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ORIGINAL RESEARCH

STRUCTURAL

Impact of Pulmonary Hypertension on Outcomes After Transcatheter Tricuspid Valve Edge-to-Edge Repair

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ABSTRACT

BACKGROUND Data regarding the association of pulmonary hypertension (PH) and outcomes in patients undergoing transcatheter tricuspid valve edge-to-edge repair (T-TEER) are scarce.

OBJECTIVES The aims of this study were: 1) to investigate the impact of PH on outcomes after T-TEER; and 2) to shed further light on the role of precapillary- and postcapillary PH in patients undergoing T-TEER for relevant tricuspid regurgitation (TR).

METHODS The study included patients from EuroTR (European Registry of Transcatheter Repair for Tricuspid Regurgitation; NCT06307262) who underwent T-TEER for relevant TR from 2016 until 2023 with available invasive evaluation of systolic pulmonary artery pressure (sPAP) using right heart catheterization. Study endpoints were procedural TR reduction, improvement in NYHA function class, and a combined endpoint of death or heart failure hospitalization (HFH) at 2 years.

RESULTS Among a total of 1,230 patients (mean age 78.6 ± 7.0 years, 51.4% women), increasing sPAP was independently associated with increasing rates of 2-year death or HFH (HR: 1.027; 95% CI: 1.003-1.052; $P = 0.030$; median survival follow-up 343 days [Q1-Q3: 114-645 days]). No significant survival differences were observed for patients with pre- vs postcapillary PH. Sensitivity analysis revealed an sPAP value of 46 mm Hg as the optimized threshold for the prediction of death or HFH. Being observed in 526 patients (42.8%), elevated sPAP (>46 mm Hg) was associated with more severe heart failure symptoms at baseline and follow-up. Importantly, NYHA functional class significantly improved and TR severity was significantly reduced irrespective of PH.

CONCLUSIONS PH is an important outcome predictor in patients undergoing T-TEER for relevant TR. In contrast to previous studies, no significant differences were observed for patients with precapillary and postcapillary PH in terms of survival free from HFH. (JACC Cardiovasc Interv. 2025;18:325-336) © 2025 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

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ABBREVIATIONS AND ACRONYMS

dPAP = diastolic pulmonary artery pressure

HFH = heart failure hospitalization

mPAP = mean pulmonary artery pressure

PCWP = pulmonary capillary wedge pressure

PH = pulmonary hypertension

PVR = pulmonary vascular resistance

RHC = right heart catheterization

sPAP = systolic pulmonary artery pressure

TPG = transpulmonary gradient

TR = tricuspid regurgitation

T-TEER = tricuspid valve transcatheter edge-to-edge repair

Transcatheter tricuspid valve edge-to-edge repair (T-TEER) has emerged as a safe and effective treatment option for patients with tricuspid regurgitation (TR). The TRILUMINATE (Clinical Trial to Evaluate Cardiovascular Outcomes in Patients Treated With the Tricuspid Valve Repair System) trial demonstrated superiority of the T-TEER procedure beyond optimal medical therapy regarding a combined endpoint of death, heart failure hospitalization (HFH), need for tricuspid valve surgery, and Kansas City Cardiomyopathy Questionnaire score improvement.[1] The study was subject to several strict eligibility criteria[2] and excluded patients with significant pulmonary hypertension (PH; systolic pulmonary artery pressure [sPAP] ≥ 70 mm Hg) or a relevant precapillary component.[1] A previous analysis from the TriValve (Transcatheter Tricuspid Valve Therapies) registry did not observe significant outcome differences in interventionally treated patients with TR after stratification for pulmonary pressures.[3] Of note, the study assessed sPAP echocardiographically, which is known to underestimate real pressure conditions because of rapid systolic pressure equalization in the presence of severe TR.[4,5] Previous studies have shown that discordance of echocardiographically and invasively measured sPAP provides prognostic value beyond the degree of PH itself.[4] Beyond that, data regarding the dedicated impact of precapillary PH in T-TEER patients are currently limited to small patient numbers.[6] The aim of this subanalysis from EuroTR (European Registry of Transcatheter Repair for Tricuspid Regurgitation) was to shed further light on the complex interaction of PH and T-TEER treatment. The aims of the study were to: 1) investigate the association of PH with outcomes after T-TEER; and 2) shed further light on the role of pre- and postcapillary PH in patients undergoing T-TEER for relevant TR.

METHODS

STUDY POPULATION AND TREATMENT. This study included patients from the EuroTR registry (NCT06307262), which is a large, retrospective, international study among patients who underwent T-TEER from 2016 until 2023 with available invasive evaluation of sPAP using right heart catheterization (RHC). Patients with concomitant mitral valve edge-to-edge repair were excluded from the analysis. Baseline differences for included and excluded patients are outlined in Supplemental Table 1. All patients remained symptomatic despite up-titration of maximum tolerated diuretic medication doses. After discussion by an interdisciplinary heart team, the decision in favor of an interventional treatment approach was made according to each center's standard of care practice. T-TEER was performed as previously described using either the PASCAL device (Edwards Lifesciences) or the MitraClip or TriClip

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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.

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TABLE 1 Study Baseline Characteristics

	All Patients (N = 1,230)	sPAP ≤46 mm Hg (n = 704)	sPAP >46 mm Hg (n = 526)	*P* Value
Clinical data				
Female (n = 1,230)	632 (51.4)	385 (54.7)	279 (53.0)	**0.007**
Age, y (n = 1,230)	78.6 ± 7.0	78.8 ± 7.0	78.2 ± 8.2	0.430
BMI, kg/m^2 (n = 1,208)	26.3 ± 5.0	25.6 ± 4.5	27.2 ± 5.5	**<0.001**
EuroSCORE II, % (n = 1,150)	4.8 (2.6-7.7)	4.2 (2.3-7.4)	5.2 (3.1-8.5)	**<0.001**
TRI-SCORE, points (n = 410)	7 (5-8)	7 (5-8)	7 (6-9)	**0.037**
TRI-SCORE, % (n = 410)	34.0 (14.0-48.0)	34.0 (14.0-48.0)	34.0 (22.0-65.0)	**0.043**
AHT (n = 1,164)	990 (85.1)	549 (82.8)	441 (88.0)	**0.013**
Dyslipidemia (n = 1,159)	566 (48.8)	315 (47.8)	251 (50.0)	0.418
Peripheral edema (n = 1,125)	786 (64.2)	422 (60.2)	364 (69.5)	**<0.001**
Ascites (n = 1,224)	172 (14.1)	86 (12.3)	86 (16.4)	**0.040**
Jugular vein distension (n = 613)	88 (14.4)	66 (20.0)	22 (7.8)	**<0.001**
Prior MI (n = 1,230)	141 (11.5)	78 (11.1)	63 (12.0)	0.625
COPD (n = 1,230)	230 (18.7)	113 (16.1)	117 (22.2)	**0.006**
DM (n = 1,163)	304 (26.1)	132 (19.9)	172 (34.3)	**<0.001**
Prior stroke (n = 881)	105 (11.9)	64 (12.9)	41 (10.7)	0.318
TV lead (n = 1,230)	364 (29.6)	194 (27.6)	170 (32.3)	0.070
AF/atrial flutter (n = 1,123)	1,123 (91.3)	645 (91.6)	478 (90.9)	0.647
CAD (545)	545 (44.3)	294 (41.8)	251 (47.7)	**0.038**
eGFR, mL/min (n = 948)	48.5 ± 23.1	51.4 ± 23.7	44.8 ± 21.8	**<0.001**
NT-proBNP, pg/mL (n = 1,184)	4,672 ± 8,046	3,857 ± 6,181	5,786 ± 9,952	**<0.001**
MRA (n = 1,229)	522 (42.5)	288 (41.0)	234 (44.5)	0.217
Loop diuretic agent (n = 1,225)	1,138 (92.9)	648 (92.7)	490 (93.1)	0.809
Thiazide diuretic agent (n = 944)	209 (22.1)	108 (20.1)	101 (24.8)	0.092
Beta-blocker (n = 1,228)	1,038 (84.5)	597 (85.0)	441 (83.8)	0.564
RASI (n = 944)	564 (59.7)	320 (59.8)	244 (59.7)	0.962
Hemodynamic data				
sPAP, mm Hg (n = 1,230)	45.9 ± 14.6	35.9 ± 6.8	59.4 ± 11.0	**<0.001**
dPAP, mm Hg (n = 1,109)	18.7 ± 7.9	14.9 ± 5.6	23.6 ± 7.6	**<0.001**
mPAP, mm Hg (n = 1,204)	29.3 ± 9.4	23.5 ± 5.6	37.1 ± 7.6	**<0.001**
PCWP, mm Hg (n = 869)	18.9 ± 7.2	15.5 ± 5.4	23.5 ± 6.6	**<0.001**
TPG, mm Hg (n = 847)	10.9 ± 5.9	8.5 ± 4.0	13.9 ± 6.4	**<0.001**
CO, mL/min (n = 590)	4.2 ± 1.5	3.9 ± 1.2	4.6 ± 1.7	**<0.001**
PVR, WU (n = 547)	2.9 ± 1.7	2.4 ± 1.3	3.5 ± 2.0	**<0.001**

Continued on the next page

system (Abbott Vascular). RHC was performed prior to T-TEER after optimized medical recompensation in a euvolemic stable situation as judged by each center.

STUDY VARIABLES AND ENDPOINTS. RHC-derived hemodynamic parameters included pulmonary artery pressures (sPAP, diastolic pulmonary artery pressure [dPAP], and mean pulmonary artery pressure [mPAP]), mean pulmonary capillary wedge pressure (PCWP), pulmonary vascular resistance (PVR) and cardiac output. The transpulmonary gradient (TPG) was calculated as the difference between mPAP and mean PCWP. Echocardiographic evaluation was performed in line with current guidelines and as previously described for the EuroTR registry.[7,8] Echocardiographic sPAP was calculated by adding estimated right atrial pressure derived from width and respiratory variability of the inferior vena cava to the maximum systolic right atrial-right ventricular pressure gradient. TR severity was assessed using a 5-grade scale[9]: mild, moderate, severe, massive, and torrential. According to current guideline recommendations, PH was defined as mPAP >20 mm Hg. Subtypes of PH were distinguished as follows: precapillary PH (PVR >2 WU), postcapillary PH (PCWP ≥15 mm Hg), and mixed pre- and postcapillary PH (PVR >2 WU and PCWP ≥15 mm Hg).[10] On the basis of a previous study of PH in the context of T-TEER, patients were additionally classified into the following categories: no significant PH (mPAP ≤30 mm Hg), significant postcapillary PH (mPAP >30 mm Hg and TPG ≤17 mm Hg), and significant precapillary PH (mPAP >30 mm Hg and TPG >17 mm Hg).[6]

Study endpoints were procedural TR reduction, improvement in NYHA functional class, and a

TABLE 1 Continued

	All Patients (N = 1,230)	sPAP ≤46 mm Hg (n = 704)	sPAP >46 mm Hg (n = 526)	*P* Value
Echocardiographic data				
LVEF, % (n = 1,200)	52.6 ± 11.4	53.0 ± 10.8	52.2 ± 12.1	0.343
LVEDD, mm (n = 1,121)	48.9 ± 8.6	47.9 ± 8.4	50.2 ± 8.6	**<0.001**
TR EROA, cm^2 (n = 1,122)	0.70 ± 0.60	0.78 ± 0.72	0.60 ± 0.37	**<0.001**
TR RegVol, mL (n = 1,047)	53.8 ± 30.8	54.1 ± 34.6	53.5 ± 25.0	0.178
TR VC, mm (n = 1,145)	11.4 ± 5.8	11.6 ± 4.6	11.1 ± 7.0	**0.010**
RV FAC, % (n = 1,013)	42.5 ± 72.7	40.5 ± 11.3	37.6 ± 11.2	**<0.001**
RV EDA, cm^2 (n = 724)	27.0 ± 9.9	26.5 ± 9.6	27.7 ± 10.1	0.085
RV ESA, cm^2 (n = 695)	17.1 ± 7.1	16.4 ± 6.7	18.0 ± 7.4	**0.002**
RVmid, mm (n = 1,018)	40.9 ± 9.0	40.2 ± 9.2	41.7 ± 8.7	**0.001**
RVbase, mm (n = 795)	49.0 ± 9.2	48.5 ± 9.6	50.0 ± 8.9	0.126
RV length, mm (n = 737)	70.3 ± 12.7	69.1 ± 12.4	71.9 ± 13.0	**0.003**
TV annular diameter, mm (n = 1,109)	44.1 ± 8.4	43.5 ± 8.0	44.8 ± 8.7	**0.016**
RAA, cm^2 (n = 1,044)	36.6 ± 13.3	36.9 ± 14.6	36.2 ± 11.2	0.704
TAPSE, mm (n = 1,185)	17.2 ± 4.6	17.4 ± 4.6	16.9 ± 4.6	**0.027**
$sPAP_{echo}$, mm Hg (n = 1,097)	43.0 ± 15.1	37.2 ± 11.1	50.4 ± 16.3	**<0.001**
Coaptation gap, mm (n = 744)	6.2 ± 2.9	6.4 ± 3.0	5.8 ± 2.8	**0.008**
Tenting height, mm (n = 709)	7.7 ± 3.3	7.9 ± 3.4	7.5 ± 3.1	0.286
Tenting area, cm^2 (n = 670)	1.91 ± 1.12	1.95 ± 1.11	1.87 ± 1.12	0.275
TR etiology (n = 1,209)				0.558
Primary	63 (5.2)	41 (5.9)	22 (4.3)	
Secondary	1,040 (86.4)	591 (85.5)	449 (87.5)	
Mixed	101 (8.4)	59 (8.5)	42 (8.2)	
MR severity (n = 1,209)				**0.042**
0+	94 (7.8)	62 (9.0)	32 (6.2)	
1+	816 (67.5)	467 (67.6)	349 (67.2)	
2+	277 (22.9)	155 (22.5)	122 (23.5)	
3+	21 (1.7)	6 (0.9)	15 (2.9)	
4+	1 (0.1)	0 (0.0)	1 (0.4)	

Values are n (%), mean ± SD, or median (Q1-Q3). *P* values in **bold** denote statistical significance.

AF = atrial fibrillation; AHT = arterial hypertension; BMI = body mass index; CAD = coronary artery disease; CO = cardiac output; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; dPAP = diastolic pulmonary artery pressure; EDA = end-diastolic area; eGFR = estimated glomerular filtration rate; EROA = effective regurgitant orifice area; ESA = end-systolic area; EuroSCORE = European System for Cardiac Operative Risk Evaluation; FAC = fractional area change; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; MI = myocardial infarction; mPAP = mean pulmonary artery pressure; MR = mitral regurgitation; MRA = mineralocorticoid receptor antagonist; NT-proBNP = N-terminal prohormone of brain natriuretic peptide; PCWP = pulmonary capillary wedge pressure; PVR = pulmonary vascular resistance; RAA = right atrial area; RASI = renin-angiotensin-aldosterone system inhibitor; RegVol = regurgitant volume; RV = right ventricular; RVbase = right ventricular basal diameter; RVmid = right ventricular midventricular diameter; sPAP = systolic pulmonary artery pressure; $sPAP_{echo}$ = echocardiographically estimated systolic pulmonary artery pressure; TAPSE = tricuspid annular plane systolic excursion; TPG = transpulmonary gradient; TR = tricuspid regurgitation; TV = tricuspid valve; VC = vena contracta; WU = Wood units.

combined endpoint of all-cause death or HFH at 2 years. This study adhered to the principles outlined in the Declaration of Helsinki and received proper ethical oversight.

STATISTICAL ANALYSIS. Data are expressed as mean ± SD or median (Q1-Q3). Independent samples were compared using the Mann-Whitney *U* test. The Wilcoxon test was used for comparison of dependent samples. Two-year rates of all-cause death or HFH were depicted using cumulative incidence curves. Independent predictors of 2-year rates of all-cause death or HFH were identified using a multivariable Cox regression model including all parameters yielding statistical significance in a univariable analysis. Time-dependent receiver-operating characteristic analysis was used to identify an optimized cutoff for sPAP with regard to 2-year death or HFH. Statistical significance of survival differences was calculated using the log-rank test. The level of statistical significance was set to a 2-sided *P* value <0.05. All analyses were performed using R version 4.0.4 (R Foundation for Statistical Computing) and SPSS version 25 (IBM).

RESULTS

BASELINE CHARACTERISTICS AND OVERALL OUTCOMES. The study included 1,230 T-TEER patients at a mean age of 78.6 ± 7.0 years (51.4% women). Detailed baseline characteristics are presented in Table 1. Torrential TR was present in 19.9%, massive TR in 31.1%, and severe TR in 46.9% of patients, as represented by a mean effective regurgitant

orifice area and regurgitant volume of 0.70 ± 0.60 cm^2 and 53.8 ± 30.8 mL, respectively. Overall, left ventricular function was preserved (left ventricular ejection fraction 52.6% ± 11.4%) and right ventricular function appeared borderline (tricuspid annular plane systolic excursion 17.2 ± 4.6 mm). Echocardiographically measured sPAP was 43.0 ± 15.1 mm Hg. Cardiac and noncardiac comorbidities were common and included arterial hypertension (85.1%), diabetes mellitus (26.1%), chronic obstructive pulmonary disease (18.7%), and previous stroke (11.9%). Surgical risk was elevated as expressed by a mean TRI-SCORE and European System for Cardiac Operative Risk Evaluation II score of 7 points (Q1-Q3: 5-8 points) (predicted in-hospital mortality after isolated tricuspid valve surgery 34.0% [Q1-Q3: 14.0%-48.0%]) and 4.8% [Q1-Q3: 2.6%-7.7%], respectively. Patients had exertional dyspnea (NYHA functional class ≥ III in 86.7%), peripheral edema (64.2%), ascites (14.1%), and jugular vein distension (14.4%).

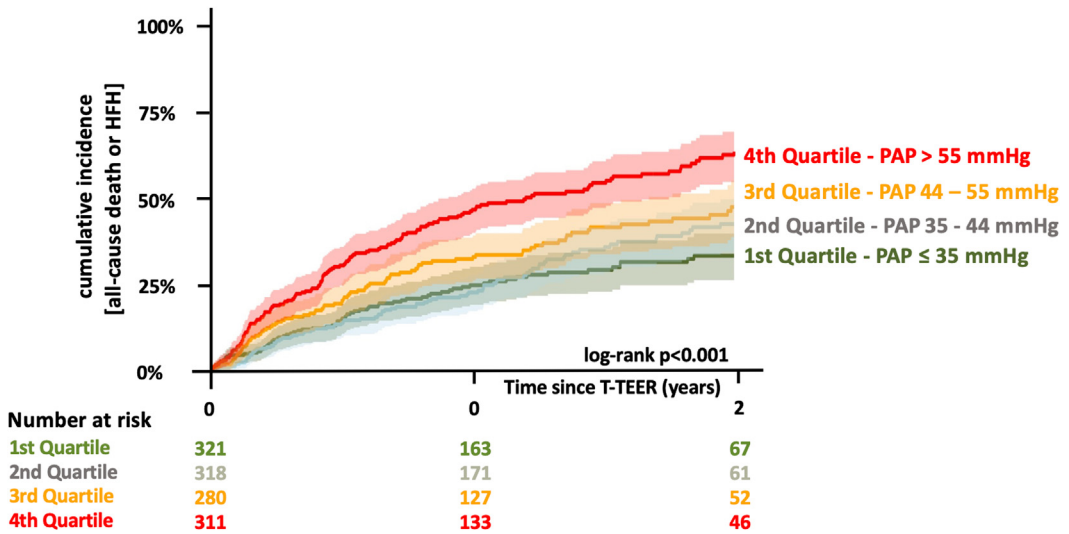
Mean $sPAP_{invasive}$, $dPAP_{invasive}$, and $mPAP_{invasive}$ were 45.9 ± 14.6, 18.7 ± 7.9, and 29.3 ± 9.4 mm Hg, respectively. Further hemodynamic data derived from RHC were cardiac output (4.2 ± 1.5 L/min), PCWP (18.9 ± 7.2 mm Hg), PVR (2.9 ± 1.7 mm Hg), and

TABLE 2 Clinical and Echocardiographic Outcomes

	All Patients (N = 1,230)	sPAP ≤46 mm Hg (n = 704)	sPAP >46 mm Hg (n = 526)	*P* Value
TR severity (n = 1,224)				**<0.001**
Moderate	26 (2.1)	14 (2.0)	32 (6.2)	
Severe	574 (46.9)	288 (41.1)	286 (54.6)	
Massive	381 (31.1)	224 (32.0)	157 (30.0)	
Torrential	243 (19.9)	174 (24.9)	69 (13.2)	
TR severity at discharge (n = 1,203)				**0.021**
Mild	572 (47.5)	319 (46.1)	253 (49.5)	
Moderate	422 (35.1)	236 (34.1)	186 (36.4)	
Severe	172 (14.3)	110 (15.9)	62 (12.1)	
Massive	25 (2.1)	20 (2.9)	5 (1.0)	
Torrential	12 (1.0)	7 (1.0)	5 (1.0)	
NYHA functional class (n = 1,224)				**0.029**
I	12 (1.0)	7 (1.0)	5 (1.0)	
II	151 (12.3)	100 (14.3)	51 (9.7)	
III	882 (72.1)	509 (72.2)	373 (71.2)	
IV	179 (14.6)	84 (12.0)	95 (18.1)	
NYHA functional class at follow-up (n = 808)				**<0.001**
I	118 (14.6)	73 (15.4)	45 (13.4)	
II	370 (45.8)	238 (50.3)	132 (39.4)	
III	276 (34.2)	143 (30.2)	133 (39.7)	
IV	44 (5.4)	19 (4.0)	25 (7.5)	

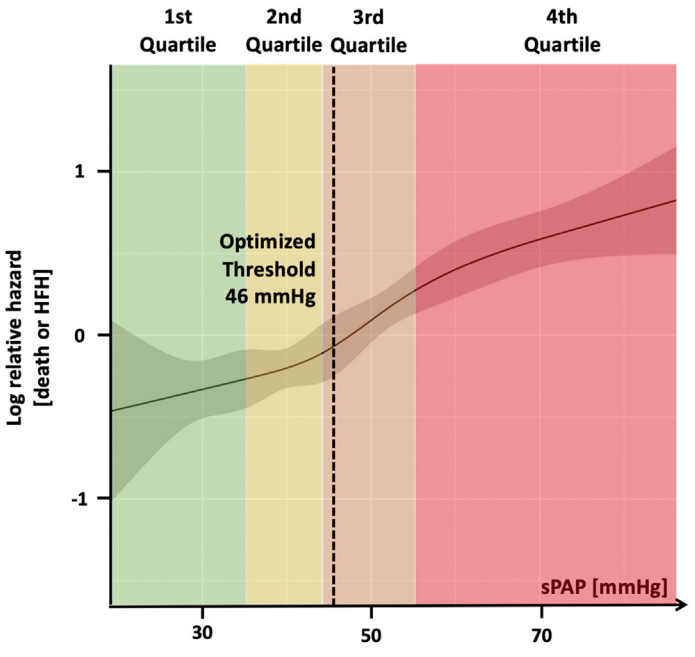
Values are n (%). *P* values in **bold** denote statistical significance.
Abbreviations as in Table 1.

FIGURE 1 Association of the Degree of Pulmonary Hypertension and 2-Year Survival Free From HFH



Increasing pulmonary hypertension (stratified by quartiles) was associated with deteriorating rates of 2-year survival free from heart failure hospitalization (HFH): first quartile, invasive systolic pulmonary artery pressure ($PAP_{invasive}$) ≤35 mm Hg; second quartile, $PAP_{invasive}$ >35 mm Hg and ≤44 mm Hg; third quartile, $PAP_{invasive}$ >44 mm Hg and ≤55 mm Hg; fourth quartile, $PAP_{invasive}$ >55 mm Hg. T-TEER = transcatheter tricuspid valve edge-to-edge repair.

FIGURE 2 Spline Curve Illustrating the Association of sPAP With Death or HFH



Increasing invasive systolic pulmonary artery pressure ($sPAP_{invasive}$) values were associated with an increasing risk for death or heart failure hospitalization (HFH).

TPG (10.9 ± 5.9 mm Hg). TR was reduced to moderate or less in 82.6% of patients and remained reduced to moderate or less in 72.7% at latest available echocardiographic follow-up examination at a median of 343 days (Q1-Q3: 111-392 days) (Table 2). Median survival follow-up was 343 days (Q1-Q3: 114-645 days). Within the overall study cohort, survival free from HFH was 70.5% (Q1-Q3: 67.7%-73.4%) after 1 year and 56.3% (Q1-Q3: 52.9%-60.0%) after 2 years. NYHA functional class improved to ≤II in 60.4% of patients at latest available follow-up (median time to follow-up 338 days [Q1-Q3: 118-393 days]).

PROGNOSTIC IMPACT OF PH IN T-TEER PATIENTS. Increasing $sPAP_{invasive}$ was associated with decreasing rates of 2-year survival free from HFH (first quartile [≤35 mm Hg]: 69.1% [Q1-Q3: 63.0%-75.7%]; second quartile [>35 and ≤44 mm Hg]: 60.5% [Q1-Q3: 53.7%-68.0%]; third quartile [>44 and ≤55 mm Hg]: 55.9% [Q1-Q3: 48.8%-64.0%]; fourth quartile [>55 mm Hg]: 40.8% [Q1-Q3: 34.5%-48.3%]; $P < 0.001$) (Figures 1 and 2). The independent predictive value of $sPAP_{invasive}$ regarding a combined endpoint of all-cause death or HFH was conformed in a multivariable Cox regression model (HR: 1.027; 95% CI: 1.003-1.052; $P = 0.030$) (Supplemental Table 2). The only independent invasive hemodynamic outcome predictor besides $sPAP_{invasive}$ was $dPAP_{invasive}$. Both parameters yielded comparable prognostic value (area under the curve 0.625 for $sPAP_{invasive}$ vs 0.649 for $dPAP_{invasive}$; $P = 0.100$). A time-dependent sensitivity analysis identified an $sPAP_{invasive}$ value of 46 mm Hg as the optimal cutoff regarding 2-year survival free from HFH. Being observed in 526 patients (42.8%), elevated sPAP (>46 mm Hg) was associated with worse survival free from HFH after T-TEER (1 year: 60.1% [Q1-Q3: 55.7%-64.9%] vs 78.3% [Q1-Q3: 75.0%-81.8%] [$P < 0.001$]; 2 years: 44.7% [Q1-Q3: 39.6%-50.4%] vs 65.6% [Q1-Q3: 61.2%-70.3%] [$P < 0.001$]) (Figure 3A). Comparable results were seen for 2-year survival (1 year: 74.7% vs 86.2% [$P < 0.001$]; 2 years: 60.3% vs 75.2% [$P < 0.001$]) (Figure 3B). At baseline and discharge, TR was more severe in patients with $sPAP_{invasive}$ ≤ 46 mm Hg (massive and torrential TR in 56.9% vs 43.2% [$P < 0.001$] at baseline and at least severe in 19.8% vs 14.1% [$P = 0.021$] at discharge). However, T-TEER significantly reduced TR irrespective of sPAP ($P < 0.001$ for both) (Figure 4A).

The presence of severe PH was associated with more severe heart failure symptoms at baseline (NYHA functional class IV in 12.0% in patients with $sPAP_{invasive}$ ≤46 mm Hg vs 18.1% in patients with $sPAP_{invasive}$ >46 mm Hg; $P = 0.029$). However, NYHA functional class significantly improved irrespective of PH ($P < 0.001$ for both) (Figure 4B). Results regarding survival, survival free from HFH, TR reduction, and symptomatic reduction were comparable when stratifying patients by sPAP ≥ 70 mm Hg vs sPAP <70 mm Hg a threshold, which has often been used as exclusion criterion for clinical trials (Supplemental Figures 1 to 3).

SUBTYPES OF PH ACCORDING TO GUIDELINE RECOMMENDATIONS. PCWP was ≥15 mm Hg in 614 patients (70.7%). Elevated PCWP yielded univariable but no multivariable prognostic significance in terms of 2-year survival free from HFH (49.6% [Q1-Q3: 44.7%-55.0%] vs 59.7% [Q1-Q3: 52.1%-68.5%]; $P = 0.005$) (Figure 5A). PVR was increased to >2 WU in 347 patients (63.4%) but did not significantly affect survival free from HFH (57.5% [Q1-Q3: 50.9%-64.9%] vs 51.3% [Q1-Q3: 43.0%-61.2%]; $P = 0.098$) (Figure 5B). The same applied for individuals with TPGs >17 mm Hg, which was observed in 14.2% of patients (44.8% [Q1-Q3: 32.9%-59.2%] vs 53.9% [Q1-Q3: 49.3%-58.7%]; $P = 0.085$) (Figure 5C). Figure 5D differentiates survival free from HFH in patients with precapillary, postcapillary, and mixed pre- and postcapillary PH. Differences in baseline characteristics for these 3 groups are presented in Supplemental Table 3.

SUBTYPES OF PH. According to the previously used definition of PH,[6] no significant difference between pre- and postcapillary PH was observed in 65.1%, 10.5%, and 24.5% of patients, respectively. Although the presence of significant either pre- or postcapillary PH was associated with significantly impaired rates of 2-year survival free from HFH, no difference was observed between both subtypes of PH ($P < 0.001$) (Figure 6).

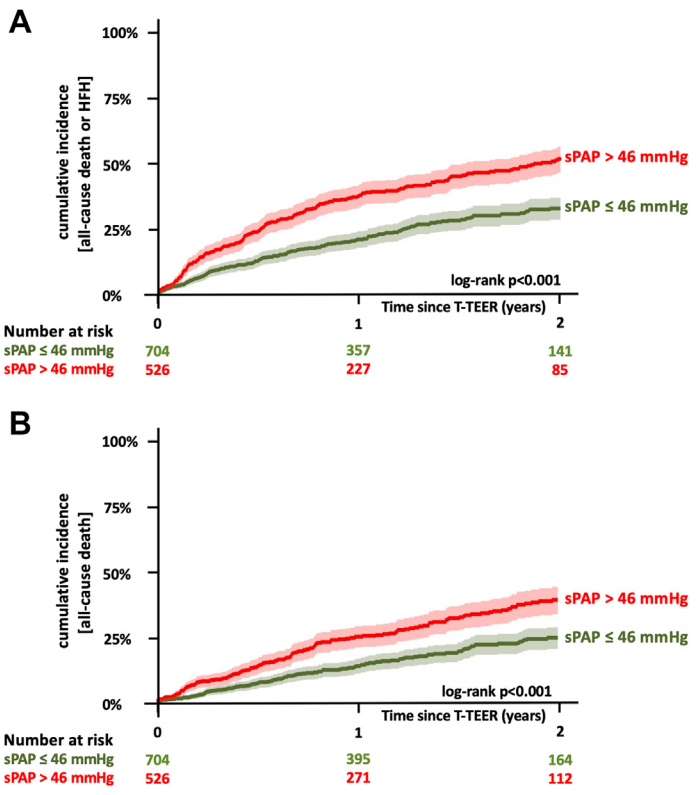
DISCUSSION

On the basis of data from the international EuroTR registry, this study gives further insights into the prognostic value of RHC-derived hemodynamic status in patients undergoing T-TEER for relevant TR. To the best of our knowledge, this is the largest population of T-TEER patients with available RHC data. Importantly, the EuroTR registry also included patients with extensive or relevant precapillary PH, who have been excluded from clinical trials in the field of T-TEER. The main findings of this study can be summarized as followed (Central Illustration): 1) the extent of PH (increasing $sPAP_{invasive}$) was significantly associated with increasing rates of mortality and HFH after T-TEER; 2) NYHA functional class improved and TR severity decreased irrespective of PH; and 3) no significant difference in survival free from HFH was observed when comparing patients with pre- vs postcapillary PH

RHC PRIOR TO T-TEER. Especially in the early days of T-TEER, the necessity of routinely performing RHC prior to the procedure was intensively discussed. In 2020, Lurz et al[4] demonstrated that echocardiographically estimated sPAP values underestimate the true pulmonary pressure conditions because of rapid systolic pressure equalization in the presence of large coaptation gaps and severe TR. Patients with discordant invasive and echocardiographic sPAP values presented with remarkably reduced 1-year survival free from HFH after the procedure (<25%). Given those findings, RHC has become an important tool in the diagnostic work-up of patients with TR being evaluated for treatment.

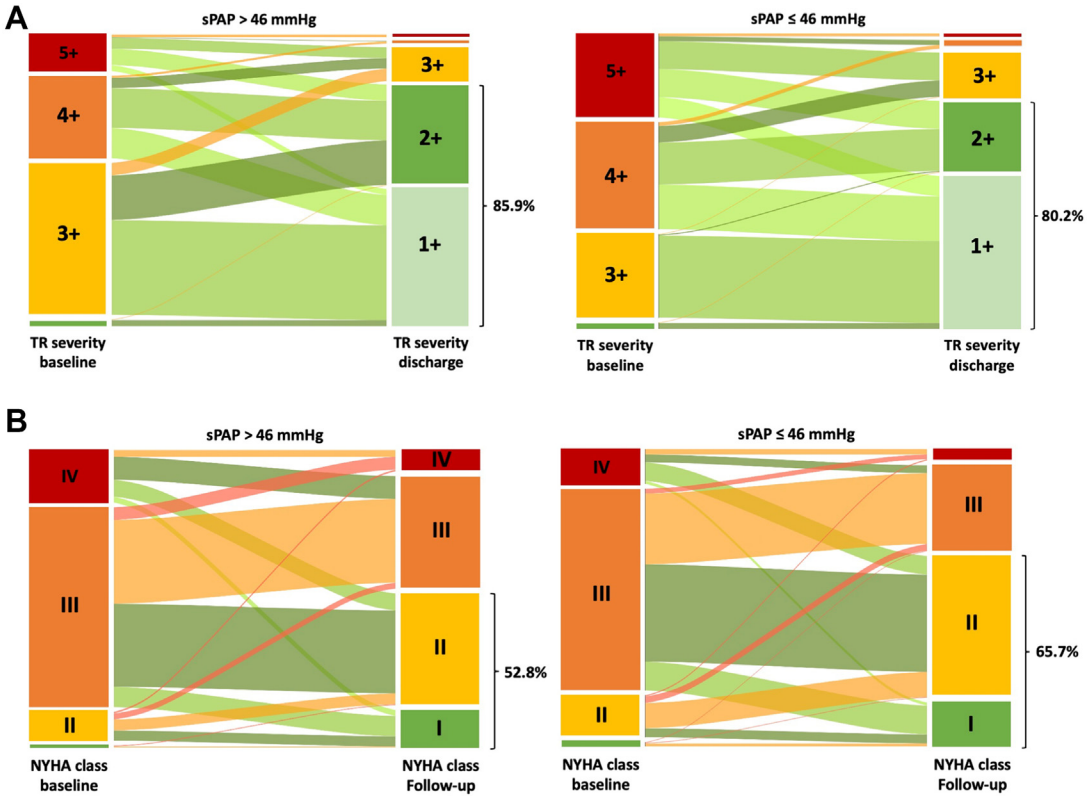
PROGNOSTIC VALUE OF PH IN T-TEER. The present study underlines the fact that sufficient TR reduction can be achieved irrespective of the presence of PH. However, the absolute degree of PH (increasing sPAP) was a major predictor for a combined endpoint of 2-year death or HFH. As represented by a higher NYHA functional class at baseline, PH itself seems to contribute to patients' symptomatic status. Excluding patients with severe PH from large randomized controlled trials seemed reasonable at the time but limits our knowledge on the benefit of T-TEER beyond medical treatment in this subgroup of patients. Given the fact that medical treatment in the setting of precapillary PH at the moment is limited to few drugs, T-TEER might be a reasonable treatment option in patients with severe PH, as approximately 40% of patients improved to NYHA functional class ≤II. Against the background of limited randomized evidence and clearly reduced survival rates, discussing the expected benefit with patients and their relatives seems crucial. However, dedicated randomized data are needed to gain a better understanding of what T-TEER can achieve in patients with excessively elevated pulmonary artery pressures. Prerequisite for adequate hemodynamic evaluation of patients with severe TR is optimized medical prehabilitation prior to RHC. In this real-world registry, patients were prepared according to the internal standards of each center. However, variability of

FIGURE 3 Impact of Pulmonary Hypertension on 2-Year Survival and 2-Year Survival Free From HFH



Patients with severe pulmonary hypertension ($sPAP_{invasive}$ >46 mm Hg) presented with significantly reduced rates of 2-year survival (B) and 2-year survival free from HFH (A) after T-TEER. Abbreviations as in Figures 1 and 2.

FIGURE 4 TR Severity and NYHA Functional Class at Baseline and Discharge Stratified by Pulmonary Hypertension



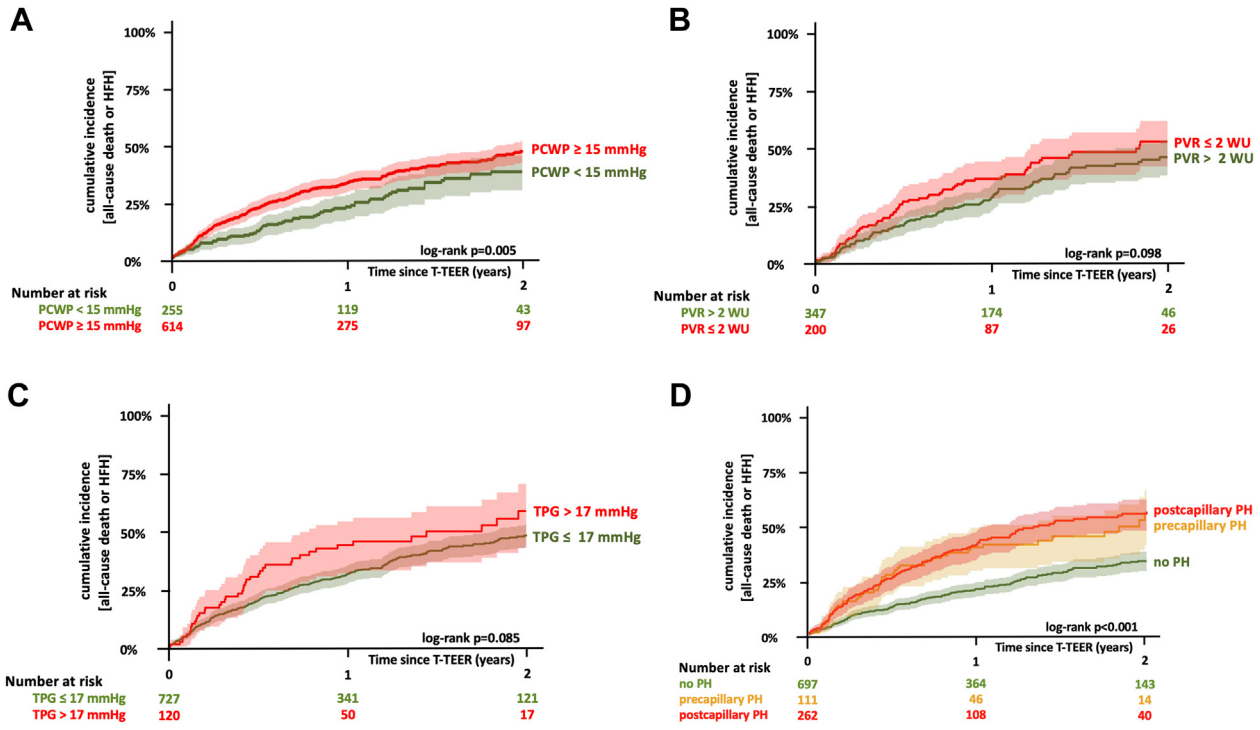
Association of invasive systolic pulmonary artery pressure ($sPAP_{invasive}$) >46 mm Hg vs ≤46 mm Hg with tricuspid regurgitation (TR) severity (at baseline and discharge, 1,200 paired samples) (A) and NYHA functional class (at baseline and follow-up, 805 paired samples) (B).

hemodynamic measurements might have an influence on prognostic considerations after T-TEER.

PRECAPILLARY- VS POSTCAPILLARY PH. In contrast to echocardiographic estimation of sPAP, RHC allows differentiation between pre- and postcapillary PH. In a multicentric cohort of 236 T-TEER patients, individuals with significant precapillary PH (mPAP >30 mm Hg and TPG >17 mm Hg) had significantly reduced 1-year survival rates compared with those without (mPAP ≤30 mm Hg) or significant postcapillary PH (mPAP >30 mm Hg and TPG ≤17 mm Hg).[6]

When applying those criteria to the considerably larger EuroTR registry, the aforementioned results could not be reproduced. In the present analysis, patients with pre- and postcapillary PH presented with equally reduced 2-year rates of survival free from HFH (precapillary 42.8% vs postcapillary 41.8%). The fact that patients with precapillary PH did not experience worse outcomes compared with those with postcapillary PH seems to be supported by the fact that stratification of patients by PCWP ≥15 mm Hg vs PCWP <15 mm Hg but not by PVR >2 WU vs PVR ≤2 WU yielded prognostic significance in terms of survival free from HFH (Figures 6A and 6B). In line with these findings, stratification of patients into precapillary, postcapillary, and mixed pre- and postcapillary PH according to recent European guidelines[10] revealed comparable 2-year survival rates free from HFH in patients with precapillary, mixed, and postcapillary PH (56.3% and 57.6%). Reasons for the discrepancy of previous studies and the result of this analysis regarding the prognostic significance of precapillary PH remain speculative. In previous studies, the subgroups of patients with precapillary PH were relatively small, and the comorbidity in the respective individuals was high, which might have confounded the comparably high mortality rates. In the meantime, patient selection seems to have improved, which possibly explains a lower overall mortality rate in patients with precapillary PH undergoing T-TEER.

FIGURE 5 Impact of Precapillary and Postcapillary PH on Survival Free From HFH After T-TEER

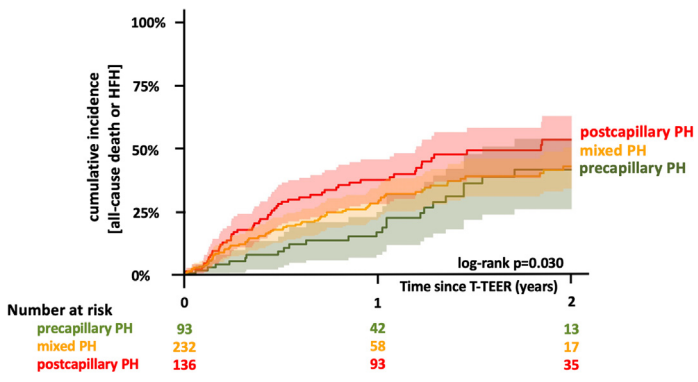


Impact of pulmonary capillary wedge pressure (PCWP) (A), pulmonary vascular resistance (PVR) (B), transpulmonary gradient (TPG) (C), and precapillary, postcapillary, and mixed precapillary and postcapillary pulmonary hypertension (PH) (D) on 2-year survival free from HFH after T-TEER. Abbreviations as in Figure 1.

The fact that especially the overall degree of PH determined outcomes after T-TEER further strengthens the role of an integrated heart team approach to TR, including not only cardiologists, cardiac surgeons, and electrophysiologists but also heart failure and PH specialists in particular. In patients with heart failure with reduced ejection fraction, up-titration of guideline-directed medical therapy and, if indicated, cardiac resynchronization therapy might reduce PCWP and hence improve PH, which might affect outcomes. Although evidence for the use of sodium-glucose cotransporter 2 inhibitors in the setting of heart failure with preserved ejection fraction in general is growing, data on the impact of this medication class on outcomes in patients with heart failure with preserved ejection fraction undergoing T-TEER for severe TR remain unavailable.

STUDY LIMITATIONS. Although this is the largest study presenting RHC data for consecutive T-TEER patients in a large multicenter approach, the analysis is subject to a number of limitations. All reported data are site reported and did not undergo core laboratory review. Of note, information regarding the medical treatment of patients with precapillary PH was not available. However, patients were considered to be on optimized medical treatment as judged by the local heart teams. Beyond that, echocardiographic

FIGURE 6 2-Year Survival Free From HFH Stratified by Significant Precapillary and Postcapillary PH



Although the presence of significant either pre- or postcapillary PH was associated with significantly impaired rates of 2-year survival free from HFH, no difference was observed for both subtypes of PH ($P < 0.001$). Abbreviations as in Figures 1 and 5.

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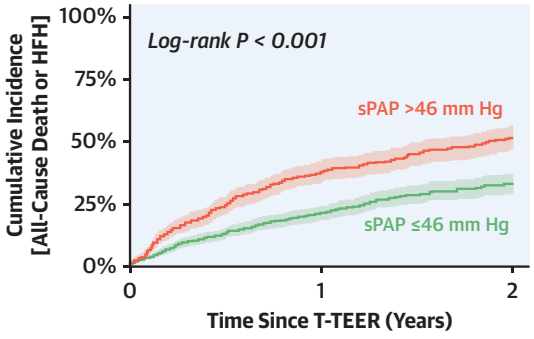
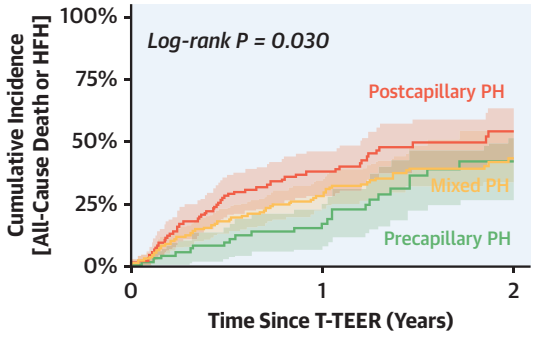
CENTRAL ILLUSTRATION Pulmonary Hypertension and T-TEER

Impact of Pulmonary Hypertension on Outcomes Following Transcatheter Tricuspid Valve Edge-to-Edge Repair (N = 1,230)

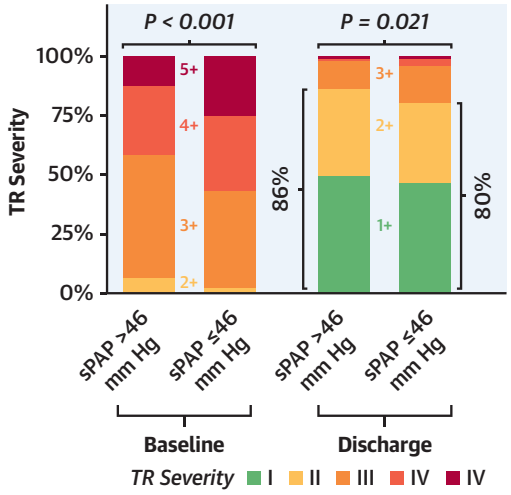
A Combined Endpoint (Death or HFH)



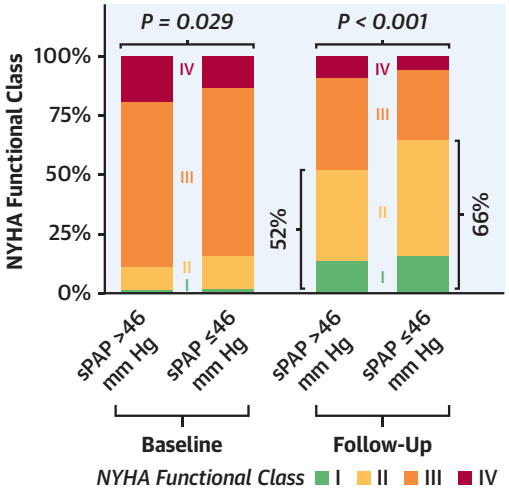


B TR Reduction and Symptomatic Improvement

Tricuspid Regurgitation



NYHA Functional Class



- The extent of pulmonary hypertension was significantly associated with increasing rates of mortality and HHF after T-TEER
- Even patients with severe PH (>46 mm Hg) presented with symptomatic improvement after T-TEER as expressed by NYHA functional class
- There was no significant difference in survival free from HFH when comparing patients with precapillary and postcapillary PH
- There was no significant difference in TR reduction when comparing patients with precapillary and postcapillary PH

Stolz L, et al. JACC Cardiovasc Interv. 2025;18(3):325–336.

HFH = heart failure hospitalization; PH = pulmonary hypertension; sPAP = systolic pulmonary artery pressure; TR = tricuspid regurgitation; T-TEER = transcatheter tricuspid valve edge-to-edge repair.

data regarding right ventricular function after T-TEER were not available.

CONCLUSIONS

In patients undergoing T-TEER for relevant symptomatic TR, increased PH was associated with progressively impaired 2-year survival free from HFH. In contrast to previous publications, pre- and postcapillary PH had comparable impact on outcomes after the procedure. Given the fact that echocardiographically measured sPAP values significantly underestimated true pressure conditions, especially in the presence of massive and torrential TR, we believe that RHC should routinely be performed within the diagnostic work-up to allow discussion of patient expectations from a T-TEER procedure, ultimately leading to a more informed and personalized approach of patient care.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr Stolz has received speaker honoraria from Edwards Lifesciences. Dr Kresoja has received travel expenses from Edwards Lifesciences. Dr von Stein has received lecture honoraria from Edwards Lifesciences. Dr Rottbauer has received speaker honoraria from Edwards Lifesciences and Abbott. Dr Denti has served as a consultant for InnovHeart, Picardia, HVR, and Approxima; and has received speaker honoraria from Abbott and Edwards Lifesciences. Dr Rassaf has received speaker honoraria and consulting fees from AstraZeneca, Bayer, Pfizer, and Daiichi-Sankyo. Dr Barreiro-Perez has received speaker fees from Abbott Vascular, Edwards Lifesciences, and Venus Medtech. Dr Adamo has received consulting fees in the past 3 years from Abbott Structural Heart and Edwards Lifesciences. Dr von Bardeleben has received institutional grants from and has served as a speaker for Abbott Vascular and Edwards Lifesciences. Dr Toggweiler has received personal honoraria from Medtronic, Boston Scientific, Biosensors, Abbott Vascular, Medira, Shockwave Medical, Teleflex, atHeart Medical, Cardiac Dimensions, Polares Medical, Amarin, Sanofi, AstraZeneca, ReCor Medical, and Daiichi-Sankyo; has received institutional research grants from Edwards Lifesciences, Boston Scientific, Fumedica, Novartis, and Boehringer Ingelheim; and holds equity in Hi-D Imaging. Dr Metra has received consulting fees in the past 3 years from Abbott Structural Heart, AstraZeneca, Bayer, Boehringer Ingelheim, Edwards Lifesciences, and Roche Diagnostics. Dr Geisler has received speaker honoraria and research grants from AstraZeneca, Bayer, Bristol Myers Squibb/Pfizer, Ferrer/Chiesi, Medtronic, and Edwards Lifesciences (all unrelated to this study). Dr Estévez-Loureiro has received speaker fees from Abbott Vascular, Edwards Lifesciences, Boston Scientific, and Venus Medtech. Dr Lüdike has received speaker honoraria and consulting fees from AstraZeneca, Bayer, Pfizer, and Edwards Lifesciences; and has received research honoraria from Edwards Lifesciences. Dr Maisano has received grant and/or research institutional support from Abbott, Medtronic, Edwards Lifesciences, Biotronik, Boston Scientific, NVT, Terumo, and Venus Medtech; has received consulting fees and personal and institutional honoraria from Abbott, Medtronic, Edwards Lifesciences, Xeltis, Cardiovalve, Occlufit, Simulands, Mtex, Venus Medtech, Squadra, and Valgen; has received royalty income from and holds intellectual property rights with Edwards Lifesciences; and is a shareholder (including share options) in Magenta, Transseptal Solutions, and 4Tech. Dr Praz has received travel expenses from Edwards Lifesciences, Abbott Vascular, Polares Medical, Medira, and Siemens Healthineers. Dr Kessler has received speaker honoraria from Edwards Lifesciences and Abbott. Dr Kalbacher has received personal fees from Abbott Medical, Edwards Lifesciences, Pi-Cardia, and Medtronic. Dr Rudolph has received research grants from Abbott Medical, Boston Scientific, and Edwards Lifesciences. Dr Iliadis has received consultant fees and travel expenses from Abbott Medical and Edwards Lifesciences. Dr Lurz has received institutional grants from Edwards Lifesciences and honoraria from Innoventrics. Dr Hausleiter has received research grant support and speaker honoraria from Edwards Lifesciences. Dr Sticchi has served on an advisory board for Edwards Lifesciences. Dr Tarantini has received speaker fees for Abbott Vascular and Edwards Lifesciences. Dr Karam has received consultant fees from Edwards Lifesciences, Boston Scientific, and Medtronic; and has received proctor fees from Abbott. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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PERSPECTIVES

WHAT IS KNOWN? PH is commonly observed in patients being evaluated for transcatheter tricuspid valve repair.

WHAT IS NEW? PH is an important outcome predictor in patients undergoing transcatheter tricuspid valve repair. There was no significant prognostic difference when comparing patients with pre- vs postcapillary PH.

WHAT IS NEXT? Randomized controlled data in patients are needed to further investigate the benefit of T-TEER beyond medical treatment explicitly in patients with severe PH.

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KEY WORDS postcapillary, precapillary, pulmonary hypertension, sPAP

APPENDIX For supplemental tables and figures as well as a list of EuroTR investigators, please see the online version of this paper.