Patient Selection and Periprocedural Imaging for Transcatheter Tricuspid Valve Interventions

A discussion of how and when various imaging modalities should be used during transcatheter tricuspid valve intervention and the anatomic and clinical characteristics that help guide patient selection.

BY KARL-PATRIK KRESOJA, MD, AND PHILIPP LURZ, MD, PHD

Severe tricuspid regurgitation (TR) affects approximately 4% of the population > 75 years, and the overall incidence is expected to increase with an aging population.[1] For a long time, severe TR was considered a mere surrogate for more advanced cardiovascular disease. However, recent research changed this paradigm by demonstrating the prognostic importance of severe TR.[2] Due to the high perioperative mortality risk, surgical tricuspid valve repair is often withheld in these patients. Minimally invasive, effective percutaneous treatment options have recently emerged with promising results, even suggesting a survival benefit compared to medical therapy alone.[3] The first-in-human successful annuloplasty using the Mitralign (Mitralign Inc.) system was reported in 2015,[4] and the first cases of successful transcatheter, edge-to-edge, tricuspid valve repair using the MitraClip (Abbott) system were reported in 2016.[5] Since then, the field of transcatheter tricuspid valve intervention (TTVI) has rapidly evolved. More than 1,000 interventions have been performed worldwide in the setting of compassionate off-label use or small proof-of-principal trials, and some dedicated devices have recently received CE Mark approval (TriClip, Abbott; Pascal, Edwards Lifesciences).[6]

The rapid development of new devices leaves interventional cardiologists with a lot of options but a scarcity of data on which devices are best suited for which patients. Currently, TTVI is based on one of three principles. The most frequently used approach is transcatheter, edge-to-edge repair to improve coaptation of the valve by either performing a bicuspidization or triple-orifice valve (coaptation enhancement).[3] The next principle is indirect annuloplasty, where the tricuspid annulus is narrowed. Lastly, orthotopic or heterotopic valve implantation has shown promising early results, but its expansion is currently stalled by difficulties in the anatomic features of the tricuspid valve.[7]

Patients currently referred for TTVI typically present at a later stage of disease, with refractory symptoms of right ventricular (RV) failure despite optimal medical treatment.[3,8,9] Before TTVI can be considered, patients should be on optimal medical therapy with the maximum tolerable diuretic dose and, in some cases, sequential nephron blockade. Each case should be discussed in a dedicated heart team; in patients at reasonable risk, a surgical approach might be favored even in the presence of isolated TR.[10] For a successful TTVI program, it is crucial to establish a team of experienced interventional cardiologists, interventional echocardiographers, cardiac surgeons, and radiologists for collaboration. Incorporating considerations of obtainable (intraprocedural) image quality and clinical and anatomic patient characteristics are of utmost importance to achieve an optimal result for each individual patient.[7] This article summarizes the latest learnings regarding patient selection and imaging requirements for different treatment approaches of TTVI.

TABLE 1. IMPORTANCE OF DIFFERENT IMAGING MODALITIES FOR PLANNING AND GUIDING TRANSCATHETER TRICUSPID VALVE INTERVENTION

	Echocardiography	Multislice CT	Fluoroscopy
Coaptation enhancement	+++	–	+
Annuloplasty	++	++	++
Orthotopic valve implantation	+++	+++	++
Heterotopic valve implantation	–	+++	+++

Adapted from Winkel MG, Brugger N, Khalique OK, et al. Imaging and patient selection for transcatheter tricuspid valve interventions. Front Cardiovasc Med. 2020;7:60. doi: 10.3389/fcvm.2020.00060

PREPROCEDURAL IMAGING MODALITIES

Comprehensive transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) evaluation of the tricuspid valve are essential to diagnosing the cause of TR, as well as for device selection. A good intraprocedural TEE image quality is mandatory in all TTVIs except for orthotopic valve implantation. Intraprocedural TEE allows for visualization of catheters and leads, identification of tricuspid valve target points, and immediate assessment of procedural success.[11] Therefore, poor intraprocedural TEE views, even in an anatomically suitable case, will usually restrict patients from TTVI. In addition, fluoroscopy facilitates steering and guidance throughout interventions. Multidetector CT can provide important insights into valve structure in patients with functional TR and is primarily necessary when patients are scheduled for transcatheter tricuspid valve implantation or annuloplasty.[12] The importance of different imaging modalities for planning and guiding currently available transcatheter procedures is shown in Table 1.

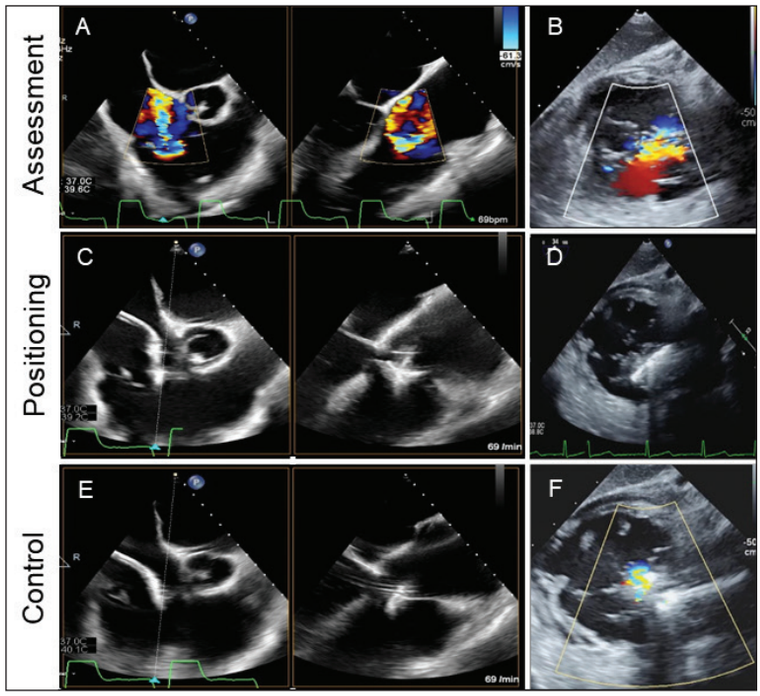

Figure 1. Intraprocedural imaging during edge-to-edge repair for TR. Using a bicommissural view with an orthogonal x-plane to visualize a modified "grasping view" (A) is necessary for edge-to-edge repair and might help in TR assessment. A transgastric view (B) is helpful to visualize the main regurgitation jet. Both the bicommissural x-plane view (C) and a transgastric view (D) can be used to guide clip positioning and leaflet grasping. Safe positioning of the deployed clip is visualized (E), and the remaining regurgitation is assessed by a transgastric view (F).

INTRAPROCEDURAL IMAGING MODALITIES

Intraprocedural imaging requirements vary depending on the TTVI approach. In edge-to-edge repair, intraprocedural TEE is crucial for visualizing the tricuspid valve leaflets and catheter positioning. The localization of the coaptation defect is best achieved by multiwindow imaging. Although three-dimensional echocardiography is useful to image and understand the tricuspid valve pathology, the limitations of spatial and, more importantly, temporal resolution need to be considered. The combination of a bicommissural view with the corresponding orthogonal x-plane view, resulting in a "grasping view" and a transgastric view, is best suited for deciding on procedural strategy but also to guide through tricuspid valve edge-to-edge repair (Figure 1A-1D). After clip deployment, adequate grasping of leaflet tissue (Figure 1E) and the extent of TR reduction (Figure 1F) should be confirmed again using a multiwindow approach.[13]

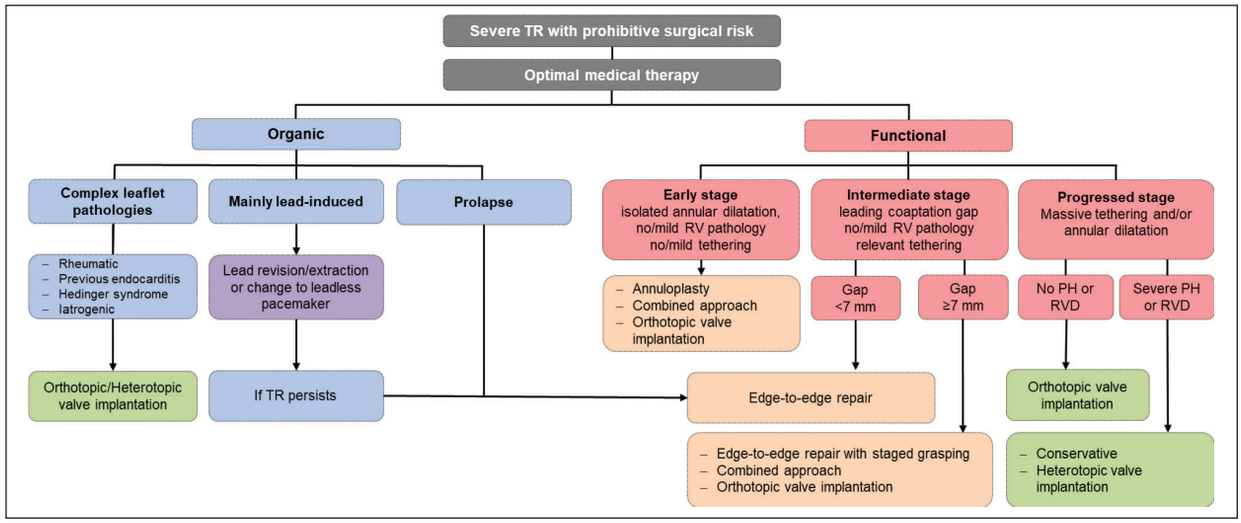

Figure 2. A proposed algorithm for treatment approach selection, considering anatomic and pathophysiologic aspects of TR. In this algorithm, PH refers to > 3 Woods units on right heart catheterization.

During annuloplasty, TEE is required to visualize the tricuspid annulus and myocardial structures based on the device used. If valve replacement is performed, positioning within the native tricuspid valve or a bioprosthetic valve can be facilitated by echocardiography and fluoroscopy.[13,14]

PATIENT SELECTION

Patient selection should involve consideration about significant comorbidities that limit life expectancy to < 1 year. End-stage liver disease, dialysis-dependent end-stage renal disease, severe lung disease, significant neurologic dysfunction, and progressive cardiac amyloidosis are comorbidities that might limit the benefits of TTVI.[15]

Because there are no head-to-head comparisons between TTVI treatment approaches, interventionalists must consider the anatomic and physiologic features of TR to find the optimal individual treatment approach. Figure 2 combines current evidence and opinions in a treatment algorithm that considers the anatomic and physiologic aspects of TR. A detailed anatomic assessment of the valve, the annulus and subvalvular apparatus, and left- and right-sided hemodynamics are crucial for further device selection.

Considerations in Patients With Primary TR

Complex and/or multiple leaflet pathologies usually are not accessible by coaptation enhancement or annuloplasty devices; therefore, ortho/heterotopic valve implantation might be considered in these patients. If TR is caused by interaction with an intracardiac lead and TR and RV dysfunction (RVD) progress, lead revision is a potential therapy to alleviate TR severity.[16] Furthermore, in some cases, lead extraction or replacement with a leadless pacemaker might also be considered as a possible treatment approach.

In cases where lead revision or extraction insufficiently alleviates TR, additional coaptation enhancement using the edge-to-edge technique has been observed as safe and was associated with TR reduction when there was an additional functional component to TR.[17,18] Coaptation enhancement for primary TR with leaflet prolapse or flail has been reported anecdotally but with promising results, and it might be considered if the prolapse is not too large and the prolapsing leaflet is graspable.[19,20]

Considerations in Patients With Functional TR

For functional TR, there is a growing body of evidence comprising prospective registries and smaller prospective studies. At earlier stages of isolated annular dilation without significant RV remodeling and leaflet tethering, an annuloplasty device might be preferred and also allow for future use of other treatment strategies. When annular dilatation is accompanied by a significant coaptation gap, coaptation enhancement might be preferred, especially if the TR jet location is in the anteroseptal or posteroseptal location and the coaptation gap is < 7 mm.[21] Larger gaps might be treatable with newer-generation devices and the ability to grasp leaflets. In clinical practice, it might be useful to intensify diuretic treatment for a short period of time prior to coaptation enhancement procedures in patients with a borderline-large coaptation gap to

TABLE 2. CURRENT EVIDENCE AND EXPERT OPINION OF FAVORABLE AND UNFAVORABLE CONDITIONS FOR PATIENTS UNDERGOING TRANSCATHETER TRICUSPID VALVE INTERVENTION

	Favorable Conditions	Unfavorable Conditions
Coaptation enhancement	▪ Degenerative TR with confined leaflet prolapse or flail ▪ Functional TR ▪ Small coaptation defect (< 7 mm) and good leaflet mobility[20,21] ▪ Antero- or posteroseptal TR jet location[21] ▪ RV lead without primary leaflet obstruction[18]	▪ Rheumatic leaflet thickening/shortening or very large leaflet prolapse ▪ Large coaptation defect (> 7 or > 10 mm*)[21] ▪ Anteroposterior jet location ▪ Poor echocardiographic visualization ▪ Primary RV lead-induced TR ▪ Disproportionate diagnosis of PH invasively and on echocardiography[8]
Annuloplasty	▪ Right atrial dilation as primary cause of TR ▪ Sufficient anatomic landing to deploy anchors with sufficient imaging views ▪ Favorable course of the RCA with relatively large distance to the tricuspid annulus	▪ Large coaptation defect (> 7 mm)† ▪ Primary RV lead-induced TR ▪ Proximal course of the RCA with risk of obstruction during annuloplasty ▪ PH (sPAP ≥ 60 mm Hg)‡
Orthotopic valve implantation	▪ Organic cause of TR with rheumatic leaflet thickening or shortening or very large leaflet prolapse ▪ Large coaptation gaps (> 7 mm) ▪ Previous surgical tricuspid valve repair or replacement ▪ Tricuspid annular dimensions suitable for valve replacement	▪ RVD (TAPSE < 16 mm or pulsed Doppler peak velocity at TDI S′ < 10 cm/s)[23‡] ▪ PH (sPAP ≥ 60 mm Hg)‡ ▪ Excessive tricuspid annular dilation (> 52 mm)[27] ▪ Risk of RCA obstruction ▪ Presence of an RV lead
Heterotopic valve implantation	▪ Organic cause of TR with rheumatic leaflet thickening or shortening or very large leaflet prolapse ▪ Large coaptation gaps (> 7 mm) ▪ Large annulus diameter (> 52 mm) ▪ PH or RVD prohibiting orthotopic valve replacement	▪ Risk of hepatic vein or azygos vein obstruction ▪ Very small distance from the cavoatrial junction and the first hepatic vein ▪ Very large vena cava diameter (> 42 mm)[28] ▪ Presence of an RV lead ▪ Contraindication for lifelong therapeutic anticoagulation

Abbreviations: PH, pulmonary hypertension; RCA, right coronary artery; RV, right ventricular; RVD, right ventricular dysfunction; sPAP, systolic pulmonary artery pressure; TAPSE, tricuspid annular plane systolic excursion; TDI, tissue Doppler image; TR, tricuspid regurgitation.

*A gap size of 7 to 10 mm might be treatable by coaptation enhancement devices when using a clip device with an additional spacer.

†Might be treatable when combining annuloplasty and coaptation enhancement.

‡Based on surgical experience of tricuspid valve repair/replacement.

temporarily reduce the gap for the intervention. In the setting of advanced RV failure with large coaptation gaps and massive annulus dilatation, tricuspid valve implantation in either the ortho- or heterotopic position might be the preferred treatment approach, especially in patients with previous surgical tricuspid valve replacement or repair. Heterotopic valve implantation might be used in cases of end-stage RV failure when a sudden increase in afterload caused by an orthotopic valve implantation might cause acute RV failure.[22,23]

Considerations in Patients With Pulmonary Hypertension

Based on surgical experience, there has been a long-standing dogma that functional TR should not be treated in patients with pulmonary hypertension (PH; systolic pulmonary artery pressure ≥ 60 mm Hg) or RVD.[10,20] However, both conditions often coexist with TR and tricuspid valve dysfunction because they cause RV pressure overload, dilation, and subsequent remodeling.[24] However, recent evidence challenged this paradigm

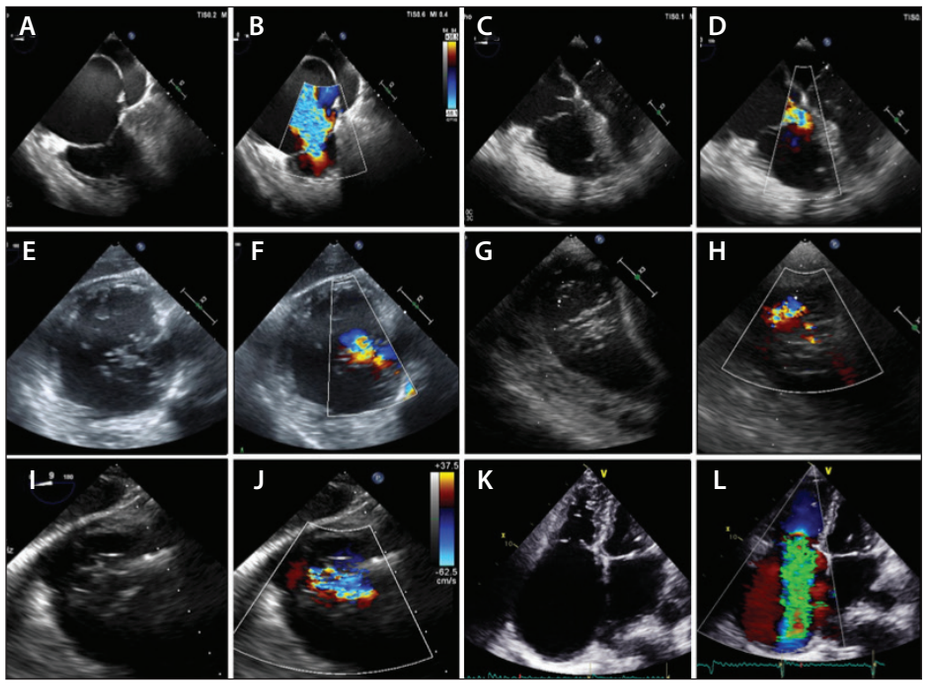

Figure 3. Functional TR due to right atrial dilatation (A, B) compared with primary TR due to leaflet prolapse (C, D). Examples of TR jet location on a transgastric view on TEE with a central to anteroseptal (E, F), posteroseptal (G, H), and anteroposterior (I, J) jet location. Example of a patient with functional torrential TR due to right atrial dilatation with a large coaptation gap of approximately 10 mm (K, L).

and suggested that patients with PH can have the same benefit as those with normal pulmonary pressures. The diagnosis of PH appears to render inferior prognosis only in the presence of a discordance between echocardiographically and invasively measured pulmonary pressure. Patients with invasive PH but no evidence of PH on TTE had the worst prognosis, indicating that TR severity might be the main driver of mortality in these patients because it alleviates the correlation of estimated and actual pulmonary pressure when measured by TTE.[8] Therefore, combining invasive and echocardiographic assessment of PH is essential for risk stratification and patient selection in TTVI.

Considerations in Patients With RVD

RVD has also been associated with poor perioperative surgical outcomes.[23,25] However, in a recent analysis of 249 patients who underwent edge-to-edge repair for severe TR between 2015 and 2018, no impact of RVD was found on traditional echocardiographic parameters (ie, tricuspid annular plane systolic excursion).[26] In contrast to the surgical experience, acute RV failure after edge-to-edge repair or indirect annuloplasty is extremely rare. Future studies on transcatheter tricuspid valve replacement will need to focus on the implications of sudden and complete TR abolishment on RV function and hemodynamics.

Conditions Favoring Specific TTVI Approaches

Table 2 summarizes the current evidence and expert opinions on when a specific TTVI approach is or is not preferred.[8,18,20,21,23,27,28] Furthermore, Figure 3 shows examples of primary and functional TR, different TR jet locations, and an example of a large coaptation gap in a patient with torrential TR. Because no randomized controlled trials are currently available to build recommendations for the use of TTVI, patient selection remains in the hands of experienced and dedicated heart teams on a case-by-case basis. The promising initial results observed with different interventional methods have generated a vast interest in the use of TTVI on a larger scale, and further research is needed to clarify the role of transcatheter interventions in the setting of severe TR.

CONCLUSION

With the field of TTVI rapidly evolving, the armamentarium and the number of possible indications for transcatheter treatment of the tricuspid valve are expanding. In absence of large randomized trials, a meticulous preprocedural workup, understanding of the tricuspid valve pathophysiology, and intraprocedural imaging are of utmost importance to achieve optimal results for the individual patient and establish a successful TTVI program. ■

1. Topilsky Y, Maltais S, Medina Inojosa J, et al. Burden of tricuspid regurgitation in patients diagnosed in the community setting. JACC Cardiovasc Imaging. 2019;12:433-442. doi: 10.1016/j.jcmg.2018.06.014
2. Enriquez-Sarano M, Messika-Zeitoun D, Topilsky Y, et al. Tricuspid regurgitation is a public health crisis. Prog Cardiovasc Dis. 2019;62:447-451. doi: 10.1016/j.pcad.2019.10.009
3. Taramasso M, Benfari G, van der Bijl P, et al. Transcatheter versus medical treatment of patients with symptomatic severe tricuspid regurgitation. J Am Coll Cardiol. 2019;74:2998-3008. doi: 10.1016/j.jacc.2019.09.028
4. Schofer J, Bijuklic K, Tiburtius C, et al. First-in-human transcatheter tricuspid valve repair in a patient with severely regurgitant tricuspid valve. J Am Coll Cardiol. 2015;65:1190-1195. doi: 10.1016/j.jacc.2015.01.025
5. Hammerstingl C, Schueler R, Malasa M, et al. Transcatheter treatment of severe tricuspid regurgitation with the MitraClip system. Eur Heart J. 2016;37:849-853. doi: 10.1093/eurheartj/ehv710
6. Nickenig G, Weber M, Lurz P, et al. Transcatheter edge-to-edge repair for reduction of tricuspid regurgitation:

6-month outcomes of the TRILUMINATE single-arm study. Lancet. 2019;394:2002-2011. doi: 10.1016/S0140-6736(19)32600-5
7. Asmarats L, Puri R, Latib A, et al. Transcatheter tricuspid valve interventions: landscape, challenges, and future directions. J Am Coll Cardiol. 2018;71:2935-2956. doi: 10.1016/j.jacc.2018.04.031
8. Lurz P, Orban M, Besler C, et al. Clinical characteristics, diagnosis, and risk stratification of pulmonary hypertension in severe tricuspid regurgitation and implications for transcatheter tricuspid valve repair. Eur Heart J. Published online March 16, 2020. doi: 10.1093/eurheartj/ehaa138
9. Orban M, Rommel K-P, Ho EC, et al. Transcatheter edge-to-edge tricuspid repair for severe tricuspid regurgitation reduces hospitalizations for heart failure. JACC Heart Fail. 2020;8:265-276. doi: 10.1016/j.jchf.2019.12.006
10. Baumgartner H, Falk V, Bax JJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 2017;38:2739-2791. doi: 10.1093/eurheartj/ehx391
11. Winkel MG, Brugger N, Khalique OK, et al. Imaging and patient selection for transcatheter tricuspid valve interventions. Front Cardiovasc Med. 2020;7:60. doi: 10.3389/fcvm.2020.00060
12. Ancona F, Agricola E, Stella S, et al. Interventional imaging of the tricuspid valve. Interv Cardiol Clin. 2018;7:13-29. doi: 10.1016/j.iccl.2017.08.010
13. Hahn RT, Nabauer M, Zuber M, et al. Intraprocedural imaging of transcatheter tricuspid valve interventions. JACC Cardiovasc Imaging. 2019;12:532-553. doi: 10.1016/j.jcmg.2018.07.034
14. Hahn RT. Imaging considerations for percutaneous tricuspid intervention. Cardiac Interv Today. 2017;11:40-42, 44-27.
15. Ho EC, Ong G, Fam NP. Transcatheter tricuspid valve intervention: a practical algorithm for patient selection. Curr Opin Cardiol. 2019;34:164-172. doi: 10.1097/HCO.0000000000000607
16. Addetia K, Harb SC, Hahn RT, et al. Cardiac implantable electronic device lead-induced tricuspid regurgitation. JACC Cardiovasc Imaging. 2019;12:622-636. doi: 10.1016/j.jcmg.2018.09.028
17. Taramasso M, Gavazzoni M, Pozzoli A, et al. Outcomes of TTVI in patients with pacemaker or defibrillator leads: data from the TriValve registry. JACC Cardiovasc Interv. 2020;13:554-564. doi: 10.1016/j.jcin.2019.10.058
18. Lurz J, Rommel K-P, Unterhuber M, et al. Safety and efficacy of transcatheter edge-to-edge repair of the tricuspid valve in patients with cardiac implantable electronic device leads. JACC Cardiovasc Interv. 2019;12:2114-2116. doi: 10.1016/j.jcin.2019.05.034
19. Braun D, Nabauer M, Massberg S, Hausleiter J. Transcatheter Repair of primary tricuspid valve regurgitation using the MitraClip system. JACC Cardiovasc Interv. 2016;9:e153-154. doi: 10.1016/j.jcin.2016.05.020
20. Hausleiter J, Braun D, Orban M, et al. Patient selection, echocardiographic screening and treatment strategies for interventional tricuspid repair using the edge-to-edge repair technique. EuroIntervention. 2018;14:645-653. doi: 10.4244/EIJ-D-17-01136
21. Besler C, Orban M, Rommel K-P, et al. Predictors of procedural and clinical outcomes in patients with symptomatic tricuspid regurgitation undergoing transcatheter edge-to-edge repair. JACC Cardiovasc Interv. 2018;11:1119-1128. doi: 10.1016/j.jcin.2018.05.002
22. Subbotina I, Girdauskas E, Bernhardt AM, et al. Comparison of outcomes of tricuspid valve surgery in patients with reduced and normal right ventricular function. Thorac Cardiovasc Surg. 2017;65:617-625. doi: 10.1055/s-0037-1604450
23. Di Mauro M, Foschi M, Tancredi F, et al. Additive and independent prognostic role of abnormal right ventricle and pulmonary hypertension in mitral-tricuspid surgery. Int J Cardiol. 2018;252:39-43. doi: 10.1016/j.ijcard.2017.11.031
24. Topilsky Y, Khanna A, Le Tourneau T, et al. Clinical context and mechanism of functional tricuspid regurgitation in patients with and without pulmonary hypertension. Circ Cardiovasc Imaging. 2012;5:314-323. doi: 10.1161/CIRCIMAGING.111.967919
25. Kim Y-J, Kwon D-A, Kim H-K, et al. Determinants of surgical outcome in patients with isolated tricuspid regurgitation. Circulation. 2009;120:1672-1678. doi: 10.1161/CIRCULATIONAHA.109.849448
26. Karam N, Mehr M, Taramasso M, et al. Value of echocardiographic right ventricular and pulmonary pressure assessment in predicting transcatheter tricuspid repair outcome. JACC Cardiovasc Interv. 2020;13:1251-1261. doi: 10.1016/j.jcin.2020.02.028
27. Asmarats L, Dagenais F, Bédard E, et al. Transcatheter tricuspid valve replacement for treating severe tricuspid regurgitation: initial experience with the NaviGate bioprosthesis. Can J Cardiol. 2018;34:1370.e5-1370.e7. doi: 10.1016/j.cjca.2018.07.481
28. Toggweiler S, Boeck B de, Brinkert M, et al. First-in-man implantation of the Tricento transcatheter heart valve for the treatment of severe tricuspid regurgitation. EuroIntervention. 2018;14:758-761. doi: 10.4244/EIJ-D-18-00440

Karl-Patrik Kresoja, MD
Department of Cardiology
Heart Center Leipzig at University Leipzig
Leipzig, Germany
Disclosures: None.

Philipp Lurz, MD, PhD
Department of Cardiology
Heart Center Leipzig at University Leipzig
Leipzig, Germany
philipp.lurz@gmx.de
Disclosures: Consultant to Abbott, Edwards Lifesciences, and Medtronic.