The Potential of Devices for HFpEF

Andrew J Stewart Coats¹ and Stefan D Anker²

1. University of Warwick, Coventry, CV4 8UW, UK
2. Institute of Innovative Clinical Trials, University Medical Centre Göttingen, Göttingen, Germany

Corresponding author:
Professor Andrew J Stewart Coats,
University of Warwick, CV4 8UW, UK
Email: ajescoats@aol.com

Abstract

The 2016 ESC/HFA HF guidelines list the very many drug and device therapies that are proven to be beneficial in terms of life prolongation and hospitalisation prevention for HFrEF. The list of recommended therapies or devices for HFpEF and HFrEF is limited to diuretics and the management of comorbidities and so far there is no clinical evidence for an electrical or mechanical device for HFpEF. The Cardiac Contractility Modulation (CCM) device that may have a role in selected HFrEF and HFrEF patients has been reviewed in another paper in this issue but here we survey the results so far of a novel device for patients with HFpEF. Despite lagging many years behind HFrEF, HFpEF patients are now being targeted with novel devices with the potential to improve symptoms, improve quality of life, reduce hospitalization and delay progression of the syndrome. The front-runner is a novel inter-atrial left atrial pressure decompression device the Corvia IASD, which currently enrolling patients in a randomized trial. This device is a CE-marked investigational, non-surgical transcatheter implant designed to provide continuous and dynamic decompression of the left atrium, in an effort to reduce symptoms, HF hospitalizations, and improve quality of life as well as potentially slowing the progression of HFpEF.

Keywords: Heart failure; Devices; HFpEF; inter-atrial shunt

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Background

The 2016 ESC/HFA HF guidelines list the very many drug and device therapies that are proven to be beneficial in terms of life prolongation and hospitalisation prevention for HFrEF. [1] The list of recommended therapies or devices for HFpEF and HFrEF is limited to diuretics and the management of comorbidities and so far there is no clinical evidence for an electrical or mechanical device for HFpEF. The Cardiac Contractility Modulation (CCM) device that may have a role in selected HFrEF and HFrEF patients has been reviewed in another chapter but here we survey the results so far of a novel device for patients with HFpEF.

Heart failure affects more than 26 million people globally. Heart failure with preserved ejection fraction (HFpEF), accounts for approximately 50% of all heart failure, affecting more than 6.2 million people in the United States and Europe, yet recommended treatment options remain limited. In contrast to the situation of HFrEF the survival risk of HFpEF has virtually

Figure 1 The Corvia InterAtrial Shunt Device (IASD®) System. The device next to a US 10 cent coin for size comparison.

Figure 2 The IASD delivery system. Panel A shows the controller of the delivery catheter system. Panel B shows the device still loaded onto the catheter delivery system and Panel C shows the device half deployed.
remained unchanged over the last two decades of progress in HF research. This is a reflection of the lack of available therapies. Drug treatments for HFpEF and HFmrEF are reviewed in Chapter 7. For HFpEF although prognosis when corrected for age and co-morbidities is lower than for HFrEF it is still unacceptably high. In addition many with this type of heart failure have difficulty breathing, find simple daily activities tiring if not impossible and are frequently hospitalized with a resultant dramatic reduction in their quality of life. Although the pathophysiology of HFpEF is complex and undoubtedly there are several phenotypes of this syndrome it is clear that a subset of patients and many of the symptoms are limited by excessive rises in left atrial pressure, in particular during exercise. This is the principal target of left atrial compression with diuretic usage and fluid balance control. The technique of using a device to lower left atrial pressures is novel and offers some potential for the large unmet need of HFpEF patients. Here we review the clinical trials data of one such device, the Corvia Medical IASD®.

The device
Corvia Medical’s InterAtrial Shunt Device (IASD) System (Figure 1) has derived from pioneering haemodynamic studies going back two decades. The device is a CE-marked investigational, non-surgical transcatheter implant designed to provide continuous and dynamic decompression of the left atrium, in an effort to reduce symptoms, HF hospitalizations, and improve quality of life as well as potentially slowing the progression of HFpEF.

The device is designed to be inserted percutaneously during a catheter-based procedure. The delivery system is used to create a controlled inter-atrial communication, with resulting flow through the IASD system between the left and right atria. This opening allows blood to flow from the high pressure left atrium to the lower pressure right atrium and can decrease the elevated left atrial pressures in HFpEF in a dynamic manner i.e. at rest and during physical activity, thereby reducing lung congestion. Figure 2 shows the implant loaded on the delivery catheter.

This device-based approach has been developed, in part based upon the observation that patients with Lutembacher’s syndrome (ASD + Mitral Stenosis and some congenital heart patients with ASD’s) are less symptomatic than those without an ASD, suggesting that left atrial decompression through an inter-atrial communication might relieve symptoms in HFpEF where like in MS left atrial pressures are elevated.[2] This thinking led to the first in man experience in patients initially with MS and subsequently in HFpEF. Simulation modelling showed the theoretical effects of such a shunt (diameter up to 12 mm) on acute rest and exercise haemodynamic data (including changes in PCWP) in patients with HFpEF. The inter-atrial shunt was predicted to lower PCWP acutely by ~3 mm Hg under simulated resting conditions (from 10 to 7 mm Hg) and by ~11 mm Hg during simulated peak exercise (from 28 to 17 mm Hg). Left ventricular cardiac output was predicted to decrease ~0.5 L/min at rest and ~1.3 L/min at peak exercise, with corresponding increases in right ventricular cardiac output. A majority of these effects were achieved with a shunt diameter of 8–9 mm, whereas minimal effects were obtained with diameters under 6 mm.[3]

Based on these data a first pilot study in patients with HFpEF was commenced.[4] Eleven patients satisfying the inclusion/exclusion criteria of symptomatic HFpEF and LVEF >45%; baseline PCWP ≥15 mmHg (at rest), or ≥25 mmHg (on exercise) were included. An IASD device was successfully implanted in all 11 using percutaneous trans-septal access via the femoral vein.
At 30 days, LV filling pressures had fallen 5.5 mmHg (19.7 ± 3.4 vs. 14.2 ± 2.7; P = 0.005. Two serious adverse events were reported (one re-hospitalization, and one implant malposition successfully treated with a new device during the index procedure). One of these implantations is shown in Figure 3 and the desired placement of the device showed figuratively in Figure 4. At one year, all patients had survived, NYHA class had decreased (Class III/IV 45 %/0 % vs. 82%/18% at baseline), six-minute walk distance had increased (315±152 meters to 343±76 meters) and MLWHF score improved (53±17 to 37±17), although these changes were not statistically significant. Over the year compared to the year pre-implantation heart failure hospitalisations decreased from affecting 6 of 11 patients with a rate per 10 patient years of 1.36 to 2 of 11 patients, and a HFH/10PY rate of 0.73. (p=0.03).

Theses encouraging early proof of concept results led to the design of the REDUCE LAP-HF Trial[6] in which patients with ejection fraction ≥40% and New York Heart Association functional class III or IV heart failure with a pulmonary pressure (PCWP) ≥15 mmHg at rest or ≥25 mm Hg during supine bike exercise were planned to be implanted with an IASD System II, and followed for three years. This trial has recently reported [7] and showed in 68 HFpEF patients (placement successful in 64 of 66) no major adverse cardiac or cerebrovascular events through 6 months. At 6 months, 31 (52%) of 60 patients had a reduction in pulmonary capillary wedge pressure at rest and 34 (58%) of 59 had a lower pulmonary capillary wedge pressure during exertion, with 39% achieving both. Exercise wedge pressure was reduced both at 20 watts (~3 mmHg, p=0.0124) and at peak exercise (~2 mmHg, p=0.0255), despite an improved exercise duration (7.3 min [SD 3.1] vs 8.2 min [3.4], p=0.03). Sustained device patency at 6 months was confirmed by left-to-right shunting (pulmonary/systemic flow ratio: 1.06 [SD 0.32] at baseline vs 1.27 [0.20] at 6 months, p=0.0004).

Conclusions
Despite lagging many years behind HFrEF, HFpEF patients are now being targeted with novel devices with the potential to improve symptoms, improve quality of life, reduce hospitalization and delay progression of the syndrome. The front-runner is a novel inter-atrial left atrial pressure decompression device the Corvia IASD, currently enrolling patients in a randomized trial.

Declaration of Interest
The author declares no conflicts of interest.

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References