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LETTERS

RESEARCH LETTER

Transcatheter Pulmonary Artery Banding for HFrEF

Initial Results: Exercise Hemodynamics From the Ongoing First-in-Human Trial

Ventricular interdependence is a physiological phenomenon due, in part, to the right ventricle (RV) and left ventricle (LV) sharing myocardial fibers, a common interventricular septum, and pericardium.[1] Under normal conditions, LV contraction assists RV contraction, whereas conversely, LV failure is often detrimental to the adjacent ventricle due to loss of LV contractility and reduced compliance, which increases pulmonary vascular resistance (PVR). The RV in patients with heart failure with reduced ejection fraction (HFrEF) is considered to be an innocent bystander that fails when increased PVR, secondary to reduced LV compliance, overwhelms RV contractility, and decoupling occurs.[2] The resistance-compliance relationship in pulmonary stenosis differs from postcapillary increased PVR in that the former is a brief, early systolic phenomenon with a normal distal pulmonary compliant vascular bed, whereas the latter is a systolic and diastolic disturbance with reduced pulmonary arterial compliance.

Therefore, RV hypertension may play a counterintuitive role when elective pulmonary artery banding (PAB) is performed in HFrEF patients with preserved RV contractility. The increased RV work generated by the proximal stenosis faces a normal or increased distal pulmonary compliance, and this energy may be transferred to the LV by mechanisms of ventricular interdependence. Initial studies of surgical PAB in infants with dilated cardiomyopathy have demonstrated significant improvements in LV function in selected patients, although this may be related to the underlying etiology and pediatric myocytic response.[3]

We hypothesized that an increase in RV pressure by purposeful PAB could assist LV systolic function through ventricular interdependence in HFrEF patients with preserved RV function, without causing RV failure. In addition, PAB could improve exercise capacity by reducing the mean wedge pressure by attenuating the pressure wave and increasing distal pulmonary compliance. A transcatheter reversible PAB device (Figure 1A) (Restore Medical) was designed to be delivered via an 18-F femoral venous sheath to each pulmonary artery with a preset constriction of 8 mm or 9 mm. This level of constriction was determined by bench testing on flow models to increase the RV pressure by 15 to 20 mm Hg at rest. Following preclinical testing, a first-in-human multicenter safety and feasibility trial (ContraBand™ Safety & Feasibility Study for Treatment of Heart Failure; NCT05230745) was approved by the ethical committees at 5 participating centers (ZNA/OCMW Antwerp, Belgium; Ethics Committee, Nemocnice Na Homolce, Prague, Czech Republic; Ethics Committee, Kaplan Medical Center, Petach Tikva, Israel; Lithuanian Bioethics Committee, Vilnius, Lithuania; and Local EC, Tbilisi Heart and Vascular Clinic, Tbilisi, Georgia). We report the preliminary results of this ongoing trial, including initial results of invasive hemodynamics during exercise.

The first-in-human trial included consecutive HFrEF patients (N = 23) with a resting mean pulmonary artery pressure <20 mm Hg and preserved RV function. Right heart catheterization with supine exercise at baseline and 6 months (Figure 1B) was introduced after the initial safety and feasibility of PAB was demonstrated. The patient cohort was of median age 63.3 years (Q1-Q3: 60.5-69.5 years), either NYHA functional class II (n = 7) or III (n = 16), and mostly of ischemic cardiomyopathy etiology (78%). The mean procedure time was 45 ± 19 minutes. Ultimately, 22 patients successfully received bilateral 8-mm (n = 12) or 9-mm (n = 10) PAB devices; immediately post-banding, the RV pressure increased from 32.7 ± 7.0 mm Hg to 48.2 ± 7.3 mm Hg. In 1 patient, the right pulmonary artery implant dislodged to the main pulmonary artery without complications. There were no other complications.

At a median follow-up of 16.6 months (1.8-27.1 months), all patients were alive without device-related hospitalizations or signs of RV failure. At 6-month evaluation (n = 21), in comparison to baseline, 6-minute walk time and Kansas City Cardiomyopathy Questionnaire Quality of Life increased (331 ± 113 m to 377 ± 115 m, and 51 ± 25.7 to 72 ± 20.3, respectively), and LV end-diastolic volume and LV

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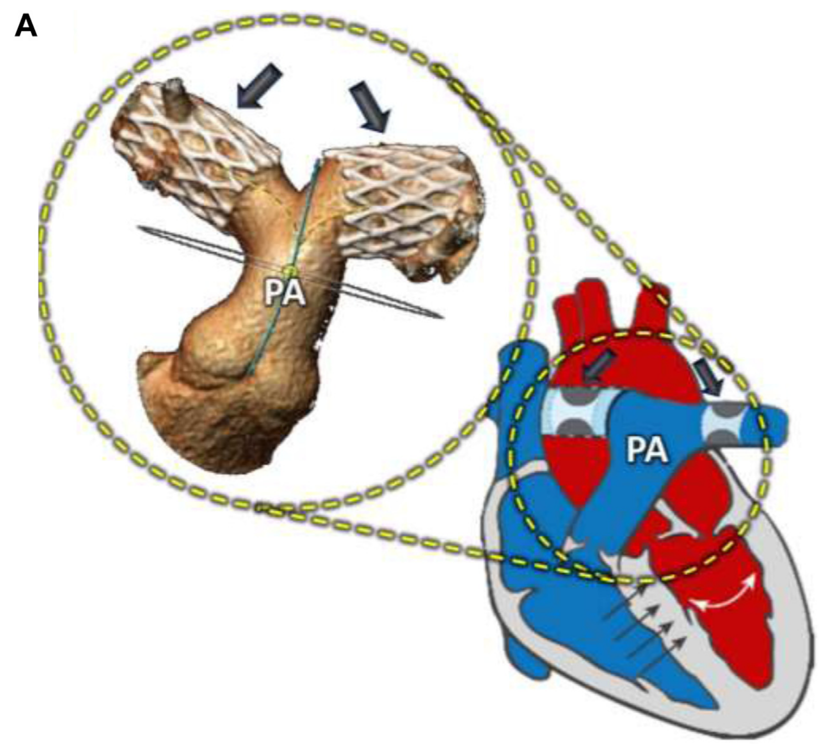
FIGURE 1 **Transcatheter PAB for HFrEF**



B	Baseline [n]		6-Months [n]		
	Rest [8]	20W [5]	Rest [8]	20W [6]	40W [4]
CO l/min	4.8±1.2	6.6±2.3	4.7±0.9	6.2±1.9	6.5±2.6
Wedge mmHg	12±4.3	31.2±8.6	11±3.5	18.7±5.8	23.5±5.4

(A) Shown in both the drawing and a computed tomography 3-dimensional reconstruction are the pulmonary artery (PA) banding (PAB) devices (arrows) placed in proximal regions of the right and left pulmonary arteries. (B) The table shows the baseline and 6-month results of invasive hemodynamics during exercise. CO = cardiac output; HFrEF = heart failure with reduced ejection fraction.

end-systolic volume decreased (223.6 ± 54.5 mL to 199.5 ± 60.1 mL, and 160.1 ± 42.6 mL to 143.1 ± 52.4 mL, respectively). LV ejection fraction was 29.0% ± 6.0% and 30.9% ± 7.8%. Cardiac output by thermodilution at 6 months (n = 12) was similar to baseline (4.6 ± 1.8 L/min vs 4.3 ± 0.8 L/min). Tricuspid annular plane systolic excursion and RV lateral longitudinal strain were unchanged (19.5 ± 3.3 mm to 18.7 ± 3.2 mm, and −22.8% ± 5.4% to −21.0% ± 7.3%, respectively).

Eight PAB patients (8-mm devices) exercised while invasive hemodynamics were monitored; 5 before and 6 after PAB, with 3 patients assessed both pre- and post-PAB. Cardiac output *increased* similarly pre- and post-banding, whereas the end-expiration mean wedge pressure was markedly lower at 20 W and plateaued with continued exercise up to 40 W (Figure 1B). Sample sizes are too small to assess significance at this stage.

In this multicenter first-in-human study, transcatheter PAB for HFrEF with preserved RV function proved to be safe at a median follow-up of 16 months and demonstrated improvements in functional parameters and LV volumes, while RV function remained preserved. Initial exercise data with a PAB showed a marked reduction in mean wedge pressure while demonstrating an *increase* in cardiac output. Therefore, the mechanism of action is not due to a direct limit on preload of the LV by flow restriction, but rather suggests that modulation of the pulmonary hemodynamics/compliance distal to the band and improved LV function due to the increase in RV afterload. Because this increase is at a fixed point in the branch pulmonary arteries and not throughout the pulmonary vascular bed, it should be likened to pulmonary stenosis and not pulmonary hypertension. The effect of PAB on the wedge pressure during exercise may also have potential in the treatment of both HFrEF and heart failure with preserved ejection fraction patients. Future randomized controlled studies are warranted to definitively assess the effect of this novel therapeutic strategy in patients with heart failure.

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Editor's Note: To view the authors' full presentation at TCTMD Shark Tank, please visit https://www.jacc.org/journal/basic-translational/tht-2024-shark-tank.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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