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ORIGINAL ARTICLE
Aortic valvular heart disease

Prognostic value of algorithm-based invasive haemodynamic assessment of paravalvular regurgitation after transcatheter aortic valve replacement with self-expanding devices—the APPOSE registry

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Abstract

Background Detecting and grading paravalvular regurgitation (PVR) following transcatheter aortic valve replacement (TAVR) remains challenging.

Aims We evaluated the prognostic value of algorithm-based invasively measured haemodynamic indices of PVR for all-cause mortality and heart failure (HF) rehospitalizations.

Methods and Results We included 727 patients who underwent TAVR with a self-expanding valve for severe native aortic stenosis between 2015 and 2021 at Radboudumc. Invasive left ventricular and aortic pressures were continuously measured and analysed offline using a validated algorithm for standardized computation of haemodynamic indices of PVR. The primary endpoint was an event-adjudicated composite of all-cause mortality and HF rehospitalization across 3-year follow-up. Algorithm-derived diastolic pressure–time index (DPTI) ≤58 and diastolic delta (DD) ≤32 mmHg were independently associated with the composite outcome (hazard ratio [HR] 1.64 [95% confidence interval (CI): 1.14, 2.37], HR 1.80 [95% CI: 1.21, 2.68], respectively). Following stratification for angiography-graded PVR, algorithm-derived invasive indices remained independently

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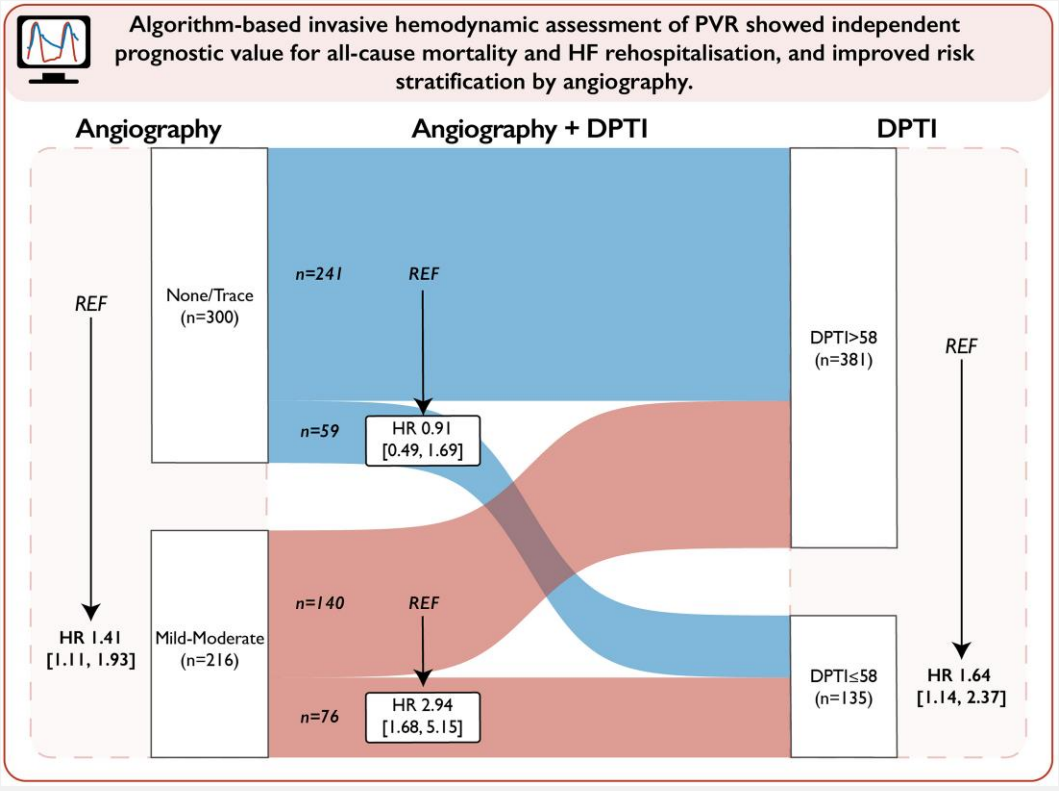
associated with the composite outcome in those with angiographic mild-moderate (HR DPTI ≤58 mmHg: 2.94, 95% CI: 1.68, 5.15) but not none/trace PVR (HR DPTI ≤58 mmHg: 0.91, 95% CI: 0.49, 1.69). Inferences remained consistent when considering only those with angiographic mild PVR (HR DPTI ≤58: 3.19, 95% CI: 1.62, 6.26).

Conclusion Algorithm-based invasive assessment of PVR showed independent prognostic value for the risk of all-cause mortality and HF rehospitalization across 3-year follow-up. Additionally, following stratification for angiography-graded PVR, haemodynamic indices remained independently associated with the composite outcome in those with angiographic mild PVR. Together, this highlights the potential of real-time automated assessment of invasive haemodynamics for risk stratification of patients undergoing TAVR.

Graphical abstract



Prognostic value and interrelation of PVR as graded by Sellers-based aortic root angiography and algorithm-based invasive haemodynamics. The Sankey plot visualizes the prognostic value and interrelation of PVR graded by Sellers-based aortic root angiography and DPTI, and is stratified for its isolated (left and right panels, respectively) and combined use (middle panel). Mild-moderate PVR as assessed by aortic root angiography was independently associated with the composite outcome of all-cause mortality or heart failure rehospitalization at 3-year post-TAVR (left panel). Similarly, DPTI ≤58 was independently associated with the composite endpoint (right panel). When stratified for angiographic PVR, DPTI ≤58 remained independently associated with the composite endpoint in those with angiographic mild-moderate (bottom part of middle panel) but not with angiographic none/trace PVR (upper part of middle panel). For this analysis, mild and moderate PVR were collapsed into a single category due to the low prevalence of ≥moderate PVR (mild PVR $n = 186$, moderate PVR $n = 30$). Hazard ratios are derived from multivariable Cox regression models for the composite outcome of all-cause mortality or HF rehospitalization at 3-year post-TAVR, with 95% confidence intervals being presented between square brackets. DPTI, diastolic pressure-time index; HR, hazard ratio; REF, reference.

Keywords Invasive haemodynamics • Paravalvular regurgitation • Heart failure • Prognosis • Transcatheter aortic valve replacement • Aortic stenosis

Introduction

Transcatheter aortic valve replacement (TAVR) represents a guideline-recommended treatment for patients with severe aortic stenosis across the surgical risk spectrum.[1,2] However, paravalvular regurgitation (PVR) is a frequent complication post-TAVR, particularly after implantation of a self-expanding valve (SEV).[3,4] This may have important implications, as PVR is associated with an increased risk of heart

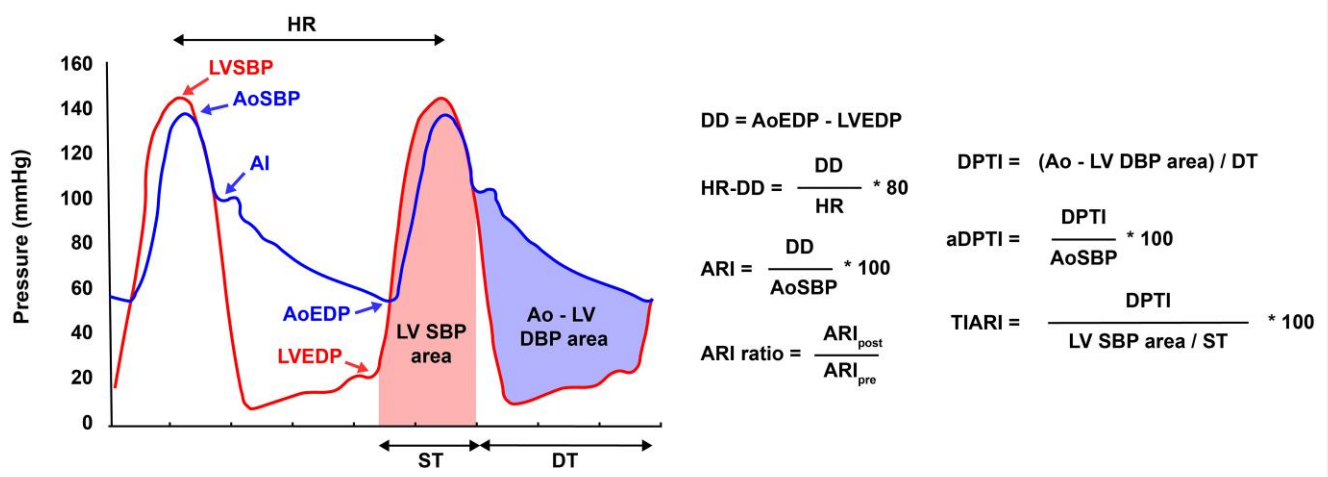


Figure 1 Computation of invasive haemodynamic indices of paravalvular regurgitation using standardized time events of the cardiac cycle. A graphical representation of invasive haemodynamic parameters of paravalvular regurgitation that were determined using the left ventricular (red) and aortic (blue) pressure signals. While parameters and time events are quantified in each cardiac cycle, they are graphically displayed across different cycles for improved clarity. Adapted from Stens *et al.*[15] aDPTI adjusted diastolic pressure time index, Ao aortic, (a)DPTI (adjusted) diastolic pressure-time index, AI aortic incisura, ARI aortic regurgitation index, DD diastolic delta, DBP diastolic blood pressure, DT diastolic time, EDP end-diastolic pressure, HR heart rate, HR-DD heart rate-adjusted diastolic delta, LV left ventricle, SBP systolic blood pressure, ST systolic time, TIARI time-integrated aortic regurgitation index

failure (HF). Moderate PVR has consistently been associated with poorer clinical outcomes[5–7] and even mild PVR seems associated with poorer prognosis or prosthesis durability.[5,8–10] Accurate, procedural diagnosis of PVR is therefore essential, especially as effective treatment options (e.g. post-dilation) are readily available to reduce PVR and the future risk of HF.

Contemporary imaging methods for grading PVR have significant limitations. Cardiac magnetic resonance is highly accurate for grading PVR, but is expensive and not feasible to perform procedurally due to logistical constraints. Alternatively, transthoracic echocardiography (TTE) and aortic root angiography are available to grade PVR. However, procedural TTE assessment of PVR is challenging, as jets are often multiple, eccentric, and irregularly shaped, which may be obscured by the TAVR frame and poor acoustic window due to the supine position and habitus of the patient.[11,12] Additionally, angiography is widely used procedurally as it captures the sum of all regurgitant jets, but grading is subjective and associated with significant inter-observer variability.[13] Consequently, contemporary imaging modalities frequently underestimate the severity of PVR compared to cardiac magnetic resonance.[12,13]

Recent studies revealed invasive haemodynamic indices to have high diagnostic value for cardiac magnetic resonance–based assessment of PVR.[14,15] However, studies evaluating its prognostic value have been inconclusive, largely due to the primary focus on all-cause mortality[16–18] instead of outcomes that are more directly linked to PVR pathophysiology such as rehospitalization for HF. A potential limitation of current procedural assessment of PVR using invasive haemodynamics is its reliance on visual or manual computation of the difference in end-diastolic left ventricular (LV) and aortic pressure (i.e. diastolic delta [DD][19]). To allow real-time assessment of PVR, we have recently developed and validated a stand-alone automated algorithm[15]; however, its role for prognosis remains unclear. An additional advantage of such algorithms is that they allow for the integration of multiple parameters across the entire cardiac cycle, which may provide a more comprehensive assessment of the haemodynamic profile.[20,21]

Using our algorithm, we assessed the prognostic value of algorithmically derived, invasively measured haemodynamic indices of PVR for the 3-year incidence of a composite outcome of all-cause mortality and HF hospitalization in patients receiving an SEV. Furthermore, we evaluated the prognostic value of algorithmically derived invasive haemodynamic indices after stratification for angiographic grading of PVR.

Methods

We retrospectively included patients who underwent TAVR with an SEV for severe native aortic stenosis between 2015 and 2021 in the Radboud University Medical Center. All patients were discussed in a multidisciplinary heart team and were deemed eligible for TAVR. The requirement of ethical approval was waived by the ethics committee of the Radboud University Medical Center, Nijmegen, The Netherlands (2022-13565). Written informed consent to re-use collected data and collect clinical follow-up data from medical files was obtained from all patients. Reporting followed the Strengthening the Reporting of Observational studies in Epidemiology guidelines (Supplementary Table S1).[22]

Contemporary grading of PVR

Procedural aortic root angiography was performed using a pigtail catheter in the ascending aorta just above the newly implanted SEV. Angiographic PVR was graded according to Sellers' criteria.[23] In addition, patients underwent transthoracic echocardiography before TAVR, before hospital discharge and at 30-days post-TAVR, and was performed according to the 2011 European and American guidelines.[24]

Invasive grading of PVR

We used two 5F fluid-filled pigtail catheters (Impulse; Boston Scientific, Marlborough, MA, USA), attached to two separate fluid management systems with integrated pressure transducers (Navilyst Medical, Marlborough, MA, USA), to simultaneously measure LV and aortic pressures 1) before pre-dilation (or before direct implantation), 2) after implantation of the SEV, and when applicable 3) after each additional periprocedural intervention such as post-dilation or implantation of a second valve. The LV pressure catheter was positioned in the mid-ventricle at the level of the papillary muscles, whilst the aortic pressure catheter was positioned near the non-coronary cusp (pre-implantation) or in the upper quadrant

of the stent frame of the SEV (post-implantation). Pressure transducers were flushed and balanced before each TAVR procedure to atmospheric pressure. Continuous haemodynamic data were captured in Mac-Lab (GE Healthcare, Chicago, IL, USA), and were exported for offline analysis. A validated rule-based algorithm[15] was used to filter cardiac cycles affected by arrhythmias or noise, and to subsequently determine systolic transvalvular pressure gradients (i.e. mean and max), as well as standardize computation of various invasive haemodynamic parameters of PVR, including the DD,[19] heart rate–adjusted DD (HR-DD),[25] aortic regurgitation index (ARI),[26] ARI ratio,[27] time-integrated ARI (TIARI),[28] and (adjusted) diastolic pressure time index (DPTI and aDPTI)[20] (*Figure 1*). Parameters were computed for each cardiac cycle and averaged. When additional interventions such as post-dilation were performed, the post-intervention values were used for analyses.

Clinical endpoints

The primary endpoint was a non-hierarchical composite of all-cause mortality or HF rehospitalization at 3-year post-TAVR, with secondary endpoints including the individual components of the primary endpoint. We screened medical files of all eligible patients in both the referral hospital and TAVR treating centre for incidence of rehospitalization for HF and all-cause mortality post-TAVR. An event-adjudication committee, whose members (G.V., M.R.) were unaware of the results of the invasive haemodynamic analyses, adjudicated rehospitalization events for HF according to the Valve Academic Research Consortium 3 (VARC-3) criteria.[29] All-cause mortality data from medical files were enriched with mortality data from the Dutch population death registry (Dutch: 'Basisregistratie Personen'). Follow-up for time-to-event outcomes was defined as the interval between TAVR and event, repeat aortic valve intervention, lost to follow-up or right-censoring at 3-year post-TAVR, whichever came first.

Statistical analyses

Summary statistics are presented as means and standard deviations (SD), medians (interquartile range [IQR]), or frequencies (%), as appropriate. We performed ordinal logistic regression to investigate the association of invasive indices with angiographic grading of PVR. Subsequently, we computed hazard ratios (HRs) and 95% confidence intervals (CIs) for the association of angiographic and invasive indices of PVR with the composite endpoint using separate multivariable Cox regression models. To assess the individual components of the composite endpoint, we used (1) multivariable Cox regression models for all-cause mortality, and (2) Finn and Gray sub-distribution hazard models for HF rehospitalization, treating all-cause mortality as a competing risk.[30] Results from Fine and Gray models are presented as sub-distribution HRs (sHRs). All multivariable analyses were performed with invasive haemodynamic indices both expressed as a binary and continuous variable. Binary analyses used previously defined cut-offs for prognosis or cardiac magnetic resonance-based diagnosis of PVR if available (i.e. DD ≤32 mmHg, HR-DD ≤25 mmHg/bpm, ARI ≤ 25, ARI ratio ≤ 0.6),[14,25–27] and if not, derived from receiver operating curves for the composite endpoint at 3 years (i.e. TIARI ≤ 60, DPTI ≤ 58, and aDPTI ≤ 28). Continuous analyses evaluated the relevance of including restricted cubic splines, and tested for non-linearity using the Wald statistic. All multivariable Cox regression models used age as the timescale[31,32] and were adjusted for variables that, based on domain knowledge, may confound the association between invasive haemodynamic indices of PVR and clinical outcomes, including sex, atrial fibrillation, diabetes, estimated glomerular filtration rate (eGFR), LV ejection fraction (LVEF), LV hypertrophy,[33] chronic obstructive pulmonary disease (COPD), pulmonary hypertension, history of coronary artery disease, and ≥moderate mitral regurgitation. Multicollinearity was checked using variance inflation factors, but no relevant multicollinearity was observed (all variance inflation factors less than three, Supplementary Table S2).

Additionally, as angiography is widely used to grade PVR procedurally, stratified analyses were performed to explore the prognostic value of invasive haemodynamic indices within each angiographic PVR stratum. For this analysis, mild and moderate PVR were collapsed into a single category due to the low prevalence of ≥moderate PVR. Analyses were repeated using data from patients with angiographic mild PVR alone.

To assess the robustness of our results, we performed several sensitivity analyses: (1) truncating follow-up data at 1- and 2-year post-TAVR, (2) using multiply imputed data (Supplemental Methods), and (3) comparing PVR rates between the Portico valve and other valves. Analyses were performed in R version 4.2.3 (Posit Software, Boston, MA, USA) using the *mice, pROC, car*, and *rms* packages. Two-tailed *P*-values <0.05 were considered statistically significant.

Results

A total of 727 patients were included. The mean age was 79.3 ± 6.6 years, with 350 (48.1%) patients being women (*Table 1*). In total, 380 (52.3%) patients had a New York Heart Association (NYHA) score ≥III and had a mean EuroSCORE II score of 3.9% ± 3.6%. The mean LVEF was 54.0% ± 11.7%, with a mean aortic valve area (AVA) of 0.78 ± 0.2 cm^2, mean gradient of 41.5 ± 14.6 mmHg, and maximal velocity of 4.11 ± 0.68 m/s. Patients were primarily treated under general anaesthesia ($n = 539$, 74.1%), with the femoral ($n = 483$, 66.4%) or subclavian ($n = 240$, 33.0%) artery being most commonly used for primary access (*Table 1*).

Assessment of PVR

Following implantation, we found no change in DD, driven by comparable increases in LV and aortic end-diastolic pressure (*Table 2*). In contrast, HR-DD and ARI significantly decreased, which was primarily driven by increases in heart rate and aortic systolic blood pressure, respectively. In addition, TIARI and DPTI increased, whilst the aDPTI decreased. Based on angiography, patients were primarily classified as having none/trace ($n = 359$, 58.1%) or mild PVR ($n = 226$, 36.6%), with 33 patients classified as moderate PVR (5.3%, *Table 3*). Haemodynamic indices were inversely associated with angiographic and TTE gradings of PVR (*Table 3*). PVR severity did not materially differ between Portico and other valves (Supplementary Table S3).

Association with clinical outcomes

During a median follow-up of 36 months (IQR: 17, 36 months; 1606 person-years), 136 patients were rehospitalized for HF (161 hospitalizations), and 178 died, corresponding to 251 composite outcome events. Using angiography, we found that moderate PVR was independently associated with an increased hazard for the composite endpoint (HR 2.01, 95% CI: 1.12, 3.58). Using algorithm-based invasive haemodynamic indices of PVR, we revealed significant linear dose–response associations with the composite outcome, where lower values corresponded to a higher risk (Supplementary Figure S1). When dichotomized, DPTI ≤58 and DD ≤32 mmHg were independently associated with an increased hazard of the composite endpoint (HR 1.64, 95% CI: 1.14, 2.37; HR 1.80, 95% CI: 1.21, 2.68, respectively, *Table 4*). Results were consistent across sensitivity analyses when follow-up data were truncated at 1 and 2 years (Supplementary Tables S4 and S5) and when using multiply imputed data (Supplementary Table S6).

Following stratification for angiographic grading of PVR, an independent association with the composite endpoint was found for DPTI ≤58 (HR 2.94, 95% CI: 1.68, 5.15, *Central Illustration*) as well as for DD ≤32 mmHg (HR 2.32, 95% CI: 1.33, 4.05) in those with angiography-graded mild-moderate PVR (mild PVR $n = 186$, moderate PVR $n = 30$). Inferences remained consistent when considering only those with angiographic mild PVR (DPTI ≤58 HR 3.19, 95% CI: 1.62, 6.26; DD ≤32 mmHg HR 2.18, 95% CI: 1.12, 4.26). Invasive indices were not associated with the composite outcome in those with angiography-graded none-trace PVR (DPTI ≤58: HR 0.91, 95% CI: 0.49, 1.69; DD ≤32 mmHg: HR 1.03, 95% CI: 0.51, 2.12).

Discussion

The APPOSE registry evaluated for the first time the association between algorithm-derived procedural invasive haemodynamic indices

Table 1 Baseline characteristics of the patients included in the APPOSE registry

	APPOSE registry (n = 727)	% missing
Demographics		
Age, years	79.3 ± 6.6	0
Sex, *n* women (%)	350 (48.1)	0
Comorbidities		
Obesity, *n* (%)	203 (27.9)	0
EuroSCORE II, %	3.9 ± 3.6	0
NYHA class III/IV, n (%)	380 (52.3)	0
PAD, *n* (%)	176 (24.2)	0
Diabetes, *n* (%)	227 (31.2)	0
Coronary heart disease, *n* (%)	413 (56.8)	0
COPD, *n* (%)	149 (20.5)	0
AF, n (%)	165 (22.7)	0
CKD-EPI-GFR, mL/min	66.7 ± 19.5	0
Pulmonary hypertension, n (%)	264 (40.5)	10.3
Pre-TAVR echocardiography		
AVA, cm^2	0.78 ± 0.21	4.5
PGmean, mmHg	41.5 ± 14.6	12.8
Vmax, m/s	4.1 ± 0.7	0.3
LVEF, %	54.0 ± 11.7	0.3
LV hypertrophy, n (%)	391 (55.1)	2.3
≥Moderate aortic regurgitation, *n* (%)	108 (15.1)	1.5
≥Moderate mitral regurgitation, *n* (%)	148 (20.4)	0
Index procedure		
Primary access, n (%)		0
Femoral	483 (66.4)	
Subclavian	240 (33.0)	
Transaortic	4 (0.6)	
General anaesthesia, n (%)	539 (74.1)	0
Predilation, n (%)	453 (66.0)	5.6
Postdilation, n (%)	102 (14.0)	0
Valve, n (%)		0
Medtronic CoreValve	25 (3.4)	
Medtronic CoreValve Evolut R	478 (65.7)	
Abbott Portico	222 (30.5)	
Abbott Navitor	2 (0.3)	

Baseline and procedure characteristics are presented as means and standard deviations, medians [interquartile range] or frequencies (%) as appropriate. AF, atrial fibrillation; AVA, aortic valve area; CKD-EPI-GFR, chronic kidney disease epidemiology collaboration equation for glomerular filtration rate; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; LV, left ventricle; NYHA, New York Heart Association; PAD, peripheral artery disease; PG, pressure gradient; Vmax peak aortic valve velocity.

Table 2 Pre- and post-procedural assessment of invasive haemodynamics

	Overall (n = 727)		
	Pre	Post	*P*
n cardiac cycles assessed	20 [12, 39]	41 [23, 77]	<.001
Individual time events			
Heart rate, bpm	66.0 ± 14.2	74.4 ± 12.9	<.001
AoEDP, mmHg	55.0 ± 11.4	58.2 ± 11.4	<.001
AoSBP, mmHg	113.7 ± 24.7	139.0 ± 27.6	<.001
LVEDP, mmHg	12.8 ± 6.3	16.0 ± 7.0	<.001
LVSBP, mmHg	159.8 ± 31.4	139.5 ± 28.0	<.001
Transvalvular systolic pressure gradients			
PGmean, mmHg	37.4 ± 16.0	2.4 ± 4.68	<.001
PGmax, mmHg	68.2 ± 25.2	22.7 ± 11.3	<.001
Indices of PVR			
DD, mmHg	42.2 ± 12.0	42.2 ± 12.5	.965
HR-DD, mmHg/bpm	54.4 ± 15.3	47.0 ± 12.9	<.001
ARI	37.8 ± 10.0	31.0 ± 9.1	<.001
TIARI	53.4 ± 12.4	61.3 ± 11.7	<.001
DPTI	56.0 ± 13.3	57.5 ± 12.8	.05
aDPTI	49.8 ± 9.2	41.9 ± 7.7	<.001
ARI ratio	0.93 ± 0.5		N/A

Data on invasive haemodynamics are presented as means and standard deviations, medians [interquartile range] or frequencies (%) as appropriate. (a)DPTI, (adjusted) diastolic pressure time index; Ao, aortic; ARI, aortic regurgitation index; DD, diastolic delta; DPTI, diastolic pressure time index; EDP, end-diastolic pressure; HR-DD, heart rate–adjusted diastolic delta; LV, left ventricular; PG, pressure gradient; SBP, peak systolic blood pressure; TIARI, time-integrated aortic regurgitation index.

of PVR and a composite outcome of all-cause mortality and rehospitalization for HF across a 3-year follow-up post-TAVR. We present the following key findings. Firstly, algorithm-derived haemodynamic indices (i.e. DPTI ≤58, and DD ≤32 mmHg) were independently associated with the composite outcome. Second, following stratification for angiography-graded PVR, algorithm-derived haemodynamic indices remained independently associated with the composite outcome in those diagnosed with angiographic mild PVR. Together, these results highlight the potential of algorithm-based invasive haemodynamics for risk stratification of patients undergoing TAVR (*Graphical abstract*).

Driven by its effects on clinical and durability outcomes of residual PVR, several studies explored the relation of invasive haemodynamic indices of PVR with future clinical events.[19,20,25–28] In contrast to most studies, who focussed on all-cause mortality only and presented mixed outcomes, we evaluated a composite endpoint of all-cause mortality and HF rehospitalization across 3 years of follow-up. The advantage is that HF rehospitalizations are more directly linked to PVR rather than all-cause mortality, especially in an elderly population of 80 years old where competing causes for death are common. This is illustrated in our own findings, as the relatively 3-year high mortality rate observed in our cohort (24.5%) likely reflects, at least in part, that follow-up for a subset of patients coincided with the global COVID-19 pandemic, underscoring the value of more PVR-specific endpoints. Furthermore, previous studies primarily used manual computation to derive haemodynamic

Table 3 Comparison of contemporary and invasive haemodynamic assessment of PVR

	Angiography ($n = 618$)				TTE at hospital discharge ($n = 689$)				TTE at 30-days post-TAVR ($n = 509$)			
	None/ Trace	Mild	Moderate	*P* for trend	None/ Trace	Mild	Moderate	*P* for trend	None/ Trace	Mild	Moderate	*P* for trend
n (%)	359 (58.1%)	226 (36.6%)	33 (5.3%)		342 (49.6%)	299 (43.4%)	48 (7.0%)		260 (51.1%)	196 (38.5%)	53 (10.4%)	
DD, mmHg	44.8 ± 11.5	40.1 ± 12.7	30.9 ± 10.8	<.001	43.8 ± 11.7	41.6 ± 12.9	33.8 ± 10.5	<.001	43.4 ± 12.3	41.4 ± 12.9	35.8 ± 10.7	.001
HR-DD, mmHg/bpm	49.9 ± 12.1	44.3 ± 12.6	34.8 ± 13.2	<.001	48.8 ± 12.4	46.2 ± 13.2	38.2 ± 11.7	<.001	48.8 ± 12.8	45.3 ± 13.6	40.9 ± 11.5	<.001
ARI	32.9 ± 8.8	29.4 ± 8.9	22.7 ± 8.3	<.001	32.2 ± 8.8	30.5 ± 9.1	25.0 ± 8.3	<.001	31.8 ± 8.8	30.8 ± 9.3	26.7 ± 8.0	.006
ARI ratio	0.90 ± 0.3	0.92 ± 0.4	1.2 ± 1.0	.029	0.92 ± 0.4	0.92 ± 0.4	1.00 ± 0.8	.715	0.93 ± 0.4	0.90 ± 0.3	1.04 ± 0.7	.597
TIARI	63.5 ± 11.6	59.6 ± 11.6	52.2 ± 10.3	<.001	62.5 ± 11.4	60.9 ± 11.8	55.3 ± 9.5	.003	61.9 ± 11.2	60.6 ± 11.8	57.1 ± 11.8	.023
DPTI	59.7 ± 12.2	55.7 ± 12.7	49.1 ± 10.9	<.001	58.4 ± 12.5	57.3 ± 13.1	51.7 ± 10.8	.025	58.5 ± 13.0	56.7 ± 12.7	53.0 ± 12.1	.014
aDPTI	43.4 ± 7.6	40.7 ± 7.6	35.7 ± 7.4	<.001	42.6 ± 7.6	41.7 ± 7.9	38.0 ± 7.4	.006	42.4 ± 7.4	42.0 ± 7.8	39.0 ± 7.6	.043

Data on invasive haemodynamic parameters of PVR are presented, and are stratified by angiography and TTE grading of PVR. Trend analyses were performed using ordinal logistic regression. Invasive haemodynamic indices of PVR were dose-dependently associated with angiographic or TTE grading of PVR. aDPTI, adjusted diastolic pressure time index; ARI, aortic regurgitation index; DD, diastolic delta; DPTI, diastolic pressure time index; HR-DD, heart rate-adjusted diastolic delta; PVR, paravalvular regurgitation; TIARI, time-integrated aortic regurgitation index; TTE, transthoracic echocardiography.

parameters instead of standardized, automated algorithms. As a result of these advantages, our study found that several invasive haemodynamic indices of PVR were independently associated with the composite endpoint (i.e. DPTI ≤58, and DD ≤32 mmHg), which are primarily exerted through increased rates of HF hospitalization. This highlights the potential of invasive haemodynamic indices to identify those at risk for future incidence of all-cause mortality and HF rehospitalization.

Current procedural diagnosis and grading of PVR is predominantly performed using Sellers-based aortic root angiography. Angiographic ≥ moderate PVR has consistently been associated with adverse clinical outcomes.[19,34,35] However, prior work has demonstrated poor agreement between angiographic ≥moderate PVR and cardiac magnetic resonance-graded ≥moderate PVR.[13] Notably, the sensitivity of angiography for detecting ≥moderate PVR on cardiac magnetic resonance substantially improved when an angiographic threshold of ≥mild PVR was applied,[13] suggesting that, in a subset of patients with angiographic mild PVR, the true severity may be underestimated compared with cardiac magnetic resonance. Consistent with this concept, previous analyses showed that the discriminatory value of aortic root angiography for cardiac magnetic resonance-based significant PVR was improved when combined with invasive haemodynamic indices.[15,36] In the present study, among patients with angiographic mild PVR, a DPTI ≤58 was independently associated with the composite endpoint. These findings suggest that invasive haemodynamic indices may identify a higher risk phenotype within those with angiographic mild PVR, and could therefore guide application of procedural strategies to reduce PVR, such as post-dilation. Together, these results may support a complimentary role for invasive haemodynamic assessment of PVR to contemporary modalities to improve post-TAVR risk stratification in patients with PVR.

From a clinical perspective, assessment of PVR through invasive haemodynamics may seem straightforward. However, current practice relies on visual inspection or manual computation, which takes time, is subject to errors and the interpretation requires careful consideration. We have previously demonstrated that automated algorithms enable continuous waveforms analyses, facilitate averaging of parameters across extended acquisition periods, and systematically exclude noisy or arrhythmia-affected cycles.[15] Algorithm-based assessment of invasive haemodynamics may allow integrating data from the entire diastole (e.g. DPTI), and may offer a more comprehensive characterization of diastolic loading than single-timepoint measures (e.g. DD). Accordingly, time-integrated indices may provide incremental prognostic information beyond single time-point measures. Importantly, such computations can be made in real time using automated algorithms, and can be scaled to work in routine haemodynamic setups. As our current study was not powered to investigate the incremental prognostic value of time-integrated over time-static indices, future studies are warranted. Collectively, these considerations underscore the need for prospective studies to evaluate the use of real-time assessment of invasive haemodynamic indices of PVR to guide clinical decision making.

Strengths and limitations

Strengths include the use of validated automated analysis software for standardized computation of invasive haemodynamic indices, and the consideration of rehospitalization for HF within the composite endpoint, which were adjudicated based on VARC-3 criteria in a central committee blinded to invasive haemodynamics. Some limitations should be considered. First, patients were primarily treated under general anaesthesia and with SEV's. Consequently, inferences (including cut-offs of haemodynamic indices) may not directly be translated to those treated under other conditions (e.g. balloon-expandable valves, conscious sedation). Secondly, angiography and TTE grading of PVR were performed as part of routine clinical practice rather than centrally adjudicated by a core laboratory. Consequently, angiographic and TTE-grading of PVR are subject to inter-observer variability, and may

Table 4 Association between angiographic and invasively measured indices of paravalvular regurgitation with clinical outcomes following three-years of follow-up

Haemodynamic variable	*n* (%)	Composite outcome (multivariable HR, 95% CI)	All-cause mortality (multivariable HR, 95% CI)	Rehospitalization for HF (multivariable sHR, 95% CI)
Transvalvular systolic pressure gradients				
PGmean ≥ 10 mmHg	31/609 (5.1%)	1.50 [0.68, 3.32]	1.96 [0.82, 4.68]	0.49 [0.12, 1.98]
PGmax ≥ 23 mmHg	271/609 (44.5%)	0.99 [0.71, 1.39]	0.93 [0.63, 1.39]	1.12 [0.75, 1.70]
Haemodynamic indices of PVR				
DD ≤ 32 mmHg	127/612 (20.8%)	**1.80 [1.21, 2.68]**	1.56 [0.99, 2.46]	**2.45 [1.49, 4.04]**
HR-DD ≤ 25 mmHg/bpm	26/591 (4.4%)	1.98 [0.98, 3.99]	1.18 [0.46, 3.04]	**3.12 [1.40, 6.95]**
ARI ≤ 25	172/612 (28.1%)	1.98 [0.99, 2.10]	**1.58 [1.03, 2.43]**	**1.71 [1.09, 2.69]**
ARI ratio ≤ 0.6	77/565 (13.6%)	1.33 [0.83, 2.12]	1.66 [0.995, 2.76]	1.38 [0.74, 2.57]
TIARI ≤ 60	365/602 (60.6%)	1.33 [0.92, 1.92]	1.24 [0.81, 1.91]	**1.69 [1.08, 2.64]**
DPTI ≤ 58	161/602 (26.7%)	**1.64 [1.14, 2.37]**	**1.55 [1.02, 2.37]**	**2.00 [1.28, 3.11]**
aDPTI ≤ 28	305/602 (50.7%)	1.41 [0.98, 2.01]	1.35 [0.89, 2.04]	**1.74 [1.10, 2.76]**
Contemporary grading of PVR				
Angiography, procedural				
- None/Trace	359/618 (58.1%)	*REF*	*REF*	*REF*
- Mild	226/618 (36.6%)	1.32 [0.95, 1.84]	1.24 [0.85, 1.80]	1.58 [0.99, 2.48]
- Moderate	33/618 (5.3%)	**2.01 [1.12, 3.58]**	1.17 [0.54, 2.52]	**4.06 [2.04, 8.10]**
TTE, hospital discharge				
- None/Trace	260/509 (51.1%)	*REF*	*REF*	*REF*
- Mild	196/509 (38.5%)	**1.39 [1.01, 1.92]**	1.38 [0.95, 2.02]	1.30 [0.83, 2.03]
- Moderate	53/509 (10.4%)	1.61 [0.90, 2.88]	1.27 [0.61, 2.64]	1.89 [0.85, 4.20]
TTE, 30-days				
- None/Trace	260/509 (51.1%)	*REF*	*REF*	*REF*
- Mild	196/509 (38.5%)	0.94 [0.66, 1.34]	1.22 [0.75, 1.98]	0.91 [0.50, 1.68]
- Moderate	53/509 (10.4%)	1.60 [0.98, 2.61]	0.68 [0.28, 1.69]	1.88 [0.84, 4.24]

Primary analyses were based on a composite outcome of all-cause mortality and rehospitalization for HF, with secondary analyses focussing on the individual components. Multivariable Cox regression and Finn and Gray models were used to compute cause-specific and subdistribution hazard ratios, respectively. Bold values indicate statistically significant results. Multivariable models included sex, atrial fibrillation, diabetes, estimated glomerular filtration rate (eGFR), left ventricular ejection fraction (LVEF), LV hypertrophy, chronic obstructive pulmonary disease (COPD), pulmonary hypertension, history of coronary artery disease, and ≥moderate mitral regurgitation as covariates. aDPTI, adjusted diastolic pressure time index; ARI, aortic regurgitation index; DD, diastolic delta; HF, heart failure; HR-DD, heart rate-adjusted diastolic delta; PG, pressure gradient; PVR, paravalvular regurgitation; TIARI, time-integrated aortic regurgitation index; TTE, transthoracic echocardiography.

have attenuated corresponding effect estimates. Thirdly, given the limited sample size, cut-offs for the DPTI, TIARI, and aDPTI were derived using the same dataset used to assess outcomes. Consequently, findings relating to these parameters may be susceptible to some degree of overfitting. Fourthly, the small sample size prevented assessment of effect modification and its influence on subgroup-specific haemodynamic cut-offs. We propose large-scale multi-centre studies to specifically focus on such questions. Finally, due to the retrospective nature of the study, residual confounding may persist despite multivariable adjustment.

Conclusion

Algorithm-based invasive haemodynamics assessment of PVR showed independent prognostic value for the risk of all-cause mortality and HF rehospitalization across three-year follow-up in TAVR patients treated with a SEV. Importantly, following stratification for angiography-graded PVR, invasive assessment of haemodynamics remained independently associated with the composite outcome in those with angiographic mild PVR. Based on these observations, we highlight the potential of diagnosis and grading of PVR using an integrated approach of angiography and real-time assessment of invasive haemodynamics for risk stratification of patients undergoing TAVR.

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Author contributions

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Supplementary data

Supplementary data are available at *European Heart Journal – Valvular and Structural Heart Disease* online.

Declarations

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Disclosure of Interest

M.H.v.W. reported receiving consulting fees from Boston Scientific and Abbott Vascular, and received speaker fees and travel grants from Medtronic and Abbott Vascular. R.J.M.v.G. reported receiving consulting and speaker's fees from Abbott Vascular, AstraZeneca, Sanofi SA, Amgen Inc, and InfraRedx Inc and receiving institutional research grant funding from Amgen Inc, InfraRedx Inc, AstraZeneca, and Sanofi SA. L.X.v.N. has received an unrestricted research grant from Haemonetics. R.H.H. has been a consultant for Medtronic. N.v.R. has received research funding from Abbott, Philips, Medtronic, and Biotronik, has served as a consultant for RainMed, Castor, and Medtronic, and received speaker fees from Abbott and Bayer. The remaining authors have nothing to disclose.

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References

1. Praz F, Borger MA, Lanz J, Marin-Cuartas M, Abreu A, Adamo M, *et al.* 2025 ESC/EACTS Guidelines for the management of valvular heart disease: developed by the task force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2025;**46**:4635–736. https://doi.org/10.1093/eurheartj/ehaf194
2. Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP, Gentile F, *et al.* 2020 ACC/AHA Guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2021;**143**:e72–227. https://doi.org/10.1161/CIR.0000000000000923
3. Abdel-Wahab M, Mehilli J, Frerker C, Neumann F-J, Kurz T, Tölg R, *et al.* Comparison of balloon-expandable vs self-expandable valves in patients undergoing transcatheter aortic valve replacement: the CHOICE randomized clinical trial. *JAMA* 2014;**311**:1503–14. https://doi.org/10.1001/jama.2014.3316
4. Tamburino C, Bleiziffer S, Thiele H, Scholtz S, Hildick-Smith D, Cunnington M, *et al.* Comparison of self-expanding bioprostheses for transcatheter aortic valve replacement in patients with symptomatic severe aortic stenosis: SCOPE 2 randomized clinical trial. *Circulation* 2020;**142**:2431–42. https://doi.org/10.1161/CIRCULATIONAHA.120.051547
5. Kodali SK, Williams MR, Smith CR, Svensson LG, Webb JG, Makkar RR, *et al.* Two-year outcomes after transcatheter or surgical aortic-valve replacement. *N Engl J Med* 2012;**366**:1686–95. https://doi.org/10.1056/NEJMoa1200384
6. Pibarot P, Hahn RT, Weissman NJ, Arsenault M, Beaudoin J, Bernier M, *et al.* Association of paravalvular regurgitation with 1-year outcomes after transcatheter aortic valve replacement with the SAPIEN 3 valve. *JAMA Cardiol* 2017;**2**:1208–16. https://doi.org/10.1001/jamacardio.2017.3425
7. Popma JJ, Adams DH, Reardon MJ, Yakubov SJ, Kleiman NS, Heimansohn D, *et al.* Transcatheter aortic valve replacement using a self-expanding bioprosthesis in patients with severe aortic stenosis at extreme risk for surgery. *J Am Coll Cardiol* 2014;**63**:1972–81. https://doi.org/10.1016/j.jacc.2014.02.556
8. Watanabe Y, Yamamoto M, Hioki H, Saito M, Omiya J, Kito K, *et al.* Long-term impact of mild paravalvular regurgitation after transcatheter aortic valve replacement: the OCEAN-TAVI registry. *JACC Cardiovasc Interv* 2025;**19**:63–75. https://doi.org/10.1016/j.jcin.2025.09.004
9. Okuno T, Tomii D, Heg D, Lanz J, Praz F, Stortecky S, *et al.* Five-year outcomes of mild paravalvular regurgitation after transcatheter aortic valve implantation. *EuroIntervention* 2022;**18**:33–42. https://doi.org/10.4244/EIJ-D-21-00784
10. Sá MP, Jacquemyn X, Van den Eynde J, Tasoudis P, Erten O, Sicouri S, *et al.* Impact of paravalvular leak on outcomes after transcatheter aortic valve implantation: meta-analysis of kaplan-meier-derived individual patient data. *Struct Heart* 2023;**7**:100118. https://doi.org/10.1016/j.shj.2022.100118
11. van Wely M, Rooijakkers M, Stens N, El Messaoudi S, Somers T, van Garsse L, *et al.* Paravalvular regurgitation after transcatheter aortic valve replacement: incidence, quantification, and prognostic impact. *Eur Heart J Imaging Methods Pract* 2024;**2**:qyae040. https://doi.org/10.1093/ehjimp/qyae040
12. Hartlage GR, Babaliaros VC, Thourani VH, Hayek S, Chrysohoou C, Ghasemzadeh N, *et al.* The role of cardiovascular magnetic resonance in stratifying paravalvular leak severity after transcatheter aortic valve replacement: an observational outcome study. *J Cardiovasc Magn Reson* 2014;**16**:93. https://doi.org/10.1186/s12968-014-0093-x
13. Frick M, Meyer CG, Kirschfink A, Altiok E, Lehrke M, Brehmer K, *et al.* Evaluation of aortic regurgitation after transcatheter aortic valve implantation: aortic root angiography in comparison to cardiac magnetic resonance. *EuroIntervention* 2016;**11**:1419–27. https://doi.org/10.4244/EIJY15M03_06
14. Rooijakkers MJP, Stens NA, van Wely MH, van der Wulp K, Rodwell L, Gehlmann H, *et al.* Diastolic delta best predicts paravalvular regurgitation after transcatheter aortic valve replacement as assessed by cardiac magnetic resonance: the APPOSE trial. *Eur Heart J Cardiovasc Imaging* 2023;**24**:1072–81. https://doi.org/10.1093/ehjci/jead033
15. Stens NA, Versteeg GAA, Rooijakkers MJP, de Lange R, Bonekamp SJH, van Wely MH, *et al.* Construct validity of automated assessment of invasively measured hemodynamics during transcatheter aortic valve replacement. *Eur Heart J Digit Health* 2025;**6**:1006–14. https://doi.org/10.1093/ehjdh/ztaf069
16. van Wely M, van der Wulp K, Rooijakkers M, Vart P, Morshuis W, van Royen N, *et al.* Aortic regurgitation index ratio is a strong predictor of 1-year mortality after transcatheter aortic valve implantation using self-expanding devices. *Semin Thorac Cardiovasc Surg* 2021;**33**:923–30. https://doi.org/10.1053/j.semtcvs.2020.11.025

17. Schoechlin S, Brennemann T, Allali A, Ruile P, Jander N, Allgeier M, *et al.* Hemodynamic classification of paravalvular leakage after transcatheter aortic valve implantation compared with angiographic or echocardiographic classification for prediction of 1-year mortality. *Catheter Cardiovasc Interv* 2018;**91**:E56–63. https://doi.org/10.1002/ccd.27384
18. Bavry AA, Aalaei-Andabili SH, Karimi A, Park K, Choi CY, Manning EW 3rd, *et al.* Comparison of different invasive hemodynamic measurements as a prediction tool for mortality after transcatheter aortic valve replacement in men: a retrospective observational study. *Cardiol Ther* 2017;**6**:251–9. https://doi.org/10.1007/s40119-017-0095-5
19. Patsalis PC, Konorza TF, Al-Rashid F, Plicht B, Riebisch M, Wendt D, *et al.* Incidence, outcome and correlates of residual paravalvular aortic regurgitation after transcatheter aortic valve implantation and importance of haemodynamic assessment. *EuroIntervention* 2013;**8**:1398–406. https://doi.org/10.4244/EIJV8I12A213
20. Höllriegel R, Woitek F, Stativa R, Mangner N, Haußig S, Fuernau G, *et al.* Hemodynamic assessment of aortic regurgitation after transcatheter aortic valve replacement: the diastolic pressure-time index. *JACC Cardiovasc Interv* 2016;**9**:1061–8. https://doi.org/10.1016/j.jcin.2016.02.012
21. Patsalis PC, Konorza TFM, Al-Rashid F, Plicht B, Hildebrandt HA, Wendt D, *et al.* Hemodynamic assessment of paravalvular aortic regurgitation after TAVI: estimated myocardial supply-demand ratio and cardiovascular mortality. *Am J Physiol Heart Circ Physiol* 2013;**304**:H1023–H8. https://doi.org/10.1152/ajpheart.00807.2012
22. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol* 2008;**61**:344–9. https://doi.org/10.1016/j.jclinepi.2007.11.008
23. Sellers RD, Levy MJ, Amplatz K, Lillehei CW. Left retrograde cardioangiography in acquired cardiac disease: technic, indications and interpretations in 700 cases. *Am J Cardiol* 1964;**14**:437–47. https://doi.org/10.1016/0002-9149(64)90027-X
24. Zamorano JL, Badano LP, Bruce C, Chan KL, Gonçalves A, Hahn RT, *et al.* EAE/ASE recommendations for the use of echocardiography in new transcatheter interventions for valvular heart disease. *Eur Heart J* 2011;**32**:2189–214. https://doi.org/10.1093/eurheartj/ehr259
25. Jilaihawi H, Chakravarty T, Shiota T, Rafique A, Harada K, Shibayama K, *et al.* Heart-rate adjustment of transcatheter haemodynamics improves the prognostic evaluation of paravalvular regurgitation after transcatheter aortic valve implantation. *EuroIntervention* 2015;**11**:456–64. https://doi.org/10.4244/EIJY14M12_08
26. Sinning JM, Hammerstingl C, Vasa-Nicotera M, Adenauer V, Lema Cachiguango SJ, Scheer AC, *et al.* Aortic regurgitation index defines severity of peri-prosthetic regurgitation and predicts outcome in patients after transcatheter aortic valve implantation. *J Am Coll Cardiol* 2012;**59**:1134–41. https://doi.org/10.1016/j.jacc.2011.11.048
27. Sinning JM, Stundl A, Pingel S, Weber M, Sedaghat A, Hammerstingl C, *et al.* Pre-procedural hemodynamic status improves the discriminatory value of the aortic regurgitation index in patients undergoing transcatheter aortic valve replacement. *JACC Cardiovasc Interv* 2016;**9**:700–11. https://doi.org/10.1016/j.jcin.2015.12.271
28. Bugan B, Kapadia S, Svensson L, Krishnaswamy A, Tuzcu EM. Novel hemodynamic index for assessment of aortic regurgitation after transcatheter aortic valve replacement. *Catheter Cardiovasc Interv* 2015;**86**:E174–9. https://doi.org/10.1002/ccd.25848
29. Généreux P, Piazza N, Alu MC, Nazif T, Hahn RT, Pibarot P, *et al.* Valve academic research consortium 3: updated endpoint definitions for aortic valve clinical research. *J Am Coll Cardiol* 2021;**77**:2717–46. https://doi.org/10.1016/j.jacc.2021.02.038
30. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. *J Am Stat Assoc* 1999;**94**:496–509. https://doi.org/10.1080/01621459.1999.10474144
31. Thiébaut AC, Bénichou J. Choice of time-scale in Cox's model analysis of epidemiologic cohort data: a simulation study. *Stat Med* 2004;**23**:3803–20. https://doi.org/10.1002/sim.2098
32. Korn EL, Graubard BI, Midthune D. Time-to-event analysis of longitudinal follow-up of a survey: choice of the time-scale. *Am J Epidemiol* 1997;**145**:72–80. https://doi.org/10.1093/oxfordjournals.aje.a009034
33. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, *et al.* Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2015;**16**:233–70. https://doi.org/10.1093/ehjci/jev014
34. Elzomor H, Neumann TJ, Boas L, Ruile P, Abdelshafy M, Elkoumy A, *et al.* Association between three-year mortality after transcatheter aortic valve implantation and paravalvular regurgitation graded by videodensitometry in comparison with visual grading. *Clin Res Cardiol* 2024;**113**:116–25. https://doi.org/10.1007/s00392-023-02280-7
35. Tateishi H, Campos CAM, Abdelghani M, Leite RS, Mangione JA, Bary L, *et al.* Video densitometric assessment of aortic regurgitation after transcatheter aortic valve implantation: results from the Brazilian TAVI registry. *EuroIntervention* 2016;**11**:1409–18. https://doi.org/10.4244/EIJV11I12A271
36. Rooijakkers MJP, Elkoumy A, Stens NA, van Wely MH, Versteeg GAA, Tsai TY, *et al.* Periprocedural assessment of paravalvular regurgitation after transcatheter aortic valve replacement using diastolic delta and videodensitometry. *J Am Heart Assoc* 2024;**13**:e035587. https://doi.org/10.1161/JAHA.124.035587