JACC: ADVANCES VOL. 2, NO. 9, 2023

EDITORIAL COMMENT

Tricuspid Regurgitation

A New Transcatheter Therapy on the Block!*

Poonam Velagapudi, MD, MS,[a] Rebecca T. Hahn, MD[b]

Secondary tricuspid regurgitation (STR) occurs in the setting of dilatation of the right atrium, tricuspid valve (TV) annulus, and/or right ventricle (RV) with intrinsically normal TV leaflets.[1] Two forms of STR are now recognized, atrial-STR characterized by absence of significant leaflet tethering, marked dilatation of the right atrium in the setting of relatively normal RV size and function, normal left ventricular (LV) function and absence of pulmonary hypertension, and ventricular-STR where leaflets appear tethered in the setting of RV dilation and/or dysfunction often in the presence of LV dysfunction, or pulmonary hypertension.[2] Although natural history studies confirm the association between mortality and increasing severity of tricuspid regurgitation (TR),[3] atrial-STR has been associated with lower mortality rates compared to ventricular-STR.[4]

Isolated TV surgery for TR is associated with high in-hospital mortality rates[5] resulting from delayed presentation or referral for intervention, low annual surgical site volumes, and the lack of Class I indications in current guidelines.[6] Transcatheter TV therapies have thus seen a rapid expansion with different mechanisms for reducing TR. Meta-analyses of early trials have suggested that all devices reduce TR and result in RV remodeling with improved forward stroke volume.[7] However, randomized trials are needed to show an improvement in mortality or heart failure hospitalizations compared to medical therapy. The multicenter TRILUMINATE (Trial to Evaluate Cardiovascular Outcomes in Patients Treated With the Tricuspid Valve Repair System Pivotal) randomized controlled trial compared 1-year outcomes of the Triclip (Abbott Structural Heart) transcatheter edge-to-edge device with medical therapy in patients with moderate to severe TR (93% FTR) at intermediate or greater risk for surgery.[8] Triclip reduced TR, had a high safety profile, and improved quality of life but failed to show a significant improvement in mortality or TV intervention, or heart failure hospitalizations. One potential reason is that patient selection resulted in a large number of atrial-STR patients which could affect the 1-year mortality. In addition, multiple studies have suggested that the tricuspid transcatheter edge to edge repair devices may be less effective in reducing TR in atrial-STR type morphologies.[9,10]

There is thus a clear need for a transcatheter annuloplasty device and yet the TriCinch system (4Tech Inc), and the Trialign system (Mitralign, Inc),[11] had significant anchoring issues and are no longer under investigation. The Cardioband device (Lifesciences) early feasibility study (NCT03382457) recently reported its 1-year results showing a progressive reduction in TR and improvement in Kansas City Cardiomyopathy Questionnaire-Overall Summary (KCCQ-OS) score over time, but minimal improvement in 6-minute walk distance.[12] The transcatheter K-clip system (Huihe Medical Technology) is a novel direct-annuloplasty device that uses a corkscrew anchor to position and secure it to the annulus, and gripping clip arms to plicate the tricuspid annulus, which may also help with anchoring. By plicating the posterior annulus, the device bicuspidizes the valve and narrows the septolateral annular dimension, thereby simulating the surgical Kay annuloplasty.[13]

In this issue of *JACC: Advances*, Xu et al[14] report the 30-day safety, performance, and efficacy

*Editorials published in *JACC: Advances* reflect the views of the authors and do not necessarily represent the views of *JACC: Advances* or the American College of Cardiology.

From the [a]Division of Cardiovascular Medicine, University of Nebraska Medical Center, Omaha, Nebraska, USA; and the [b]Columbia University Irving Medical Center, New York-Presbyterian Hospital, New York, New York, USA.

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.

ISSN 2772-963X https://doi.org/10.1016/j.jacadv.2023.100668

TABLE 1 Comparison of Transcatheter Tricuspid Valve Annular Devices

	Trialign 30 d (n = 15)[11]	Cardioband 30 d (n = 37)[12,16]	Cardioband 1 y (n = 37)[12]	K-Clip 30 d (n = 39)[14]
Age, y	73.6 ± 6.6	77.5 ± 7.5	77.5 ± 7.5	73.0 (IQR: 66-76)
Female	86.7%	75.7%	75.7%	68.2%
NYHA functional class III/IV baseline	66.7%	64.9%	64.9%	79.5%
NYHA functional class III/IV 30-day results	0%	25%	8%	5.1%
Baseline severe TR	(PISA EROA = 0.51 ± 0.18 cm^2)[a]	22.2%	22.2%	56.4%
Baseline > severe TR		77.7%	77.7%	43.6%
30 d TR ≤ moderate	(PISA EROA = 0.32 ± 0.18 cm^2)[a]	45.4%	73%	71.8%
TV annulus baseline	Area = 12.3 ± 3.1 cm^2	SL diam = 4.56 mm	SL diam = 4.56 mm	Area = 17.1 ± 4.8 cm^2
TV annulus 30-day results	Area = 11.3 ± 2.7 cm^2	SL diam = 38.8 mm	SL diam = 35.1 mm	Area = 12.5 ± 3.6 cm^2
KCCQ-OS baseline	(MLWHF 47.4 ± 17.6)	53 ± 25[b]	57.3 ± 24.3	64.9 ± 15.1
KCCQ-OS 30-day results	(MLWHF 20.9 ± 14.8)	69 ± 24[b]	76.4 ± 23.7	75.9 ± 11.8
6MWD baseline	245.2 ± 110.1 m	245.8 ± 125.3 m[a]	245.8 ± 125.3 m	284.6 ± 111.6 m
6MWD 30-day results	298.0 ± 107.6 m	247.0 ± 124.2 m[a]	(Δ7.2 ± 132.7 m)	362.7 ± 116.5 m

[a]The extended grading scheme was developed after publication of the SCOUT (Percutaneous Tricuspid Valve Annuloplasty System for Symptomatic Chronic Functional Tricuspid Regurgitation) trial. [b]From Hahn et al[11] with 30 patients.

6MWD = 6-minute walk distance; EROA = effective regurgitant orifice area; KCCQ-OS = Kansas City Cardiomyopathy Questionnaire Overall Score; MLWHF = Minnesota Living with Heart Failure Questionnaire; PISA = proximal isovelocity surface area; SL diam = septolateral diameter; TR = tricuspid regurgitation.

outcomes of 39 patients with ≥ grade 4 STR NYHA functional class ≥ II, intermediate or high surgical risk with a Tri-Score ≥4, and LV ejection fraction ≥40%. The patients underwent transthoracic echocardiography, transesophageal echocardiography with 3 dimensional, and cardiac tomography angiography, providing accurate measurements of the TV, RV, and right coronary artery (RCA). The procedure was meticulously performed with imaging guidance. The mean age of the study patients was 73 years, 69% were female, and 80% had NYHA functional class III/IV disease. All patients had 100% implantation/success rates, and 77% had ≥2 grade reduction in TR. Notably, there was a reduction in TV and RV measurements with significant improvement in NYHA class (95% NYHA class I/II), 6-minute walk distance, and KCCQ score at 30 days. The procedure was safe, with a 2.6% major adverse events rate at 30 days. There were no deaths.

In the current study, 75% of the screened patients met the study inclusion criteria and all had a successful procedure, suggesting that this therapy may be suitable for a large proportion of patients with TR. All echocardiograms were evaluated in an independent core laboratory and safety events were monitored by an independent clinical event committee, thus increasing the validity of these findings. In this context, the absence of any 30-day death or rehospitalization for heart failure and a reduction of at least 2 grades of TR in 77% of patients is remarkable in light of the results of prior annuloplasty studies (Table 1). A significant reduction in TV annular diameter, circumference, and area demonstrated device efficacy in annulus reconstruction, indicating the versatility of the device in tackling various anatomies. The main strength of the K-Clip is the possibility of reducing the TV annular dimensions without crossing the valve or remodeling the leaflets. Though there is a theoretical risk to the RCA due to its proximity to the TV annulus, the single anchor per device significantly limits this risk and indeed, there were no RCA-related complications or interventions required in the study.

This study has several limitations. The results of this study may not be applicable to the general population, given that the study was performed by operators at a single center in China. Transcatheter therapies for TR are complex procedures requiring comprehensive intraprocedural imaging and have a learning curve, and thus outcomes may not be similar if performed by less experienced operators. The TV has 2 posterior leaflets in more than a third of patients presenting for trials[15] and whether a simple posterior plication will obtain similar results in all morphologies requires further study. Although the short-term outcomes are promising, this trial lacks long-term follow-up to determine if TR reduction and clinical improvements are sustained at 1 year and beyond. Given that the study lacks a comparator arm, the outcomes of this therapy compared to surgery, medical therapy, or other transcatheter therapies are unknown.

In conclusion, a large armamentarium of transcatheter devices is likely needed to treat the broad spectrum of anatomic challenges associated with different etiologies of TR. The TV annuloplasty device should be one of those transcatheter options and the current study is encouraging, showing that a simple annular repair device can show similar short-term reductions in TR as transcatheter edge to edge repair repair devices, with improvements in symptoms, quality of life, and functional capacity. The K-clip system thus appears to be a promising transcatheter therapy in the treatment of TR that requires further evaluation in larger randomized controlled trials before widespread use.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr Velagapudi has received speaker fees from Abiomed, Medtronic, Opsens, and Shockwave; and fees for participating in advisory boards for Abiomed and Sanofi. Dr Hahn has received speaker fees from Abbott Structural, Baylis Medical, Edwards Lifesciences, Medtronic and Philips Healthcare, Siemens Healthineers; has institutional consulting contracts for which she receives no direct compensation with Abbott Structural, Edwards Lifesciences, Medtronic and Novartis; and is Chief Scientific Officer for the Echocardiography Core Laboratory at the Cardiovascular Research Foundation for multiple industry-sponsored tricuspid valve trials, for which she receives no direct industry compensation.

ADDRESS FOR CORRESPONDENCE: Dr Poonam Velagapudi. E-mail: Poonamchou@gmail.com.

REFERENCES

1. Hahn RT. Tricuspid regurgitation. *N Engl J Med*. 2023;388:1876-1891.

2. Hahn RT, Badano LP, Bartko PE, et al. Tricuspid regurgitation: recent advances in understanding pathophysiology, severity grading and outcome. *Eur Heart J Cardiovasc Imaging*. 2022;23(7):913-929.

3. Offen S, Playford D, Strange G, Stewart S, Celermajer DS. Adverse prognostic impact of even mild or moderate tricuspid regurgitation: insights from the National Echocardiography Database of Australia. *J Am Soc Echocardiogr*. 2022;35:810-817.

4. Gavazzoni M, Heilbron F, Badano LP, et al. The atrial secondary tricuspid regurgitation is associated to more favorable outcome than the ventricular phenotype. *Front Cardiovasc Med*. 2022;9:1022755.

5. Chen Q, Bowdish ME, Malas J, et al. Isolated tricuspid operations: the Society of Thoracic Surgeons Adult Cardiac Surgery Database Analysis. *Ann Thorac Surg*. 2023;115:1162-1170.

6. Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2021;77(4):e25-e197.

7. Sannino A, Ilardi F, Hahn RT, et al. Clinical and echocardiographic outcomes of transcatheter tricuspid valve interventions: a systematic review and meta-analysis. *Front Cardiovasc Med*. 2022;9:919395.

8. Sorajja P, Whisenant B, Hamid N, et al. Transcatheter repair for patients with tricuspid regurgitation. *N Engl J Med*. 2023;388:1833-1842.

9. Lurz P, Besler C, Schmitz T, et al. Short-term outcomes of tricuspid edge-to-edge repair in clinical practice. *J Am Coll Cardiol*. 2023;82(4):281-291.

10. Tanaka T, Sugiura A, Kavsur R, et al. Leaflet-to-annulus index and residual tricuspid regurgitation following tricuspid transcatheter edge-to-edge repair. *EuroIntervention*. 2022;18(2):e169-e178.

11. Hahn RT, Meduri CU, Davidson CJ, et al. Early feasibility study of a transcatheter tricuspid valve annuloplasty: SCOUT trial 30-day results. *J Am Coll Cardiol*. 2017;69:1795-1806.

12. Gray WA, Abramson SV, Lim S, et al. 1-Year outcomes of cardioband tricuspid valve reconstruction system early feasibility study. *J Am Coll Cardiol Intv*. 2022;15:1921-1932.

13. Kay JH, Maselli-Campagna G, Tsuji KK. Surgical treatment of tricuspid insufficiency. *Ann Surg*. 1965;162:53-58.

14. Xu H, Li W, Lee AP, et al. 30-day outcomes of transcatheter tricuspid annuloplasty with the K-clip system: a single-center, observational study. *JACC: Adv*. 2023;2:100671.

15. Hahn RT, Weckbach LT, Noack T, et al. Proposal for a Standard echocardiographic tricuspid valve nomenclature. *J Am Coll Cardiol Img*. 2021;14(7):1299-1305.

16. Davidson CJ, Lim DS, Smith RL, et al. Early feasibility study of cardioband tricuspid system for functional tricuspid regurgitation: 30-day outcomes. *J Am Coll Cardiol Intv*. 2021;14:41-50.

KEY WORDS transcatheter tricuspid valve repair, tricuspid regurgitation