

CASE REPORT

INTERMEDIATE

CLINICAL CASE

Heterotopic Transcatheter Tricuspid Valve Replacement in a Patient With Carcinoid Heart Disease



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ABSTRACT

Neuroendocrine tumors can lead to carcinoid heart disease with subsequent development of severe tricuspid regurgitation due to thickening and restriction of the tricuspid leaflets. We present a patient who underwent successful heterotopic transcatheter tricuspid valve replacement for torrential tricuspid regurgitation due to carcinoid heart disease. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2022;4:101679) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

A 70-year-old female patient was referred to our clinic from an outside hospital with right-sided heart failure due to torrential tricuspid regurgitation (TR) for further diagnostics and treatment planning. The patient reported exertional dyspnea (New York Heart Association [NYHA] functional class IV), occasional thoracic discomfort, and a history of syncope. Physical examination revealed distinct peripheral edema, ascites, pleural

effusion, and jugular vein distension. Auscultation revealed a 2/6 systolic murmur in position of the tricuspid valve (TV) and attenuated breath sounds over the right lung. Laboratory testing showed elevated N-terminal pro-B-type natriuretic peptide levels, as well as cardiorenal¹ and cardiohepatic syndrome² (Table 1). Electrocardiography at admission revealed regular sinus rhythm with a known left bundle branch block. At the time of admission, the patient was being treated with the maximum tolerated dose of diuretic medication (60 mg/d torsemide and 10 mg/d xipamide).

LEARNING OBJECTIVES

- To understand the difficulties regarding the interventional treatment of tricuspid regurgitation with carcinoid heart disease.
- To keep heterotopic transcatheter tricuspid valve replacement in mind as a treatment option for patients with tricuspid regurgitation due to carcinoid heart syndrome.

MEDICAL HISTORY

The patient had recently undergone laparoscopic surgery for removal of an indeterminate ovarian tumor. Pathologic examination of the surgical specimen (15 × 10 × 6 cm) revealed the presence of a cystic ovarian teratoma with portions of a

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ABBREVIATIONS AND ACRONYMS

CT = computed tomography

MRI = magnetic resonance imaging

NYHA = New York Heart Association

TR = tricuspid regurgitation

TV = tricuspid valve

carcinoid tumor (positive staining for chromogranin and synaptophysin). After surgery, the patient was transferred to the external cardiology department owing to progressive right-side heart failure. Echocardiographic evaluation revealed the torrential TR. In the presence of a severe cardiorenal syndrome, the patient needed intermittent hemodialysis. Significant coronary artery disease was excluded by coronary angiography. Left ventricular systolic function was normal. Right heart catheterization showed no evidence of pulmonary hypertension (systolic pulmonary arterial pressure 25 mm Hg; inferior vena cava v-wave 17 mm Hg). Furthermore, the patient reported a history of paroxysmal atrial fibrillation and heparin-induced thrombocytopenia type II. Abdominal ultrasound showed signs of venous hepatic congestion with beginning cirrhosis.

INVESTIGATIONS

In our department, echocardiographic evaluation (transthoracic and transesophageal) revealed torrential TR with a false-low triangular continuous-wave Doppler signal. TR quantification by means of the proximal isovelocity surface area method was not applicable owing to atrioventricular pressure equalization³ (Figures 1 and 2). TR led to dilation of the inferior vena cava and flow reversal within the hepatic veins. All 3 TV leaflets were severely restricted, leading to a large coaptation gap (3-dimensional gap area 5.5 cm², 2-dimensional coaptation gap in the septolateral direction 3.2 cm) (Figure 1). Right ventricular (RV) function was preserved, while end-diastolic RV dimensions indicated

significant RV enlargement (RV ejection fraction 50.8%). RV to pulmonary artery coupling was preserved (0.84 mm/mm Hg). Echocardiographic imaging further showed a circular pericardial effusion (15 mm).

Positron emission tomography (Ga-68 DOTA-TOC) and abdominal magnetic resonance imaging (MRI) revealed no evidence of local tumor recurrence or lymphogenic or distant metastases. Cardiac MRI confirmed significant RV dilation and TR (regurgitant volume 84 mL (Figure 2). Furthermore, TR was accompanied by perihepatic and perisplenic ascites, as well as right-side pleural effusion (Figure 2). For further therapy planning, full-cycle computed tomography (CT) of the TV was performed.

MANAGEMENT

After discussion in the interdisciplinary heart team consisting of cardiac surgeons, interventional cardiologists, and heart failure specialists, the decision for an interventional TR treatment was made. TRI Score (8 points, 48% in-hospital mortality) and LaPar Score (12% mortality risk, 38% major morbidity risk) were indicative for advanced surgical risk.^{4,5} Owing to the large coaptation gap, severely restricted TV leaflets, and significant TV annular dilation, neither an “edge-to-edge” tricuspid valve repair nor an orthotopic TV replacement (as compassionate use) were suitable. After anatomy and hemodynamics were found to be suitable for a heterotopic TV replacement, treatment of TR was successfully performed using the TricValve (P&F) system (Central Illustration). As previously described, the implantation of 2 biological valves made of bovine pericardium placed inside self-expanding nitinol-covered stents in the superior and inferior vena cava was performed with the use of inguinal venous access under fluoroscopic and transthoracic echocardiographic guidance as previously described.^{6,7} Video 1 shows an RV angiogram after device placement. Chest X-ray and transthoracic echocardiography confirmed the regular valve positioning (Figure 3). Another 5 days later, the patient was discharged home.

DISCUSSION

Given the presence of torrential TR due to severely restricted TV leaflets combined with the history of a histologically proven neuroendocrine tumor, the most likely diagnosis in the present case was carcinoid heart disease. The latter is a rare condition with a prevalence of 1 to 2 per 100,000 people

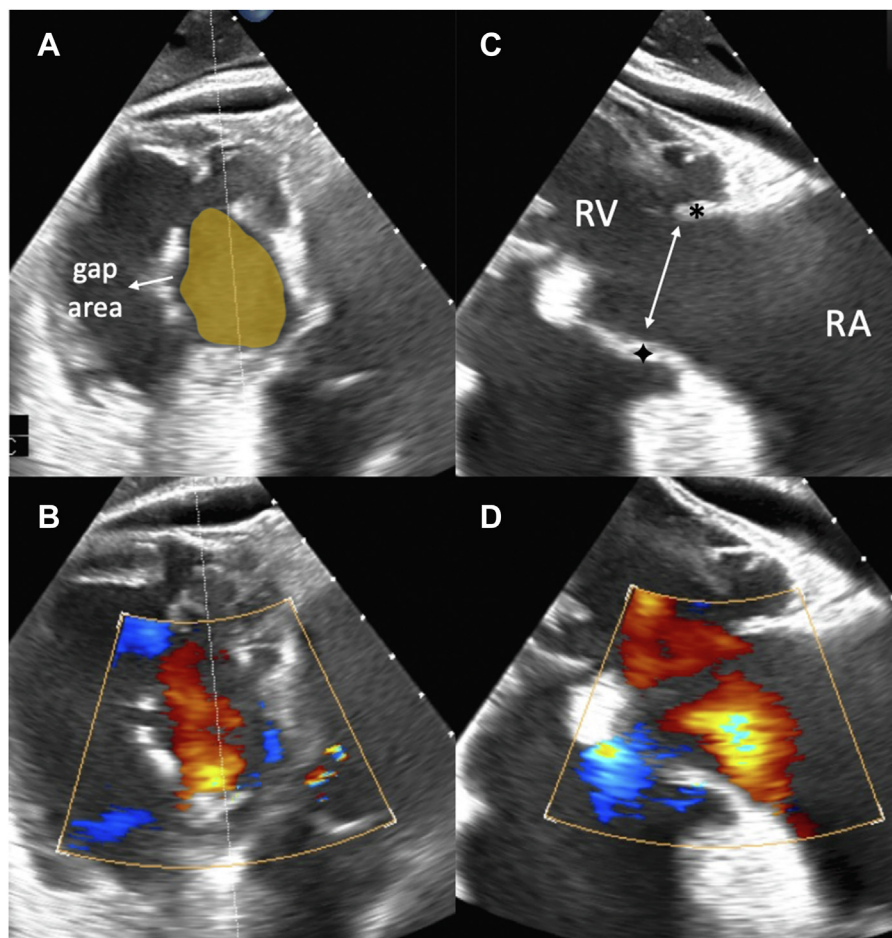
TABLE 1 Laboratory Evaluation

eGFR, mL/min (≥ 60 mL/min)	23
Creatinine, mg/dL (0.5–1.0 mg/dL)	2.1
Urea, mg/dL (17–49 mg/dL)	94
Bilirubin, mg/dL (≤ 1.2 mg/dL)	2.9
AST, U/L (≤ 34 U/L)	23
ALT, U/L (≤ 34 U/L)	16
GGT, U/L (≤ 39 U/L)	323
Alkaline phosphatase, U/L (35–105 U/L)	189
NT-proBNP, pg/mL (≤ 623 pg/mL)	905
Chromogranin A, ng/mL (≤ 94 ng/mL)	544
Serotonin, ng/mL (117–192 ng/mL)	71

Normal values for each parameter are indicated in parentheses.

ALT = alanine transaminase; AST = aspartate transaminase; GGT = gamma glutamyltransferase; eGFR = estimated glomerular filtration rate; N-terminal pro-B-type natriuretic peptide.

FIGURE 1 Transesophageal Echocardiography

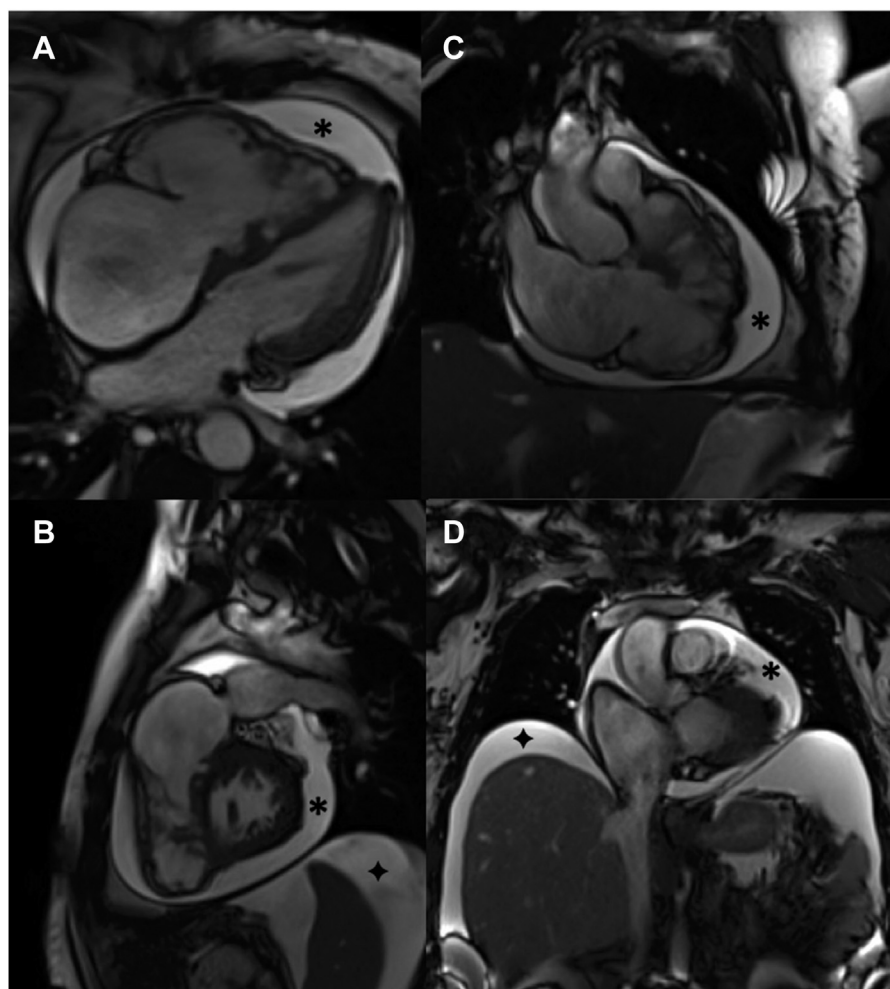


Transesophageal echocardiographic evaluation reveals a large coaptation gap during systole with subsequent torrential tricuspid regurgitation. **(A and B)** Transgastric view: severely restricted tricuspid valve leaflets with large coaptation gap. **(C and D)** Cross-sectional view derived from the transgastric angulation: severe restriction of the septal (*) and anterior (+) tricuspid valve leaflets leading to a large coaptation gap. RA = right atrium; RV = right ventricle.

per year⁸ being associated with neuroendocrine tumors. It is currently thought that serotonin and other neuroendocrine substances produced by the respective neoplasms lead to fibrosis, thickening, and immobilization of the TV leaflets, chordae tendineae, and papillary muscles.⁹⁻¹¹ Unlike in our case, further progression of the disease can also lead to the development of pulmonary stenosis.¹² Surgical removal of the ovarian tumor might have prevented such disease progression in our patient. Owing to inactivation of endocrine substances within the pulmonary microvasculature, carcinoid heart disease usually does not affect the mitral or

aortic valve.¹³ Of note, the gynecologic surgery was curative in our patient, with comprehensive oncologic work-up (MRI, positron emission tomography-CT) showing no evidence of either local tumor residues or metastases. This was of particular importance because the bicaval stents of the replacement system contain biological valves, which are known to degenerate quickly in the presence of an active neuroendocrine malignancy.¹⁴

Torrential TR as seen in the present case is associated with severe symptoms of right-side heart failure, secondary organ damage [eg, cardiohepatic and cardiorenal syndrome] impaired quality of life and

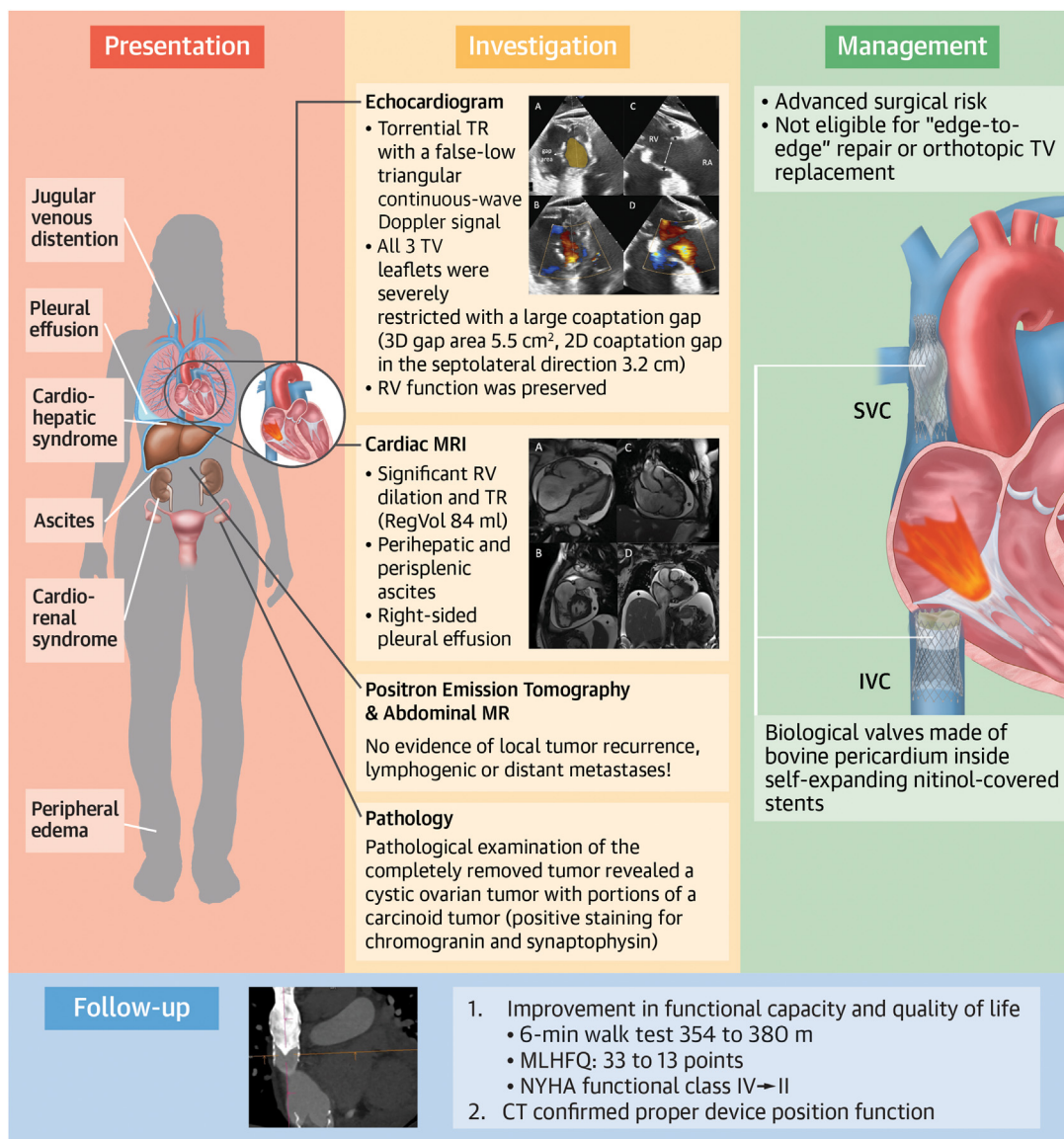
FIGURE 2 Magnetic Resonance Imaging

Cardiac magnetic resonance imaging of the heart in (A) 4-chamber, (B) 3-chamber, and (C) short-axis views. The patient presented with concomitant pericardial effusion (*) and ascites (+).

limited life expectancy. Surgical tricuspid valve replacement is known to be associated with high periprocedural mortality.¹⁵ Especially in old patients with advanced or prohibitive surgical risk, alternative interventional treatment options can be considered.¹⁶ Owing to the complicated anatomy with restricted, almost immobile, leaflets and severely dilated RV dimensions, transcatheter tricuspid valve edge-to-edge repair and orthotopic transcatheter TV replacement (TTVR) are often inapplicable in the context of carcinoid heart disease. By definition, heterotopic transcatheter TV replacement does not depend on the anatomy of the TV itself. The bicaval stents of the TV replacement system prevent backflow from the

volume-overloaded right atrium into the systemic circulation by implanting valve-containing stents into the superior and inferior venae cavae.⁶ Early outcome data after heterotopic TV replacement showed high rates of procedural success (up to 94%), low complication rates, and significant reduction of heart failure-related symptoms accompanied by significant quality of life improvement.^{7,17,18} In accordance with these results, our patient presented with a significant improvement of heart failure-related symptoms after 6 months (no edema, no pleural effusion, no ascites). Diuretic medication at follow-up comprised torsemide (20 mg/d) and spironolactone (25 mg/d). Similar to pre-existing literature, RV dimensions and

CENTRAL ILLUSTRATION Heterotopic TTVR in a Patient With TR and Carcinoid Heart Disease



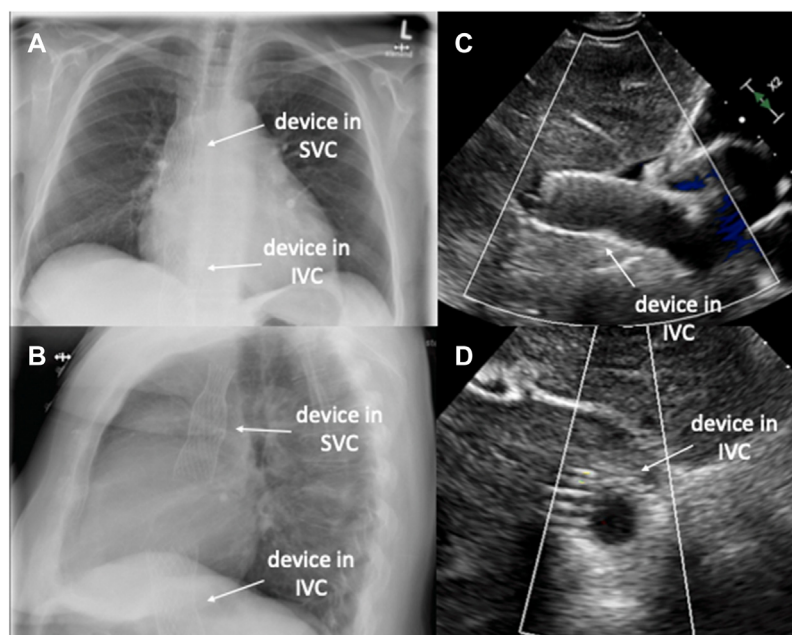
Stolz L, et al. J Am Coll Cardiol Case Rep. 2022;4(23):101679.

Presentation, investigation, management, and follow-up of a patient with carcinoid heart disease who received heterotopic transcatheter tricuspid valve replacement. CT = computed tomography; IVC = inferior vena cava; MLHFQ = Minnesota Living With Heart Failure Questionnaire; MR = magnetic resonance; MRI = magnetic resonance imaging; NYHA = New York Heart Association; SVC = superior vena cava; TR = tricuspid regurgitation; TTVR = transcatheter TV replacement; TV = tricuspid valve.

function remained unchanged during follow-up.⁶ To assess the durability of transcatheter heterotopic TV replacement in the setting of carcinoid heart disease, the patient will undergo regular follow-up visits including cardiologic and oncologic monitoring.

FOLLOW-UP

At 6-month follow-up, the patient presented in a significantly improved health status (NYHA II) without clinical evidence of peripheral edema or

FIGURE 3 Postinterventional Imaging

(A and B) Caval stents within the superior (SVC) and inferior (IVC) venae cavae in a chest X-ray. (C and D) View derived from transthoracic echocardiography, showing the device located in the IVC.

TABLE 2 Baseline and Follow-Up Imaging

	Baseline	Follow-Up
Echocardiography		
RV end-diastolic area, cm ² (8–20 cm ²)	15.0	16.9
RV end-systolic area, cm ² (3–11 cm ²)	30.3	30.8
RV fractional area change, % (≥35%)	50.0	45.1
RV ejection fraction (3D), % (≥45%)	50.8	47.2
RV free wall longitudinal strain, % (≤−20%)	−15.4	−19.2
TV annular diameter, mm (<40 mm)	46.4	48.5
TR max PG, mm Hg (≤30 mm Hg)	14.3	15.1
IVC diameter, mm (≤21 mm)	25.0	18.1
RA area, mm ² (≤18 mm ²)	25.8	32.5
TAPSE, mm (≥17mm)	21.0	23.2
LV ejection fraction, % (≥60%)	63.0	60.2
Magnet resonance imaging		
RV end-diastolic volume, mL (<176 mL)	263	^a
RV end-systolic volume, mL (<104 mL)	133	^a
RV ejection fraction, % (≥45%)	49	^a
RegVol, mL	84	^a
RV forward SV, mL (>50 mL)	46	^a
Computed tomography		
RV end-diastolic volume, mL (<177 mL)	256	252
RV end-systolic volume, mL (<78 mL)	128	122
RV ejection fraction, % (≥45%)	48	51

Normal values for each parameter are indicated in parentheses. ^aNo MRI at follow-up performed.

3D = 3-dimensional; IVC = inferior vena cava; LV = left ventricle; RegVol = regurgitant volume; PG = pressure gradient; RA = right atrial; RV = right ventricular; SV = stroke volume; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation; TV = tricuspid valve; VTI = velocity time integral.

ascites. She denied dizziness, syncope, thoracic discomfort, and nycturia. Both 6-minute walking test distance and quality of life according to the Minnesota Living With Heart Failure Questionnaire improved (6MWD: 354 to 380 m; MLHFQ: 33 to 13 points). Echocardiographic (Videos 2A and 2B) and CT follow-up examinations (Video 3) revealed no significant changes in RV function or dimensions (Table 2). Pericardial effusion was constant in size. Laboratory follow-up revealed no significant changes in renal or hepatic function.

CONCLUSIONS

TR in the context of carcinoid heart syndrome is often associated with challenging TV anatomy, which a few years ago would have lacked appropriate therapeutic options. As demonstrated in the present case, heterotopic tricuspid valve replacement is a reasonable interventional treatment

approach for these patients and may reduce heart failure symptoms.

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KEY WORDS carcinoid heart disease, right-side heart failure, tricuspid regurgitation, tricuspid valve replacement

APPENDIX For supplemental videos, please see the online version of this paper.