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Editorial

The role of percutaneous tricuspid regurgitation interventions in the current clinical practice: tackling a heterogenous disease

El papel de las intervenciones percutáneas en la insuficiencia tricuspídea en la práctica actual: abordando una enfermedad heterogénea

Zach Rozenbaum,[a,b] Sharon Bruoha,[a] and Azeem Latib[a,c,*]

[a] *Division of Cardiology, Montefiore Medical Center, Albert Einstein School of Medicine, New York, NY, United States*
[b] *Sackler Faculty of Medicine, Tel-Aviv University, Israel*
[c] *Division of Cardiology, Department of Medicine, University of Cape Town, Cape Town, South Africa*

Severe tricuspid regurgitation (TR) is known to be independently associated with adverse prognosis.[1] Its importance is further emphasized by the prevalence of this entity, particularly in the aging population.[2] Until the past few years, surgical management was the only available effective treatment for isolated severe TR. Operative mortality, nonetheless, remains high.[3] Moreover, surgery is associated with a 45% recurrence rate after 5 years,[4] and recent data suggest that surgery may not improve the survival rate in isolated severe cases of TR.[5] Accordingly, guidelines recommend TR surgery as a class 1 indication only with concomitant left-sided valvular surgery.[6] Conversely, patients with prohibitive surgical risk managed conservatively were shown to have dismal outcomes.[7] Fortunately, the emergence of percutaneous devices expanded the horizon of TR treatment.

TACKLING THE MULTI-MECHANISTIC PATHOLOGY

TR is the product of various pathophysiological mechanisms including right ventricular (RV) dilatation with consequential leaflet tethering, tricuspid annular dilatation with subsequent mal-coaptation, atrial fibrillation causing further annular dilation through atrial enlargement, and abnormalities in the tricuspid valve leaflets and apparatus. At a certain point, regurgitation itself becomes an etiology through a vicious circle of RV and atrial remodeling. Accordingly, numerous percutaneous devices are being developed for transcatheter tricuspid valve repair (TTVr) and replacement (TTVR). They can be classified according to their mechanism—leaflet approximation, direct suture or ring annuloplasty and valve implantation that can be orthotopic—implantation in the anatomic tricuspid location or heterotopic implantation in the cavoatrial junction. The long-term stability of the orthotopic valve may be compromised due to the structural changes of the valvular apparatus over time that faces increased postoperative afterload. Some valves minimize this effect by not entirely relying on radial forces such as the Lux-Valve (Ningbo Jenscare Biotechnology, China) that attaches to the septum. Of note, a shortcoming of the Lux-valve is the thoracotomy requirement. An approach to relief RV pressure due to increased afterload is the Trisol valve (TriSol Medical, Israel) that induces leaflet coaptation by using a dome-shaped structure that enables larger RV closing volume. Additional orthotopic valves like the Intrepid (Medtronic, United States)—that received the Food and Drug Administration Breakthrough Device designation—and the Evoque (Edwards Lifesciences, United States) are showing encouraging results. Heterotopic valve implantation had been reported as double-valve implantation (inferior and superior vena cava), as well as single valve solely into the inferior vena cava. Nevertheless, the vena cavae can show substantial dynamic variations in size as well, particularly in self-expanding valves applying radial force on the compliant vessel, whereas right atrial enlargement can generate a funnel-shaped cavoatrial junction, thus increasing the risk of valve migration. Since the procedure results in the ventricularization of the right atrium, persistent overload can cause morphological changes and adversely impact the cardiac function.

Additional anatomical considerations play a role in device selection including the course of the right coronary artery, proximity to the atrioventricular node, and or/bundle of His (in this regard, the NaviGate valve—NaviGate Cardiac Structures, United States—has short graspers, and termed atrial winglets to prevent compression of the conduction system[8]), the dimensions of the inferior vena cava and its orientation relative to the right atrium (that can impact device stability and introduce difficulties achieving coaxiality), the size of the tricuspid annulus (large annuli may be modified as with the TriCinch—4Tech Cardio, Ireland—,[9] that mimics the Kay procedure), the distance between the tricuspid annulus and the RV apex, the size of the iliac vein (eg, the Cardiovalve—Cardiovalve, Israel—and the Evoque utilize a relatively low profile), the presence of an intracardiac shunt, short leaflet length (with an insufficient grasping area), thickened nonpliable leaflets, coaptation gap and depth (usually over ~7mm is a predictor of leaflet approximation failure), tethering severity, the tenting area and height, the location of the regurgitant jet, the number of leaflets (eg, 3 or 4), a proper annular shelf, and the juxtaposed noncoronary sinus relative to the device anchoring to the anterior and septal leaflet commissures (that may be compromised by the anchoring mechanism).

Multiple factors must, therefore, be taken into observed when considering a patient for TTVr/TTVR, and a thorough evaluation is warranted. In advanced stages of the disease manifesting as severe

* **Corresponding author.**
E-mail address: alatib@gmail.com (A. Latib).

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RV enlargement, considerable tethering or very large annuli, TTVr and TTVR may not be technically feasible. The anatomical characteristics can exceed the device capabilities, eg, the maximum length of Cardioband (Edwards Lifesciences, United States) tricuspid system is 120 mm. Even if the intervention is technically possible with advanced disease, irreversible damage to the RV structure and function may impede clinical improvement. Nevertheless, the point of no return is not clear, and patients with RV dysfunction and pulmonary hypertension have the potential to improve.[10]

Finally, the patient's characteristics must be reviewed as certain trials excluded patients with specific comorbidities like chronic kidney disease or systolic pulmonary artery pressure > 70 mmHg.

OUTCOMES OF PERCUTANEOUS TRICUSPID VALVE INTERVENTIONS

TriValve is the largest TTVr registry available predominantly describing edge-to-edge repair with MitraClip (Abbott Vascular, United States) in the tricuspid position. Use of MitraClip was described as bicuspidization of the tricuspid valve,[11] by approximating the posterior or anterior leaflet to the septal leaflet (while anterior to the posterior leaflet clipping may distort the valvular apparatus). Devices operating with similar mechanisms are the TriClip (Abbott Structural Heart, United States), and the PASCAL (Edwards Lifesciences, United States).

Table 1. Outcome data with transcatheter tricuspid valve devices

	Leaflet approximation devices					Annuloplasty devices				
Device (company) or procedure	MitraClip (Abbott Vascular, United States)[12]	TriClip (Abbott Structural Heart, United States)[13]	PASCAL (Edwards Lifesciences, United States)[14]	TriCinch (4Tech Cardio, Ireland)[9]	Mistral (Mitralix, Israel)[15]	FORMA (Edwards Lifesciences, United States)[16]	Millipede (Boston Scientific, United States)[17]	Cardioband (Edwards Lifesciences, United States)[18,19]	Trialign (Mitralign, United States)[20]	PASTA[21]
No.	249	85	34	1	7	29	2	30	15	1
TR grade improvement after 30 days			Yes		Yes	Yes	Yes	Yes	Yes	
Significant improvement in QoL measures after 30 days			Yes		Yes	Yes		No	Yes	
Mortality after 30 days			0%		0%	0%		6.7%	0%	
TR grade improvement after 6 months		Yes		Yes				Yes		
Significant improvement in QoL measures after 6 months		Yes		Yes				Yes		No
Mortality after 6 months		5%		0%				10%		0%
TR grade improvement after 1 year	Yes	Yes				Yes (N = 16)				
Significant improvement in QoL measures after 1 year	Yes	Yes				Yes (N = 16)				
Mortality after 1 year	20%	7.1%				0% (N = 16)				
TR grade improvement after 2 years								Yes		
Significant improvement in QoL measures after 2 years								Yes		
Mortality after 2 years								26.7%		

(Continues)

Table 1. Outcome data with transcatheter tricuspid valve devices *(Continued)*

	Orthotopic valve implantation						Heterotopic valve implantation		
Device (company)	NaviGate (NaviGate Cardiac Structures, United States)[22]	Trisol (TriSol Medical, Israel)[23,*]	Lux-Valve (Ningbo Jenscare Biotechnology, China)[24,25]	Evoque (Edwards Lifesciences, United States)[26]	Cardiovalve (Cardiovalve, Israel)[27]	Intrepid (Medtronic, United States), NCT04433065*	TricValve (P+F Products + Features, Austria)[28]	Sapien in ring (Edwards Lifesciences, United States)[28]	Tricento (New Valve Technology, Switzerland)[29]
No.	5		12	25	1		7	14	1
TR grade improvement after 30 days			Yes	Yes					
Significant improvement in QoL measures after 30 days			Yes	Yes					
Mortality after 30 days			8.3%	0%					
TR grade improvement after 6 months	Yes								
Significant improvement in QoL measures after 6 months	Yes								Yes
Mortality after 6 months	0%								0%
TR grade improvement after 1 year			Yes					No	
Significant improvement in QoL measures after 1 year			Yes					No	
Mortality after 1 year			16.6%					57%	
TR grade improvement after 2 years					Yes				
Significant improvement in QoL measures after 2 years					Yes				
Mortality after 2 years					0%				

* No clinical follow-up data available yet.
QoL, quality of life; TR, tricuspid regurgitation.

Patients from studies describing the various devices were heterogenous and vary significantly from one to the other. Also, the 30-day mortality rate ranges from 0% to 13% with significant improvement in TR grade, and in the quality of life according to published data (table 1). Notable longer-term outcomes include a 20% mortality rate at 1-year follow-up in the MitraClip cohort,[12] and a 26% mortality rate after 2 years in the Cardioband cohort.[18] Currently, prospective efficacy data mostly rely on quality-of-life scores and TR grade. However, it was shown that patients with procedural failure have a significantly higher mortality rate,[30] suggestive that patients would fare worse without the procedure. Moreover, a registry-based propensity-matched study that compared TTVr to conservative treatment showed symptomatic and survival benefits.[31] Currently, 3 TTVr devices have received the CE marking: Cardioband, TriClip, and PASCAL system for the management of TR, but none have been approved by the U.S. Food and Drug Administration. Consequently, most percutaneous tricuspid interventions are applicable in trial settings or as compassionate use.

In conclusion, TTVR/TTVr devices are becoming considerably more viable options. Surgical, and most certainly, conservative treatment of patients with severe TR are not ideal choices and expanding treatment possibilities towards percutaneous approaches is, therefore, an obvious choice. Results from ongoing trials have been anticipated, which will hopefully be followed by the approval of additional devices.

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A. Latib has served on advisory boards or as consultant for Medtronic, Boston Scientific, Edwards Lifesciences, Abbott, and VDYNE. The remaining authors have no relations to disclose.

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