure hospitalizations and cardiovascular death despite high initial expectations in the Prospective Comparison of ARNI (angiotensinreceptor-neprilysin inhibitor) with ARB (angiotensin-receptor blocker) Global Outcomes in HF with Preserved Ejection Fraction trial (PARAGON-HF) [12]. Follow up review of PARAGON-HF data, however, suggested benefits in specific sub groups of HFpEF patients [13]. The apparent benefit in some patients, but not others, suggests heterogeneity within the pathophysiology of HFpEF. This heterogeneity appears to have consequences more profound than the HFrEF population and may contribute to the lack of proven guideline-directed medical therapies for HFpEF when compared to HFrEF. Moving forward, appropriately

☆ Ethical statement: None

* Corresponding author.
E-mail address: Sitaramesh.emani@osumc.edu (S. Emani).

https://doi.org/10.1016/j.tcm.2020.09.004
1050-1738/

identifying and subsequently matching therapies to clinical phenotypes of HFpEF may lead to better outcomes. Specifically, patients that demonstrate abnormalities in left atrial filling pressures, which occurs in many forms of heart failure, represents a particular group for whom interatrial shunt devices may provide benefit.

Importance of left atrial pressure in heart failure

Pulmonary pressures (especially pulmonary diastolic pressure, PAD) in heart failure patients are known to correlate with outcomes [14,15]. The Chronicle Offers Management of Heart Failure Study (COMPASS-HF) study incorporated pressure monitoring capabilities into right-ventricular leads of cardiac rhythm devices (*i.e.,* pacemakers and defibrillators) in an effort to track, and potentially impact, HF status. Although the primary outcome was not met, analysis of COMPASS-HF data demonstrated elevations of estimated PAD were associated with an increased risk of worsening HF; the inability to meet the primary outcome was likely related to lack of protocol-driven management when abnormal pressures were recorded [16,17]. Subsequent investigations evaluated the role of controlling PAD in improving patient outcomes by using an implantable hemodynamic monitoring system. In the CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients (CHAMPION) trial, a pulmonary artery pressure sensor was implanted in both HFrEF and HFpEF patients. Notable in CHAMPION was protocol-directed management to specific hemodynamic targets (*e.g.* to a specific PAD goal) in the active therapy arm. CHAMPION demonstrated that managing patients to a specific hemodynamic target resulted in less HF hospitalizations and improved outcomes both in the short and long term [18,19]. Of particular significance was the ability to improve outcomes in both HFrEF and HFpEF, reinforcing the importance of hemodynamic profiles across the range of ejection fractions in heart failure [20].

In heart failure hemodynamics, the use of PAD pressure can serve as a surrogate for left-sided filling pressures, including left atrial pressures [21]. Abnormal elevations in left atrial pressures, specifically, are linked to worsening heart failure symptoms [4,22]. Ultimately, remote hemodynamic monitoring trials have shown positive results due to the ability to reduce left atrial pressure. The importance of left atrial pressure is further underscored by a move towards direct left atrial pressure monitoring, which are currently being developed and may have improved fidelity over pulmonary arterial pressure monitoring [23].

Special consideration needs to be given to a subset of heart failure patients who present with dyspnea on exertion but have normal resting left atrial pressures on invasive testing. When considering these patients, it is important to understand that the primary symptom burden occurs with effort and not while inactive. It follows then that measurements acquired in a resting state may not reveal symptom etiology. If, after eliminating other causes of dyspnea, these patients undergo invasive exercise hemodynamic testing, substantial elevations in left-sided filling pressures may be noted and generally correspond to symptom onset [24]. Importantly, these patients, despite normal resting measurements, are at risk of poor heart failure outcomes [25]. From these collective data rises a need to directly treat elevated left atrial pressures in HF patients.

Left atrial decompression as a therapeutic strategy

Selective left atrial decompression as a therapeutic strategy for heart failure likely traces its roots to observations from other patient populations. Historically, patients with left-sided valve disease and concomitant atrial septal defects tend to have better outcomes than would be expected with left-sided valve disease alone, with the postulated mechanism being the presence of left-right shunting across the interatrial septum allowing decompression of the left atrium [26]. Conversely, closure of atrial septal defects, either surgically or by transcatheter techniques, can result in abrupt elevations of left atrial pressures and precipitate the onset of acute heart failure [27,28]. These observations suggest that anatomic manipulation of the atrial septum can allow modulation of left atrial pressures, and by extension, heart failure.

Such ideas led to the use of percutaneous balloon septostomy in severe, refractory cases of heart failure complicated by hypoxemia and pulmonary edema while being treated with extracorporeal membrane oxygenation [29-32]. In one small series of 9 patients, blade septostomy followed by balloon septostomy resulted in a 50% reduction in left atrial pressures; moreover, 7 of the 9 patients survived [32]. In a larger series of 64 patients, balloon septostomy resulted in a 66% reduction in left atrial pressures without developing right-left shunting [30].

Importantly, from the smaller study, post septostomy shunts had long-term patentcy in only two of the 7 survivors, implying only transient therapeutic benefits from this approach if applied to more chronic scenarios [32]. When considering chronic heart failure patients, more durable solutions are needed and have prompted the development of device-based shunt therapies as a novel therapeutic strategy. At present, three main designs exist, and all remain investigational with ongoing clinical testing to prove safety and efficacy.

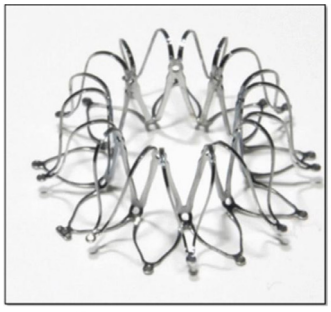
Interatrial shunt device

The InterAtrial Shunt Device (IASD, Corvia Medical, Tewksbury, MA, USA) is a nitinol device with a 19 mm outer diameter and a central opening diameter of 8 mm designed to sit across the interatrial septum [Fig. 1A]. Delivery of the device occurs by obtaining femoral venous access (16 Fr) followed by a standard trans-septal puncture. The IASD delivery system is then placed across the atrial septum, the left atrial disc is exposed and retracted to the septum, and the right atrial disc is unsheathed to secure the device in place. Device placement creates a reinforced anatomic communication between the left and right atria that physiologically allows a pressure-dependent left-to-right flow. [Fig. 1B and 1C]. The goal of the device is to allow left atrial decompression when left atrial pressures would be at their highest values, thus mitigating hemodynamically-driven dyspnea.

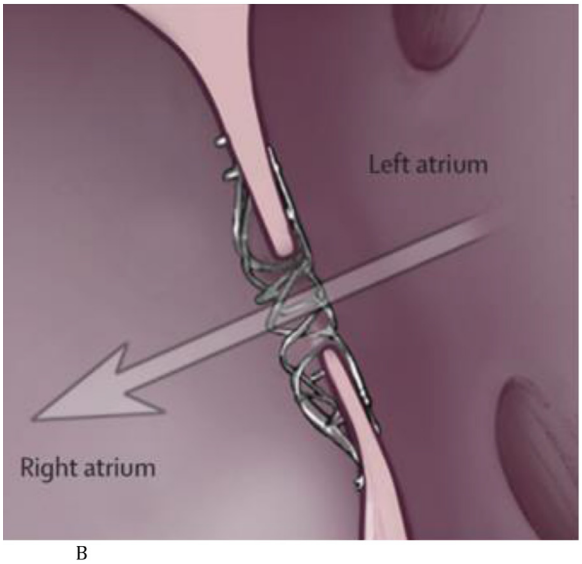
The creation of an interatrial shunt creates a mismatch between pulmonary and systemic flow (Qp:Qs), and carries a risk of worsening right-sided heart failure. Traditionally, however, Qp:Qs ratios $< 1.5:1$ are known to be well-tolerated and without deleterious right-sided changes. Based on patients affected by congenital atrial septal defects, such shunts are typically not considered for primary closure (which, theoretically, should counterbalance current clinical practice aimed at closing PFOs, not creating them) [33]. This parameter was integrated into the design of the IASD, which targets a Qp:Qs of 1.3:1 and increased flow with activity, and ultimately yielded the inner diameter of 8 mm using computational modeling [34].

The IASD underwent initial safety and feasibility testing in the Reduce Elevated Left Atrial Pressure in Patient with Heart Failure (REDUCE LAP-HF) trial [35]. REDUCE LAP-HF was a multicenter, unblinded, single-arm study that enrolled HFpEF patients (EF >40%) with exertional dyspnea graded at NYHA class II or worse. Primary eligibility was based on the presence of elevated left atrial pressures (assessed by the pulmonary capillary wedge pressure [PCWP] $>$ 15 mmHg at rest or $\geq$ 25 mmHg with exercise) and right atrial pressures that were lower than left atrial pressures. Invasive exercise hemodynamics were assessed using a recumbent bike and a prescribed graded exercise routine based on

Please cite this article as: S. Emani, D. Burkhoff and S.M. Lilly, Interatrial shunt devices for the treatment of heart failure, Trends in Cardiovascular Medicine, https://doi.org/10.1016/j.tcm.2020.09.004



A



B

Fig. 1. A: InterAtrial Shunt Device (IASD, Corvia Medical Inc., Tewkesbury, MA,USA). *Reproduced with permission from Corvia.*
Figure 1B: Schematic illustrating IASD device placed across atrial septum allowing for flow from the left atrium to the right atrium. *Reproduced with permission from Corvia.*
Figure 1C: Transthoracic echo with color Doppler demonstrating flow from the left atrium to the right atrium. *Reproduced with permission from Corvia.*

previously published protocols, starting at 0 W with an increase of 20 W after three-minute intervals to a point of patient-reported exhaustion or PCWP values ≥ 25 mmHg [36]. A total of 68 patients were enrolled, of which 64 underwent device implant. Mean EF was 47%, with most patients being NYHA functional class III (46%). The study evaluated co-primary endpoints comprised of safety and performance of the IASD at 6 months as well as changes in clinical status (functional capacity). No complications were reported related to the insertion of the device either at the time of implant or at the 6-month mark [35].

REDUCE LAP-HF demonstrated placement of an IASD resulted in a reduction in left atrial pressures at rest in 52% of patients, lower exercise left atrial pressures in 58%, and 39% showing a reduction in both phases. Sustained left-to-right shunting was demonstrated at 6 months, with an average resting Qp:Qs of 1.06:1 and an average Qp:Qs of 1.27:1 at peak exercise [35].

The same cohort of patients was followed for one year, with 60 patients achieving follow up through 12 months (3 patient deaths, including one due to stroke, and one lost to follow up between 6 and 12 months). In the patients evaluated at 1 year, 6-minute walk distance was greater at 12 months compared to baseline (363 m *vs* 331 m), and NYHA functional class was overall improved, with most patients achieving functional class I or II. Minnesota Living with Heart Failure scores were likewise improved at 12 months [37]. Taken together, the 6 and 12 month results of REDUCE LAP-HF suggested sustained hemodynamic and clinical benefits with the use of the IASD while maintaining a favorable safety profile.

Following the results of REDUCE LAP-HF, a Phase 2 randomized trial was conducted to focus on the HFpEF phenotype with exercise-induced hemodynamic abnormalities (specifically, those with an exercise PCWP ≥ 25 mmHg) [38]. The resultant REDUCE LAP-HF I trial was a randomized, multi-center trial comparing the IASD to placebo (sham procedure). Primary inclusion criteria were an NYHA functional status ≥ III, and exercise PCWP ≥25 mmHg, and a right atrial pressure less than left atrial pressure estimations. The primary endpoint was reduction in exercise PCWP at 1 month along with standard safety endpoints. A total of 44 patients were enrolled in a 1:1 fashion. At 1 month follow up, exercise PCWP was significantly lower in the IASD group, and no major adverse events were reported [39]. Subsequent analysis through the 1 year mark demonstrated a one class improvement in NYHA functional classification (conducted by blinded observers), and suggested a reduction in heart failure hospitalizations with the IASD. Noteworthy was the fact that all IASD devices were patent at 1 year, and no differences in adverse events between groups was seen [40].

Although encouraging, the results of the Phase 2 REDUCE LAP-HF I trial do not represent definitive proof of IASD efficacy in improving heart failure outcomes. More definitive evidence is expected from the pivotal randomized trial, REDUCE LAP-HF II (NCT03088033), currently being conducted. The trial has a target enrollment of 608 patients that will be randomized to IASD implant or a control arm. Inclusion criteria are similar to REDUCE LAP-HF I, with key criteria including age ≥40 years, EF ≥40%, current or recent NYHA Class III HF, recent need for intravenous diuretics, and exercise PCWP ≥ 25 mmHg (with PCWP greater than RAP ≥5 mmHg [41]. Although not specifically mentioned in the study design, the age criteria likely represents an effort to screen out patients less common forms of HF, including congenital and infiltrative disorders, in favor of a more "average" phenotype; indeed the mean age of HfPEF patients in the U.S. is >70 years [42]. In addition to safety measures, the primary outcome will be incidence of worsening heart failure and changes in measured quality of life through 24 months. Although biomarker analysis is not included in the primary or secondary endpoint analysis, planned subgroup analysis will focus on biomarker data [41]. Until these results are available, the IASD device will remain a promising, but unproven and investigational device.

V-Wave device

The V-Wave device (V-Wave Ltd, Caesarea, Israel) is another device designed for placement across the interatrial septum. Although it is a nitinol structure similar to the IASD, it has a unique hourglass shape with an ePTFE covering aimed at preventing tissue ingrowth [43] [Fig. 2]. Early iterations also included a one-way valve to ensure only left-to-right shunting [43]. This preliminary valve design, however, demonstrated a high rate of shunt stenosis or occlusion at 12 months due to pannus infiltration of the valve [44]. A design modification preserved the hour-glass shape but eliminated the valve component; instead, a 5.1 mm central opening was created. The V-Wave device is delivered via femoral venous access (14 Fr) following an interatrial septal puncture. The left atrial portion is expanded within the left atrium and then secured back to the interatrial septal. Device deployment is completed with the expansion of the right atrial portion [43]. In preclinical studies, the V-Wave device showed improvements in left atrial pressure, right atrial pressure, ejection fraction, and survival [45].

Please cite this article as: S. Emani, D. Burkhoff and S.M. Lilly, Interatrial shunt devices for the treatment of heart failure, Trends in Cardiovascular Medicine, https://doi.org/10.1016/j.tcm.2020.09.004

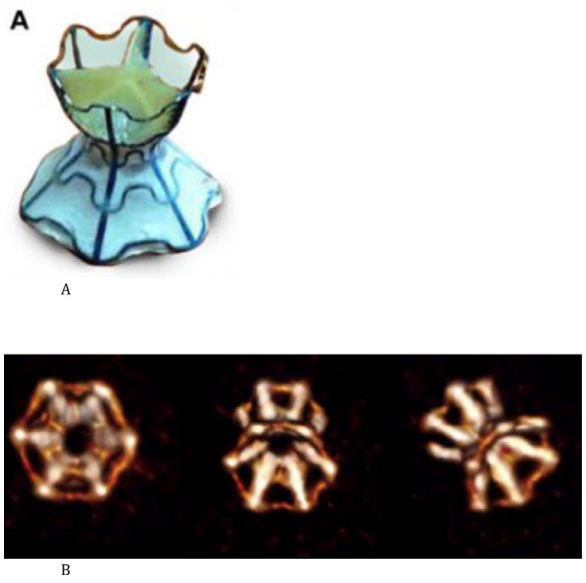


Fig. 2. A: Preliminary design of the V-Wave device (V-Wave Ltd., Caesarea, Isreal) including ePTFE coating and the incorporation of a one-way valve. *Reproduced with permission from V-Wave.*
Figure 2B: Computed tomography imaging and reconstruction of the V-Wave device post implant. *Reproduced with permission from V-Wave.*

Early clinical studies were conducted using the original V-Wave device (with valve design). A 10 patient proof-of-concept study was conducted among patients with HFrEF (EF ≤40%) who were NYHA functional class III or IV with a PCWP ≥15 mmHg. No periprocedural complications were noted; however one patient died prior to the specified 3-month follow up. Of surviving patients, 89% improved to NYHA functional class I or II, and 6-minute walk distance improved by 75 m. From a hemodynamic standpoint, PCWP and cardiac output both improved at 3 months [46].

A follow up, non-randomized trial enrolling 38 patients was conducted thereafter. In this trial, a mix of HFrEF and HFpEF patients were included. The first generation V-Wave device was successfully implanted in all patients, with only 1 periprocedural complication (pericardial tamponade). Despite early initial success, one-year follow up results were diminished due to reduced shunt patency in 50% of the patients (either stenosis or closure). As mentioned, pannus infiltration was implicated in the loss of patency, which eventually prompted the design of a second-generation device. In patients who maintained shunt patency, however, improvements were noted in ejection fraction, 6-min walk distance, and PCWP [44].

Testing of the second-generation device (*i.e.,* without valve) is currently underway. With an aim to enroll and randomize 500 patients to either V-Wave implant or a control arm, the Reducing Lung Congestion Symptoms in Advanced Heart Failure (RELIEVE-HF, NCT03499236) trial seeks to evaluate the safety of the V-Wave device while also evaluating a composite endpoint of death, heart transplant or ventricular assist device implantation, heart failure hospitalizations, and change in 6-min walk distance. Unlike the REDUCE LAP-HF II study of the IASD, the V-Wave device will be tested across a broad range of ejection fractions, not just in HFpEF patients. Similar to the IASD, the V-Wave device remains investigational and without definitive evidence of efficacy until these trial results become available.

Atrial flow regulator

The Atrial Flow Regulator (AFR; Occlutech, Istanbul, Turkey) represents a third device aimed at affecting interatrial flow in heart failure patients. The device is comprised of two nitinol mesh discs that anchor the device across the interatrial septum leaving a central canal open [Fig. 3]. Three sizes are available (6, 8, and 10 mm, corresponding to canal diameter), which are delivered via femoral venous access (10–12 Fr based on device size) following a transseptal puncture. The placement of the AFR allows for bidirectional flow depending on intracardiac hemodynamics [47].

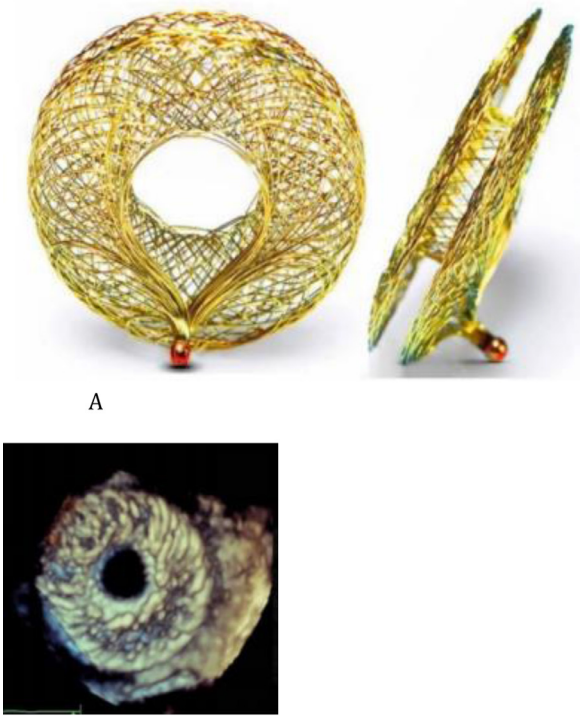


Fig. 3. A: Atrial Flow Regulator device (AFR; Occlutech, Istanbul, Turkey) [42].
Figure 3B: AFR device as seen by three-dimensional echocardiography [42].

Initial experience with the AFR system has not been with standard heart failure patients, but rather has involved patients with pulmonary hypertension. For these patients, in whom severe right heart failure can occur, the creation of a right-to-left shunt could be beneficial. Indeed, case-reports and small case series have been presented in which the AFR was successfully implanted and generated the desired right-to-left shunt. Moreover, the patients in whom the device was implanted had signs of clinical improvement. The AFR device remained patent through short term follow up [47,48].

Because the AFR has the capacity for bidirectional flow, its use in heart failure to decompress the left atrium has been postulated. The Pilot Study to Assess Safety and Efficacy of a Novel Atrial Flow Regulator in Heart Failure Patients (PRELIEVE; NCT03030274) is currently enrolling as the first step to evaluate the hypothesis that the ASR can improve outcomes in HFrEF patients. Pending results, additional trials will likely be required to prove potential benefits.

Conclusions

The prominent role played by elevated left atrial pressures in heart failure symptom etiology and prognosis is driving novel solutions aimed at decompressing the left atrium. Current pharmacologic therapies may achieve lower left atrial pressures, but do so through indirect mechanisms involving preload and afterload. Newer, device-based therapies are under development with the

Please cite this article as: S. Emani, D. Burkhoff and S.M. Lilly, Interatrial shunt devices for the treatment of heart failure, Trends in Cardiovascular Medicine, https://doi.org/10.1016/j.tcm.2020.09.004

goal of allowing direct reduction in left atrial pressures through the creation of a left-to-right shunt.

In addition to short- and intermediate-term improvements in heart failure, attention will need to be paid to complications related to device implant and maintenance. Current trials are evaluating procedural safety, which is of particular importance given the need for a transseptal puncture. Previous investigational devices utilizing transseptal techniques were plagued by complications [49]; but experience with the technique has matured since that time and will hopefully minimize adverse events. Additionally, the presence of a fixed device on the interatrial septum may lead to late complications similar to those seen when PFO closure devices are implanted. Such complications include the late formation of thrombus on the device, and/or an increased incidence of atrial arrhythmias [50]. Answers to these questions may not come from pivotal trial results; therefore ongoing diligence to monitor and evaluate patients receiving interatrial shunt devices will be required in the long term.

Despite these concerns, unique design aspects, as well as application to a range of heart failure patients, provides immense potential for therapeutic improvements; however such devices remain investigational at this point while ongoing clinical trials build an appropriate evidence base to support their use.

Acknowledgments

The authors did not receive any funding related to this manuscript.

References

[1] Heidenreich PA, Albert NM, Allen LA, Bluemke DA, Butler J, Fonarow GC, et al. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. Circ Heart Fail 2013;6(3):606–19.
[2] Jencks SF, Williams MV, Coleman EA. Rehospitalizations among patients in the medicare fee-for-service program. N Engl J Med 2009;360(14):1418–28.
[3] Miller LW, Guglin M. Patient selection for ventricular assist devices: a moving target. J Am Coll Cardiol 2013;61(12):1209–21.
[4] Freed BH, Shah SJ. Stepping out of the left ventricle's shadow: time to focus on the left atrium in heart failure with preserved ejection fraction. Circ Cardiovasc Imaging 2017;10(4).
[5] Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J 2016;37(27):2129–200.
[6] Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Colvin MM, et al. 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: a Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation 2017;136:e137–61.
[7] Iwano H, Little WC. Heart failure: what does ejection fraction have to do with it? J Cardiol 2013;62(1):1–3.
[8] Krittanawong C, Kukin ML. Current management and future directions of heart failure with preserved ejection fraction: a contemporary review. Curr Treat Options Cardiovasc Med 2018;20(4):28.
[9] Tsao CW, Lyass A, Enserro D, Larson MG, Ho JE, Kizer JR, et al. Temporal trends in the incidence of and mortality associated with heart failure with preserved and reduced ejection fraction. JACC Heart Failure 2018;6(8):678–85.
[10] Zakeri R, Cowie MR. Heart failure with preserved ejection fraction: controversies, challenges and future directions. Heart 2018;104(5):377–84.
[11] Pitt B, Pfeffer MA, Assmann SF, Boineau R, Anand IS, Claggett B, et al. Spironolactone for heart failure with preserved ejection fraction. N Engl J Med 2014;370(15):1383–92.
[12] Solomon SD, McMurray JJV, Anand IS, Ge J, Lam CSP, Maggioni AP, et al. Angiotensin-neprilysin inhibition in heart failure with preserved ejection fraction. N Engl J Med 2019;381(17):1609–20.
[13] Jackson AM, Jhund PS, Solomon SD, McMurray JJV. Response by Jackson et al. to letter regarding article, "Effects of Sacubitril-Valsartan versus valsartan in women compared with men with heart failure and preserved ejection fraction: insights from PARAGON-HF. Circulation 2020;142(1):e5–6.
[14] Morley D, Brozena SC. Assessing risk by hemodynamic profile in patients awaiting cardiac transplantation. Am J Cardiol 1994;73(5):379–83.
[15] Stevenson LW, Tillisch JH, Hamilton M, Luu M, Chelimsky-Fallick C, Moriguchi J, et al. Importance of hemodynamic response to therapy in predicting survival with ejection fraction less than or equal to 20% secondary to ischemic or nonischemic dilated cardiomyopathy. Am J Cardiol 1990;66(19):1348–54.
[16] Bourge RC, Abraham WT, Adamson PB, Aaron MF, Aranda JM Jr, Magalski A, et al. Randomized controlled trial of an implantable continuous hemodynamic monitor in patients with advanced heart failure: the COMPASS-HF study. J Am Coll Cardiol 2008;51(11):1073–9.
[17] Stevenson LW, Zile M, Bennett TD, Kueffer FJ, Jessup ML, Adamson P, et al. Chronic ambulatory intracardiac pressures and future heart failure events. Circ Heart Fail 2010;3(5):580–7.
[18] Abraham WT, Adamson PB, Bourge RC, Aaron MF, Costanzo MR, Stevenson LW, et al. Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial. Lancet 2011;377(9766):658–66.
[19] Abraham WT, Stevenson LW, Bourge RC, Lindenfeld JA, Bauman JG, Adamson PB, et al. Sustained efficacy of pulmonary artery pressure to guide adjustment of chronic heart failure therapy: complete follow-up results from the CHAMPION randomised trial. Lancet 2016;387(10017):453–61.
[20] Adamson PB, Abraham WT, Bourge RC, Costanzo MR, Hasan A, Yadav C, et al. Wireless pulmonary artery pressure monitoring guides management to reduce decompensation in heart failure with preserved ejection fraction. Circ Heart Fail 2014;7(6):935–44.
[21] Falicov RE, Resnekov L. Relationship of the pulmonary artery end-diastolic pressure to the left ventricular end-diastolic and mean filling pressures in patients with and without left ventricular dysfunction. Circulation 1970;42(1):65–73.
[22] Wolsk E, Kaye D, Borlaug BA, Burkhoff D, Kitzman DW, Komtebedde J, et al. Resting and exercise haemodynamics in relation to six-minute walk test in patients with heart failure and preserved ejection fraction. Eur J Heart Fail 2018;20(4):715–22.
[23] Perl L, Soifer E, Bartunek J, Erdheim D, Kohler F, Abraham WT, et al. A novel wireless left atrial pressure monitoring system for patients with heart failure, first ex-vivo and animal experience. J Cardiovasc Transl Res 2019.
[24] Borlaug BA, Nishimura RA, Sorajja P, Lam CS, Redfield MM. Exercise hemodynamics enhance diagnosis of early heart failure with preserved ejection fraction. Circ Heart Fail 2010;3(5):588–95.
[25] Dorfs S, Zeh W, Hochholzer W, Jander N, Kienzle RP, Pieske B, et al. Pulmonary capillary wedge pressure during exercise and long-term mortality in patients with suspected heart failure with preserved ejection fraction. Eur Heart J 2014;35(44):3103–12.
[26] Askey JM, Kahler JE. Longevity in extensive organic heart lesions: a case of Lutembacher's syndrome in a man aged 72. Ann Intern Med 1950;33(4):1031–6.
[27] Beyer J. Atrial septal defect: acute left heart failure after surgical closure. Ann Thorac Surg 1978;25(1):36–43.
[28] Ewert P, Berger F, Nagdyman N, Kretschmar O, Dittrich S, Abdul-Khaliq H, et al. Masked left ventricular restriction in elderly patients with atrial septal defects: a contraindication for closure? Catheter Cardiovasc Interv 2001;52(2):177–80.
[29] Aiyagari RM, Rocchini AP, Remenapp RT, Graziano JN. Decompression of the left atrium during extracorporeal membrane oxygenation using a transseptal cannula incorporated into the circuit. Crit Care Med 2006;34(10):2603–6.
[30] Baruteau AE, Barnetche T, Morin L, Jalal Z, Boscamp NS, Le Bret E, et al. Percutaneous balloon atrial septostomy on top of venoarterial extracorporeal membrane oxygenation results in safe and effective left heart decompression. Eur Heart J Acute Cardiovasc Care 2018;7(1):70–9.
[31] Johnston TA, Jaggers J, McGovern JJ, O'Laughlin MP. Bedside transseptal balloon dilation atrial septostomy for decompression of the left heart during extracorporeal membrane oxygenation. Catheter Cardiovasc Interv 1999;46(2):197–9.
[32] Seib PM, Faulkner SC, Erickson CC, Van Devanter SH, Harrell JE, Fasules JW, et al. Blade and balloon atrial septostomy for left heart decompression in patients with severe ventricular dysfunction on extracorporeal membrane oxygenation. Catheter Cardiovasc Interv 1999;46(2):179–86.
[33] Stout KK, Daniels CJ, Aboulhosn JA, Bozkurt B, Broberg CS, Colman JM, et al. 2018 AHA/ACC guideline for the management of adults with congenital heart disease: a report of the american college of cardiology/American heart association task force on clinical practice guidelines. J Am Coll Cardiol 2019;73(12):e81–e192.
[34] Kaye D, Shah SJ, Borlaug BA, Gustafsson F, Komtebedde J, Kubo S, et al. Effects of an interatrial shunt on rest and exercise hemodynamics: results of a computer simulation in heart failure. J Card Fail 2014;20(3):212–21.
[35] Hasenfuss G, Hayward C, Burkhoff D, Silvestry FE, McKenzie S, Gustafsson F, et al. A transcatheter intracardiac shunt device for heart failure with preserved ejection fraction (REDUCE LAP-HF): a multicentre, open-label, single-arm, phase 1 trial. Lancet 2016;387(10025):1298–304.
[36] Borlaug BA, Kane GC, Melenovsky V, Olson TP. Abnormal right ventricular-pulmonary artery coupling with exercise in heart failure with preserved ejection fraction. Eur Heart J 2016;37(43):3293–302.
[37] Kaye DM, Hasenfuss G, Neuzil P, Post MC, Doughty R, Trochu JN, et al. One-year outcomes after transcatheter insertion of an interatrial shunt device for the management of heart failure with preserved ejection fraction. Circ Heart Fail 2016;9(12). doi:10.1161/CIRCHEARTFAILURE.116.003662.
[38] Feldman T, Komtebedde J, Burkhoff D, Massaro J, Maurer MS, Leon MB, et al. Transcatheter interatrial shunt device for the treatment of heart failure: rationale and design of the randomized trial to REDUCE Elevated Left Atrial Pressure in Heart Failure (REDUCE LAP-HF I). Circ Heart Fail 2016;9(7). doi:10.1161/CIRCHEARTFAILURE.116.003025.

Please cite this article as: S. Emani, D. Burkhoff and S.M. Lilly, Interatrial shunt devices for the treatment of heart failure, Trends in Cardiovascular Medicine, https://doi.org/10.1016/j.tcm.2020.09.004

[39] Feldman T, Mauri L, Kahwash R, Litwin S, Ricciardi MJ, van der Harst P, 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(4):364–75.
[40] Shah SJ, Feldman T, Ricciardi MJ, Kahwash R, Lilly S, Litwin S, et al. One-year safety and clinical outcomes of a transcatheter interatrial shunt device for the treatment of heart failure with preserved ejection fraction in the Reduce Elevated Left Atrial Pressure in Patients With Heart Failure (REDUCE LAP-HF I) trial: a randomized clinical trial. JAMA Cardiol 2018;3(10):968–77.
[41] Berry N, Mauri L, Feldman T, Komtebedde J, van Veldhuisen DJ, Solomon SD, et al. Transcatheter interatrial shunt device for the treatment of heart failure: rationale and design of the pivotal randomized trial to REDUCE Elevated Left Atrial Pressure in Patients with Heart Failure II (REDUCE LAP-HF II). Am Heart J 2020;226:222–31.
[42] Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM. Trends in prevalence and outcome of heart failure with preserved ejection fraction. N Engl J Med 2006;355(3):251–9.
[43] Amat-Santos IJ, Del Trigo M, Bergeron S, Pibarot P, Altisent O, Campelo–Parada F, et al. Left atrial decompression using unidirectional left-to-right interatrial shunt: initial experience in treating symptomatic heart failure with preserved ejection fraction with the W-wave device. JACC Cardiovasc Intervent 2015;8(6):870–2.
[44] Rodes-Cabau J, Bernier M, Amat-Santos IJ, Ben Gal T, Nombela-Franco L, Garcia Del Blanco B, et al. Interatrial Shunting for heart failure: early and late results from the first-in-human experience with the V-wave system. JACC Cardiovasc Intervent 2018;11(22):2300–10.
[45] Eigler NL, del Rio CL, Verheye S, McConnell PI, Lilly SM, George R, et al. Cardiac unloading with an implantable interatrial shunt in heart failure: serial observations in an ovine model of ischemic cardiomyopathy. Struct Heart 2017;1(1–2):40–8.
[46] Del Trigo M, Bergeron S, Bernier M, Amat-Santos IJ, Puri R, Campelo-Parada F, et al. Unidirectional left-to-right interatrial shunting for treatment of patients with heart failure with reduced ejection fraction: a safety and proof-of-principle cohort study. Lancet 2016;387(10025):1290–7.
[47] Patel MB, Samuel BP, Girgis RE, Parlmer MA, Vettukattil JJ. Implantable atrial flow regulator for severe, irreversible pulmonary arterial hypertension. EuroIntervention 2015;11(6):706–9.
[48] Rajeshkumar R, Pavithran S, Sivakumar K, Vettukattil JJ. Atrial septostomy with a predefined diameter using a novel occlutech atrial flow regulator improves symptoms and cardiac index in patients with severe pulmonary arterial hypertension. Catheter Cardiovasc Interv 2017;90(7):1145–53.
[49] Abraham WT. Hemodynamic monitoring in advanced heart failure: results from the LAPTOP-HF trial. HFSA 20th Annual Scientific Meeting Orlando, FL; 2016.
[50] Staubach S, Bertog S, Wunderlich N, Sievert H. Late complications of transcatheter closure of patent foramen ovale: new technology and new outcomes. Future Cardiol 2009;5(5):503–10.

Please cite this article as: S. Emani, D. Burkhoff and S.M. Lilly, Interatrial shunt devices for the treatment of heart failure, Trends in Cardiovascular Medicine, https://doi.org/10.1016/j.tcm.2020.09.004