# Transcatheter tricuspid valve repair/replacement should be offered to all patients with severe tricuspid regurgitation: pros and cons

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# Pros: TTVI should be considered in all patients with severe TR

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Severe tricuspid regurgitation (TR) has been repeatedly shown to be associated with poor prognosis and increased mortality, yet it continues to be undertreated and managed conservatively<sup>1</sup>. Transcatheter repair and replacement technologies are emerging to address this large unmet clinical need and, in our opinion, should be offered to all patients with severe TR for the following reasons.

## **INEFFECTIVENESS OF MEDICAL THERAPY**

While diuretic therapy may improve symptoms and temporarily reduce the degree of TR, it has not been shown to have a demonstrable effect on the natural history of tricuspid valve disease or hard clinical outcomes. New heart failure drugs have been associated with a clear benefit in patients suffering from mitral regurgitation and left-sided heart failure but not for those who have severe TR and concomitant right-sided heart failure. As the

natural history of TR is ill-defined, the trend of treating patients with diuretics and only referring them for intervention when diuretics fail has resulted in many patients presenting for intervention with advanced disease and severe right ventricular dysfunction. By this point, these patients may not benefit from any intervention<sup>1</sup>.

# HIGH RISK OF ISOLATED TRICUSPID VALVE SURGERY

Surgical data continue to demonstrate a high risk of poor outcomes after isolated tricuspid valve (TV) intervention, which has probably been the strongest factor in the low number of patient referrals<sup>2</sup>. Transcatheter therapies are more attractive due to the lower rates of complications, morbidity and mortality.

#### IMPROVEMENT OF PROGNOSIS AND QUALITY OF LIFE

Patients treated with currently available transcatheter therapies for TR have better outcomes in terms of both quality of life and prognosis compared with those managed medically. This result is consistent across a broad range of patients, even those with modest reductions in TR<sup>3</sup>.

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#### **COMPLICATIONS**

Contemporary transcatheter tricuspid valve therapies have an overall low rate of complications and, so, can be safely proposed to patients with severe TR. Recent studies have demonstrated a good safety profile for both transcatheter repair and replacement techniques.

#### **CUSTOMISATION OF TRANSCATHETER THERAPY**

Patients with severe TR can have a broad spectrum of clinical and anatomical features. Notwithstanding that most of these therapies are still in the initial phase of development, we can foresee a future where the complementary safety and efficacy profile of these therapies can allow us to address different clinical stages of the disease and anatomical scenarios.

#### TRANSCATHETER TRICUSPID VALVE REPAIR

Transcatheter tricuspid valve repair is an extremely safe procedure and has been shown to improve symptoms, quality of life and right ventricular remodelling. The relatively straightforward screening process allows for wider patient candidacy with suitable anatomy. The amount of residual TR after valve repair is usually higher than that after replacement; nonetheless, this may be

helpful in reducing the risk of afterload mismatch in patients with concomitant advanced right ventricular dysfunction<sup>4</sup>.

#### TRANSCATHETER TRICUSPID VALVE REPLACEMENT

Transcatheter tricuspid valve replacement is a predictable and highly effective therapy that can address multiple different anatomies. The procedure is usually fast and reproducible with low residual TR. Initial clinical experiences with orthotopic valve replacement have shown excellent early outcomes and good valve haemodynamics; moreover, the compatibility of most transcatheter tricuspid valve replacement prostheses with a valve-in-valve procedure allows for lifetime management<sup>5</sup>. A heterotopic valve replacement may offer an important palliative option in patients with advanced disease.

## Conflict of interest statement

A. Latib is on the advisory board and/or has consulted for Edwards Lifesciences, V-dyne, Medtronic, Abbott, and Boston Scientific. A. Mangieri received speaking honoraria from Boston Scientific and Abbott Vascular; fees and speaking honoraria from Concept Medical; and an institutional grant from Boston Scientific.

# Cons: TTVI is not the first choice in all patients with severe TR

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Severe tricuspid regurgitation is a prevalent disease which leads to progressive right-sided heart failure and is associated with increased mortality. TR is rarely caused by structural valvular defects but is mostly driven by adverse right heart remodelling due to left heart disease, pulmonary hypertension (PH) and atrial fibrillation (AF). The prognostic impact of TR is largely underestimated in clinical practice, and isolated tricuspid valve (TV) surgery is often associated with poor outcomes. Consequently, patients with TR are undertreated and often referred too late to heart valve specialists. Transcatheter tricuspid valve intervention (TTVI) techniques have been proven to be safe, and prospective registries suggest its efficacy. However, not every patient with severe TR is suitable for interventional therapy, and randomised controlled trials evaluating this treatment are still ongoing.

# PATIENTS WITH SEVERE TR UNDERGOING LEFT-SIDED VALVE SURGERY/INTERVENTION

Whereas isolated TV surgery is associated with high mortality, in particular in secondary TR, concomitant TV repair during left-sided valve surgery appears effective and not associated with additive risk. Thus, TV surgery in patients with severe primary or secondary TR who are undergoing left-sided valve surgery stands out as a class I recommendation in current guidelines<sup>6</sup>. Also, accumulating evidence suggests that transcatheter therapies of left-sided valvular heart disease facilitate reverse remodelling of the right ventricle resulting in a substantial reduction of TR severity. For example,

TR improvement was recently reported in patients undergoing transcatheter mitral valve repair: TR reduction from severe to none/mild or moderate was reported in 38% and 12% of patients, respectively, after transcatheter mitral valve repair. In other words, careful observation of patients' past left-sided valvular interventions is of critical importance prior to reassessing TR in these patients.

## PATIENTS WITH SEVERE PULMONARY HYPERTENSION

PH on the basis of pulmonary arterial disease or left heart disease is a prevalent cause of secondary TR. On the one hand, severe PH negatively impacts outcomes after TTVI, particularly when echocardiography underestimates systolic pulmonary artery pressure. Conversely, PH regression following specific pharmacological interventions or pulmonary thrombendarteriectomy in chronic thromboembolic PH facilitates reverse right ventricular remodelling and contributes to a significant TR reduction. Consequently, patients with significant PH are not optimal candidates for TTVI and should be first offered specific PH therapy, including medical or surgical therapy for pulmonary arterial hypertension, and medical/interventional therapy for left heart disease.

# PATIENTS WITH ATRIAL FIBRILLATION

AF may give rise to TR, despite preserved left ventricular function and normal systolic pulmonary artery pressure, via right atrial enlargement and TV annular dilation (atrial TR). Rhythm control therapy may facilitate reverse right atrial remodelling and regression of atrial TR<sup>10</sup>. Hence, TTVI should be restricted to patients with atrial TR and failed rhythm control therapy and/or persistence of TR despite AF resolution.

In conclusion, TTVI is not the first choice in patients requiring left-sided heart surgery and may be deferred in patients with treatable causes of TR, such as left heart disease, pulmonary hypertension and AF. In every case, a thorough work-up of the patient, a critical evaluation of clinical trial participation and a close

follow-up by a team dedicated to the entire spectrum of tricuspid therapy are paramount.

# **Conflict of interest statement**

The authors have no conflicts of interest to declare.

## References

- 1. Prihadi EA, van der Bijl P, Gursoy E, Abou R, Mara Vollema E, Hahn RT, Stone GW, Leon MB, Ajmone Marsan N, Delgado V, Bax JJ. Development of significant tricuspid regurgitation over time and prognostic implications: new insights into natural history. *Eur Heart J.* 2018;39:3574-81.
- 2. Zack CJ, Fender EA, Chandrashekar P, Reddy YNV, Bennett CE, Stulak JM, Miller VM, Nishimura RA. National Trends and Outcomes in Isolated Tricuspid Valve Surgery. *J Am Coll Cardiol*. 2017;70:2953-60.
- 3. Taramasso M, Benfari G, van der Bijl P, Alessandrini H, Attinger-Toller A, Biasco L, Lurz P, Braun D, Brochet E, Connelly KA, de Bruijn S, Denti P, Deuschl F, Estevez-Loureiro R, Fam N, Frerker C, Gavazzoni M, Hausleiter J, Ho E, Juliard JM, Kaple R, Besler C, Kodali S, Kreidel F, Kuck KH, Latib A, Lauten A, Monivas V, Mehr M, Muntané-Carol G, Nazif T, Nickening G, Pedrazzini G, Philippon F, Pozzoli A, Praz F, Puri R, Rodés-Cabau J, Schäfer U, Schofer J, Sievert H, Tang GHL, Thiele H, Topilsky Y, Rommel KP, Delgado V, Vahanian A, Von Bardeleben RS, Webb JG, Weber M, Windecker S, Winkel M, Zuber M, Leon MB, Hahn RT, Bax JJ, Enriquez-Sarano M, Maisano F. Transcatheter Versus Medical Treatment of Patients With Symptomatic Severe Tricuspid Regurgitation. *J Am Coll Cardiol*. 2019;17; 74:2998-3008.
- 4. Montalto C, Sticchi A, Crimi G, Laricchia A, Khokhar A, Giannini F, Ferlini M, Colombo A, Latib A, Mangieri A. Functional and Echocardiographic Improvement After Transcatheter Repair for Tricuspid Regurgitation: A Systematic Review and Pooled Analysis. *JACC Cardiovasc Interv.* 2020;13:2719-29.
- 5. Fam NP, von Bardeleben RS, Hensey M, Kodali SK, Smith RL, Hausleiter J, Ong G, Boone R, Ruf T, George I, Szerlip M, Näbauer M, Ali FM, Moss R, Bapat V, Schnitzler K, Kreidel F, Ye J, Deva DP, Mack MJ, Grayburn PA, Peterson MD,

- Leon MB, Hahn RT, Webb JG. Transfemoral Transcatheter Tricuspid Valve Replacement With the EVOQUE System: A Multicenter, Observational, First-in-Human Experience. *JACC Cardiovasc Interv.* 2021;14:501-11.
- 6. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, Capodanno D, Conradi L, De Bonis M, De Paulis R, Delgado V, Freemantle N, Haugaa KH, Jeppsson A, Jüni P, Pierard L, Prendergast BD, Sádaba JR, Tribouilloy C, Wojakowski W. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *EuroIntervention*. 2022;17:e1126-96.
- 7. Kavsur R, Iliadis C, Spieker M, Brachtendorf BM, Tiyerili V, Metze C, Horn P, Baldus S, Kelm M, Nickenig G, Pfister R, Westenfeld R, Becher MU. Predictors and prognostic relevance of tricuspid alterations in patients undergoing transcatheter edge-to-edge mitral valve repair. *EuroIntervention*. 2021;17:827-34.
- 8. Lurz P, Orban M, Besler C, Braun D, Schlotter F, Noack T, Desch S, Karam N, Kresoja KP, Hagl C, Borger M, Nabauer M, Massberg S, Thiele H, Hausleiter J, Rommel KP. Clinical characteristics, diagnosis, and risk stratification of pulmonary hypertension in severe tricuspid regurgitation and implications for transcatheter tricuspid valve repair. *Eur Heart J.* 2020;41:2785-95.
- 9. Medvedofsky D, Aronson D, Gomberg-Maitland M, Thomeas V, Rich S, Spencer K, Mor-Avi V, Addetia K, Lang RM, Shiran A. Tricuspid regurgitation progression and regression in pulmonary arterial hypertension: implications for right ventricular and tricuspid valve apparatus geometry and patients outcome. *Eur Heart J Cardiovasc Imaging*. 2017;18:86-94.
- 10. Markman TM, Plappert T, De Feria Alsina A, Levin M, Amankwah N, Sheth S, Gertz ZM, Schaller RD, Marchlinski FE, Rame JE, Frankel DS. Improvement in tricuspid regurgitation following catheter ablation of atrial fibrillation. *J Cardiovasc Electrophysiol.* 2020;31:2883-8.