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ORIGINAL ARTICLE

Construct validity of automated assessment of invasively measured hemodynamics during transcatheter aortic valve replacement

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Aims Paravalvular regurgitation (PVR) is frequently observed following Transcatheter Aortic Valve Replacement (TAVR). Periprocedural monitoring of invasive hemodynamics has shown promise for diagnosis of PVR, but automated software options are lacking. We aimed to develop a rule-based algorithm for automated assessment of hemodynamic indices of PVR, and evaluate its construct validity and discriminatory value for cardiac magnetic resonance (CMR)-derived relevant PVR compared to standard manual hemodynamic assessment.

Methods and results Left ventricular and aortic pressures were invasively measured during TAVR using fluid-filled pigtail catheters. To evaluate construct validity of automated vs. manual assessment of invasive hemodynamics, we compared (i) proportion of cardiac cycles affected by arrhythmias/noise, (ii) pressure gradients, and (iii) PVR indices. Additionally, we compared the discriminatory value of automatically and manually determined PVR indices for CMR-determined relevant PVR at 30-days. In total, 77 patients were enrolled (664 cardiac cycles). Automated filtering of cardiac cycles affected by arrhythmias/noise had a high sensitivity (95.2%) and specificity (86.4%). In addition, excellent agreement was observed between automated and manual computation of mean gradients pre- and post-TAVR [39.3 ± 12.1 vs. 37.5 ± 11.9 mmHg, intra-class correlation coefficient (ICC): 0.916; 1.92 ± 5.87 vs. 1.14 ± 5.89, ICC: 0.957, respectively], and PVR indices [diastolic delta (DD): 41.7 ± 12.4 vs. 40.6 ± 12.3 mmHg, ICC: 0.982, respectively]. Automated and manual assessment of DD showed comparable discriminatory value for relevant PVR [area under the curve (AUC): 0.81 vs. 0.80, respectively].

Conclusion Rule-based, automated assessment of hemodynamic indices of PVR showed excellent construct validity and discriminatory value for CMR-determined relevant PVR, supporting its use for real-time evaluation and risk stratification in TAVR patients.

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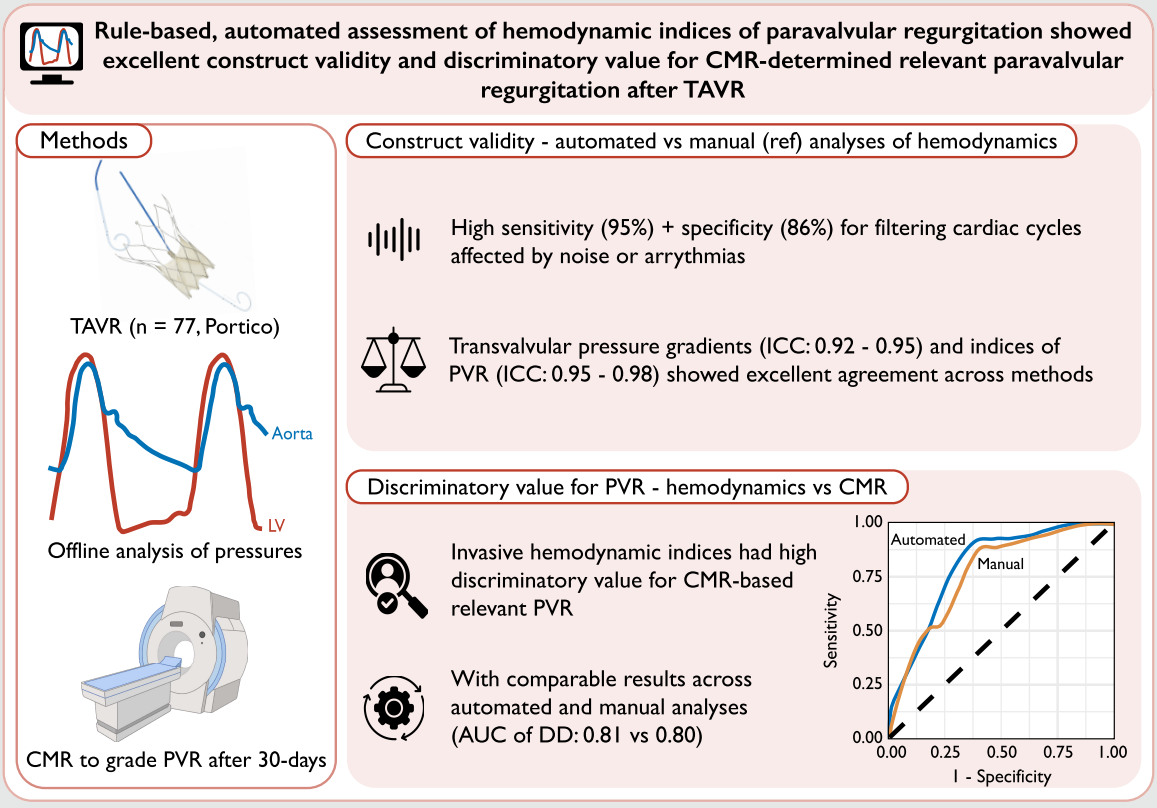
Graphical Abstract



Construct validity and discriminatory value for CMR-determined relevant PVR of automated assessment of invasively measured hemodynamics during TAVR. AUC, area under the receiver operating curve; CMR, cardiac magnetic resonance; DD, diastolic delta; PVR, paravalvular regurgitation; TAVR, transcatheter aortic valve replacement.

Keywords Automated algorithms • Construct validity • Hemodynamics • Paravalvular aortic regurgitation • Transcatheter aortic valve replacement

Introduction

Transcatheter aortic valve replacement (TAVR) is a well-established treatment for patients with severe symptomatic aortic stenosis across the surgical risk spectrum.[1–5] A frequent observation following TAVR is the incidence of paravalvular regurgitation (PVR), which occurs in response to incomplete sealing of the aortic annulus. Despite improvements in valve design, operator experience, and implantation technique during the last decade, the incidence of mild PVR remains high.[6] Interventions are readily available in the catheterization laboratory to reduce the severity of PVR, highlighting the need for accurate periprocedural diagnosis of PVR. Whilst two-dimensional flow measurements of cardiac magnetic resonance (CMR) have shown high accuracy for the assessment of PVR,[7–10] they are expensive, and periprocedural practically not feasible due to logistical constraints. Alternatively, several imaging modalities (i.e. aortic root angiography, transthoracic echocardiography) are available to perform periprocedural assessment of PVR. However, these techniques typically show significant inter-observer variability[7,11] due to their subjective and/or semi-quantitative approach. Unsurprisingly, contemporary methods frequently underestimate PVR severity compared with two-dimensional flow CMR measurements.[7,11]

Relevant PVR immediately affects cardiac hemodynamics, and consequently LV function.[12] Invasive monitoring of LV and aortic hemodynamics after TAVR has therefore shown great promise for the assessment of PVR.[13] Current periprocedural assessment of PVR through invasive hemodynamics in the catheterization laboratory, however, remains limited to visual evaluation or labour-intensive manual computation of the difference in end-diastolic LV and aortic pressure [i.e. diastolic delta (DD)].[14] Advanced hemodynamic indices of PVR that integrate data across the entire diastole[15,16] require advanced real-time computations, and are not frequently used in clinical practice. The introduction of automated software in the catheterization laboratory may allow quantitative and real-time hemodynamic assessment of PVR and transvalvular pressure gradients, and subsequently inform clinical decision making following valve replacement. In facilitating this process, the aim of the present study was to develop a rule-based algorithm for automated assessment of invasively measured hemodynamic indices of PVR, and evaluate its construct validity and discriminatory value for CMR-derived relevant PVR compared with standard manual assessment of hemodynamics.

Methods

Population and design

The APPOSE study (NCT04281771) was an investigator-initiated, single-centre prospective cohort study evaluating the association between invasively measured hemodynamics and PVR as quantified by CMR at

30-days, and its design and inclusion and exclusion criteria have been described before.[13,17] The present study represents a sub-analysis to evaluate the construct validity of an automated algorithm, and discriminatory value of automatically derived indices for CMR-based relevant PVR. All patients were accepted for a TAVR procedure by consensus of a multi-disciplinary heart team, and TAVR procedures were performed according to (inter-) national guidelines. A self-expanding valve (Portico, Abbott Structural Heart, Minneapolis, USA) was implanted in all patients, with valve sizes ranging between 23 and 29 mm. The study protocol was approved by the Medical Research Ethics Committee East-Netherlands (2019-5535) and institutional review board of the Radboud university medical centre. Written informed consent was obtained from all patients prior to enrolment.

Invasively measured hemodynamics

We used NAMIC-pressure sensors (Navilyst Medical, Marlborough, MA, USA) integrated in two 5F fluid-filled pigtail catheters (Impulse; Boston Scientific, Marlborough, USA) during the TAVR procedure to simultaneously measure continuous LV and aortic pressures (i) before pre-dilatation (or before direct implantation), (ii) after implantation of the TAVR bioprosthesis, and when applicable (iii) after each additional periprocedural intervention such as post-dilation or implantation of a second valve (hereafter 'phases'). Pressure sensors were calibrated before every TAVR procedure. In case of bradycardia, the temporary pacemaker in the right ventricle was used to pace at a rate of 80 beats/min. Hemodynamic data were captured in Mac-Lab (GE Healthcare, Chicago, USA) or Sensis Vibe (Siemens Healthcare, Erlangen, Germany), and were exported for offline use. From each exported file, we extracted a random segment of four consecutive cardiac cycles for each phase, equalling a minimum of eight cardiac cycles to be evaluated for each patient. In case of multiple post-dilations, we considered each balloon dilation an individual phase.

Manual assessment of hemodynamics

Manual assessment of invasive hemodynamics was performed using a custom user interface (Python Software Foundation, Wilmington, USA), and included (i) assessment whether each extracted cardiac cycle was affected by arrhythmias or significant noise, and (ii) annotation of relevant time events across each extracted cardiac cycle, including end-diastole, end-systole, and peak systole in the LV and aortic pressure signals. To assess construct validity of automated vs. manual assessment of invasively measured hemodynamics, one observer (N.A.S.) annotated hemodynamic segments from all patients. To evaluate the robustness of this assessment of construct validity of automated assessment, a second independent observer (G.A.A.V.) repeated the annotation process for all patients. In addition, two additional observers (M.J.P.R. and R.L.) independently assessed a random subset of 30 patients. Annotations of the four observers (N.A.S., G.A.A.V., M.J.P.R., and R.L.) on these 30 patients were compared to quantify inter-observer variability of manual assessment. Additionally, intra-observer variability of manual assessment was assessed by having one observer (N.A.S.) re-annotate the same random subset of 30 patients following a 1 month interval. Observers were trained in cardiovascular physiology and were blinded to patient and procedure characteristics, as well as to manual annotations of other observers and results of automated analyses.

Automated assessment of hemodynamics

A rule-based algorithm was designed to automate (i) filtering of cardiac cycles affected by arrhythmias and noise, (ii) detection of time events across each cardiac cycle (i.e. end-systole, end-diastole, peak systole of LV and aortic signal) (*Figure 1A*), and (iii) computation of transvalvular pressure gradients and indices of PVR. Raw pressure signals were filtered using a low-pass filter to remove high frequency noise. Segments in the continuous pressure signal where both catheters were *in situ* were automatically identified. Curvature analyses were performed to detect the aortic incisura and LV end-diastolic pressure (LVEDP) across all cycles[18] (see Supplementary material online, *Figure S1*). In addition, LV and aortic peak systolic blood pressure (SBP), and end-diastolic aortic pressure were defined as the highest and lowest value during mid-systole and late-diastole, respectively. To establish a window for transvalvular pressure gradient measurements, we defined ejection time as the interval between first pressure crossover of the LV and aortic pressure signals during early systole, and the aortic incisura (i.e. closing of aortic valve).[19] The aortic incisura pressure was subsequently mapped onto the LV pressure to identify the LV end-systolic pressure. Obtained time events in each cardiac cycle were used to quantify transvalvular pressure gradients (i.e. mean and peak-to-peak gradient) and several hemodynamic indices of PVR (i.e. the DD,[14] heart rate-adjusted DD [HR-DD],[20] aortic regurgitation index [ARI],[21] time-integrated ARI [TIARI][15] and adjusted diastolic pressure-time index [aDPTI][16]) for each individual cycle (*Figure 1B* and *C*). In addition, the ARI ratio was calculated as the mean ARI of all post-TAVR cycles divided by the mean ARI of all pre-TAVR cycles for each participant.[22] Automated analyses were independently performed by each observer (N.A.S., G.A.A.V., M.J.P.R., and R.L.), and were repeated by one observer (N.A.S.) following a 1-month interval.

Cardiac magnetic resonance

All patients underwent a CMR scan 4–6 weeks post-TAVR using a commercially available 1.5T CMR scanner. CMR data were used to evaluate the discriminatory value of automatically derived indices for relevant PVR. In summary, flow acquisitions were performed during successive breath holds, using both a high (at least 180 cm/s) and low (75 cm/s) velocity encoding to quantify forward and regurgitant volume, respectively. CMR-derived regurgitant fraction (CMR-RF) was subsequently computed by dividing the regurgitant volume by the forward volume, multiplied by 100 (Medis Suite MR (Medis Medical Imaging, Leiden, The Netherlands). Relevant PVR was defined as a CMR-RF >20%.[7]

Statistical analyses

To evaluate differences of automated vs. manual filtering in the proportion of cardiac cycles affected by noise and arrhythmias, we computed its sensitivity, specificity, positive (PPV), and negative predictive value (NPV). Agreement in hemodynamic parameters and individual time events was assessed using Bland–Altman analyses and intra-class correlation coefficients (ICC) in three contexts: (i) between manual and automated assessment by a single observer (i.e. construct validity), (ii) across repeated manual and automated assessments by the same observer (i.e. within-observer variability), and (iii) across manual and automated assessments of four observers (i.e. between-observer variability). ICC values for absolute agreement of single measures were estimated using two-way random effects models for construct validity and between-observer variability, while intra-observer variability was evaluated using a two-way mixed effects model. Furthermore, we compared the discriminatory value of manual and automated assessment of hemodynamic indices of PVR for CMR-determined relevant PVR at 4–6 weeks post-TAVR using the area under the receiver operating curve (AUC; ROC). To assess the potential added value of averaging results over multiple cycles, we compared the discriminatory value of hemodynamic indices of PVR when manually computed for a singular cardiac cycle or when automatically computed across four cycles. Finally, to explore the potential additive value of automated assessment of invasive hemodynamics to angiogram (Sellers)-based grading of PVR severity, we performed ROC and decision curve analyses.[23] Data were presented as means and standard deviations (SD), medians [inter-quartile range (IQR)] or frequencies (%) as appropriate. Analyses were performed in Python version 5.4.1 (Python Software Foundation, Wilmington, USA), and R version 4.2.3 (R Foundation for Statistical Computing, Vienna, Austria) using the *irr*,[24] *pROC*,[25] and *dca*[26] packages. Two-tailed *P*-values < 0.05 were considered statistically significant.

Results

Patient characteristics of the 77 patients are presented in *Table 1*. Patients had a mean age of 80.4 year, were predominantly female ($n = 41$, 53.2%), and had a left ventricular ejection fraction of 54.2% ± 8.4%. Patients were primarily treated under conscious sedation ($n = 60$, 77.9%). Post-dilation was performed in 15 patients (19.5%), and a second valve was implanted in two patients (2.6%) due to migration of the initial TAVR bioprosthesis.

Construct validity

Out of the 664 cardiac cycles that were extracted for manual and automated assessment ($n = 296$ pre-implantation, $n = 308$

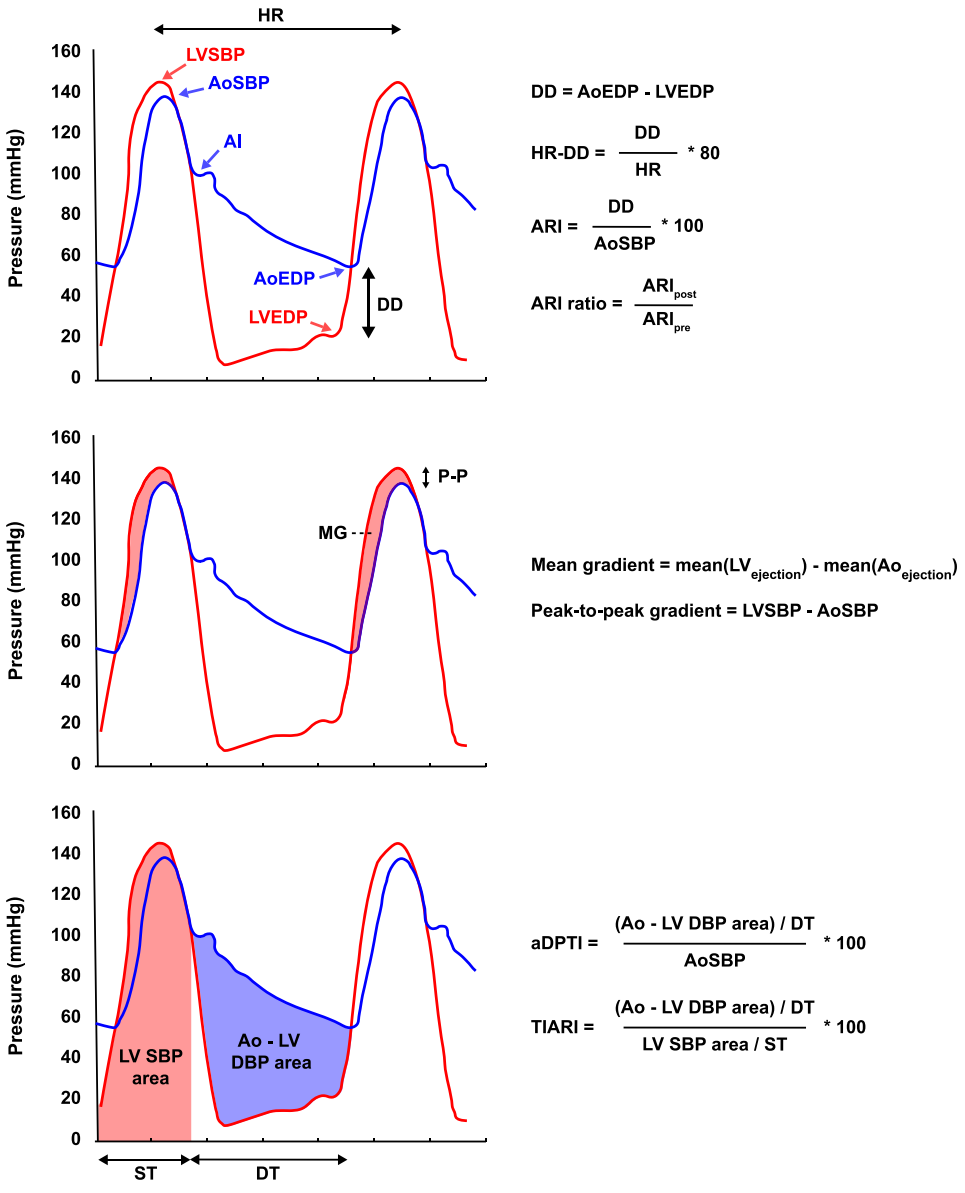


Figure 1 A graphical representation of time events and key parameters quantified in each cardiac cycle through automated and manual assessment of invasive left ventricular and aortic pressure signals. The top panel illustrates all time events identified in each cardiac cycle, which were then used to compute the parameters of interest. The middle panel focuses on the calculation of transvalvular pressure gradients. The bottom panel presents invasive hemodynamic parameters of PVR that require advanced computations and integrate data across the entire diastole. While parameters and time events are quantified in each cardiac cycle, they are graphically displayed across different cycles for improved clarity. aDPTI, adjusted diastolic pressure-time index; Ao, aortic; AI, aortic incisura; ARI, aortic regurgitation index; DD, diastolic delta; EDP, end-diastolic pressure; HR, heart rate; HR-DD, heart rate adjusted diastolic delta; LV, left ventricle; MG, mean gradient; P-P, peak to peak gradient; SBP, systolic blood pressure; DBP, diastolic blood pressure; TIARI, time-integrated aortic regurgitation index.

post-implantation, $n = 52$ post-dilation, $n = 8$ after implantation of second valve), 116 vs. 103 cycles were annotated as affected by noise/arrhythmias by automated and manual assessment, respectively. Sensitivity, specificity, PPV and NPV of automated filtering affected cycles by noise or arrhythmias were high (sensitivity: 95.2%, specificity: 86.4%, PPV: 97.4%, NPV: 76.7%, *Table 2*), and remained consistent when stratified for pre- and post-TAVR cycles (see Supplementary material online, *Table S1*). Stratified analyses for noise and arrhythmias showed comparable inferences (noise: sensitivity: 98.7%, specificity: 81.0%, PPV: 99.4%, NPV: 54.8%; arrhythmias: sensitivity: 99.1%, specificity: 86.6%, PPV: 98.1%, NPV: 93.4%), with the rule-based algorithm filtering additional cycles based on noise compared with manual assessment ($n = 31$ vs. $n = 21$) (*Table 2*). Automated computation of pre- and post-TAVR mean gradients yielded excellent agreement to manual assessment (automated vs. manual pre-TAVR: 39.3 ± 12.1 vs. 37.5 ± 11.9 mmHg, ICC: 0.916; post-TAVR: 1.92 ± 5.87 vs. 1.14 ± 5.89, ICC: 0.957, *Table 3*). In addition, automated computation of post-TAVR invasive hemodynamic indices of PVR showed excellent

Table 1 Baseline characteristics of the 77 patients included in the APPOSE cohort study

	Full cohort	CMR-RF ≤ 20%	CMR-RF > 20%
n (%)	77 (100)	62 (80.5)	15 (19.5)
Demographics			
Age, years	80.4 ± 5.1	80.5 ± 5.0	80.4 ± 5.9
Sex, *n* men (%)	36 (46.8)	27 (43.5)	9 (60)
BMI, kg/m^2	27.3 ± 4.0	27.1 ± 4.0	28.1 ± 4.1
Obesity, *n* (%)	17 (22.1)	12 (19.4)	5 (33.3)
Smoker, *n* (%)	5 (6.5)	3 (4.8)	2 (13.3)
Medical history			
STS, %	2.38 ± 0.96	2.38 ± 0.93	2.35 ± 1.11
NYHA class III/IV, *n* (%)	30 (39.0)	24 (38.8)	6 (40.0)
Diabetes, *n* (%)	20 (26.0)	13 (21.0)	7 (46.7)
Coronary heart disease, *n* (%)	41 (53.2)	33 (53.2)	8 (53.3)
COPD, *n* (%)	10 (13.0)	8 (12.9)	2 (13.3)
Atrial fibrillation, *n* (%)	17 (22.1)	14 (22.6)	3 (20.0)
MDRD-GFR, mL/min	64.8 ± 17.5	66.7 ± 17.0	57.0 ± 17.8
Haemoglobin, mmol/L	7.9 ± 0.9	8.0 ± 0.9	7.6 ± 1.0
Pre-TAVR echocardiography			
AVA, cm^2	0.79 ± 0.18	0.78 ± 0.19	0.80 ± 0.11
Mean gradient, mmHg	45.2 ± 12.4	44.9 ± 11.6	46.5 ± 15.7
Vmax, m/s	4.3 ± 0.6	4.3 ± 0.6	4.3 ± 0.6
LVEF, %	54.2 ± 8.4	54.8 ± 8.3	51.7 ± 8.4
≥Moderate aortic regurgitation, *n* (%)	7 (9.1)	6 (9.7)	1 (6.7)

Results are presented for the full cohort, as well as stratified for relevant PVR at 30-days as quantified by CMR. Data are presented as means and SDs, medians [inter-quartile range], or frequencies (%) as appropriate.
AF, atrial fibrillation; AVA, aortic valve area; BMI, body mass index; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; MDRD-GFR, modification of diet in renal disease—glomerular filtration rate; NYHA, New York Heart Association functional classification; STS, Society of Thoracic Surgeons; Vmax, aortic valve maximum velocity.

agreement with manual assessment (DD: 41.7 ± 12.4 vs. 40.6 ± 12.3 mmHg, ICC: 0.982; ARI: 30.1 ± 10.5 vs. 29.2 ± 10.2 mmHg, ICC: 0.984; TIARI: 50.9 ± 9.5 vs. 51.5 ± 9.3, ICC: 0.981, *Table 3*). Identification of individual time events in the cardiac cycle were consistent across manual and automated assessment (see Supplementary material online, *Table S2*). Inferences on construct validity of automated assessment did not change when hemodynamic segments of all patients were manually annotated by a different observer (see Supplementary material online, *Tables S3* and S4).

Within- and between-observer variability

Automated computation of hemodynamic indices showed no within- (see Supplementary material online, *Table S5*) and between-observer variability (see Supplementary material online, *Table S6*). In contrast, manual computation of hemodynamic indices showed little within- (see Supplementary material online, *Table S5*) and between-observer variability (see Supplementary material online, *Table S6*).

Relation with CMR

The CMR was performed 41 ± 14 days after TAVR. The mean CMR-RF was 12.4% ± 9.3%, and 15 patients (19.5%) were diagnosed with relevant PVR by CMR. When averaged across four consecutive cycles, automated computation of invasive hemodynamic indices of PVR showed comparable discriminatory value for relevant PVR (quantified by CMR) compared with manual computation (*Figure 2*). Specifically, the DD showed the highest discriminatory value (AUC: 0.81, 95% CI: 0.69, 0.93; *Figure 2*), and did not show significant over- or underestimation across the spectrum of the DD (see Supplementary material online, *Figure S2*). Manually computing the DD in a singular cardiac cycle yielded numerically lower discriminatory value compared with when hemodynamic indices of PVR were automatically computed and averaged across four consecutive cycles (AUC manual DD from 1 cycle: 0.77, 95% CI: 0.66, 0.89; AUC automated across 4 cycles: 0.81, 95% CI: 0.69, 0.93; Supplementary material online, *Figure S3*). Compared with angiography alone, addition of automated computation of the DD increased the discriminatory value for CMR-derived relevant PVR (angiography: AUC: 0.70, 95% CI: 0.56, 0.84; angiography + DD: AUC: 0.81, 95% CI: 0.69, 0.92) (see Supplementary material online, *Figure S4*, left panel), especially in those with a low to intermediate treatment probability of relevant PVR (see Supplementary material online, *Figure S4*, right panel).

Discussion

We developed a rule-based algorithm for automated assessment of hemodynamic indices of PVR, and evaluated its construct validity and discriminatory value for CMR-derived relevant PVR. We present the following key findings. First, automated filtering of cardiac cycles affected by cardiac arrhythmias or noise demonstrated excellent sensitivity and specificity compared with standard manual filtering. Second, automated computation of transvalvular pressure gradients and hemodynamic indices of PVR showed excellent agreement with manual assessment of invasive hemodynamics, with no within- and between-observer variability. Third, hemodynamic indices of PVR exhibited a high discriminatory value for 30-day relevant PVR as quantified

Table 2 Automated vs. manual filtering of cardiac cycles affected by significant noise or arrhythmias.

		Automated assessment		
		Normal	**Affected by noise/arrhythmias**	**Total**
Manual assessment	Normal	534	27	561
	Affected by noise/arrhythmias	14	89	103
	Total	548	116	664

		Automated assessment		
		Normal	**Affected by noise**	**Total**
Manual assessment	Normal	629	14	643
	Affected by noise	4	17	21
	Total	633	31	664

		Automated assessment		
		Normal	**Affected by arrhythmias**	**Total**
Manual assessment	Normal	577	5	582
	Affected by arrhythmias	11	71	82
	Total	588	76	664

Filtering cycles affected by both noise and arrythmias: Sensitivity: 95.2%, Specificity: 86.4%, PPV: 97.4%, NPV: 76.7%
Filtering cycles affected by noise: Sensitivity: 97.8%, Specificity: 81.0%, PPV: 99.4%, and NPV: 54.8%
Filtering cycles affected by arrhythmias: Sensitivity: 99.1%, Specificity: 86.6%, PPV: 98.1%, and NPV: 93.4%
Number of cycles filtered by the algorithm and by manual assessment have been cross-tabulated. Sensitivity, specificity, PPV, and NPV have been presented for automated vs. manual (reference) filtering of cycles affected by significant noise or arrhythmias (upper table), and separately for noise (middle table) and arrhythmias (lower table).
NPV, negative predictive value; PPV, positive predictive value; TAVR, transcatheter aortic valve replacement.

by CMR, with comparable results between automated and manual computation. Together, these findings confirm the construct validity and diagnostic utility of automated assessment of invasive hemodynamics for post-TAVR quantification of PVR (Graphical Abstract). Its implementation into clinical practice may facilitate real-time monitoring of invasive hemodynamic indices of PVR and serve as an adjunct to contemporary diagnostic modalities to enhance risk stratification in patients undergoing TAVR.

Invasive hemodynamic assessment has shown great promise for the diagnosis of PVR,[13] although its current clinical application is often limited to visual estimation of the DD from a single cardiac cycle. Although manual hemodynamic assessment is reproducible with minimal between- and within-observer variability, it remains labour-intensive. Automated assessment, in contrast, enables real-time computation of invasive hemodynamic indices and eliminates observer variability. Novel technologies to automate PVR assessment have been proposed,[27] but are dependent on the use of the SavvyWire guidewire. In our study, we developed a stand-alone automated algorithm and demonstrated that the automated quantification of transvalvular pressure gradients and indices of PVR showed excellent agreement with manually derived values. In addition, automated filtering of cycles affected by arrhythmias or significant noise showed excellent sensitivity and specificity. The lower NPV was primarily driven by an increased number of cycles being filtered due to significant noise compared with manual assessment. However, given the high prevalence of pre-existing or new-onset arrhythmias, and noise within pressure signals,[28–30] thorough filtering is essential. As a result, automated filtering may actually outperform manual filtering, as subtle deviations may be filtered as well. These advancements highlight the advantages of automated over manual hemodynamic assessment for precise quantification of PVR severity.

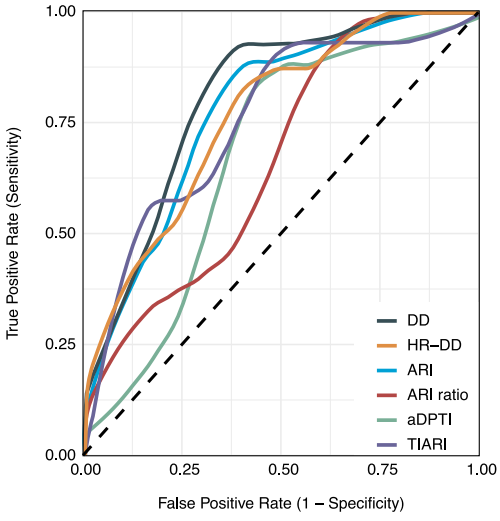
To assess the clinical relevance of automated assessment of hemodynamic indices of PVR, we related hemodynamic indices of PVR to relevant PVR as determined by CMR at 30-days, and compared their discriminatory value to manual computations. When manually and automatically assessed, the DD demonstrated the highest discriminatory value for relevant PVR. Nonetheless, manual computation of the DD in clinical practice typically uses data from a single cardiac cycle only. Automated analysis, in contrast, enables averaging data across multiple cardiac cycles, or even multiple minutes of data collection, and may therefore better capture temporal trends in post-TAVR hemodynamics due to the altered flow state. Indeed, when the DD was automatically computed across multiple cycles, the discriminatory value for relevant PVR was numerically improved (see Supplementary material online, *Figure S3*). Manually averaging data across multiple cycles is challenging to perform real-time. Together, automated assessment of invasive hemodynamics facilitates data integration across multiple cycles and streamlines analysis, potentially enabling more precise quantification of PVR severity.

To further explore the potential role of automated assessment of invasive hemodynamic indices of PVR within clinical practice, we compared its discriminatory value relative to angiography. Addition of the DD to angiography increased the discriminatory value for relevant PVR at 30-days as quantified by CMR (see Supplementary material online, *Figure S4*, left panel). Importantly, this improvement was primarily driven by an increased net benefit in those with a low to intermediate treatment probability of PVR (see Supplementary material online, *Figure S4*, right panel). This observation is clinically relevant, as these patients may be at an increased risk of being misclassified due to the underestimation of PVR severity by contemporary imaging modalities.[7,11]

Table 3 Construct validity of automated vs. manual assessment of invasive hemodynamics

	Manual (mean ± SD)	Automated (mean ± SD)	Δ (mean ± SD)	[LOA, UOA]	ICC [95% CI]
Pre-TAVR ($n = 257$ cycles)					
Mean gradient, mmHg	39.3 ± 12.1	37.5 ± 11.9	1.8 ± 4.6	[−7.20, 10.85]	0.916 [0.867, 0.944]
Peak-to-peak gradient, mmHg	53.1 ± 17.3	53.6 ± 17.3	−0.4 ± 1.7	[−3.67, 2.83]	0.995 [0.993, 0.996]
Post-TAVR ($n = 291$ cycles)					
Mean gradient, mmHg	1.92 ± 5.87	1.14 ± 5.89	0.8 ± 1.6	[−2.25, 3.81]	0.957 [0.916, 0.975]
Peak-to-peak gradient, mmHg	1.94 ± 6.17	2.26 ± 6.08	−0.3 ± 1.9	[−4.07, 3.43]	0.950 [0.937, 0.960]
DD, mmHg	41.7 ± 12.4	40.6 ± 12.3	1.1 ± 2.1	[−2.99, 5.16]	0.982 [0.963, 0.990]
HR-DD, mmHg/b.p.m.	47.4 ± 16.2	46.1 ± 15.8	1.3 ± 2.5	[−3.67, 6.21]	0.985 [0.970, 0.991]
ARI	30.1 ± 10.5	29.2 ± 10.2	0.9 ± 1.6	[−2.31, 4.12]	0.984 [0.964, 0.991]
ARI ratio	0.87 ± 0.32	0.85 ± 0.32	0.03 ± 0.1	[−0.11, 0.16]	0.975 [0.956, 0.985]
aDPTI	35.4 ± 7.1	35.9 ± 7.1	−0.5 ± 1.2	[−2.87, 1.83]	0.983 [0.971, 0.989]
TIARI	50.9 ± 9.5	51.5 ± 9.3	−0.6 ± 1.7	[−3.96, 2.83]	0.981 [0.972, 0.987]

Table on the construct validity of automated vs. manual computation of various hemodynamic parameters. ICC values for absolute agreement of single measures were estimated using two-way random effects models. Results are stratified by TAVR phase.
aDPTI, adjusted diastolic pressure-time index; ARI, aortic regurgitation index; CI, confidence interval; DD, diastolic delta; HR-DD, heart-rate adjusted diastolic delta; ICC, intra-class correlation coefficient; LOA, lower limit of agreement; SD, standard deviation; TIARI, time-integrated aortic regurgitation index; UOA, upper limit of agreement.



	Manual (AUC, 95%CI)	Automated (AUC, 95%CI)
DD	0.80 [0.68,0.92]	0.81 [0.69,0.93]
HR–DD	0.75 [0.62,0.89]	0.77 [0.63,0.90]
ARI	0.76 [0.63,0.89]	0.78 [0.65,0.91]
ARI ratio	0.69 [0.55,0.84]	0.68 [0.53,0.84]
aDPTI	0.68 [0.54,0.83]	0.67 [0.52,0.82]
TIARI	0.74 [0.60,0.89]	0.75 [0.60,0.90]

Figure 2 Receiver operating curve of invasively measured hemodynamic indices of PVR for relevant PVR at 30-days as quantified by CMR. Receiver operating curves reflect the discriminatory value of automated assessment of invasive hemodynamics for relevant PVR at 30-days as quantified by CMR. Curves were smoothed to enhance clarity. The DD had the highest discriminatory value for relevant PVR, with no observed differences across automated and manual assessment of invasive hemodynamics. aDPTI, adjusted diastolic pressure-time index; ARI, aortic regurgitation index; CMR, cardiac magnetic resonance; DD, diastolic delta; HR-DD, heart rate-adjusted diastolic delta; TIARI, time-integrated aortic regurgitation index.

Furthermore, even none/trace PVR can lead to elevated LVEDP in LVs with an increased wall stiffness, comparable to the effect of moderate PVR in more compliant LVs.[31] Our findings suggest that the addition of the DD to angiography-based diagnosis of PVR may enhance risk stratification, particularly in patients with seemingly trivial PVR which otherwise would not be treated. Consequently, clinical implementation of invasive hemodynamics to evaluate the severity of PVR may guide decision-making on post-dilation procedures. Evaluation of the safety of such procedures should be made on a case-by-case basis, balancing the risk of residual PVR and post-dilation-related complications such as landing zone rupture or stroke. Future studies are warranted to elucidate the implications of real-time invasive hemodynamic assessment as a complementary tool to contemporary imaging techniques for the diagnosis and management of PVR.

Limitations

Some limitations should be addressed. First, all patients were treated using a self-expanding Abbott Portico bioprosthesis. Consequently, the discriminatory value of invasive hemodynamic indices of PVR cannot directly be

generalized to other self-expanding or balloon-expandable devices. Nonetheless, we believe the construct validity of automated assessment of invasive hemodynamics is unlikely to be related to a valve platform. Second, the incidence of CMR-based relevant PVR was low ($n = 15$). Future studies are warranted to confirm the diagnostic value of hemodynamic indices of PVR. Third, whilst CMR may be the most accurate method to grade PVR, its accuracy may be affected by flow artefacts, flow turbulence and inclusion of coronary artery diastolic flow in the total regurgitant volume. Finally, the use of CMR might have led to selection bias, as patients with contra-indications for CMR or those with an overall poorer health status might have been more likely to decline participation.

Conclusion

Automated assessment of hemodynamic indices of PVR using a rule-based algorithm showed excellent agreement with standard manual assessment of hemodynamics. In addition, automated computation of invasive hemodynamic indices of PVR exhibited high discriminatory value for relevant PVR at 30-days post-TAVR as determined by CMR, with no observed differences from manual assessment. Our findings underscore the potential of automated assessment of hemodynamic indices of PVR, supporting the integration of automated algorithms into clinical practice for real-time evaluation and risk stratification of patients undergoing TAVR.

Supplementary material

Supplementary material is available at *European Heart Journal – Digital Health*.

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Data availability

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

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