JACC: CARDIOVASCULAR IMAGING VOL. 19, NO. 7, 2026

PUBLISHED BY ELSEVIER

Letters

RESEARCH LETTER

Impact of Inflow Gradients on Mortality and Heart Failure Hospitalizations Following Transcatheter Tricuspid Valve Edge-to-Edge Repair

Insights from the PASTE Registry

Although transcatheter tricuspid valve edge-to-edge repair (T-TEER) effectively reduces tricuspid regurgitation (TR),[1,2] the prognostic impact of iatrogenic tricuspid valve (TV) stenosis remains debated. Previous studies suggested no association but were often underpowered without core laboratory supervision.[3,4] Furthermore, the discrepancy between intraprocedural (IP) gradients measured by transesophageal echocardiography (TEE) and discharge (DC) gradients measured by transthoracic echocardiography as well as changing right ventricular (RV) preload conditions complicate intraprocedural decision making. We leveraged the large, multicenter PASTE (PASCAL for Tricuspid Regurgitation) registry to assess the association among TV inflow gradients, procedural success, and 1-year clinical outcomes.

The PASTE registry is a core laboratory supervised, prospective, observational, multicenter study including 903 consecutive patients treated with the PASCAL system at 16 European centers. The local ethics committee at each participating center granted ethical approval. The primary endpoint was a composite of 1-year all-cause mortality or heart failure hospitalization (HFH). Procedural success was defined as residual TR ≤2+ at discharge.

Median age was 80.9 years (Q1-Q3: 77.0-84.0 years) and a high burden of comorbidities (TRI-SCORE [risk score for predicting in-hospital mortality in patients undergoing isolated TV surgery]: 22.0%). Baseline TV inflow gradients were low (median 1.2 mm Hg). T-TEER effectively reduced TR to ≤2+ in 85.2% of patients.

We observed a significant increase in gradients following repair. Median gradients increased significantly after repair (median increase: 0.65 mm Hg [Q1-Q3: 0.2-1.2 mm Hg] from IP TEE to DC transthoracic echocardiography; $P < 0.001$). Correlation between IP and DC gradients was moderate ($r = 0.446$), with Bland-Altman analysis revealing that IP TEE frequently underestimates the final gradient, particularly at higher values.

Using natural cubic splines in Cox regression modeling, we identified an association between DC gradients and the primary endpoint. Through multiple validation methods including clinical HR threshold analysis and CI-based criteria, a DC gradient of >4 mm Hg (HR: 1.74 mm Hg [95% CI: 1.34-2.26 mm Hg]) emerged as the optimal discriminatory threshold for adverse outcomes (**Figure 1**). Patients with DC gradients >4 mm Hg (n = 68) had significantly lower 1-year survival compared with those with gradients ≤4 mm Hg (62.2% vs 84%, respectively). In univariable analysis, a DC gradient >4 mm Hg was associated with a 2.5-fold increased risk of the primary composite endpoint (HR: 2.49 mm Hg [95% CI: 1.65-3.74 mm Hg]; $P < 0.001$).

Multivariable logistic regression identified smaller TV annulus diameter, larger vena contracta width, and higher baseline gradient as independent predictors of elevated DC gradients, whereas anatomical phenotype or number of devices did not differ between gradient groups.

Crucially, the impact of elevated gradients was strongly modified by the extent of TR reduction. Multivariable Cox regression confirmed that both residual TR >2+ (HR: 1.78 [95% CI: 1.22-2.60]; $P = 0.003$) and DC gradients >4 mm Hg (HR: 2.22 [95% CI: 1.4-3.6]; $P < 0.001$) were independent predictors of 1-year mortality or HFH.

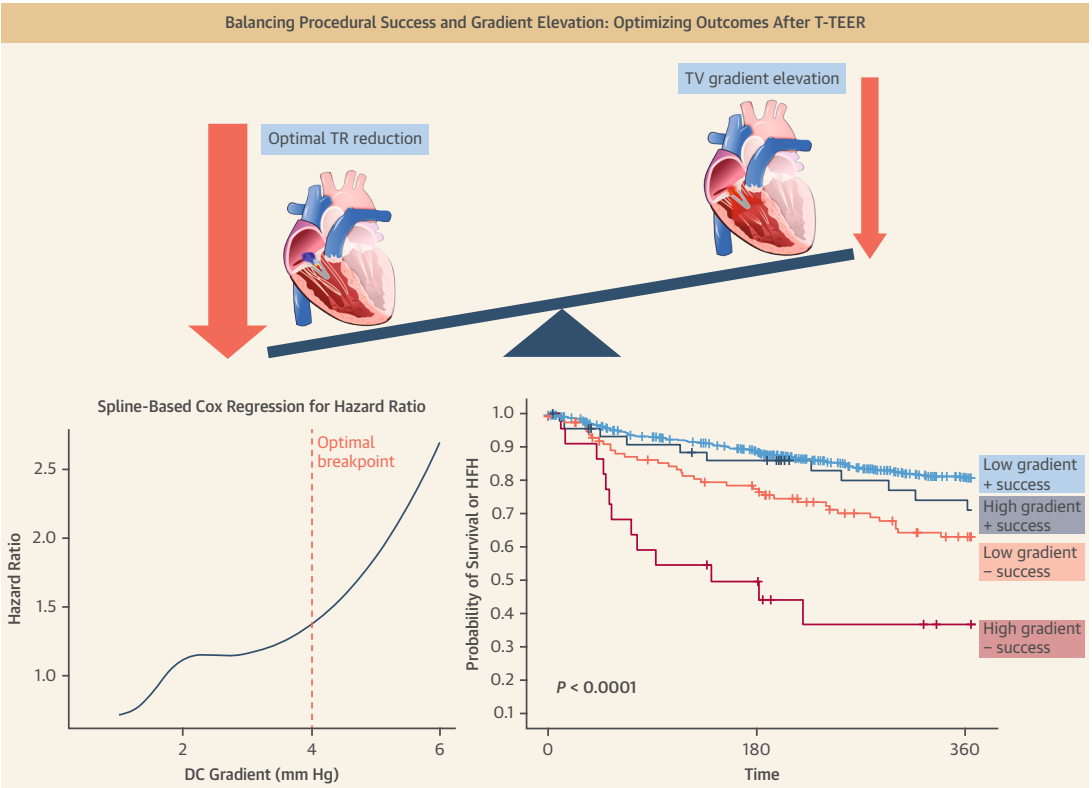
To understand the clinical trade-off, we stratified patients into 4 groups based on gradients (High: >4 mm Hg vs Low: ≤4 mm Hg) and residual TR (Success: ≤2+ vs Failure: ≥3+) (**Figure 1**).

- Best outcome: patients with low gradient + successful repair.
- Mitigated risk: patients with high gradient + successful repair did not show a statistically significant difference in outcomes compared with the reference group (HR: 1.50 [95% CI: 0.80-2.78]; $P = 0.200$).
- Worst outcome: patients with high gradient + unsuccessful repair had the highest event rates (HR: 5.50 [95% CI: 3.10-9.77]; $P < 0.001$).

Furthermore, symptomatic improvement (NYHA functional class) was observed in >60% of patients with successful TR reduction, whereas only 41% of

ISSN 1936-878X/$36.00 https://doi.org/10.1016/j.jcmg.2026.01.011

FIGURE 1 **Prognostic Impact of Discharge Gradients**



(Left) Spline-based Cox regression with optimal breakpoint calculation (red dashed line) for the primary endpoint across discharge mean gradients. (Right) Kaplan-Meier estimates stratified by discharge gradient (≤4 vs >4 mm Hg) and procedural success (TR ≤2+ vs ≥3+). DC = discharge; HFH = heart failure hospitalization; TR = tricuspid regurgitation; T-TEER = transcatheter tricuspid valve edge-to-edge repair; TV = tricuspid valve.

patients with elevated gradients and residual TR experienced symptomatic benefit.

These findings from the largest core laboratory-adjudicated cohort identify TV gradients after T-TEER with the PASCAL system as a relevant prognostic marker. We identified a discharge gradient >4 mm Hg as a critical threshold for increased mortality and HFH. This aligns with observations in mitral TEER, where gradients >4 or 5 mm Hg have been linked to adverse events.[5]

Our multivariable analysis provides mechanistic insight into gradient elevation indicating that gradient elevation results from anatomical constraints and baseline disease severity rather than device number or leaflet anatomy.

However, our data suggest that the goal of achieving TR ≤2+ should take precedence. Procedural success mitigated the risk associated with gradients >4 mm Hg, whereas residual TR exacerbated it. This implies that a modestly elevated gradient may be an acceptable trade-off if it facilitates significant TR reduction. Conversely, leaving the patient with significant residual TR and a high gradient leads to futile outcomes. Balancing this trade-off remains a complex challenge, particularly as gradients may impose additional stress to the right atrium (RA), leading to more congestion and lower RV remodeling capacity. Given the observed mean increase of ~0.7 mm Hg from IP to DC, an intraprocedural TEE mean gradient of ≤3 mm Hg appears to be a safe target to avoid discharge gradients >4 mm Hg.

In conclusion, these findings suggest that prioritizing TR reduction may be advisable, potentially

justifying the acceptance of modestly elevated gradients if necessary to achieve procedural success.

Our findings are derived exclusively from the PASCAL system, and extrapolation to other T-TEER devices requires caution. Importantly, the lack of invasive hemodynamic validation (eg, RA pressure or central venous pressure) and heart rate adjustment of gradients complicates the distinction between true iatrogenic stenosis and flow-dependent elevation related to loading conditions or altered RV-RA coupling. Finally, the small sample size in high-gradient subgroups limits statistical power, warranting caution regarding generalizability.

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No funding was received for this study. Among the full cohort of patients in the registry, data collection for the Hamburg patients was supported by a grant from the German Heart Foundation. Dr Stolz has received speaker honoraria from Edwards Lifesciences. Dr Hausleiter has received speaker honoraria from Edwards Lifesciences. Dr Rassaf has received research funding from the Deutsche Forschungsgemeinschaft and Abbott; and honoraria for lectures or advisory boards from AstraZeneca, Bayer, Berlin Chemie, Bristol Myers Squibb, Boehringer Ingelheim, Daiichi-Sankyo, Medtronic, Novartis, and Pfizer. Dr Luedike has received grants and speaker honoraria from Edwards Lifesciences. Dr Gerçek has received consulting fees from Edwards and funding from the Ruhr University Bochum (Advanced Clinician Scientist). Dr Kalbacher has received personal fees from Abbott Vascular, Edwards Lifesciences, Medtronic Inc, and Pi-Cardia Ltd. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.
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.

REFERENCES

1. Sorajja P, Whisenant B, Hamid N, et al. Transcatheter repair for patients with tricuspid regurgitation. *N Engl J Med*. 2023;388(20):1833–1842.

2. Stolz L, Kresoja KP, von Stein J, et al. Residual tricuspid regurgitation after tricuspid transcatheter edge-to-edge repair: insights into the EuroTR registry. *Eur J Heart Fail*. 2024;26(8):1850–1860.

3. Orban M, Orban MW, Braun D, et al. Clinical impact of elevated tricuspid valve inflow gradients after transcatheter edge-to-edge tricuspid valve repair. *EuroIntervention*. 2019;15(12):e1057–e1064.

4. Coisne A, Scotti A, Taramasso M, et al. Prognostic value of tricuspid valve gradient after transcatheter edge-to-edge repair: insights from the TriValve Registry. *JACC Cardiovasc Interv*. 2023;16(6):706–717. https://doi.org/10.1016/j.jcin.2023.01.375

5. Neuss M, Schau T, Isotani A, Pilz M, Schöpp M, Butter C. Elevated mitral valve pressure gradient after MitraClip implantation deteriorates long-term outcome in patients with severe mitral regurgitation and severe heart failure. *JACC Cardiovasc Interv*. 2017;10(9):931–939.