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Positive Outcomes in Patients with Resolved Pulmonary Hypertension Following TAVI: Insights from the LAPLACE-TAVI Registry

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Abstract

Pulmonary hypertension (PH) is a frequent complication in patients with aortic stenosis (AS) and is generally associated with adverse outcomes. However, the clinical significance of changes in PH following transcatheter aortic valve implantation (TAVI) has not been fully elucidated. We examined data from a prospective, multicenter TAVI registry across six Japanese institutions, estimating pulmonary artery systolic pressure through echocardiographic transtricuspid pressure gradient (TRPG). A total of 2,056 patients were categorized based on pre-TAVI TRPG into a PH-negative group (TRPG < 30 mmHg, n = 1,407, 61.9 percent) and a PH-positive group (TRPG ≥ 30 mmHg, n = 649, 28.6 percent). The PH-positive cohort was further divided after TAVI (4.1 ± 5.3 days) into Recovered PH (TRPG < 30 mmHg, n = 253) and Persistent PH (TRPG ≥ 30 mmHg, n = 396). Over a median follow-up of 1.8 years, the primary endpoint was a composite of cardiovascular death and heart failure hospitalization, with secondary endpoints including each component individually. Kaplan-Meier analysis demonstrated higher event rates in the Persistent PH group, and multivariate Cox regression revealed that each 10 mmHg decrease in TRPG post-TAVI was associated with a 24% reduction in risk of the primary endpoint (HR: 0.76, 95% CI: 0.64–0.90, p = 0.002). These findings indicate that resolution of PH may partially underlie the improved prognosis observed after TAVI in AS patients with elevated pulmonary pressures.

Keywords: TAVI, Pulmonary hypertension, TRPG, Echocardiography, Prognosis, Severe AS

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Introduction

Aortic stenosis (AS) is the most common valvular heart disorder and its prevalence continues to rise worldwide due to an aging population [1]. While surgical aortic valve replacement (SAVR) has long been the standard definitive treatment for severe AS, transcatheter aortic valve implantation (TAVI) has emerged as a less invasive alternative, initially reserved for high-risk or inoperable patients [2, 3]. With improvements in device technology, operator experience, and procedural techniques, TAVI is now increasingly offered to lower-risk patients [3–6]. This expansion underscores the need for precise preoperative risk assessment and reliable prediction of long-term outcomes [7, 8].

PH commonly develops in AS as elevated left atrial pressure from increased left ventricular afterload induces pulmonary arteriolar constriction, resulting in secondary

PH [9, 10]. Prior studies in SAVR patients demonstrated that preoperative PH is linked to higher postoperative mortality [11], whereas reductions in pulmonary arterial pressure following surgery are associated with better outcomes [12–14]. Despite these insights, the prognostic impact of PH improvement after TAVI remains insufficiently studied. To address this gap, we analyzed a multicenter Japanese TAVI registry, focusing on changes in TRPG-derived pulmonary pressures after TAVI and their relationship with long-term cardiovascular outcomes [15].

Materials and Methods

Patient cohort

We conducted a retrospective examination of data from a prospective, multicenter registry involving individuals treated with transcatheter aortic valve implantation (TAVI) at six hospitals in Japan (comprising four university hospitals and two municipal facilities). This registry, named the LAPLACE TAVI registry (aLliAnce for exPloring cLinical prospects of AortiC valvE disease), included contributions from Sakakibara Heart Institute, Juntendo University Hospital, Yamagata University Hospital, Hirosaki University Hospital, Mie University Hospital, and Kawasaki Saiwai Hospital. The study complied with the Declaration of Helsinki and obtained ethical clearance from the respective institutional review boards: Sakakibara Heart Institute (IRB-ID: 17-048), Juntendo University Hospital (IRB-ID: 17-263), Yamagata University Hospital (IRB-ID: 2019-407), Hirosaki University Hospital (IRB-ID: 2020-040), Mie University Hospital (IRB-ID: H2021-049), and Kawasaki Saiwai Hospital (IRB-ID: R4-13). The registry is listed in the University Medical Information Network Japan-Clinical Trials Registry under UMIN000031133. All patients gave written informed consent for inclusion in the registry.

Measurement of TRPG, E/A, and E/e' using echocardiography before and after TAVI

Patients received standard two-dimensional and Doppler transthoracic echocardiography (TTE) at their treating centers, in line with published guidelines [16]. Echocardiograms were performed an average of 33.3 ± 33.8 days before TAVI and 4.1 ± 5.3 days afterward. Tricuspid regurgitation (TR) was examined in views such as the apical four-chamber, parasternal short-axis, or right ventricular inflow tract. Severity grading of TR and mitral regurgitation (MR) followed recommended criteria [17]. While pulmonary hypertension (PH) is ideally confirmed by mean pulmonary artery pressure through right heart catheterization or, noninvasively, by estimating right ventricular systolic pressure (TRPG plus estimated right atrial pressure) [18], inferior vena cava measurements were not recorded in this registry. Thus, elevated pulmonary pressure (PH) was defined as TRPG ≥ 30 mmHg [16, 19, 20]. Mitral inflow patterns (E and A waves) were recorded from apical two- or four-chamber views, and mitral annular tissue velocities (e') were captured from the four-chamber view at the septal or lateral sites. The ratios E/A and E/e' were derived by dividing the E-wave peak by the A-wave peak and by e', respectively [21].

Study cohort, endpoints, and follow-up

From the full LAPLACE TAVI registry, we excluded cases without TRPG values (n = 216), yielding 2056 patients who had TAVI performed between May 17, 2010, and June 30, 2021. Patients were initially stratified by baseline (pre-TAVI) TRPG into those without PH (TRPG < 30 mmHg; PH(−) group; n = 1407, representing 61.9 percent) and those with PH (TRPG ≥ 30 mmHg; PH(+) group; n = 649, 28.6 percent). The PH(+) cohort was then further classified according to early post-TAVI TRPG (assessed 4.1 ± 5.3 days post-procedure) into a recovered subgroup (post-TAVI TRPG < 30 mmHg; n = 253) and a persistent subgroup (post-TAVI TRPG ≥ 30 mmHg; n = 396).

The main endpoint was a composite of cardiovascular death or admission for heart failure occurring after the TAVI procedure. Individual components—cardiovascular death and heart failure admission—served as secondary endpoints. Maximum follow-up reached 10.6 years, with a median of 1.8 years.

Statistical analysis

Continuous variables were reported either as mean ± standard deviation or median with interquartile range (IQR), depending on normality assessed via the Shapiro-Wilk test, while categorical data were expressed as counts and percentages. Group comparisons of continuous variables were conducted using one-way ANOVA or Kruskal-Wallis tests, as appropriate. Time-to-event outcomes were analyzed with Kaplan-Meier curves, and differences between groups were evaluated using the log-rank test. The association between TRPG, treated as a continuous variable, and study endpoints was assessed using Cox proportional hazards models in both univariate and multivariate frameworks. Covariates for multivariate analyses were selected based on clinical relevance and univariate results. Two multivariate models were constructed: Model 1 included TRPG (per −10 mmHg), age, and sex; Model 2 additionally adjusted for AF/AFL, peripheral arterial disease, pacemaker implantation, prior stroke, diabetes mellitus, hemoglobin, albumin, eGFR, and log-transformed NT-proBNP. Statistical significance was defined as $p < 0.05$. Analyses were performed using JMP Pro 12.0 (SAS Institute Inc, Cary, NC, USA) and SPSS version 27 (IBM Corp, Armonk, NY, USA).

Results and Discussion

Baseline characteristics, medications, procedural features, and devices in PH (−) and PH (+) groups, and recovered vs. persistent PH subgroups

Baseline characteristics, comorbidities, medication use, procedural details, and THV types were first compared between patients without PH (TRPG < 30 mmHg; PH (−), n = 1,407) and those with PH (TRPG ≥ 30 mmHg; PH (+), n = 649) **(Table 1)**. Patients in the PH (+) group were older, more frequently male, and had a higher prevalence of prior heart failure, more severe NYHA functional class, AF/AFL, previous coronary interventions, and pacemaker implantation. Conventional cardiovascular risk factors such as hypertension, diabetes, and dyslipidemia were similar between groups. TAVI risk scores were higher in the PH (+) cohort. Biomarkers reflecting cardiac and renal function, including NT-proBNP and serum creatinine, were elevated in patients with PH. Echocardiography revealed more advanced mitral and tricuspid regurgitation in the PH (+) group. Regarding medications, beta-blockers, diuretics, and anticoagulants were more commonly prescribed among PH (+) patients. TAVI procedural approaches and THV types (balloon- vs. self-expandable) and sizes did not differ between groups.

Within the PH (+) cohort, patients were further classified after TAVI into those with recovered PH (TRPG < 30 mmHg; n = 253) and persistent PH (TRPG ≥ 30 mmHg; n = 396) **(Table 2)**. Age, BMI, NYHA class, procedural risk scores, and most comorbidities were comparable between these subgroups, except for AF/AFL, which was more frequent in the Persistent PH group. Echocardiographic measures related to AS—including aortic valve area, mean and peak transvalvular gradients, and severity of aortic and mitral regurgitation—showed no significant differences. Notably, LVEF was paradoxically higher in patients with Persistent PH. Medication use was largely similar between subgroups, except oral anticoagulants, which were more common in the Persistent PH group, likely due to the higher prevalence of AF/AFL. Procedural approaches and device characteristics were comparable, though the THV size implanted was smaller in the Persistent PH subgroup.

Table 1. Baseline Characteristics of Patients with and without Pulmonary Hypertension (PH)

Variable	p-Value	PH (+) (n = 649, 31.6%)	PH (−) (n = 1,407, 68.4%)
Demographics			
Age, years	0.0011	84.9 ± 5.3	84.1 ± 5.3
Male, n (%)	0.0284	196 (30.2%)	494 (35.1%)
BMI, kg/m²	<0.0001	21.8 ± 3.7	22.7 ± 3.7
NYHA class III/IV, n (%)	<0.0001	371 (57.7%)	614 (44.1%)
Logistic EuroSCORE, %	<0.0001	18.6 (17.6–19.7)	14.7 (14.2–15.2)
EuroSCORE II, %	<0.0001	8.0 (7.3–8.7)	5.8 (5.4–6.1)
STS-PROM, %	<0.0001	8.3 (7.8–8.7)	6.4 (6.2–6.6)
Comorbidities			
Prior heart failure, n (%)	<0.0001	146 (40.0%)	221 (24.6%)
Hypertension, n (%)	0.84	499 (77.1%)	1,074 (76.7%)
Diabetes mellitus, n (%)	0.46	140 (21.6%)	324 (23.0%)
Dyslipidemia, n (%)	0.18	347 (53.5%)	797 (56.7%)
AF/AFL, n (%)	<0.0001	216 (33.8%)	281 (20.2%)
Cancer, n (%)	0.08	104 (16.0%)	270 (19.2%)
Prior stroke, n (%)	0.23	65 (10.0%)	166 (11.8%)
COPD, n (%)	0.29	64 (10.0%)	119 (8.5%)
CKD (stage ≥3), n (%)	0.0192	464 (71.5%)	933 (66.3%)
PAD, n (%)	0.0007	129 (20.1%)	198 (14.1%)
Old myocardial infarction, n (%)	0.33	40 (6.2%)	72 (5.1%)
History of coronary revascularization, n (%)	0.0148	122 (18.8%)	332 (23.6%)
p-PTAV, n (%)	0.27	19 (2.9%)	30 (2.1%)

Pacemaker implantation, n (%)	0.0212	50 (5.9%)	72 (5.1%)
Laboratory Findings			
NT-proBNP, pg/mL	0.0002	4,777 (3,710–5,844)	2,704 (2,139–3,270)
Creatinine, mg/dL	0.0003	1.10 ± 0.9	0.98 ± 0.6
eGFR, mL/min	0.0002	50.3 ± 19.2	53.6 ± 18.4
Hemoglobin, g/dL	<0.0001	11.3 ± 1.6	11.6 ± 1.6
Albumin, g/dL	0.0001	3.7 ± 0.5	3.8 ± 0.4
Echocardiography			
LVEF, %	0.0162	59.9 ± 12.4	61.1 ± 10.0
AVA, cm²	0.0002	0.66 ± 0.21	0.70 ± 0.21
Peak gradient, mmHg	0.0152	88.3 ± 33.8	84.8 ± 29.4
Mean gradient, mmHg	0.0128	51.0 ± 21.1	48.7 ± 17.9
AR ≥ moderate, n (%)	0.99	52 (8.0%)	113 (8.0%)
MR ≥ moderate, n (%)	<0.0001	92 (14.2%)	76 (5.4%)
TR ≥ moderate, n (%)	<0.0001	105 (16.2%)	33 (2.4%)
TRPG, mmHg	<0.0001	38.6 ± 9.4	21.9 ± 4.7
Medications			
Beta-blockers, n (%)	<0.0001	281 (43.4%)	437 (31.1%)
ACEIs/ARBs, n (%)	0.24	362 (55.9%)	747 (53.1%)
Statins, n (%)	0.50	331 (51.1%)	741 (52.7%)
Diuretics, n (%)	<0.0001	379 (58.5%)	580 (41.2%)
Oral anticoagulants, n (%)	<0.0001	239 (36.8%)	311 (22.1%)
Procedural Characteristics			
Procedure duration, min	0.64	81.5 (78–85)	82.5 (80.5–85.0)
Fluoroscopy time, min	0.73	22.2 (21.3–23.0)	22.3 (21.8–22.9)
Contrast volume, mL	0.80	63.3 (60.0–66.7)	62.8 (60.7–65.0)
Conscious sedation, n (%)	0.0134	404 (62.3%)	954 (67.8%)
Transfemoral approach, n (%)	0.08	599 (93.0%)	1,329 (94.9%)
Valve size, mm	0.16	24.7 ± 2.4	24.9 ± 2.4
Balloon-expandable, n (%)	0.0096	413 (69.5%)	988 (71.3%)

Abbreviations: BMI, body mass index; AF/AFL, atrial fibrillation or flutter; COPD, chronic obstructive pulmonary disease; PAD, peripheral artery disease; OMI, old myocardial infarction; p-PTAV, percutaneous transcatheter aortic valvuloplasty; PMI, pacemaker implantation; NT-proBNP, N-terminal pro B-type natriuretic peptide; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; AVA, aortic valve area; AR, aortic regurgitation; MR, mitral regurgitation; TR, tricuspid regurgitation; TRPG, transtricuspid pressure gradient.

Table 2. Baseline Features of Recovered vs. Persistent Pulmonary Hypertension (PH) Groups

Variable	p-Value	Persistent PH (n = 396, 61.0%)	Recovered PH (n = 253, 39.0%)
Demographics			
Age, years	0.15	85.1 ± 5.4	84.5 ± 5.1
Male, n (%)	0.0273	107 (27.0%)	89 (35.2%)
BMI, kg/m²	0.24	21.9 ± 3.7	21.6 ± 3.5
NYHA class III/IV, n (%)	0.49	222 (56.6%)	149 (59.4%)

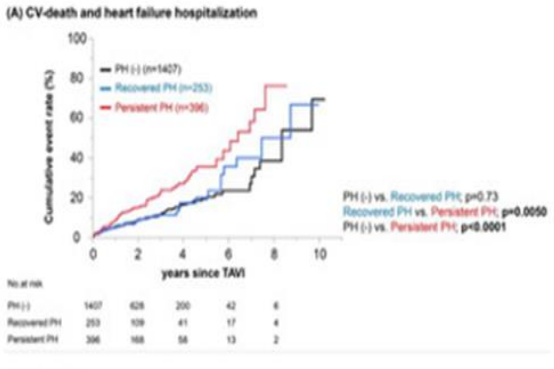
Logistic EuroSCORE, %	0.78	18.5 (17.3–19.8)	18.8 (17.1–20.6)
EuroSCORE II, %	0.64	7.9 (7.0–8.7)	8.2 (7.0–9.4)
STS-PROM, %	0.57	8.4 (7.8–9.0)	8.1 (7.4–8.8)
Comorbidities			
Prior heart failure, n (%)	0.73	94 (37.6%)	52 (35.9%)
Hypertension, n (%)	0.22	311 (78.7%)	188 (74.6%)
Diabetes mellitus, n (%)	0.48	89 (22.5%)	51 (20.2%)
Dyslipidemia, n (%)	0.24	219 (55.3%)	128 (50.6%)
AF/AFL, n (%)	0.0066	148 (37.9%)	68 (27.4%)
Cancer, n (%)	0.32	68 (17.2%)	36 (14.2%)
Prior stroke, n (%)	0.21	35 (8.8%)	30 (11.9%)
COPD, n (%)	0.77	38 (9.7%)	26 (10.4%)
CKD (stage ≥3), n (%)	0.22	290 (73.2%)	174 (68.8%)
PAD, n (%)	0.27	74 (18.7%)	55 (22.3%)
Old myocardial infarction, n (%)	0.14	20 (5.1%)	20 (7.9%)
History of coronary revascularization, n (%)	0.61	72 (18.2%)	50 (19.8%)
p-PTAV, n (%)	0.25	14 (2.4%)	5 (2.0%)
Pacemaker implantation, n (%)	0.45	33 (8.3%)	17 (6.7%)
Laboratory Findings			
NT-proBNP, pg/mL	0.60	4,991 (3,422–6,560)	4,406 (3,332–5,481)
Creatinine, mg/dL	0.72	1.11 ± 0.9	1.09 ± 0.9
eGFR, mL/min	0.0371	49.0 ± 18.9	52.2 ± 20.0
Hemoglobin, g/dL	0.0188	11.2 ± 1.6	11.5 ± 1.7
Albumin, g/dL	0.89	3.7 ± 0.5	3.7 ± 0.5
Echocardiography			
LVEF, %	0.0138	60.9 ± 11.3	58.4 ± 13.8
AVA, cm^2	0.33	0.67 ± 0.20	0.65 ± 0.23
Peak gradient, mmHg	0.50	87.7 ± 34.0	89.5 ± 33.8
Mean gradient, mmHg	0.24	50.1 ± 21.5	52.2 ± 20.5
AR ≥ moderate, n (%)	0.27	28 (7.1%)	24 (9.5%)
MR ≥ moderate, n (%)	0.67	58 (14.7%)	34 (13.4%)
TR ≥ moderate, n (%)	0.0169	75 (18.9%)	30 (11.9%)
TRPG, mmHg	0.0001	39.7 ± 9.4	36.9 ± 9.0
Medications			
Beta-blockers, n (%)	0.49	176 (44.4%)	105 (41.7%)
ACEIs/ARBs, n (%)	0.65	224 (56.6%)	138 (54.8%)
Statins, n (%)	0.96	202 (51.0%)	129 (51.2%)
Diuretics, n (%)	0.92	231 (58.3%)	148 (58.7%)
Oral anticoagulants, n (%)	0.0423	158 (39.9%)	81 (32.0%)
Procedural Characteristics			
Procedure duration, min	0.44	82.5 (78–87)	79.8 (75–84)
Fluoroscopy time, min	0.42	21.9 (20.8–23.0)	22.6 (21.3–23.8)
Contrast volume, mL	0.42	64.4 (60.1–68.7)	61.6 (56.2–67.1)
Conscious sedation, n (%)	0.0161	261 (65.9%)	143 (56.5%)
Transfemoral approach, n (%)	0.88	366 (92.9%)	233 (93.2%)

Valve size, mm	0.0028	24.5 ± 2.4	25.1 ± 2.4
Balloon-expandable, n (%)	0.31	257 (67.1%)	156 (63.2%)

Long-term outcomes of cardiovascular death and heart failure hospitalization across PH status post-TAVI

During the follow-up, 245 of the 2,056 patients (11.9%) experienced the primary composite endpoint of cardiovascular (CV) death or heart failure-related hospitalization. Breaking this down by pulmonary hypertension status, the rates were 10.0 percent (n = 141) in the PH-negative group, 11.9 percent (n = 30) in those whose PH resolved after TAVI (Recovered PH), and 18.7 percent (n = 74) in the Persistent PH group. Looking specifically at CV mortality, the overall rate was 5.5 percent (n = 113), with 4.3 percent (n = 61) in PH-negative, 5.9 percent (n = 15) in Recovered PH, and 9.3 percent (n = 37) in Persistent PH patients. Hospitalizations due to heart failure occurred in 8.1% of all participants (n = 166), comprising 7.0 percent (n = 98) in PH-negative, 6.3 percent (n = 16) in Recovered PH, and 13.1 percent (n = 52) in Persistent PH.

Kaplan-Meier curves without adjustment indicated that patients with Persistent PH had a markedly higher cumulative incidence of the primary endpoint compared with both PH-negative and Recovered PH groups, which showed similar event rates **(Figure 1a)**. Separate analyses for CV death and heart failure hospitalization mirrored this pattern, with Persistent PH patients demonstrating the worst outcomes, while the other two groups had closely overlapping incidence curves **(Figures 1b and 1c)**.



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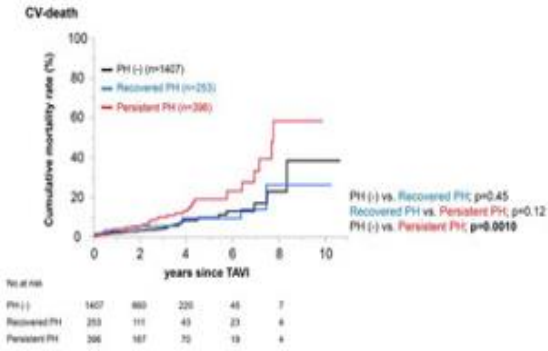

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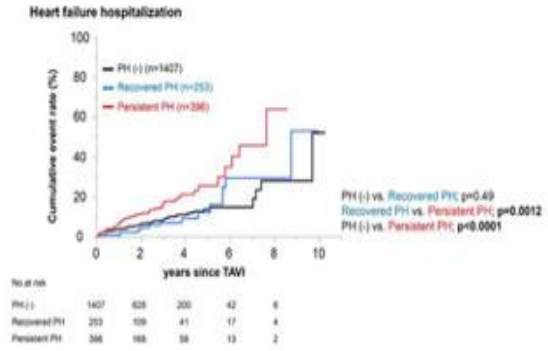


c)

Figure 1. Long-Term Outcomes After TAVI According to Pulmonary Hypertension Status

Kaplan-Meier survival plots showing cumulative events for patients without PH (black), those whose PH resolved after TAVI (Recovered PH, blue), and those with Persistent PH (red). Panels depict the combined endpoint of cardiovascular death or heart failure hospitalization (a), cardiovascular mortality alone (b), and heart failure hospitalization alone (c), with accompanying risk tables indicating cumulative incidence over time.

Prognostic significance of TRPG reduction evaluated by cox regression models

To examine the relationship between changes in tricuspid regurgitation pressure gradient (TRPG) and clinical outcomes, univariate and multivariate Cox proportional hazards models were employed, treating TRPG as a continuous measure. Analyses included both the full cohort and the subgroup with PH prior to TAVI. In multivariate models, a 10 mmHg decline in TRPG was assessed after adjusting for variables identified in univariate analyses and baseline differences between Recovered and Persistent PH patients **(Tables 1 and 2)**.

Univariate modeling showed that factors such as diabetes, atrial fibrillation/flutter, prior stroke, peripheral artery disease, pacemaker implantation, hemoglobin, albumin, estimated glomerular filtration rate, and NT-proBNP

levels were significantly associated with the composite endpoint. Based on this, three analytic models were constructed: an unadjusted model, Model 1 adjusted for age and sex, and Model 2 including age, sex, diabetes, atrial fibrillation/flutter, pacemaker implantation, prior stroke, hemoglobin, albumin, eGFR, and log-transformed NT-proBNP.

Among patients with pre-TAVI PH, a 10 mmHg reduction in TRPG corresponded to a significantly lower risk of the composite outcome of CV death and heart failure hospitalization in both univariate and multivariate analyses (HR: 0.82, 95 percent CI: 0.70–0.96, p = 0.0095; HR: 0.80, 95 percent CI: 0.69–0.94, p = 0.0064; HR: 0.76, 95 percent CI: 0.64–0.90, p = 0.0020). TRPG reduction also independently predicted reduced risk of heart failure hospitalization (HR: 0.75, 95 percent CI: 0.63–0.90, p = 0.0016; HR: 0.75, 95 percent CI: 0.63–0.90, p = 0.0018; HR: 0.70, 95 percent CI: 0.57–0.87, p = 0.0011), while no significant association was observed for CV death alone.

Extending this analysis to the full cohort (PH-negative and PH-positive) confirmed that a decrease of 10 mmHg in TRPG was consistently linked with a lower incidence of heart failure hospitalization across all models. Additionally, in Model 2, TRPG reduction was significantly associated with decreased risk of the composite primary outcome.

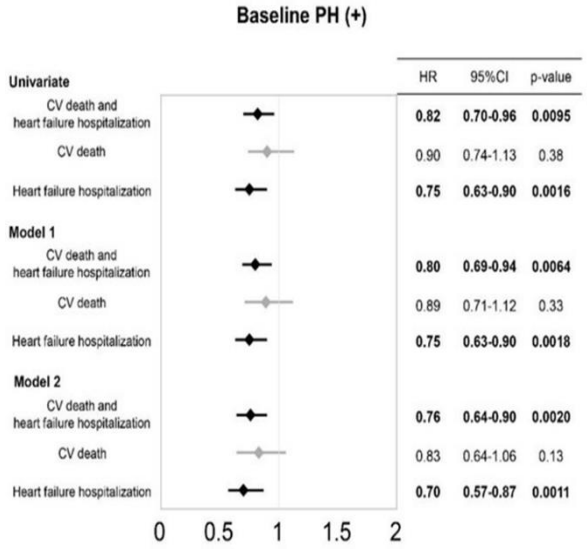


Figure 2. Risk Estimates Associated with Reductions in TRPG Among Patients with Pulmonary Hypertension at Baseline

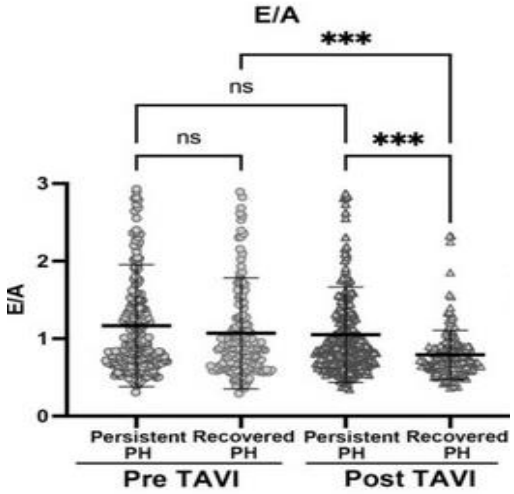
This figure presents hazard ratios corresponding to a 10 mmHg drop in tricuspid regurgitation pressure gradient (TRPG), obtained from both univariate and multivariable Cox regression models. The analysis focused on the primary composite outcome—cardiovascular mortality or hospitalization for heart failure—in patients who had pulmonary hypertension (PH) prior to the procedure. The first adjusted model (Model 1) accounted for age, gender, and baseline TRPG. The more comprehensive model (Model 2) included additional covariates: age, gender, TRPG, atrial fibrillation or flutter, peripheral artery disease, prior pacemaker placement, previous stroke, diabetes, hemoglobin levels, serum albumin, estimated glomerular filtration rate (eGFR), and logarithmically transformed NT-proBNP.

Evolution of echocardiographic parameters reflecting left atrial pressure burden ater TAVI in patients with resolved versus ongoing pulmonary hypertension

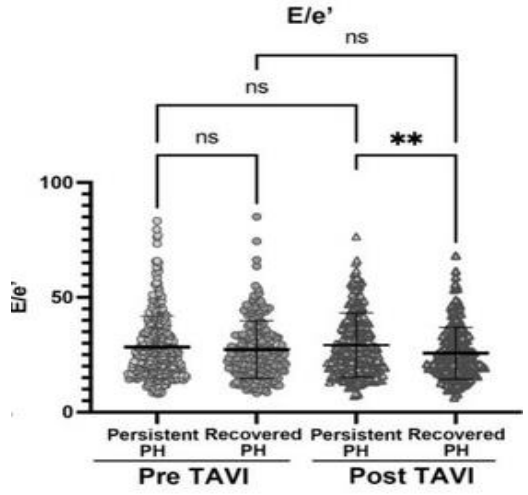
To better understand why TRPG decline following transcatheter aortic valve implantation (TAVI) was linked to better prognosis in this cohort, we compared changes in key echocardiographic markers of left ventricular filling pressure between the groups with persistent PH and those who recovered from PH. These markers included the E/A ratio (early to late diastolic mitral inflow velocities) and the E/e' ratio (early mitral inflow velocity to early diastolic mitral annular velocity).

As depicted in the left panel of **Figure 3**, pre-TAVI E/A values were nearly identical in both groups. Post-procedure, however, the Recovered PH group showed a clear decrease in E/A, whereas no such change occurred in the Persistent PH group. As a result, E/A values after TAVI were notably lower in patients whose PH resolved.

The right panel of **Figure 3** shows a parallel pattern for E/e': after TAVI, this ratio was markedly reduced in the Recovered PH group compared to the Persistent PH group, with a mild decline from baseline observed only in those who recovered from PH.



a)



b)

Figure 3. Variations in E/A and E/e' Ratios Before and After TAVI in PH Patients. Figure legend: Pre- and post-TAVI comparisons of E/A (left) and E/e' (right) ratios in patients with Persistent and Recovered PH. Differences between time points and groups were analyzed using one-way ANOVA. ** indicates $p < 0.01$ and *** indicates $p < 0.001$.

This study investigated how changes in pulmonary hypertension (PH), assessed via echocardiographic TRPG before and shortly after TAVI, relate to long-term outcomes, including the composite of cardiovascular (CV) death and heart failure hospitalization, as well as each component separately. Key observations include: (1) PH, defined as TRPG ≥ 30 mmHg, was present in 28.6% of AS patients undergoing TAVI, with 38.9% of these patients demonstrating a post-TAVI normalization of PH comparable to those without baseline PH; (2) patients whose PH resolved after TAVI exhibited significantly lower risks of the composite endpoint, CV death, and heart failure hospitalization; and (3) echocardiographic markers of diastolic function and left ventricular (LV) filling pressures, specifically E/A and E/e' ratios, improved after TAVI in the Recovered PH group, while remaining unchanged in the Persistent PH group.

TAVI has rapidly evolved as a primary treatment option for severe AS, with expanding indications to include lower-risk patients, driven by device improvements and procedural refinements [3–6, 22]. Accurate risk stratification after TAVI is therefore increasingly critical for guiding management strategies [23, 24].

PH is a well-recognized complication of severe AS, with prevalence estimates ranging from 29% to 56% in prior studies using invasive or non-invasive methods [9, 25–28]; our findings of 28.6% align with this range. PH in AS typically arises from LV pressure overload and diastolic dysfunction, leading to elevated left atrial pressures [28–31]. Historical data indicate that preoperative PH predicts higher perioperative mortality and reduced long-term survival following aortic valve replacement [17]. Relief of AS by either SAVR or TAVI reduces LV, left atrial, mitral valve, and pulmonary vascular load, which can result in PH resolution. Residual PH post-TAVI has been linked to worse survival, and the likelihood of PH improvement appears to depend on the extent of AS-induced cardiovascular remodeling [32, 33].

Most prior studies on PH dynamics and outcomes relied on invasive pressure measurements [32, 33]. By contrast, this study utilized TRPG, a non-invasive echocardiographic parameter reflecting pulmonary artery systolic pressure and pulmonary vascular resistance [15, 34], to assess right ventricular load before and after TAVI. Across the full cohort, TRPG remained largely unchanged, but in patients with baseline PH, TRPG significantly decreased following TAVI. Additionally, E/A and E/e' ratios, indicative of diastolic dysfunction, improved only in the Recovered PH group. These findings suggest a relationship between TRPG and diastolic function indices, implying that TAVI can facilitate not only PH recovery but also reverse cardiac remodeling in patients without advanced irreversible changes, potentially improving prognosis. In contrast, patients with advanced remodeling and persistent PH may derive limited benefit in terms of reduced mortality and heart failure risk [35].

Importantly, a 10 mmHg reduction in TRPG was independently associated with a lower risk of the primary outcome in multivariate analysis, primarily through a reduction in heart failure hospitalization. These results underscore the potential value of earlier TAVI intervention in AS patients, before extensive cardiovascular remodeling leads to the development of PH.

Several factors should be considered when interpreting these results. Firstly, the retrospective nature of the study, combined with a relatively small cohort, may have left residual confounding factors unaccounted for, despite adjustments for TRPG and other covariates in multivariate analyses. Secondly, this study relied on TRPG derived from non-invasive echocardiography as a proxy for pulmonary hypertension, pulmonary artery systolic pressure, and pulmonary vascular resistance, without validation through invasive right heart catheterization [36]. Nevertheless, the study benefits from the use of a prospective multicenter TAVI registry, allowing for detailed pre- and post-procedural echocardiographic assessments that can inform long-term prognostic evaluation and assist in determining optimal timing for TAVI in severe AS patients.

Conclusion

This analysis of a prospective TAVI registry indicates that patients with PH who experience a decrease in TRPG after TAVI have a notably lower risk of the combined endpoint

of cardiovascular death and heart failure hospitalization, compared to patients whose TRPG remains unchanged, highlighting the potential prognostic importance of post-TAVI pulmonary pressure improvement.

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Conflict of interest: None

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Ethics statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board (IRB) of Sakakibara Heart Institute (IRB-ID: 17-048), Juntendo University Hospital (IRB-ID: 17-263), Yamagata University Hospital (IRB-ID: 2019-407), Hirosaki University Hospital (IRB-ID: 2020-040), Mie University Hospital (IRB-ID: H2021-049), and Kawasaki Saiwai Hospital (IRB-ID: R4-13), respectively, and the registry is publicly registered in the University Medical Information Network Japan-Clinical Trials Registry, (UMIN000031133).
Written informed consent has been obtained from the patients to publish this paper.

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