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InterAtrial Shunt Device (IASD®) implantation — a novel treatment method for heart failure with preserved ejection fraction

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Abstract

Heart failure with preserved ejection fraction (HFpEF) is a condition with complex pathophysiology and clinical profile. No treatment has been proven to reduce mortality or reduce morbidity in a meaningful way. In the era of percutaneous cardiac interventions, a novel method of reducing left atrial pressure by creating an iatrogenic interatrial shunt has been introduced. We present a report of implantation of InterAtrial Shunt Device (IASD®) in three consecutive patients.

Key words: heart failure, preserved ejection fraction, interventions

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INTRODUCTION

A subgroup of patients with symptoms of heart failure (HF) does not present with dilated left ventricular (LV) dimensions or reduced LV ejection fraction (LVEF). The terms 'heart failure with preserved ejection fraction' (HFpEF) or 'diastolic HF' have been used to describe this population [1, 2]. The incidence of HFpEF is rising, but there is still no treatment that has been proven to reduce mortality or reduce morbidity in a meaningful way in HFpEF [3–8]. Patients suffering from HFpEF are elderly and symptomatic, and their quality of life is often very poor [9, 10].

Exercise intolerance in HFpEF patients is associated with an increase in left atrial pressure and impaired LV diastolic function [11, 12].

Historically, a combination of mitral stenosis and atrial septal defect (Lutembacher's syndrome) has been described [13]. Patients with this combination had better outcomes than patients with 'pure' mitral stenosis. This could be related to reduction of left atrium pressure via the atrial septal defect.

The REDUCe Elevated Left Atrial Pressure in Patients with Heart Failure (REDUCE LAP-HF) trial was conducted to assess the InterAtrial Shunt Device (IASD®) (Corvia Medical Inc., Tewksbury, MA, USA) performance and safety in symptomatic patients with HFpEF.

This paper presents our initial experience with IASD® implantation in three consecutive patients.

METHODS

We enrolled three patients with known HFpEF, who met inclusion criteria (adults aged > 40 years, HFpEF with New York Heart Association [NYHA] II–IV functional class, LVEF > 40%, increased pulmonary capillary wedge pressure (PCWP) > 15 mm Hg at rest, or > 25 mm Hg during supine ergometry). Detailed protocol and design of the REDUCE LAP-HF trial were described elsewhere [14, 15]. The study protocol was approved by the local bioethics committee. All patients gave written informed consent.

All enrolled patients underwent right heart catheterisation with assessment of cardiac output and haemodynamic parameters at rest and during supine bicycle exercise, at baseline, six and 12 months after device implantation. Haemodynamic assessment was done according to acknowledged standards [16].

Implantation of the device was performed percutaneously (on a separate hospitalisation from the screening) via the

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Table 1. Patient characteristics and results

Parameter	Patient M.A.			Patient G.L.			Patient B.A.		
	Before procedure	Six months after procedure	12 months after procedure	Before procedure	Six months after procedure	12 months after procedure	Before procedure	Six months after procedure	12 months after procedure
Patient characteristics									
Age [years]	73			66			61		
Sex	Female			Female			Male		
NYHA class	II	II	II	II	II	I	II	II	I
BMI [kg/m^2]	36.7	34.1	35.6	31.8	31.7	32.2	33.2	31.7	31.7
Comorbidities	AF (cardiac pacemaker implanted due to symptomatic bradycardia), arterial hypertension, type 2 DM, CKD, hypothyroidosis (L-thyroxine supplementation)			Arterial hypertension			Hyperlipidaemia, right bundle branch block		
Haemodynamics, resting									
Mean RA pressure [mm Hg]	6	5	12	0	10	3	4	15	4
PA pressure systolic/diastolic [mm Hg]	39/13	59/22	58/17	23/7	37/15	32/8	40/20	48/12	26/6
Mean RV pressure [mm Hg]	17	14	20	8	21	12	7	25	9
Mean PCWP [mm Hg]	25	15	13	7	11	10	13	17	4
Mean arterial pressure [mm Hg]	100	126	121	119	119	129	120	119	97
Cardiac output [L/min]	4.1	4.9	5.8	5.1	4.9	6.3	8.5	7.7	5.9
Cardiac Index [L/min/m^2]	2.2	2.6	3.0	2.7	2.6	3.2	3.7	3.3	2.6
Oxygen saturation Arterial/SVC/IVC/PA [%]	92/59.4/60.6/ /60.0	92/64/74.1/ /72.3	90/72.1/71.6/ /71.7	99/66.7/NA/ /73	97/62/NA/ /77.1	97/65.4/NA/ /75.5	96/74.3/72.5/ /74.6	95/70.7/71.4/ /75.2	94/74.8/73.4/ /72.7
Haemodynamics, supine bike exercise									
Mean RA pressure [mm Hg]	17	19	21	12	11	10	10	22	9
PA pressure systolic/diastolic [mm Hg]	61/22	68/27	77/16	61/35	67/28	58/17	58/28	62/23	41/8
Mean RV pressure [mm Hg]	20	NA	NA	NA	NA	NA	NA	NA	NA
Mean PCWP [mm Hg]	35	26	36	31	25	28	25	19	10
Mean arterial pressure [mm Hg]	111	121	128	179	150	134	112	130	94
Cardiac output [L/min]	6.1	8.8	10.1	9.1	11.1	10.6	13.2	10.1	10.1
Cardiac index [L/min/m^2]	3.2	4.7	5.3	4.8	5.9	5.4	5.7	4.4	4.4
Oxygen saturation Arterial/SVC/IVC/PA [%]	94/55/20.8/ /38.6	87/38.7/NA/ /35.9	89/46.6/NA/ /36.3	94/64.9/NA/ /35.9	93/51.7/NA/ /51.8	92/56.7/NA/ /76.3	84/NA/67.2/ /55	94/65.7/NA/ /49.3	96/48/NA/ /48.4

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Table 1. cont. Patient characteristics and results

Parameter	Patient M.A.			Patient G.L.			Patient B.A.		
	Before procedure	Six months after procedure	12 months after procedure	Before procedure	Six months after procedure	12 months after procedure	Before procedure	Six months after procedure	12 months after procedure
Echocardiography									
LA diameter [mm]	53	51	51	41	42	41	43	40	45
LA volume [mL]	80	109	116	75	85	63	102	100	93
RA size (area from the apical four chamber view) [cm^2]	17	46	23	15.5	15	16	22	17	19.8
LVEDD [mm]	56	55	52	55	51	49	53	49	47
LVESD [mm]	38	37	34	35	37	27	41	31	33
LVEF [%]	53	50	52	58	55	53	55	66	69
E/e'	13	16	14	13	11	9.8	8.7	10.8	11
TAPSE [mm]	18	16	17	21	21	18	26	26	22
Aortic regurgitation	None	None	None	None	None	Mild/trivial	None	Mild/trivial	None
Mitral regurgitation	Moderate	Moderate	Moderate	Mild/trivial	Moderate	Moderate	Mild/trivial	Mild/trivial	None
Tricuspid regurgitation	Moderate	Moderate	Moderate	Mild/trivial	Moderate	Moderate	Mild/trivial	Mild/trivial	None
Pulmonary regurgitation	None	Mild/trivial	Mild/trivial	None	Moderate	Moderate	Mild/trivial	None	None
Other parameters									
Peak VO_2 [mL/kg/min]	13.4	14.7	16.2	19.7	17.9	20.2	29.4	20.8	25.1
6MWT distance [m]	300	180	235	170	330	345	520	490	500
Dyspnea (Borg Scale 6–20) before/end of test	7/14	3/10 (modified Borg Scal 0-10)	6/15	8/19	0/7 (modified Borg Scale 0–10)	6/10	7/8	6/10	8/12
Fatigue (Borg Scale 6–20) before/end of test	8/20	5/10 (modified Borg Scale 0–10)	13/17	7/18	0/4 (modified Borg Scale 0–10)	8/10	7/10	7/17	8/12
MLWHF total score	73	81	55	64	5	19	40	27	15
NT-proBNP [pg/mL]	1084	1098	1182	254	229	175	92	177	101

6MWT — six-minute walk test; AF — atrial fibrillation; BMI — body mass index; CKD — chronic kidney disease; DM — diabetes mellitus; E/e' — the ratio of mitral peak velocity of early filling (E) to early diastolic mitral annular velocity (e'); IVC — inferior vena cava; LA — left atrium; LVEDD — left ventricular end-diastolic diameter; LVEF — left ventricular ejection fraction; LVESD — left ventricular end-systolic diameter; MLWHF — Minnesota Living With Heart Failure Form; NA — not available; NT-proBNP — N-terminal pro B-type natriuretic peptide; NYHA — New York Heart Association; PA — pulmonary artery; PCWP — pulmonary capillary wedge pressure; RA — right atrium; RV — right ventricle; SVC — superior vena cava; TAPSE — tricuspid annular plane systolic excursion

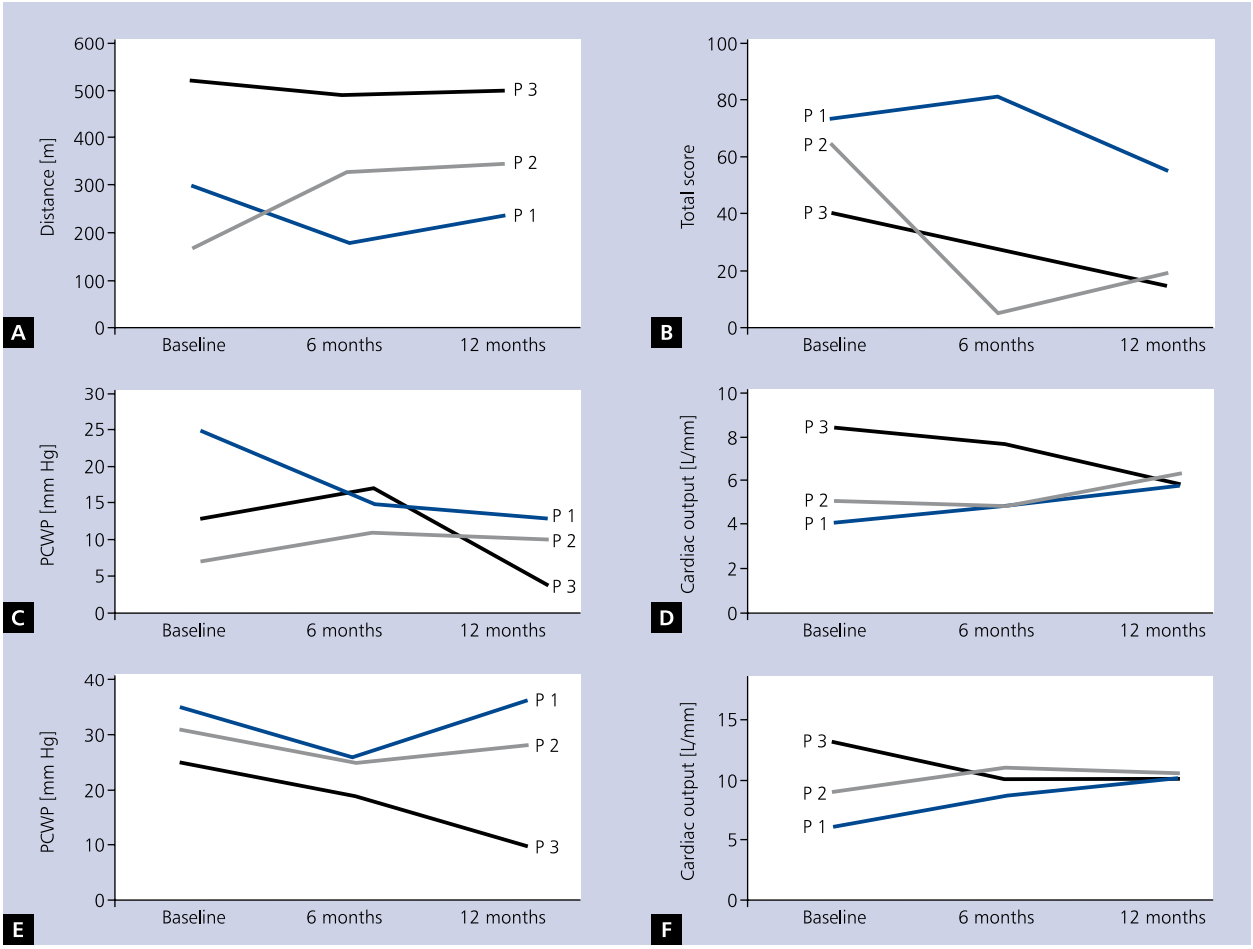

Figure 1. Selected haemodynamic parameters (invasive study), exercise capacity, and quality of life in three patients — 12 months observation; **A.** Six-minute walk test; **B.** Minnesota Living with Heart Failure form; **C.** Pulmonary capillary wedge pressure (PCWP), resting; **D.** Cardiac output resting; **E.** Pulmonary capillary wedge pressure (PCWP), exercise; **F.** Cardiac output exercise; P — patient

femoral vein. Transseptal puncture of the interatrial septum was done using fluoroscopy and transoesophageal echocardiographic guidance, and the device was positioned using an over-the-wire technique. Two patients not receiving oral anticoagulants for atrial fibrillation were prescribed aspirin (75 mg once daily) indefinitely, and clopidogrel (75 mg once daily) for six months. One patient with atrial fibrillation treated with oral anticoagulants continued on existing oral anticoagulants (warfarin) after the procedure. Endocarditis prophylaxis was advised for a minimum of six months post-implantation.

RESULTS

We successfully implanted the IASD® device in three patients between April 8, 2015 and June 11, 2015 using the techniques described above. We did not observe any major adverse cardiac or cerebrovascular event, including death, stroke, myocardial infarction, pulmonary or systemic embolism, or need for surgical intervention throughout the 12-month follow-up period.

Detailed clinical, locally assessed echocardiography and haemodynamic parameters are shown in Table 1. Figure 1 shows the dynamics of significant haemodynamic parameters, exercise capacity, and quality of life in 12-month observation.

Baseline mean PCWP, mean pulmonary pressure, mean right atrial pressure, and cardiac output increased during exercise are shown in Table 1.

At six and 12 months follow-up we observed reduction of PCWP at rest in two of three patients, and during exercise in two of three patients. All three patients had echocardiographic evidence of left-to-right atrial flow. Cardiac output measured with thermodilution was increased in two of three patients. Right atrial pressure at rest was higher in two of three patients, and during supine exercise in one of three patients (in one patient we initially observed increase in right atrial pressure after six months, which subsequently decreased).

Echocardiography showed changes in chamber volumes as described in Table 1. There were no significant changes in N-terminal pro B-type natriuretic peptide (NT-proBNP)

concentrations. In two of three patients NYHA class improved (II to I), and six-minute walk distance improved in one of three patients. In every patient, the Minnesota Living with Heart Failure total score decreased meaningfully (> 15 points) compared to baseline at 12-month follow-up.

DISCUSSION

The pathophysiology of HFpEF is complex and multifactorial. Many co-morbidities (i.e. arterial hypertension, atrial fibrillation, coronary artery disease, diabetes, obesity, chronic kidney disease, anaemia, chronic obstructive pulmonary disease) contribute to the clinical profile and symptom development in patients with HFpEF [17–20]. According to the current guidelines, HFpEF can be diagnosed if LVEF is equal to or more than 50% (the most recent European Society of Cardiology guidelines on HF defined "mid-range" HF in patients with LVEF 40–49%); however, most of the HFpEF trials included patients with LVEF ≥ 40% [21]. No treatment has been proven to reduce mortality or morbidity in HFpEF so far, so the treatment is focused on relieving symptoms, and improving exercise capability and quality of life [3–8]. Our data, as well as other invasive haemodynamic studies, showed that patients with HFpEF present with increased PCWP during exercise [11, 12]. According to the REDUCE LAP-HF study, novel IASD® device implantation leads to reduction in exercise PCWP, which is consistent with atrial decompression and a reduction in LV end-diastolic volume. Peak exercise PCWP was reduced after device implantation, despite an increase in exercise capacity; this parameter has been associated with mortality in studies on patients with HFpEF [12].

Our observations of three patients are in line with previously reported REDUCE LAP-HF trial results [14, 22]. Partial improvement in terms of haemodynamic parameters was seen, and patients reported better quality of life. The latter may be related to the placebo effect, because there was no clear evidence of better exercise capacity and the levels of NT-proBNP were virtually the same in 12-month observation. REDUCE LAP-HF was a small, open-label, non-randomised study with limited data on mortality. Blinded randomised trials (including a control procedure) with long-term follow-up are ongoing to confirm the IASD® device safety and effectiveness.

CONCLUSIONS

The observations to date show that the IASD® device implantation is a promising method in terms of symptom reduction, quality of life, and safety.

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Conflict of interest: *Michał Kosowski and Piotr Kubler declare no conflict of interest; the remaining authors received honoraria as investigators.*

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InterAtrial Shunt Device (IASD®) — nowa metoda inwazyjnego leczenia niewydolności serca z zachowaną frakcją wyrzutową lewej komory

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Streszczenie

Niewydolność serca z zachowaną frakcją wyrzutową lewej komory (HFpEF) jest stanem o złożonej patofizjologii i profilu klinicznym. Żadna z dotychczas proponowanych metod leczenia nie przyniosła efektu w zakresie redukcji zachorowalności i śmiertelności. W czasach ciągłego postępu inwazyjnych metod terapii chorób serca i naczyń zaproponowano metodę przezskórnego wytworzenia połączenia między przedsionkami w celu redukcji ciśnienia w lewym przedsionku. W niniejszej pracy zaprezentowano raport z implantacji urządzenia InterAtrial Shunt Device (IASD®) u trzech pacjentów.

Słowa kluczowe: niewydolność serca, zachowana frakcja wyrzutowa, leczenie inwazyjne

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