International Journal of Cardiology 187 (2015) 227–228

Contents lists available at ScienceDirect

International Journal of Cardiology

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

Letter to the Editor

Clinical outcome of transcatheter treatment of heart failure with preserved or mildly reduced ejection fraction using a novel implant

Filip Malek [a,*], Petr Neuzil [a], Finn Gustafsson [b], David M. Kaye [c,d], Antony Walton [d], Martin Mates [a], Lars Søndergaard [b], Nikolaj Ihlemann [b], Justin A. Mariani [d], Vivek Reddy [e]

[a] Na Homolce Hospital, Prague, Czech Republic
[b] Dept. of Cardiology, Rigshospitalet, Copenhagen, Denmark
[c] IDI Baker Institute, Australia
[d] Alfred Hospital, Melbourne, Australia
[e] Mount Sinai School of Medicine, NY, USA

ARTICLE INFO

Article history:
Received 9 February 2015
Accepted 17 March 2015
Available online 18 March 2015

Keywords:
Heart failure with preserved ejection fraction
Interatrial septal device
Heart failure hospitalizations

Chronic heart failure with preserved ejection fraction (HFpEF) is common and treatment options are limited [1]. Strategies for effectively reducing symptoms and improving outcome in patients with HF and reduced ejection fraction (HFrEF) have not been successful in subjects with HFpEF [2].

The prognosis of HFpEF is similar to HFrEF and chronic HFpEF accounts for 50% of all HF hospitalizations (HFH) with the incidence HFpEF increasing worldwide [3].

Elevated filling pressures in the patients with HFpEF have been associated with an increased risk of cardiovascular hospitalization and resting PCWP > 12 mm Hg has been associated with increased mortality [4].

We hypothesized that creation of a small permanent atrial septal defect in patients with elevated left ventricle (LV) filling pressure (i.e. pulmonary capillary wedge pressure = PCWP) in chronic HFpEF would lower left sided filling pressures and, in turn, relieve dyspnea, without adverse hemodynamic sequelae, and potentially reduce HFH and improve quality of life.

The objective of this prospective non-randomized study was to evaluate the safety and potential benefits of the Interatrial Septal Device System (IASD®, DC Devices Inc., Tewksbury, MA, USA) in the treatment of chronic symptomatic HFpEF despite optimal medical management. The primary outcome measure was serious adverse device events through 30-days. Secondary outcome measures included procedural success, NYHA class, PCWP, and other hemodynamic variables during right heart catheterization, six-minute walk distance, HF hospitalizations, and quality-of-life (assessed by Minnesota Living With Heart Failure). Patients with left ventricular ejection fraction (LVEF) ≥ 45% and at least on HF hospitalization within the prior year, or with persistent NYHA III class symptoms, were included. The main hemodynamic inclusion criterion was: PCWP at rest ≥ 15 mm Hg or during exercise ≥ 25 mm Hg. The IASD is an implant comprised of Nitinol (outer diameter 19 mm), which is inserted percutaneously in the interatrial septum to produce a permanent 8 mm atrial septal communication.

The 30-day results have previously been reported [5]. Eleven patients were enrolled. Patients were elderly, impaired in terms of functional capacity, quality of life, and suffered from multiple comorbidities. Mean LVEF was 57%, and elevated left sided filling pressures was documented in all. Cardiac index was reasonably preserved at rest. The MAGGIC score at baseline was 22, and 82% of patients had a MLWHF score > 45.

At early follow-up PCWP had significantly decreased by 28% from 19.0 ± 5 to 14 ± 3 mm Hg ($p = 0.005$). Right atrial pressure and systolic pulmonary artery pressure were unchanged. Patient symptoms improved, NYHA class decreased from 100% in NYHA Class III/IV to 45% ($p = 0.044$), six-minute walk distance increased from 322 ± 151 m to 368 ± 123 m ($p = 0.025$), and quality of life improved from 53 ± 17 to 18 ± 19 ($p = 0.005$).

At one year, all patients survived, NYHA class decreased (Class III/IV 45%/0% vs. 82%/18% at baseline; $p = 0.017$), six-minute walk distance increased (315 ± 152 m to 343 ± 76 m; p = NS) and MLWHF score improved (53 ± 17 to 37 ± 17; $p = 0.057$) (Table 1).

Heart failure hospitalization (HFH) during the prior year affected 55% of patients (6 of 11) with a rate per 10 patient years (HFH/10PY) of 1.36. In the post-procedural year, HFH requiring IV diuretics occurred in 18% (2 of 11) of the patients, and the HFH/10PY rate decreased significantly to 0.73. ($p = 0.03$). Recurrent HFH occurred in 33% (2 of 6) of the patients with prior year HFH.

* Corresponding author at: Dept. of Cardiology, Cardiovascular Center, Na Homolce Hospital, Roentgenova Street 2, 150 30 Prague 5, Czech Republic.

http://dx.doi.org/10.1016/j.ijcard.2015.03.198
0167-5273/

Table 1
Clinical results compared to baseline.

	HFH		NYHA class		6 MWTD (M)		MLWHF	
	Prior year	Year after	Baseline	1 Year	Baseline	1 Year	Baseline	1 Year
Median	1	0	3	2.5	334	364	58	29.5
Range	0 to 6	0 to 5	III–IV	II–III	52–540	240–494	17–70	14–62
Mean	1.5	0.8[1]	3.2	2.5[2]	309.6	351.7[3]	54.9	36.3[4]
STDEV	1.90	1.75	0.42	0.53	158.8	79.4	17.0	16.5

HFH = heart failure hospitalizations, 6MWTD = six minute walk test distance, MLWHF = Minnesota Living With Heart Failure, STDEV — standard deviation.
[1] p = 0.030 vs. baseline.
[2] p = 0.017 vs. baseline.
[3] p = NS vs. baseline.
[4] p = 0.057 vs. baseline.

Average daily dose of furosemide increased from 60 ± 66 mg/day to 95 ± 143 mg/day (NS), primarily due to increases in two patients with recurrent HFH. At one year, there was no new onset AF, all patients (64%) in sinus rhythm (SR) at baseline remained in SR at one year.

There were no major adverse cardiac or cerebral events through 12 months of follow-up. A total of seventeen SAEs were reported in 7 patients through 12 months of follow-up. Seven (41%) of these events occurred in one patient with a history of six HF hospitalizations in the 12-months prior to the implantation of IASD, and five of these seven were repeat HF hospitalizations requiring IV diuretics. Three events were repeat heart failure related hospitalizations in a single patient who developed ventricular ectopy and systolic HF.

The present study demonstrated the sustained one year clinical benefit of an inter-atrial shunt device, developed to reduce LA pressure. At one year, in this highly symptomatic patient population, survival free from (HFH) requiring IV diuretics, with improved quality of live was 73%.

In conclusion, placement of the IASD in a cohort of HFpEF patients produced decrease of filling pressures and was associated with clinical improvement at one year in most patients. Current therapeutic options in HFpEF are ineffective, and the results of this study support further investigations to potentially improve symptoms and even outcome in this underserved population.

Conflict of interest

Dr. Vivek Reddy holds stock options in DC Devices, Inc., and is currently conducting research sponsored by this company. Dr. Antony Walton and Dr. Petr Neuzil have received research money in connection with the study. All other authors declare no potential conflict of interest.

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