Effect of Pulmonary Hypertension Hemodynamic Presentation on Clinical Outcomes in Patients With Severe Symptomatic Aortic Valve Stenosis Undergoing Transcatheter Aortic Valve Implantation

Insights From the New Proposed Pulmonary Hypertension Classification

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Background—Pulmonary hypertension (PH) frequently coexists with severe aortic stenosis, and PH severity has been shown to predict outcomes after transcatheter aortic valve implantation (TAVI). The effect of PH hemodynamic presentation on clinical outcomes after TAVI is unknown.

Methods and Results—Of 606 consecutive patients undergoing TAVI, 433 (71.4%) patients with severe aortic stenosis and a preprocedural right heart catheterization were assessed. Patients were dichotomized according to whether PH was present (mean pulmonary artery pressure, ≥25 mm Hg; n=325) or not (n=108). Patients with PH were further dichotomized by left ventricular end-diastolic pressure into postcapillary (left ventricular end-diastolic pressure, >15 mm Hg; n=269) and precapillary groups (left ventricular end-diastolic pressure, ≤15 mm Hg; n=56). Finally, patients with postcapillary PH were divided into isolated (n=220) and combined (n=49) subgroups according to whether the diastolic pressure difference (diastolic pulmonary artery pressure−left ventricular end-diastolic pressure) was normal (<7 mm Hg) or elevated (≥7 mm Hg). Primary end point was mortality at 1 year. PH was present in 325 of 433 (75%) patients and was predominantly postcapillary (n=269/325; 82%). Compared with baseline, systolic pulmonary artery pressure immediately improved after TAVI in patients with postcapillary combined (57.8±14.1 versus 50.4±17.3 mm Hg; *P*=0.015) but not in those with precapillary (49.0±12.6 versus 51.6±14.3; *P*=0.36). When compared with no PH, a higher 1-year mortality rate was observed in both precapillary (hazard ratio, 2.30; 95% confidence interval, 1.02–5.22; *P*=0.046) and combined (hazard ratio, 3.15; 95% confidence interval, 1.43–6.93; *P*=0.004) but not isolated PH patients (*P*=0.11). After adjustment, combined PH remained a strong predictor of 1-year mortality after TAVI (hazard ratio, 3.28; *P*=0.005).

Conclusions—Invasive stratification of PH according to hemodynamic presentation predicts acute response to treatment and 1-year mortality after TAVI. **(*Circ Cardiovasc Interv*. 2015;8:e002358. DOI: 10.1161/CIRCINTERVENTIONS.114.002358.)**

Key Words: aortic valve ■ catheterization ■ hemodynamics ■ hypertension ■ hypertension, pulmonary

Pulmonary hypertension (PH) frequently coexists with severe aortic stenosis (AS) and confers a worse prognosis.[1,2] Transcatheter aortic valve implantation (TAVI) is an alternative therapeutic modality to surgical aortic valve replacement (SAVR) for patients with symptomatic severe AS who are either inoperable or high risk for conventional SAVR.[3–5] Patient selection for TAVI relies on clinical and anatomic factors, and risk assessment is a critical component of the procedural planning.[6] Previous studies have shown PH to be a predictor of mortality after TAVI.[7–11] However, studies to date have focused mainly on PH severity rather than hemodynamic presentation and used noninvasive measurements of pulmonary artery systolic pressure (PASP), which correlate only modestly with invasive measurements.[12] According to

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WHAT IS KNOWN

- Pulmonary hypertension (PH) as assessed by noninvasive echocardiography frequently coexists with severe aortic stenosis and confers a worse prognosis among patients undergoing conventional surgical aortic valve replacement.
- PH is a heterogeneous entity, and invasive evaluation of pulmonary artery pressures is the gold standard method to define PH and assess PH severity.

WHAT THE STUDY ADDS

- This article examined the effect of PH hemodynamic presentation on clinical outcomes after transcatheter aortic valve implantation using data derived from invasive evaluation according to the new updated PH hemodynamic definitions.
- Patients with precapillary PH and combined postcapillary and precapillary PH have the worst outcomes after transcatheter aortic valve implantation, whereas patients with isolated postcapillary PH have outcomes similar to patients with no pulmonary PH.

guidelines, right heart catheterization (RHC) remains the gold standard for the accurate diagnosis of PH.[13]

PH is a heterogeneous entity, and according to the updated clinical classification of PH (5th World Symposium on PH, Nice, 2013), 5 groups are recognized (Figure 1).[14,15] Group 2 or postcapillary PH is because of left-sided heart disease and can be distinguished from the other 4 noncardiogenic PH groups (collectively categorized as precapillary PH) according to whether left ventricular (LV) filling pressures are elevated or not. Moreover, left-sided PH can be further stratified into isolated (reversible) and combined postcapillary and precapillary (±reversible) subgroups depending on whether the diastolic pressure difference (DPD) is normal or elevated (Figure 1).[15] Whether PH hemodynamic presentation may help further risk stratify patients undergoing TAVI is unknown. We therefore aimed to assess the effect of PH hemodynamic presentation on clinical outcomes after TAVI using patients without PH as a reference group.

Methods

Patient Population

We performed an analysis of prospectively collected data that included all patients who underwent TAVI at our institution between August 2007 and December 2012. Patients were deemed high risk or inoperable for conventional SAVR by a multidisciplinary heart team. Patient flow is shown in Figure 2. Only patients with severe symptomatic AS (indexed aortic valve area, <0.6 cm^2/m^2) undergoing a preprocedural RHC were considered for inclusion. Of 606 consecutive patients undergoing TAVI during the inclusion period, 471 (78%) patients had a preprocedural RHC. The 135 (22%) patients without a RHC were excluded from this analysis. A further 38 patients were excluded for the reasons shown in Figure 2. The remaining 433 patients with severe symptomatic native valve AS were dichotomized according to whether PH (invasive mean pulmonary artery pressure [mPAP], ≥25 mm Hg) was present (n=325) or not (n=108). Patients with PH were further dichotomized into precapillary (LV end-diastolic pressure [LVEDP], ≤15 mm Hg; n=56) and postcapillary (LVEDP, >15 mm Hg; n=269) subtypes. Finally, patients with postcapillary PH were dichotomized into isolated postcapillary (n=220) and combined postcapillary and precapillary (n=49) subtypes based on whether the DPD was normal (<7 mm Hg) or elevated (≥7 mm Hg). DPD was calculated as diastolic PAP minus LVEDP.[15] In 8 patients, the aortic valve was not crossed and the mean pulmonary arterial wedge pressure was substituted for the LVEDP for group categorization in these patients. This study complies with the Declaration of Helsinki, was approved by the local ethics committee, and all patients provided informed written consent.

Right and Left Heart Catheterization

All included patients underwent diagnostic coronary angiography and complete left and RHC for hemodynamic assessment before TAVI as previously described.[16] Pulmonary artery and intracardiac pressures were measured and recorded using fluid-filled catheters connected to pressure transducers.

Cardiac output (CO) was determined using the modified Fick method with estimated oxygen consumption (VO_2) as previously described and was indexed to body surface area to calculate the cardiac index.[16] Stroke volume was calculated as CO/heart rate and was indexed to body surface area to calculate the stroke volume index. AS severity and arterial and global afterload were calculated as

Definition	Characteristics	Clinical Group(s)*
Pulmonary hypertension (PH)	Mean PA ≥25 mmHg	All
Pre-capillary PH	Mean PA ≥25 mmHg PAWP or LVEDP ≤15mmHg CO normal or reduced	1. Pulmonary arterial hypertension 3. PH due to lung diseases 4. Chronic thromboembolic PH 5. PH with unclear and/or multifactorial mechanisms
Post-capillary PH	Mean PA ≥25 mmHg PAWP or LVEDP >15mmHg CO normal or reduced	2. PH due to left heart disease 2.1. Systolic dysfunction 2.2. Diastolic dysfunction 2.3. Valvular disease 2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies
Isolated post-capillary	DPD <7 mmHg	
Combined post- and pre-capillary	DPD ≥7 mmHg	

*Clinical groups classified according to the 2013 Nice Classification of Pulmonary Hypertension.[14,15]

Figure 1. Hemodynamic definitions of pulmonary hypertension (PH) according to the Proceedings of the 5th World Symposium on Pulmonary Hypertension.[14,15] CO indicates cardiac output; DPD, diastolic pressure difference; LVEDP, left ventricular end-diastolic pressure; PA, pulmonary artery; and PAWP, pulmonary arterial wedge pressure.

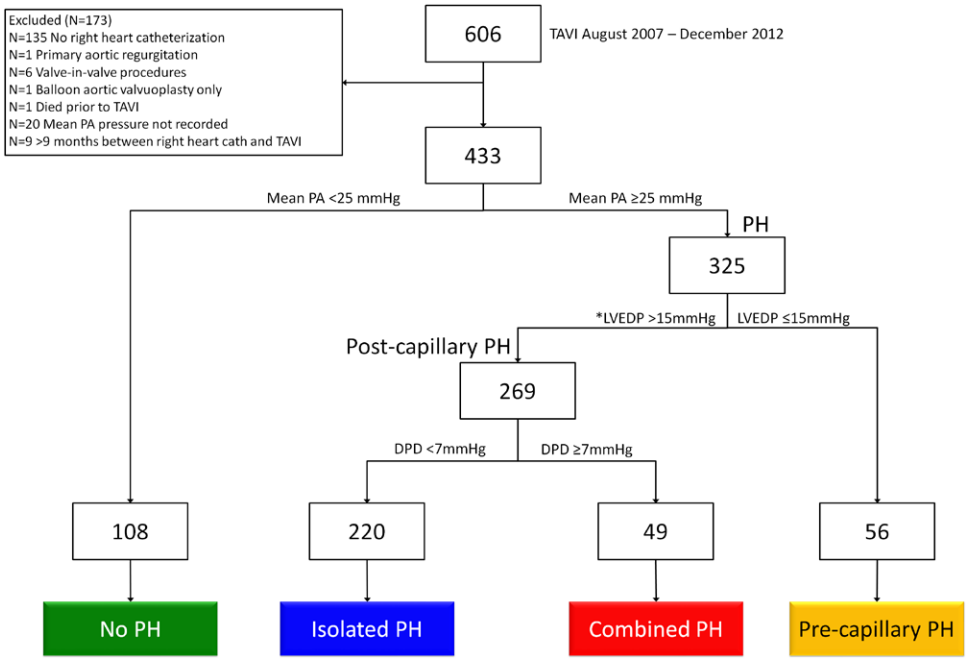

Figure 2. Patient flow. DPD indicates diastolic pressure difference; LVEDP, left ventricular end-diastolic pressure; PA, pulmonary artery pressure; PH, pulmonary hypertension; and TAVI, transcatheter aortic valve implantation. *In 8 patients, the aortic valve was not crossed during preprocedural right heart catheterization, and the pulmonary arterial wedge pressure was used for group categorization in these patients.

previously described.[16] LVEDP was measured at the *Z*-point, which is identified as the point at which the slope of the ventricular pressure upstroke changes on the LV pressure tracing, which corresponds to the R wave on the electrocardiographic tracing. Measurements of LVEDP were made at the end of expiration.

Pulmonary vascular resistance was calculated as transpulmonary gradient/CO (Woods units) and transpulmonary gradient×80/CO (dynes s per cm^5). Pulmonary arterial compliance was calculated as the stroke volume/(sPAP−dPAP), sPAP indicating the systolic PA pressure and dPAP diastolic PA pressure.[17] Right ventricular stroke work index was calculated as stroke volume index×(mPAP−mRAP)×0.0136, with mRAP indicating mean right atrial pressure.[18] A DPD of ≥7 mm Hg is associated with more advanced pulmonary vascular remodeling.[19]

Echocardiography

Transthoracic 2-dimensional echocardiography was performed at baseline using commercially available ultrasound systems (iE33, Philips Medical systems). Acquired images were transferred to a workstation for offline analysis (Syngo Dynamics Workplace, version 9.5, Siemens Medical Solutions, Inc). LV geometric assessment was performed as recommended, and LV mass was calculated using the Devereux formula and indexed to body surface area.[20] LV ejection fraction (LVEF) was calculated according to the Simpsons method. Mitral, aortic, and tricuspid valve regurgitation were evaluated using spectral and color-Doppler images and graded as trivial, mild, moderate, and severe, as recommended.[21] Right ventricular systolic function was assessed using tricuspid annular plane systolic excursion and the pulsed Doppler peak velocity at the annulus as previously described.[22] Aortic valve area was assessed using the continuity equation and indexed to the body surface area.[23] The mean transaortic valve gradient was measured using continuous wave Doppler in the apical 5-chamber view.[23] Maximal tricuspid regurgitant jet velocity combined with central venous pressure measured using the inferior caval vein respiratory variation was used to calculate the PASP.

Transcatheter Aortic Valve Implantation

TAVI was performed as previously described.[24] Vascular access was transfemoral using the Edwards SAPIEN/XT (Edwards Lifesciences, Irvine, CA) or the Medtronic CoreValve Revalving System (Medtronic Inc., Minneapolis, MN), transapical for the Edwards SAPIEN/XT or self-expanding Symetis ACURATE TA valve (Symetis Inc, Switzerland) or transsubclavian using the Medtronic CoreValve Revalving System.

Clinical Follow-Up

Adverse events were assessed in hospital, and regular clinical follow-up was performed at 1, 6, and 12 months by means of a clinical visit or standardized telephone interview. All suspected events were adjudicated by a clinical event committee comprising a cardiac surgeon and an interventional cardiologist. Baseline clinical and procedural characteristics and all follow-up data were entered into a dedicated database, held at an academic clinical trials unit (CTU Bern, Bern University Hospital, Bern, Switzerland) responsible for central data audits and maintenance of the database.

Study End Points

Clinical end points were defined according to the criteria of the Valve Academic Research Consortium-2 consensus document.[25] Primary end point was all-cause mortality at 1 year. Secondary end points included cardiovascular death, major adverse cardiovascular and cerebrovascular events (composite of all-cause mortality, major stroke, and myocardial infarction [MI]), and the composite of death and major stroke at 30 days and 1 year. Other end points included cerebrovascular events (major stroke, minor stroke, and transient ischemic attack) and MI at 30 days and 1 year. In addition, bleeding (life-threatening and major), acute renal failure, vascular complications (major and minor), and rates of pacemaker implantation were assessed at 30 days. New York Heart Association (NYHA) functional class status was assessed at baseline and 1-year follow-up. LVEF, right ventricular function, and PASP were assessed on discharge echocardiography.

Statistics

All patients included into this study were divided into 4 groups as follows: (1) no PH (n=108; mPAP, <25 mm Hg; reference group); (2) precapillary PH (n=56; mPAP, ≥25 mm Hg; LVEDP, ≤15 mm Hg;

precapillary group); (3) postcapillary isolated PH (n=220; mPAP, ≥25 mm Hg; LVEDP, >15 mm Hg; DPD, <7 mm Hg; isolated group); (4) combined postcapillary and precapillary PH (n=49; mPAP, ≥25 mm Hg; LVEDP, >15 mm Hg; DPD, ≥7 mm Hg; combined group).

Discrete data were summarized as counts with percentages with *P* values from χ^2 or Fisher exact tests, whereas continuous data were presented as means±SD with *P* values from 1-way ANOVAs when normally distributed or medians (interquartile range) for skewed data using *P* values from Kruskal–Wallis tests (Tables 1–4). Counts and incidence rates of clinical outcomes at 30-day and 1-year follow-up were computed from Kaplan–Meier life tables for the 4 groups (Table 5; Table I in the Data Supplement). Cox regression was used to compute hazard ratios (HRs) of outcomes (and 95% CI). The proportional hazards assumption was verified for Cox models. Adjusted HRs were estimated from multivariable Cox regressions, adjusting for age, sex, body mass index, diabetes mellitus, previous coronary artery bypass graft surgery, peripheral vascular disease, previous MI, coronary artery disease, LVEF ≤30%, and chronic obstructive pulmonary disease (Table 6). These variables were selected as they are well known to be associated with adverse outcomes after TAVI. No adjustments were made for multiple comparisons. Changes in left and right ventricular function and PASPs after TAVI (difference between discharge and baseline) were analyzed overall and within each group using a linear mixed model taking into account the within-patient correlation (Table 7). Two sided *P* values of <0.05 were considered as statistically significant. All analyses were performed using Stata version 13.0.

Results

Baseline Characteristics

Patient flow is shown in Figure 2. Mean age was 82.4±5.3 years. When compared with isolated and no PH groups, patients with combined and precapillary PH had a significantly higher prevalence of atrial fibrillation (19% versus 15% versus 53% versus 39%; *P*<0.001, respectively) and had significantly higher surgical risk scores (Society for Thoracic Surgeons score, 7.2±5.9% versus 5.9±3.3% versus 7.0±3.6% versus 8.2±5.6%; *P*=0.011 and logistic EuroSCORE 24.1±13.8% versus 18.3±11.0% versus 31.0±15.8% versus 23.9±13.2%; *P*<0.001, respectively). All 3 PH groups were significantly more symptomatic according to NYHA functional status when compared with patients with no PH. Significantly more patients with precapillary PH were taking oral anticoagulation, angiotensin-converting enzyme/angiotensinogen receptor II blockers, and calcium channel blockers when compared with other groups (Table 1).

Echocardiographic and Invasive Hemodynamic Characteristics

Echocardiographic and invasive hemodynamic data are summarized in Tables 2 and 3, respectively. Both isolated and combined PH patients had smaller aortic valve areas when compared with patients with no PH. Patients with combined PH had a lower LVEF when compared with other groups. Both combined and precapillary PH patients had worse right ventricular function and a higher prevalence of moderate to severe tricuspid regurgitation. Patients with combined PH had a higher prevalence of moderate to severe mitral regurgitation when compared with patients with no PH. RHC was performed a median of 20 days (interquartile range, 8–39 days) before TAVI. When compared with no PH groups, combined and precapillary PH patients had lower COs, cardiac indices, faster heart rates, higher pulmonary vascular resistances, lower pulmonary arterial compliances, and higher transpulmonic gradients. Patients with combined PH had a worse severity of PH when compared with both other PH groups, whereas patients with isolated PH had a significantly worse severity of PH when compared with precapillary patients.

Procedural Characteristics

Procedural data are summarized in Table 4. Most patients underwent TAVI via the transfemoral route with 14% of patients undergoing either staged or concomitant percutaneous coronary intervention.

Clinical Outcomes

One-year clinical follow-up was completed for 415 of 433 (96%) patients. Unadjusted and adjusted clinical events at 1-year follow-up are presented in Tables 5 and 6, respectively. Although there were no significant differences in all-cause mortality between groups at 30 days, a trend toward a higher rate of cardiac mortality was observed among patients with precapillary PH at 30 days when compared with those without PH (unadjusted HR, 5.11; 95% confidence interval (CI), 0.99–26.35), but this did not reach statistical significance (*P*=0.051). There were no statistically significant differences in other clinical end points at 30 days between the study groups (Table I in the Data Supplement).

Mortality over time ≤12 months for all-cause mortality and cardiac death among patients stratified according to the presence or absence of PH is shown in Figure 3 and stratified according to the 4 hemodynamic subgroups in Figure 4.

When compared with patients without PH, patients with PH had a statistically significant higher overall mortality rate at 1 year (19.7% versus 10.3%; unadjusted HR, 2.03; 95% CI, 1.07–3.85; *P*=0.030; Figure 3; Table II in the Data Supplement). After adjustment, PH remained a predictor for all-cause mortality at 1 year (adjusted HR, 1.95; 95% CI, 1.01–3.76; *P*=0.046; Table III in the Data Supplement).

When stratified according to the 4 hemodynamic subgroups, patients with precapillary PH had a higher rate of death (10.3% versus 21.7%; unadjusted HR, 2.30; 95% CI, 1.02–5.22; *P*=0.046) compared with patients without PH, which was driven mainly by cardiac death (unadjusted HR, 3.00; 95% CI, 1.14–7.88; *P*=0.026) at 1 year. After adjustment, however, differences in death (adjusted HR, 1.90; 95% CI, 0.83–4.35; *P*=0.13) and cardiac death (adjusted HR, 2.25; 95% CI, 0.85–5.97; *P*=0.11) were no longer significant. No statistically significant differences in death (adjusted HR, 1.75; 95% CI, 0.88–3.49; *P*=0.11) or cardiac death (adjusted HR, 1.55; 95% CI, 0.65–3.71; *P*=0.33) were observed between no PH and isolated PH groups. When compared with patients with no PH, those with combined PH had a higher rate of death (10.3% versus 29.0%; unadjusted HR, 3.15; 95% CI, 1.43–6.93; *P*=0.004) driven predominantly by cardiac death (unadjusted HR, 3.84; 95% CI, 1.49–9.91; *P*=0.005) at 1 year. After adjustment for age, sex, body mass index, diabetes mellitus, previous coronary artery bypass graft, previous MI, peripheral vascular disease, coronary artery disease, chronic obstructive pulmonary disease, and LVEF ≤30%, combined PH remained a strong predictor for death (adjusted HR, 3.28; 95% CI, 1.43–7.53; *P*=0.005) and cardiac death (adjusted HR, 3.81; 95% CI, 1.40–10.36; *P*=0.009) at 1 year.

Table 1. Baseline Characteristics

		PH			
	No PH n=108	Precapillary n=56	Isolated n=220	Combined n=49	*P* Value
Age, y	81.7±5.4	82.9±4.1	82.6±5.2	82.2±6.2	0.48
Female, sex, n (%)	48 (44)	33 (59)	124 (56)†	32 (65)	0.059
Height, cm	165.2±8.0	166.5±7.8	164.4±8.6	163.7±7.2	0.27
Weight, kg	72.6±15.5	73.9±17.1	71.2±14.5	70.0±13.9	0.50
Body mass index, kg/m^2	26.5±5.1	26.6±5.8	26.3±5.0	26.2±5.1	0.95
Body surface area, m^2	1.8±0.2	1.9±0.2	1.8±0.2	1.8±0.2	0.42
Cardiac risk factors					
Diabetes mellitus, n (%)	31 (29)	23 (41)	58 (26)	14 (29)	0.20
Hypercholesterolemia, n (%)	75 (69)	34 (61)	145 (66)	31 (63)	0.70
Hypertension, n (%)	95 (88)	45 (80)	189 (86)	40 (82)	0.52
Current smoker, n (%)	11 (12)	6 (11)	15 (7)	6 (15)	0.36
Past medical history					
Coronary artery disease, n (%)	63 (58)	35 (63)	144 (65)	28 (57)	0.53
Multivessel disease, n (%)	27 (69)	14 (61)	54 (70)	7 (47)	0.32
Previous myocardial infarction, n (%)	17 (16)	9 (16)	34 (15)	5 (10)	0.80
Previous coronary artery bypass graft, n (%)	10 (9)	4 (7)	13 (6)	3 (6)	0.73
Previous percutaneous coronary intervention, n (%)	35 (32)	18 (32)	58 (26)	8 (16)	0.16
Previous stroke, n (%)	5 (5)	2 (4)	7 (3)	2 (4)	0.93
Peripheral vascular disease, n (%)	24 (22)	13 (23)	37 (17)	14 (29)	0.24
Chronic obstructive pulmonary disease, n (%)	18 (17)	14 (25)	34 (15)	10 (20)	0.38
Renal failure (GFR<60 mL/min per 1.73 m^2)	74 (81)	37 (80)	148 (84)	37 (84)	0.93
Baseline cardiac rhythm					
Atrial fibrillation, n (%)	8 (15)	19 (53)*	21 (19)	12 (39)‡	<0.001
Symptoms					
Syncope, n (%)	20 (19)	9 (16)	28 (13)	3 (6)	0.18
NYHA functional class					
NYHA III/IV, n (%)	60 (59)	44 (80)*	157 (76)†	40 (83)‡	0.002
CCS angina status					
CCS III/IV, n (%)	19 (18)	9 (16)	31 (14)	5 (10)	0.65
Risk assessment					
Logistic EuroScore (%)	15.4 (10.0–25.0)	22.5 (12.1–32.5)*	22.0 (13.4–31.6)†	29.0 (17.3–43.9)‡	<0.001
STS score (%)	4.7 (3.5–7.9)	6.8 (4.3–9.8)*	5.7 (4.0–8.0)†	6.0 (4.5–9.1)‡	0.016
Medications					
Aspirin, n (%)	75 (70)	31 (55)	147 (67)	27 (56)	0.14
Clopidogrel, n (%)	29 (27)	9 (16)	42 (19)	5 (10)	0.08
Oral anticoagulation, n (%)	21 (20)	28 (50)*	46 (21)	17 (35)‡	<0.001
Diuretic, n (%)	72 (67)	45 (80)	153 (70)	38 (79)	0.19
β-blocker, n (%)	51 (48)	30 (54)	121 (55)	26 (54)	0.64
ACEi/ARB, n (%)	38 (36)	34 (61)*	78 (36)	18 (38)	0.005
Ca channel blocker, n (%)	21 (20)	9 (16)	46 (21)	2 (4)‡	0.049
Statin, n (%)	58 (54)	24 (43)	109 (50)	19 (40)	0.29
Laboratory values					
Brain natriuretic peptide, pg/mL	174.5 (106.0–358.3)	256.0 (113.5–534.5)	358.0 (158.5–876.5)†	624.0 (274.0–1510.0)‡	<0.001

Depicted are mean±SD with *P* values from ANOVAs or counts (%) with *P* values from χ^2 tests. For skewed variables depicted are median (interquartile range) with *P* values from Kruskal–Wallis test. Body surface area is computed using Haycock formula. GFR is computed using Cockroft–Gault formula. ACEi/ARB indicates angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; CCS, Canadian Cardiovascular Society; GFR, Glomerular filtration rate; NYHA, New York Heart Association; PH, pulmonary hypertension; and STS, Society of Thoracic Surgeons.

*P<0.05, no PH vs precapillary PH.

†P<0.05, no PH vs isolated PH.

‡P<0.05, no PH vs combined PH.

Table 2. Echocardiographic Characteristics

	No PH n=108	PH			*P* Value
		Precapillary n=56	Isolated n=220	Combined n=49	
Aortic stenosis severity					
Aortic valve area, cm^2	0.65±0.22	0.62±0.26	0.57±0.22†	0.54±0.20‡	0.008
Indexed aortic valve area, cm^2/m^2	0.36±0.12	0.33±0.14	0.32±0.12†	0.31±0.12‡	0.034
Aortic maximal velocity, cm/s	3.82±1.11	3.78±0.88	4.08±0.82	3.66±0.75	0.15
Mean gradient, mm Hg	42.3±16.9	40.1±17.1	44.1±17.3	40.0±15.9	0.26
Peak gradient, mm Hg	68.0±25.2	59.4±23.5	71.9±27.2	60.2±23.1	0.019
LV geometry and 2D measurements					
LV end-systolic diameter, mm	32.9±10.4	31.6±11.5	33.2±11.9	39.0±13.1	0.20
LV end-diastolic diameter, mm	48.9±9.8	46.0±9.8	48.0±10.6	50.2±9.0	0.63
LV mass index, g/m^2	142.6±43.7	149.6±60.8	150.7±42.0	143.3±39.0	0.80
LV systolic function					
LV ejection fraction, %	56.9±13.1	54.6±13.4	51.2±15.4†	44.2±15.9‡	<0.001
RV systolic function					
TAPSE, mm	19.2±4.6	16.4±4.8	18.9±5.6	15.4±4.8‡	0.016
DTI, cm/s	12.2±2.8	10.9±4.2	11.7±2.7	10.3±2.8‡	0.09
Associated valvular abnormality					
Aortic regurgitation					
None	22 (23%)	15 (28%)	46 (23%)	8 (16%)	0.36
Mild	67 (69%)	34 (64%)	130 (66%)	34 (69%)	
Moderate	8 (8%)	4 (8%)	21 (11%)	6 (12%)	
Severe	0 (0%)	0 (0%)	0 (0%)	1 (2%)	
Mitral regurgitation	…	…	…	…‡	<0.001
None	8 (8%)	2 (4%)	15 (7%)	5 (10%)	
Mild	77 (76%)	39 (70%)	145 (69%)	18 (37%)	
Moderate	15 (15%)	14 (25%)	46 (22%)	20 (41%)	
Severe	1 (1%)	1 (2%)	4 (2%)	6 (12%)	
Tricuspid regurgitation	…	…*	…	…‡	<0.001
None	21 (22%)	8 (16%)	46 (24%)	9 (19%)	
Mild	68 (71%)	25 (49%)	118 (63%)	26 (55%)	
Moderate	7 (7%)	17 (33%)	22 (12%)	9 (19%)	
Severe	0 (0%)	1 (2%)	2 (1%)	3 (6%)	
Right sided hemodynamics					
RV–RA gradient, mm Hg	31.1±8.9	40.5±10.3*	41.1±12.2†	48.2±12.6‡	<0.001
Central venous pressure, mm Hg	7.9±3.9	10.1±8.8	8.9±3.7	10.3±4.5‡	0.07
Pulmonary artery systolic pressure, mm Hg	39.0±10.9	50.7±15.8*	50.2±13.6†	58.4±14.4‡	<0.001

Depicted are mean±SD with *P* values from ANOVAs or counts (%) with *P* values from Fisher exact tests. DTI indicates pulse Doppler peak velocity at the annulus; LV, left ventricle; PH, pulmonary hypertension; RA, right atrial; RV, right ventricle; and TAPSE, tricuspid annular plane systolic excursion.

*$P<0.05$, no PH vs precapillary PH.

†$P<0.05$, no PH vs isolated PH.

‡$P<0.05$, no PH vs combined PH.

Both precapillary (HR, 2.24; 95% CI, 1.05–4.76; $P=0.04$) and combined PH (HR, 2.86; 95% CI, 1.36–6.01; $P=0.006$) had a higher incidence of the composite end point of death or major stroke at 1 year. After adjustment, only combined PH remained as a predictor or death or major stroke (adjusted HR, 3.10; 95% CI, 1.41–6.79; $P=0.005$). Combined PH was also a predictor of the composite end point of death, major stroke, or MI at 1 year (adjusted HR, 3.13; 95% CI, 1.49–6.58; $P=0.003$) after adjustment. No statistically significant differences in the other end points were observed at 1 year.

NYHA Functional Class Improvement

NYHA functional class improvement at baseline and 12 months is shown in Figure 5. At 12-month follow-up, 13.2% and 10.0% of patients with precapillary PH and combined PH remained in NYHA>II functional class when compared

Table 3. Invasive Hemodynamic Characteristics

	No PH n=108	PH			*P* Value
		Precapillary n=56	Isolated n=220	Combined n=49	
Aortic stenosis severity					
Aortic valve area, cm^2	0.63±0.23	0.57±0.26	0.55±0.25†	0.51±0.20‡	0.009
Indexed aortic valve area, cm^2/m^2	0.35±0.13	0.32±0.15	0.31±0.14†	0.29±0.12‡	0.014
Peak-to-peak gradient, mm Hg	48.2±23.1	46.1±28.2	55.5±26.8†	47.1±26.6	0.016
Mean gradient, mm Hg	43.1±16.2	39.8±16.0	44.2±17.4	38.2±15.4	0.08
Systemic vascular load					
Systolic arterial pressure, mm Hg	133.8±25.7	125.8±23.6	138.6±30.7	135.6±27.4	0.023
Diastolic arterial pressure, mm Hg	61.8±12.4	63.0±12.1	66.6±14.2†	71.4±14.3‡	<0.001
Mean arterial pressure	90.2±16.5	88.6±14.8	95.5±18.8†	97.9±16.9‡	0.003
Systemic vascular resistance, mm Hg/min per L	1805±543	1942±714	1938±644	2264±769‡	0.001
LV systolic function					
Ejection fraction, %	58.5±13.3	54.7±13.4	51.3±15.3†	43.7±16.1‡	<0.001
LV systolic pressure, mm Hg	183.5±31.4	171.5±33.3*	194.1±35.7†	186.4±31.3	<0.001
LV end diastolic pressure, mm Hg	17.0±6.7	11.2±2.8*	26.0±6.4†	21.9±4.7‡	<0.001
Stroke volume, mL	54.7±14.4	46.0±14.5*	50.7±15.3†	38.8±13.7‡	<0.001
Stroke volume index, mL/m^2	30.5±7.2	25.6±7.3*	28.4±7.8†	21.9±7.2‡	<0.001
Cardiac output, L/min	4.0±0.9	3.6±1.0*	3.8±1.0	3.3±1.2‡	0.001
Cardiac index, L/min m^2	2.3±0.4	2.0±0.5*	2.1±0.5	1.9±0.6‡	<0.001
Heart rate, bpm	74.7±10.7	80.8±15.8*	77.7±13.4	89.5±22.2‡	<0.001
Right sided hemodynamics					
PA systolic pressure, mm Hg	32.2±5.8	51.5±11.6*	56.1±12.1†	73.9±16.3‡	<0.001
PA systolic pressure ≥60 mm Hg, n (%)	0 (0%)	14 (25%)*	75 (34%)†	40 (82%)‡	<0.001
PA diastolic pressure, mm Hg	10.5±4.0	19.6±5.6*	22.3±6.0†	33.6±5.8‡	<0.001
Mean PA pressure, mm Hg	18.9±4.3	33.1±6.7*	36.4±7.6†	50.1±7.9‡	<0.001
Pulmonary arterial compliance, mL/mm Hg	1.5±0.5	0.9±0.3*	0.9±0.4†	0.6±0.3‡	<0.001
Diastolic pulmonary gradient, mm Hg	–6.3±7.5	8.4±6.9*	-3.7±6.2†	11.6±4.9‡	<0.001
Transpulmonic gradient, mm Hg	2.1±7.5	21.9±7.8*	10.3±7.9†	28.3±7.6‡	<0.001
Pulmonary vascular resistance, dynes s per cm^5	45.7±160.0	539.5±281.1*	246.6±206.9†	745.2±292.6‡	<0.001
Pulmonary vascular resistance, Wood units	0.6±2.0	6.7±3.5*	3.1±2.6†	9.3±3.7‡	<0.001
RV systolic pressure, mm Hg	33.8±7.0	49.1±13.8*	54.9±11.9†	72.2±16.7‡	<0.001
RV diastolic pressure, mm Hg	6.0±3.4	8.3±4.9*	11.1±4.9†	14.8±5.2‡	<0.001
RA mean pressure, mm Hg	4.5±3.5	8.3±5.2*	8.6±4.4†	12.0±4.9‡	<0.001
Right ventricular stroke work index, g m per m^2 per beat	6.0±2.2	8.6±3.3*	10.4±3.3†	11.4±5.0 ‡	<0.001

Depicted are mean±SD with *P* values from ANOVAs. LV indicates left ventricle; PA, pulmonary artery; PH, pulmonary hypertension; RA, right atrial; and RV, right ventricle.

*$P<0.05$, no PH vs precapillary PH.

†$P<0.05$, no PH vs isolated PH.

‡$P<0.05$, no PH vs combined PH.

with 9.0% and 7.9% of patients with isolated and no PH, respectively.

Echocardiographic Outcomes

Acute changes in biventricular function and PASPs are shown in Table 7. Significant improvements in right ventricular function and PASPs were observed in both isolated and combined PH groups. No statistically significant improvements in right ventricular function or PASP were observed in the precapillary PH group (Figure 6).

Discussion

This study demonstrates that PH hemodynamic presentation affects procedural outcome of patients undergoing TAVI. We found that when compared with patients without PH, 1-year mortality was higher in both precapillary and combined PH patients but not in patients with isolated PH. These findings have relevant clinical implications because PH is frequent in patients undergoing TAVI with a prevalence reported in previous studies between 10% and 42%.[9,26–30] In our study, 3 quarters of patients (75%) with symptomatic severe AS

Table 4. Procedural Characteristics

	No PH n=108	PH			*P* Value
		Precapillary n=56	Isolated n=220	Combined n=49	
Access route					
Femoral, n (%)	83 (77)	47 (84)	182 (83)	37 (76)	0.27
Apical, n (%)	25 (23)	9 (16)	33 (15)	11 (22)	
Subclavian, n (%)	0 (0)	0 (0)	5 (2)	1 (2)	
Valve type					
Medtronic CoreValve, n (%)	53 (49)	30 (54)	120 (55)	31 (63)	0.10
Edwards Sapien valve, n (%)	54 (50)	23 (41)	98 (45)	16 (33)	
Symetis valve, n (%)	1 (1)	3 (5)	2 (1)	2 (4)	
Procedural specifications					
Device success, n (%)	100 (93)	45 (82)	186 (86)	42 (86)	0.17
No device success; AR ≥2+, n (%)	8 (7)	10 (18)	26 (12)	6 (12)	0.25

Depicted are counts (%) with *P* values from Fisher exact tests. No pairwise comparison (no PH vs precapillary PH, no PH vs isolated PH, and no PH vs combined PH) was significant at α of 0.05. AR indicates aortic regurgitation; and PH, pulmonary hypertension.

undergoing TAVI had PH based on preprocedural invasive hemodynamic evaluations and almost one third had severe PH (invasive PASP, ≥60 mm Hg).

Several studies have demonstrated that PH affects outcomes in patients with severe AS independent of the treatment modality. Malouf et al[2] reported that patients with severe PH and AS had a poor prognosis when treated conservatively but had a high perioperative mortality with conventional SAVR. Similarly, Melby et al[31] reported that operative mortality was nearly doubled in patients undergoing conventional SAVR in the presence of PH and that PH resulted in a decreased long-term survival. A PASP of >60 mm Hg has been described as a strong independent predictor of both in-hospital and long-term mortality among patients undergoing SAVR.[32] Among TAVI patients, previous studies reported PH to be an independent predictor of late, rather than early, mortality after the procedure.[7,8] Tamburino et al[7] reported that PASP >60 mm Hg was an independent predictor of overall, but not early, mortality among patients with severe AS undergoing TAVI. Similarly, in a subanalysis of the French Aortic National CoreValve and Edwards (FRANCE 2) Registry (n=2435), Lucon et al[8] observed no significant effect of PH severity on 30-day mortality, but severe PH (PASP, >60 mm Hg) was an independent predictor of 1-year mortality.

Concordant with these previous findings, PH was associated with worse clinical outcomes at 1 year in our study when compared with patients without PH. However, PH hemodynamic presentation is heterogeneous with various underlying

Table 5. Unadjusted Clinical Outcomes at 1 y

	Reference	PH			Precapillary vs No PH		Isolated vs No PH		Combined vs No PH	
	No PH n=108	Precap n=56	Isolated n=220	Combined n=49	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
1-y Follow-Up										
All-cause death, n (%)	11 (10.3)	12 (21.7)	37 (17.1)	14 (29.0)	2.30 (1.02–5.22)	0.046	1.73 (0.88–3.39)	0.11	3.15 (1.43–6.93)	0.004
Cardiovascular death, n (%)	7 (6.7)	10 (18.2)	23 (10.8)	11 (23.6)	3.00 (1.14–7.88)	0.026	1.68 (0.72–3.92)	0.23	3.84 (1.49–9.91)	0.005
Cerebrovascular events	7 (6.6)	4 (7.8)	7 (3.3)	4 (8.2)	1.13 (0.33–3.87)	0.84	0.50 (0.17–1.42)	0.19	1.33 (0.39–4.54)	0.65
Major stroke, n (%)	4 (3.7)	4 (7.8)	6 (2.8)	4 (8.2)	1.98 (0.49–7.90)	0.34	0.74 (0.21–2.64)	0.65	2.31 (0.58–9.22)	0.24
Minor stroke, n (%)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	…	…	…	…	…	…
Transient ischemic attack, n (%)	3 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)	…	…	…	…	…	…
Myocardial infarction, n (%)	2 (2.0)	0 (0.0)	4 (1.9)	2 (4.5)	…	…	…	…	…	…
All-cause death or major stroke, n (%)	13 (12.1)	14 (25.3)	41 (18.9)	15 (31.0)	2.24 (1.05–4.76)	0.037	1.61 (0.86–3.01)	0.13	2.86 (1.36–6.01)	0.006
All-cause death, major stroke, or MI, n (%)	15 (14.0)	14 (25.3)	42 (19.3)	16 (33.1)	1.92 (0.93–3.98)	0.08	1.42 (0.79–2.57)	0.24	2.65 (1.31–5.36)	0.007

Depicted are counts (incidence rates, %). HRs (95% [CI]) are from Cox Regressions. CI indicates confidence interval; HR, hazard ratio; MI, myocardial infarction; and PH, pulmonary hypertension.

Table 6. Adjusted Clinical Outcomes at 1 y

	Precapillary vs No PH		Isolated vs No PH		Combined vs No PH	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
1-y Follow-Up						
All-cause death, n (%)	1.90 (0.83–4.35)	0.13	1.75 (0.88–3.49)	0.11	3.28 (1.43–7.53)	0.005
Cardiovascular death, n (%)	2.25 (0.85–5.97)	0.11	1.55 (0.65–3.71)	0.33	3.81 (1.40–10.36)	0.009
All-cause death or major stroke, n (%)	1.94 (0.90–4.18)	0.09	1.67 (0.88–3.15)	0.12	3.10 (1.41–6.79)	0.005
All-cause death, major stroke, or MI, n (%)	1.74 (0.83–3.65)	0.14	1.52 (0.83–2.79)	0.17	3.13 (1.49–6.58)	0.003

Depicted are counts (incidence rates, %). Adjusted HRs (95% [CI]) are from multivariable Cox regressions, adjusting for age, sex, diabetes mellitus, body mass index, previous coronary artery bypass grafting, previous myocardial infarction, peripheral vascular disease, coronary artery disease, left ventricular ejection fraction ≤30%, chronic obstructive pulmonary disease known to be associated with these adverse outcomes. CI indicates confidence interval; HR, hazard ratio; MI, myocardial infarction; and PH, pulmonary hypertension.

pathophysiological mechanisms. In general, based on the proceedings of the 5th World Symposium on PH in Nice, 2013, 3 hemodynamic presentations of PH are recognized: precapillary, isolated postcapillary, and combined postcapillary and precapillary PH (Figure 1), and this replaces the older PH classification, which was based on the proceedings of the 4th World Symposium on PH (Figure I in the Data Supplement).[14,15] Either the LVEDP or pulmonary arterial wedge pressure can be used for hemodynamic stratification of PH and the use of either variable did not substantially change the group classification in this study (Table IV in the Data Supplement).[13] This study is the first to assess the effect of PH hemodynamic presentation on clinical outcomes after TAVI using the updated invasive definitions.

Postcapillary PH

Postcapillary or left-sided PH is the most common form of PH in Western countries.[33] In this study, postcapillary PH accounted for the vast majority (82%) of PH among patients with symptomatic severe AS undergoing TAVI and was mostly comprised of isolated postcapillary PH. Left-sided PH was observed to have markedly different long-term prognostic implications after TAVI depending on whether the DPD was normal (ie, isolated postcapillary) or elevated (ie, combined postcapillary and precapillary). Patients with combined PH had significantly worse 1-year outcomes. Patients with combined PH were observed to have a more insidious form of PH on RHC when compared with patients with isolated PH. PH severity was worse among patients with combined PH leading to a more impaired right ventricular function when compared with patients with isolated PH. In addition, pulmonary vascular resistance was elevated suggesting intrinsic changes in the pulmonary vascular bed. By definition, all patients with combined PH had a DPD of ≥7 mm Hg, which has previously been shown to be associated with more advanced pulmonary vascular remodeling.[19] Conversely, in isolated postcapillary PH, the elevation of PASP is thought to be solely due to the passive backward transmission of an increased LV filling pressure (LVEDP, ≥15 mm Hg). The hemodynamic characteristics of patients with isolated PH in this study support this hypothesis, with patients with isolated PH having near normal PVR values. Isolated postcapillary PH is considered reversible, and this may explain why clinical outcomes of patients with isolated PH were similar to patients without PH after TAVI. In patients with severe AS and LV hypertrophy, it may be expected that diastolic LV dysfunction persists after TAVI, causing persistent postcapillary PH in the majority of patients and this could be prognostically relevant. Further studies are needed to assess whether diastolic dysfunction after TAVI is related to persistence of postcapillary PH.

Precapillary PH

Precapillary PH is less common than postcapillary PH but is a far more heterogeneous entity.[14] In our study, it accounted for less than one fifth of PH among patients with symptomatic severe AS undergoing TAVI but was associated with worse clinical outcomes and less functional improvement at 1 year when compared with patients without PH. The relative number of patients classified as precapillary PH in the present analysis seems to be surprisingly high (13%), as most

Table 7. Changes in Left and Right Ventricular Function and Pulmonary Artery Systolic Pressure After Transcatheter Aortic Valve Implantation

				Pulmonary Hypertension								
	No Pulmonary Hypertension			Precapillary			Isolated			Combined		
	Baseline	Discharge	*P* Value	Baseline	Discharge	*P* Value	Baseline	Discharge	*P* Value	Baseline	Discharge	*P* Value
LVEF, %	56.8±13.2	57.5±9.5	0.82	54.9±13.2	54.8±12.9	0.46	51.3±15.5	54.3±13.0	<0.001	44.1±16.1	48.5±14.9	0.008
TAPSE, mm	19.2±4.6	20.2±5.3	0.37	16.1±4.8	18.2±6.1	0.11	19.0±5.7	20.7±6.4	0.060	15.7±4.7	18.5±4.9	0.056
DTI, cm/s	12.2±2.8	13.8±4.1	0.006	11.2±4.4	12.3±2.2	0.39	11.8±2.7	13.7±3.6	<0.001	10.3±2.9	12.0±2.8	0.024
PASP, mm Hg	39.0±10.9	38.1±9.6	0.61	49.0±12.6	51.6±14.3	0.36	50.2±13.7	44.9±14.3	0.001	57.8±14.1	50.4±17.3	0.015

Depicted are crude mean±SD with *P* values from a linear mixed model taking into account the within-patient correlation (random intercept). Eight patients who died in hospital (before discharge) are excluded from the model. DTI indicates pulse Doppler peak velocity at the annulus; LVEF, left ventricular ejection fraction; PASP, pulmonary artery systolic pressure; and TAPSE, tricuspid annular plane systolic excursion.

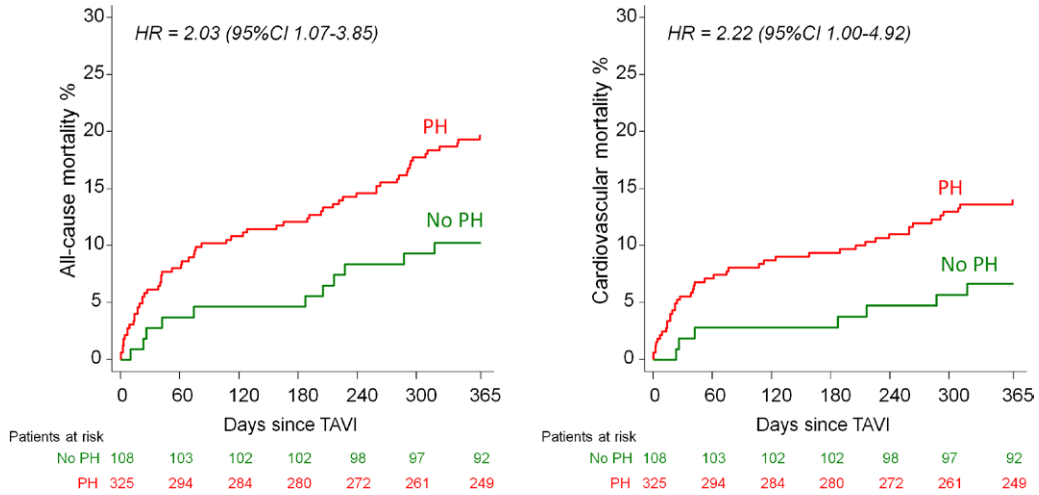

Figure 3. Kaplan–Meier analysis of death (**A**) and cardiovascular death (**B**) at 1 year among patients with and without pulmonary hypertension (PH; invasive mean pulmonary artery pressure ≥25 mm Hg) at baseline. CI indicates confidence interval; HR, hazard ratio; and TAVI; transcatheter aortic valve implantation.

patients would be expected to have postcapillary PH. However, Kaple et al[33] reported in an entirely separate cohort of patients, a similar proportion of patients (20/168; 12%) with severe AS undergoing TAVI to have precapillary (pulmonary arterial wedge pressure, <15 mm Hg; mPAP, ≥25 mm Hg) PH on invasive hemodynamic evaluation. It should be noted that left heart disease (and not pulmonary vascular disease) may still be the reason for PH even if the LVEDP/pulmonary arterial wedge pressure is <15 mm Hg, particularly in patients pretreated with diuretics. However, no significant differences in the proportion of patients taking diuretics were observed between groups (Table 1). Furthermore, patients with precapillary PH had entirely different echocardiographic and invasive hemodynamic characteristics when compared with patients with postcapillary PH. For example, patients with precapillary PH had a less severe form of AS and better LV systolic function when compared with patients with postcapillary PH. Conversely, patients with precapillary PH had similar degrees of RV dysfunction when compared with patients with combined PH and a higher prevalence of moderate to severe tricuspid regurgitation when compared with all other groups. Furthermore, patients with precapillary PH had lower PA pressures but higher PVR values when compared with patients with isolated PH, suggesting that this group is a bona fide discrete entity. Moreover, PASPs and RV function improved in both postcapillary groups, but not in the precapillary group, further supporting the hypothesis that PH was not because of left-sided heart disease among this patient cohort.

Clinical Implications

This study suggests that the stratification of PH according to the hemodynamic presentation is useful for risk stratification of patients with severe AS being considered for TAVI. Determination of the DPD among patients with severe AS and left-sided PH predicts long-term outcomes after TAVI. Furthermore, hemodynamic stratification of PH also predicts

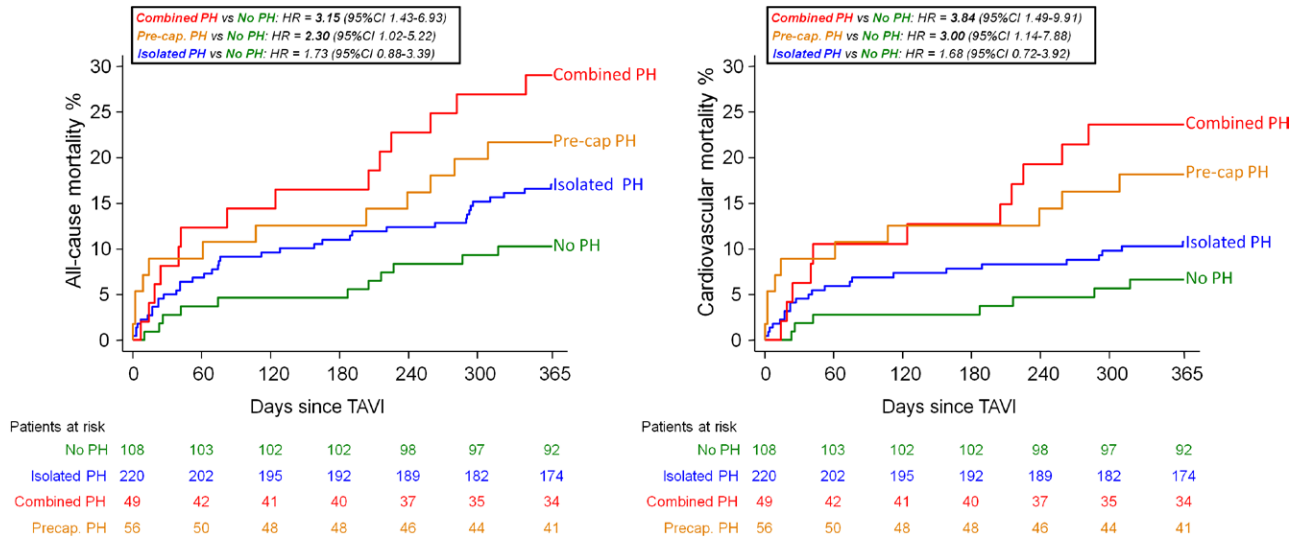

Figure 4. Kaplan–Meier analysis of death (**A**) and cardiovascular death (**B**) at 1 year comparing patients with isolated postcapillary pulmonary hypertension (PH), combined postcapillary and precapillary PH, and precapillary PH with patients without PH. CI indicates confidence interval; HR, hazard ratio; and TAVI; transcatheter aortic valve implantation.

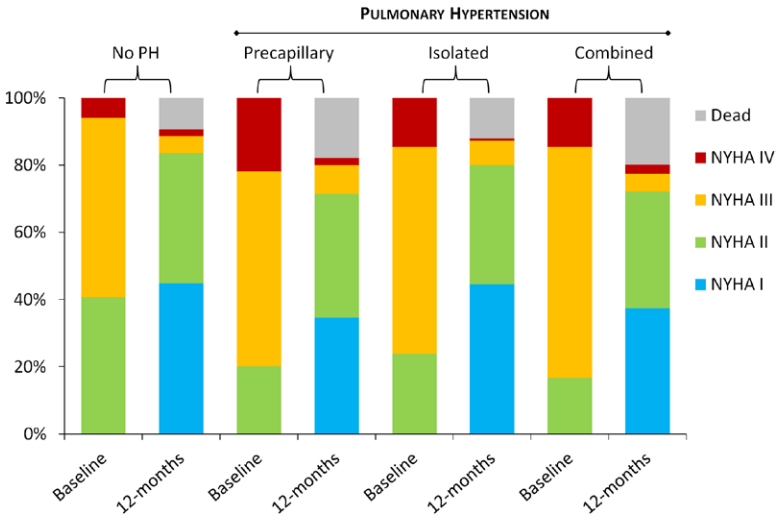

Figure 5. Functional status expressed by the New York Heart Association (NYHA) classification at baseline and 1 year follow-up among patients with severe aortic stenosis and isolated postcapillary pulmonary hypertension (PH), combined postcapillary and precapillary PH, precapillary PH, and no PH.

response to treatment. In contrast to patients with postcapillary PH, neither RV function nor PASP improved after TAVI in patients with precapillary PH, and functional improvement was less at 1-year follow-up. Whether a more tailored therapy with pulmonary vasodilator therapy (eg, Bosentan, Epoprostenol, or Sildenafil) would benefit patients with precapillary PH after TAVI is unknown. This study also raises questions on the most appropriate management of patients with combined postcapillary and precapillary PH. Currently, the mainstay of treatment for left-sided PH is treatment of the underlying cause. However, in this study, we observed worse outcomes among patients with combined PH after TAVI. Whether more targeted therapy with pulmonary vasodilator therapies, such as phosphodiesterase-5 inhibitors, would improve outcomes among patients with combined PH remains unknown.[34]

Limitations

First, this is a single-center observational study and therefore may not reflect general practice. However, all data were collected prospectively and all events were adjudicated by a clinical event committee comprising interventional cardiologists and cardiac surgeons. Second, only patients with preprocedural RHC were included in this study, and therefore, this is not a consecutive patient series. Therefore, the true prevalence of PH in severe AS may have been overestimated because the inclusion of only patients with preprocedural RHC may have led to an enrichment of patients with PH. However, the majority of patients (71%) undergoing TAVI during the inclusion period were included. Third, invasive PAPs were only measured before TAVI but not afterward. Therefore, changes in PASPs before and after TAVI were measured noninvasively using echocardiography, which would not be expected to be as accurate as invasive measurements. Fourth, echocardiographic follow-up beyond discharge is not reported, therefore precluding PASP and right ventricular function assessment during longer term follow-up. Fifth, there are limitations involved with using estimated, rather than direct, oxygen consumption for the calculation of CO as previously described in detail.[16] Sixth, in places where each of precapillary, isolated, and combined PH are compared against no PH, one should strictly declare statistical significance if $P<0.05/3=0.017$, but in this study, we used $P<0.05$ to declare statistical significance. Only pairwise comparisons were performed in this study with no PH being the reference group. In addition, all significant P values for no PH versus combined PH were $P<0.017$ in both the unadjusted (Table 5) and adjusted (Table 6) analyses, and therefore this would not have substantially changed the main findings of this study. In addition, the P values for no PH versus isolated PH were not significant regardless of whether $P<0.05$ or $P<0.017$ was used. Only the unadjusted clinical outcomes of no PH versus precapillary PH may have been affected by using $P<0.05$ instead of $P<0.017$. However, in the adjusted analysis, no PH versus precapillary PH was no longer significant for differences in all-cause mortality and cardiovascular death

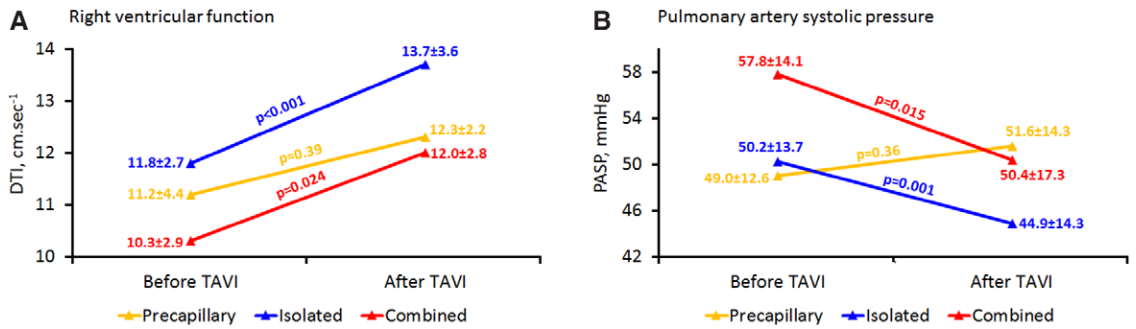

Figure 6. Changes in right ventricular systolic function (pulsed Doppler peak velocity [DTI] at the annulus; **A**) and pulmonary artery systolic pressure (PASP; **B**) measured noninvasively before and after transcatheter aortic valve implantation (TAVI) among patients with pulmonary hypertension. Data taken from Table 7.

(P>0.05), and therefore, the main findings remain unaffected. Finally, a fluid challenge was not performed in patients with a low LVEDP, which may have unmasked patients with occult postcapillary PH. However, Hoeper et al[35] have stated that this technique requires meticulous evaluation and standardization before its use in clinical practice can be recommended.

Conclusions

PH is present in the majority of patients undergoing TAVI in the current era and is comprised predominantly of postcapillary PH. Invasive stratification of PH according to hemodynamic presentation predicts the acute response to therapy and 1-year mortality after TAVI.

Disclosures

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