

Non-invasive determination of pressure recovery by cardiac MRI and echocardiography in patients with severe aortic stenosis: short and long-term outcome prediction

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Abstract

Objective: To assess the influence of pressure recovery (PR)-corrected haemodynamic parameters on outcome in patients with aortic stenosis.

Methods: Aortic stenosis severity parameters were corrected for PR (increase in static pressure due to decreasing dynamic pressure), assessed using transthoracic echocardiography (TTE) or cardiac magnetic resonance imaging (CMR), in patients with aortic stenosis. PR, indexed PR (iPR) and energy loss index (ELI) were determined. Factors that predicted all-cause mortality, and 9-month or 10-year New York Heart Association classification ≥ 2 were assessed using Cox proportional hazards regression.

Results: A total of 25 patients, aged 68 ± 10 years, were included. PR was 17 ± 6 mmHg using CMR, and CMR correlated with TTE measurements. PR correction using CMR data reduced the AS-severity classification in 12–20% of patients, and correction using TTE data reduced the

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AS-severity classification in 16% of patients. Age (Wald 4.774) was a statistically significant predictor of all-cause mortality; effective orifice area (Wald 3.753) and ELI (Wald 3.772) almost reached significance.

Conclusions: PR determination may result in significant reclassification of aortic stenosis severity and may hold value in predicting all-cause mortality.

Keywords

Aortic valve stenosis, pressure recovery, cardiac MR, echocardiography, reclassification, outcome prediction

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Introduction

In patients with aortic stenosis, decisions regarding time of intervention are based on the severity of aortic stenosis and patient symptoms. In clinical practice, transthoracic echocardiography (TTE) is the primary imaging modality for evaluating aortic stenosis severity. Many studies have reported discrepancies between noninvasively estimated echocardiographic gradients using the Bernoulli equation and invasively measured gradients across the aortic valve. The phenomenon of pressure recovery (PR) has been proposed to explain the often-overestimated echocardiographic pressure gradients compared with invasively determined pressure gradients.¹⁻³

Besides aortic flow misvaluation, studies have demonstrated that PR seems to be an important factor in aortic stenosis grading.⁴ Moreover, and particularly in patients with severe forms of aortic stenosis, calculating the energy loss coefficient (ELCo) might improve risk stratification.⁵

Pressure recovery represents the reconversion of maximal kinetic energy in the vena contracta distal to the aortic stenosis into potential energy in the ascending aorta. The extent of PR is smaller when kinetic energy is lost by the dissipation of energy in the form of flow turbulences. The course of the blood stream during left ventricular

(LV) systolic ejection is schematically outlined in Figure 1. Based on the fluid mechanics principles first described by Clark et al.,⁶ formulas for noninvasive determination of the extent of PR have been developed and have been applied in several previous echocardiographic studies.^{1,3,7-10} A further stage is the concept of indexed pressure recovery (iPR), which has been developed in order to approximate clinical importance by relating PR values to the maximal pressure gradient of the individual patient. Finally, the energy loss index (ELI), as another parameter to assess PR, integrates valve orifice areas, areas of the aorta and body composition.^{2,9} Therefore, the width of the ascending aorta is the most important parameter for noninvasive estimation of PR.

To date, ascending aorta measurements for evaluating PR have been performed using echocardiography, most commonly at the site of the sinotubular junction (STJ).¹¹ Cardiac magnetic resonance imaging (CMR) allows an exact depiction of cardiac and vascular anatomy, and has an advantage compared with echocardiography, in that it provides complete coverage of the whole ascending aorta.¹² However, the estimation of haemodynamics, particularly maximal aortic velocity at the vena contracta, affords multiple measurements, and at best, a flexible alignment of flow

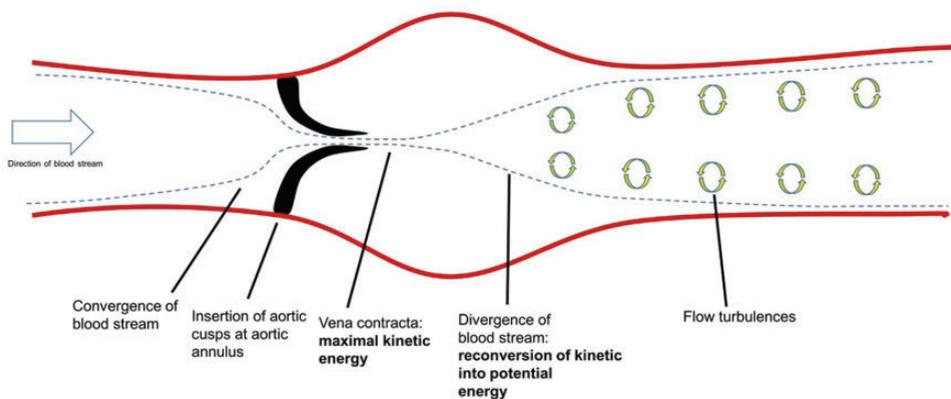


Figure 1. Schematic drawing of the course of the blood stream during left ventricular (LV) systolic ejection from the LV outflow tract to the tubular ascending aorta.

velocity measurement planes during systole/diastole, which is not easily achievable with standard software packages in CMR. In this case, echocardiography has clear advantages. The uneven distribution in assessment of morphologic and haemodynamic parameters between echocardiography and CMR have led to the idea of a hybrid approach, combining flow data derived from echocardiography with morphologic data from CMR.

The main aims of the present study were: (1) to test the feasibility of a combined echocardiography and CMR protocol for estimating PR, iPR and ELI at different aortic levels and different time-points in the cardiac cycle; (2) to compare PR, iPR and ELI assessments between echocardiography (alone) and CMR (hybrid approach); and (3) to determine the influence of PR on outcome in patients with aortic stenosis.

Patients and methods

Study population

This prospective study included sequentially enrolled patients with severe degenerative aortic stenosis who were being treated at the University Hospital Wuerzburg. CMR

examinations were conducted between January 2005 and May 2007, and patients were followed for a maximum of 10 years, up to between January 2015 and May 2017. Patients with classic CMR contraindications were excluded from the study. Other aspects of the included CMR data (e.g. LV outflow calculations) have been published previously,¹³ however there is no overlap with the data presented here. The severity of aortic stenosis was classified according to echocardiographic results. Data for patient outcome were collected from the cardiology outpatient clinic records. Missing data points were integrated by direct telephone calls with the patients or their relatives.

Ethics approval for the study was obtained from the institutional review board (University Wuerzburg EA 2003/2006) and each patient provided written informed consent.

Echocardiographic imaging technique

Transthoracic echocardiography was performed with patients in a supine left lateral position, using a VIVID7 3.5-MHz ultrasound scanner (GE Ultrasound, Horten, Norway), and standard echocardiographic procedure for the evaluation of left and

right heart dimensions and valvular heart disease.

Cardiac MRI technique

Cardiac magnetic resonance imaging was performed using a 1.5T MRI (Magnetom Symphony Quantum, Siemens Healthineers, Erlangen, Germany) with a 12-channel body phased-array coil (6 elements in the front and 6 elements in the back integrated into the spine-array). An electrocardiogram-gated balanced steady-state free precession technique (TR, 4.3 ms; TE, 2.15 ms; flip angle, 70°; temporal resolution <50 ms) was used for morphologic imaging. For the analysis of LV mass and volumes, short-axis views were acquired (10–12 consecutive 8-mm slices, depending on heart size). For assessment of the aortic supravalvular area, including the ascending aorta, the same sequence was planned in the 3-chamber view (3CV).

Measurement methods

Echocardiography velocity measurements were performed at the level of the LV outflow tract (LVOT) and the aortic valve. The effective orifice area (EOA) was calculated based on the continuity equation using diameter measurements at the level of the LVOT in the parasternal long-axis view and velocity time index at the level of the LVOT and the aorta. Ascending aorta measurements were performed at the level of the STJ at the end of diastole (Figure 2).⁸ The STJ was chosen, as it is considered to be the best measurement location for PR.¹⁴ The LVOT diameter was measured in mid-systole, inner edge to inner edge, and accounting for the fact that the LVOT has an elliptical shape in almost 90% of patients.^{15,16}

For CMR, the LV mass and volumes (plus index for body surface area) were determined using ARGUS software



Figure 2. Representative transthoracic echocardiography (TTE) image (parasternal long axis view, end-diastolic) showing the ascending aorta and diameter measurement at the level of the sinotubular junction (STJ).

(Siemens Healthineers). Aortic diameters were determined on 3CV images. Due to better coverage of the ascending aorta, diameter measurements were performed at different aortic levels by diameter linings in steady-state free precession (SSFP) sequences: aortic annulus, Sinus of Valsalva (SoV), STJ and the proximal tubular ascending aorta (AoA) (Figure 3).

Distances between aortic-measurement planes and the aortic annulus were measured, and the distance of the STJ was referred to as ‘height of SoV’, as previously described.¹⁷ All AoA diameter measurements were performed at two different time-points in the cardiac cycle (the beginning and end of systole).

Aortic areas were calculated using the following formula:

$$A = \left(\frac{d}{2}\right)^2 \times \pi \quad (1)$$

Where A = area; d = diameter

Pressure recovery, iPR and ELI were calculated using echocardiographic velocity measurements and by insertion of ascending aorta diameter measurements, determined either by echocardiography

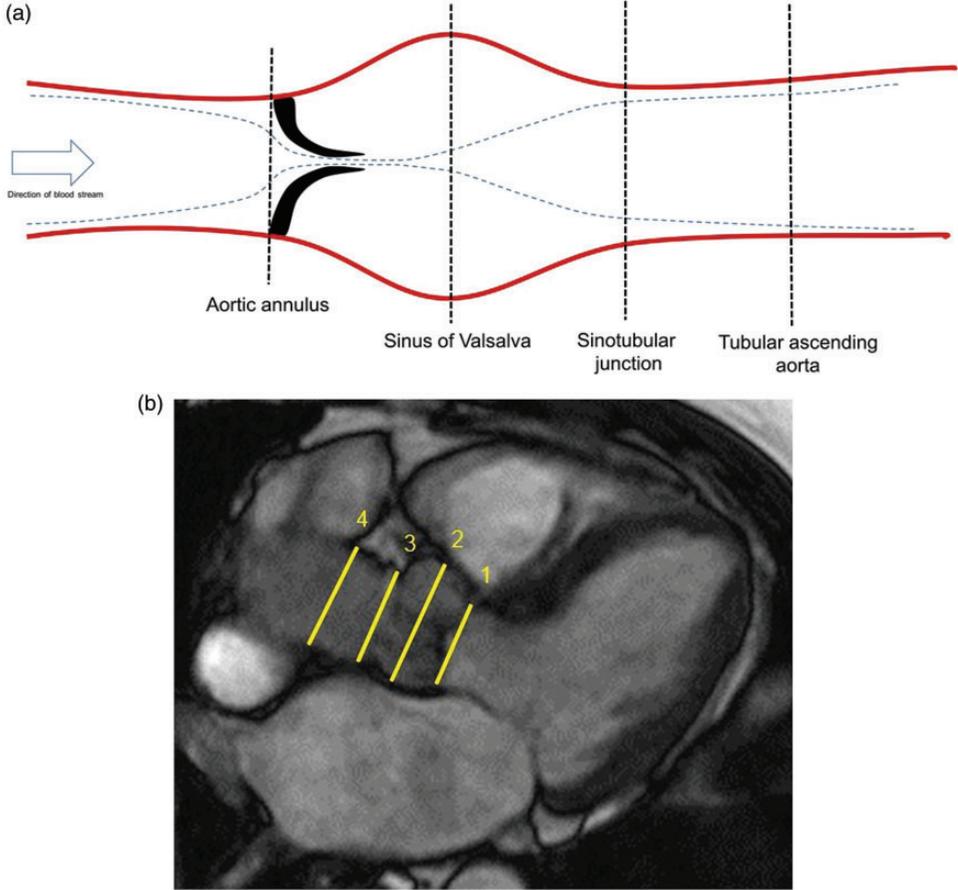


Figure 3. (a) Schematic drawing and (b) representative steady-state free precession (SSFP)-cine cardiac magnetic resonance image (3 chamber view) of the ascending aorta showing diameter measurement positions: 1, aortic annulus; 2, Sinus of Valsalva (SoV); 3, sinotubular junction (STJ); and 4, proximal tubular ascending aorta.

(one anatomic site: STJ) or by CMR (three anatomic sites: SoV, STJ, AoA).

PR (mmHg) was calculated by the formula:

$$PR = \frac{4 \times v_{max}^2 \times 2 \times EOA}{A_A \times \left(1 - \frac{EOA}{A_A}\right)} \quad (2)$$

Where PR = pressure recovery; V_{max} = maximal velocity across the aortic valve; EOA = effective orifice area; AA = ascending aorta

iPR (%) was calculated by the formula:

$$iPR = \frac{PR}{p_{max}} \quad (3)$$

Where iPR = index pressure recovery; P_{max} = maximal pressure gradient across the aortic valve

ELCo (cm^2) was calculated using the formula:

$$ELCO = \frac{EOA \times A_A}{A_A - EOA} \quad (4)$$

Where ELCo = energy loss coefficient

ELI (cm^2/m^2) was calculated by the following formula (indexed for body surface area [BSA]):

$$ELI = \frac{\frac{EOA \times A_A}{A_A - EOA}}{BSA} \quad (5)$$

Where ELI = energy loss index

Clinically relevant pressure recovery was defined as an iPR value $>20\%$.¹¹ For ELI, a cut-off value of $0.6 \text{ cm}^2/\text{m}^2$ was used.^{8,10,18}

Statistical Analyses

All results are presented as mean \pm SD or n (%) prevalence. Data were compared by application of Mann–Whitney U -test and Wilcoxon-Rank-Sum test. Cox proportional hazards linear regression analyses were performed and correlation coefficients were determined. Data were analysed using SPSS software, version 19.0 (IBM, Armonk, NY, USA), and a P value <0.05 was considered statistically significant.

Results

Basic morphological parameters (CMR) and functional parameters (echocardiography)

A total of 25 patients (18 male and seven female; mean age, 68 ± 10 years) with severe degenerative aortic stenosis were included. The study population characteristics are summarized in Table 1. According to CMR, the LV mass index (LVMI) was $100 \pm 27 \text{ g}/\text{m}^2$, LV volume indices were $79 \pm 29 \text{ ml}/\text{m}^2$ (LV end-diastolic volume index) and $36 \pm 23 \text{ ml}/\text{m}^2$ (LV end-systolic volume index), the stroke volume index was $42 \pm 14 \text{ ml}/\text{m}^2$ and the ejection fraction was $57 \pm 13\%$. All patients had aortic supra-valvular flow turbulences on cine images.

Table 1. Demographic, clinical and medication data for patients with severe degenerative aortic stenosis.

Demographic parameter	
Patients included	25
Age (years)	68 ± 10
Male: female	18: 7
BSA (kg/m^2)	1.91 ± 0.22
Height (cm)	170 ± 10
Weight (kg)	80 ± 15
Medication	
Diuretics	17/25 (68%)
Statins	13/25 (52%)
ACE-inhibitors/AT IIra	12/25 (48%)
Beta blocker	12/25 (48%)
Calcium antagonists	6/25 (24%)
Clinical parameter	
Hypertension	20/25 (80%)
Hyperlipidaemia	12/25 (48%)
Coronary artery disease	9/25 (36%)
Diabetes	7/25 (28%)
Renal insufficiency	2/25 (8%)
Smoker	6/25 (24%)
NYHA I	0/25 (0%)
NYHA II	7/25 (28%)
NYHA III	15/25 (60%)
NYHA IV	2/25 (8%)

Data presented as mean \pm SD or n (%) prevalence.

BSA, body surface area; ACE, angiotensin-converting-enzyme; AT IIra, angiotensin II receptor antagonists; NYHA, New York Heart Association classification.

The echocardiographic functional parameters are summarized in Table 2.

Aortic dimension measured by CMR

The CMR measurements at the beginning of systole varied depending on measurement position and revealed a range of aortic diameters at different levels, from 2.59 to 3.31 cm (area, $5.41\text{--}8.75 \text{ cm}^2$). The highest diameter values distal to the annulus were found at the proximal tubular ascending aorta (diameter, $2.98 \pm 0.41 \text{ cm}$, area, $7.09 \pm 1.92 \text{ cm}^2$), and the smallest values were found at the STJ (diameter, $2.77 \pm 0.44 \text{ cm}$, area, $6.18 \pm 1.89 \text{ cm}^2$).

Table 2. Haemodynamic analysis by transthoracic echocardiography (TTE) in patients with severe degenerative aortic stenosis.

Parameter		Parameter	
V_{\max}	4.34 ± 0.83	V_{mean}	3.30 ± 0.76
P_{\max}	78 ± 29	P_{mean}	51 ± 22
PR_{TTE}	15 ± 4	iPR_{TTE}	0.21 ± 0.07
VTI_{LVOT}	23 ± 6	VTI_{AK}	102 ± 25
EOA (cm ²)	0.85 ± 0.24	EOAi (cm ² /m ²)	0.46 ± 0.16
ELCO (cm ²)	0.99 ± 0.34	ELI (cm ² /m ²)	0.53 ± 0.22
$d_{\text{TTE_LVOT}}$ (cm)	2.3 ± 0.1	$A_{\text{TTE_LVOT}}$ (cm ²)	4.0 ± 0.4
$d_{\text{TTE_STJ}}$ (cm)	3.0 ± 0.33	$A_{\text{TTE_STJ}}$ (cm ²)	7.33 ± 1.57

Data presented as mean \pm SD.

V_{\max} , maximal velocity across the aortic valve; p_{\max} , maximal pressure gradient across the aortic valve; PR, pressure recovery; VTI, velocity time integral; LVOT, left ventricular outflow tract; EOA, effective orifice area; ELCO, energy loss coefficient; d, diameter; STJ, sinotubular junction; V_{mean} , mean velocity across the aortic valve; P_{mean} , mean pressure gradient across the aortic valve; iPR, index pressure recovery; AK, aortic valve; EOAI, indexed aortic orifice area; ELI, energy loss index; A, area.

Table 3. Pressure recovery (PR), iPR and energy loss index using aortic areas in three-chamber view using cardiac magnetic resonance imaging (CMR).

Anatomic site	Parameter			
	PR (mmHg)	iPR (%)	ELCO (cm ²)	ELI (cm ² /m ²)
Beginning of systole				
SoV	15 ± 5.6	21 ± 7.4	1.1 ± 0.36	0.59 ± 0.23
STJ	20 ± 7.8	27 ± 9.2	1.2 ± 0.41	0.64 ± 0.26
Ascending aorta	18 ± 6.3	24 ± 7.8	1.1 ± 0.37	0.61 ± 0.23
End of systole				
SoV	14 ± 7.5	20 ± 7.0	1.10 ± 0.35	0.59 ± 0.23
STJ	19 ± 7.2	26 ± 9.2	1.17 ± 0.40	0.63 ± 0.26
Ascending aorta	17 ± 6.9	23 ± 8.8	1.14 ± 0.37	0.61 ± 0.23

SoV, Sinus of Valsava; STJ, sinotubular junction; iPR, index pressure recovery; ELCO, energy loss coefficient; ELI, energy loss index.

Determination of PR, iPR and ELI by CMR

Pressure recovery, iPR and the respective ELI measurements for both time points (beginning and end of systole), and at the three aortic areas, are listed in Table 3. All values showed only small absolute variations in dependency of measurement position, with the parameters slightly higher at the STJ and the ascending aorta, but without statistically significant differences.

Mean aortic PR values at the beginning of systole were as follows: PR, 17 ± 6.0

mmHg; iPR, $24 \pm 7\%$; ELCO, 1.14 ± 0.37 cm²; and ELI, 0.61 ± 0.23 cm²/m².

Comparison of CMR and TTE measurements

Aortic diameter measurements with TTE (STJ) were slightly larger compared with CMR measurements (mean differences, 0.27 ± 0.42 cm; $P=0.011$). PR and iPR determined by TTE showed a high correlation with CMR measurements (PR, $r=0.73$

[$P < 0.001$]; and iPR, $r = 0.69$ [$P < 0.001$]; Figure 4).

Pressure recovery and its impact on aortic stenosis-severity classification

The PR values were applied to clinical severity, and reclassification rates for echocardiography and CMR are summarized in Figure 5. Severe aortic stenosis by indexed EOA (EOAi)_{TTE} was present in 18/25 patients (72%). Echocardiographic PR-correction resulted in severe aortic stenosis by ELI in 14/25 of patients (56%). Thus 4/25 (16%) patients were reclassified using TTE.

For CMR, the incidence of clinically relevant pressure recovery showed remarkable variances depending on the measurement position (varying between 48% and 68%). Correspondingly, a downward classification was calculated for 12–20% of patients,

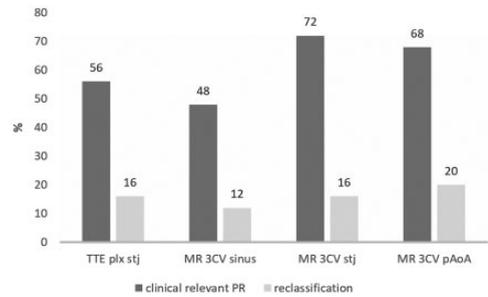


Figure 5. Frequency of clinically relevant pressure recovery (dark grey) and aortic stenosis severity reclassification (light grey) depending on imaging modality (transthoracic echocardiography [TTE] versus steady-state free precession [SSFP]-cardiac magnetic resonance imaging [CMR] in 3-chamber view [3CV]) and measurement location for CMR (sinus, Sinus of Valsalva; stj, sinutubular junction; or pAoA, proximal tubular ascending aorta); TTE measurements were obtained at the end of diastole, and SSFP measurements at the beginning of systole. Plx, parasternal long axis.

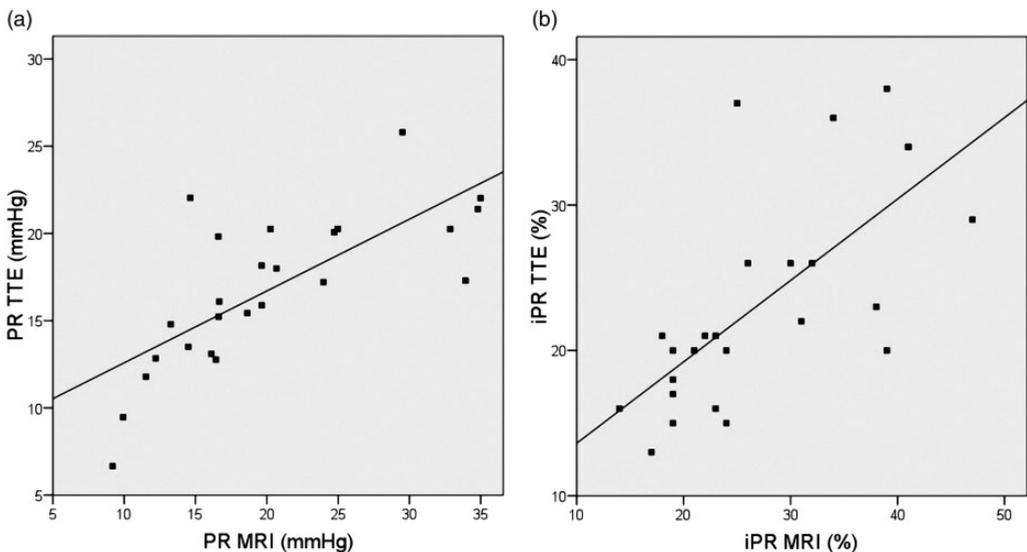


Figure 4. Scatter plots showing correlation between cardiac magnetic resonance imaging (MRI) and transthoracic echocardiography (TTE) results for (a) pressure recovery (PR), $r = 0.73$ ($P < 0.001$); and (b) index pressure recovery (iPR), $r = 0.69$ ($P < 0.001$), measured at the sinutubular junction.

partly exceeding the frequency of reclassification by echocardiography (Figure 5). The individual change in aortic stenosis severity for each patient is illustrated in Figure 6, which compares non-corrected EOA assessment with corrected assessment implementing aortic measurement by CMR.

Influence of sex, age, and pressure gradients

Female patients had significantly higher iPR values compared with male patients

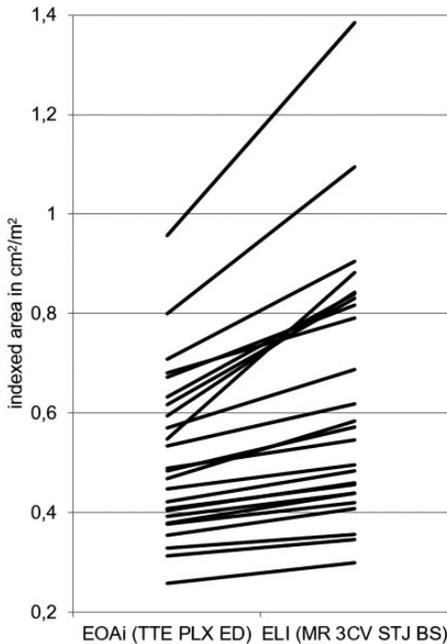


Figure 6. Changes of aortic stenosis severity from transthoracic echocardiography (TTE) measurements and cardiac magnetic resonance imaging (MR) in 3-chamber view (3CV) measurements without consideration versus with consideration of pressure recovery (PR). EOA_i, effective orifice area index; PLX, parasternal long axis; ED, end of diastole; ELI, energy loss index; STJ, sinutubular junction; BS, beginning of systole.

(0.28 ± 0.07 versus 0.21 ± 0.06 ; $P = 0.02$), but PR values were comparable between male and female patients (PR, 20.2 ± 9.8 mmHg [female] versus 20.3 ± 7.3 mmHg [male]; $P = 0.27$). Female patients displayed smaller aortic area compared with male patients (female, 4.7 ± 1.2 cm² versus male, 6.8 ± 1.8 cm²; $P = 0.009$). There was no statistically significant correlation of PR and iPR with age. PR showed a positive correlation with P_{\max} ($r = 0.59$; $P = 0.002$), and iPR was inversely correlated with P_{\max} ($r = -0.43$; $P = 0.03$).

Prediction of short- and long-term outcome

All patients underwent surgical valve replacement. A total of seven out of 25 patients died during follow-up (maximum 10 years). One patient died immediately after cardiac surgery for valve replacement, one patient died during post-operative rehabilitation, one patient died due to heart failure 4 years after cardiac surgery, and four patients died due to cancer (colorectal cancers, oesophageal cancer, and T-cell lymphoma).

Results for prediction of overall mortality are summarized in Table 4. Whereas age had a significant predictive value ($P = 0.029$), sex clearly did not ($P = 0.842$). The pressure recovery parameters, EOA_i and ELI, almost reached the level of significance.

No statistically significant effects were found for predicting clinical worsening according to the New York Heart Association (NYHA) classification, either in the first 9 months following the imaging studies, or during the longer 10-year follow-up (Table 5).

Table 4. Cox regression analysis for predicting all-cause mortality in patients with severe degenerative aortic stenosis.

Characteristic	Univariable			Wald
	HR	95% CI	Statistical significance	
Age	1.186	1.018, 1.381	$P = 0.029$	4.774
Sex	1.178	0.237, 5.846	$P = 0.842$	0.040
EOAi	60.638	0.953, 3 858	$P = 0.053$	3.753
ELI	16.443	0.9775, 277	$P = 0.052$	3.772

HR, hazard ratio; CI, confidence interval; EOAI, effective orifice area index; ELI, energy loss index.

Table 5. Cox regression analysis for 9-month NYHA ≥ 2 and 10-year NYHA ≥ 2 in patients with severe degenerative aortic stenosis.

Characteristic	Univariable			Univariable		
	9-month NYHA ≥ 2			10-year NYHA ≥ 2		
	HR	95% CI	Wald	HR	95% CI	Wald
Age	1.068	0.988, 1.154	2.743	1.048	0.976, 1.125	1.646
Sex	2.180	0.483, 9.835	1.027	1.766	0.475, 6.575	0.720
EOAi	1.476	0.048, 45.495	0.050	0.291	0.003, 26.400	0.288
ELI	1.414	0.126, 15.923	0.079	0.287	0.011, 7.659	0.555

NYHA, New York Heart Association classification; HR, hazard ratio; CI, confidence interval; EOAI, effective orifice area index; ELI, energy loss index.

There were no statistically significant correlations (all $P > 0.05$).

Discussion

CMR measurements of aortic dimension for PR determination

To the best of the authors' knowledge, this is the first study using CMR for the estimation of PR. Considering fluid mechanics principles, the extent of PR depends on the relation between aortic stenosis severity and aortic root dimensions.^{6,17} In a clinical context, the dimension of the aortic root is regarded as one of the most important parameters for the noninvasive determination of PR.¹ The applied SSFP sequences are suitable for anatomic measurements, due to their good blood-tissue contrast,¹⁸ and are available in every routine cardiac CMR site.

Regarding temporal variation in measurements during the cardiac cycle, there were only small variations in the present study, with a subtle increase in distances between the annulus and the different measurement sites from the beginning to the end of systole. A similar increase of aortic dimension at the level of annulus has been reported previously.¹⁹

In terms of spatial variations, most echocardiographic PR studies report measuring the size of the ascending aorta at one site (the STJ). For example, Baumgartner et al.¹ measured PR at 4–5 cm distal to the stenosis and stated that PR is completed at this site. Another group reported measuring the aortic cross-sectional area at the 'middle part' of the ascending aorta, as pressure recovery occurred at this site in their

observations.²⁰ In contrast, Bahlmann et al.⁷ measured at different levels of the ascending aorta, and a mean value of the different measurement locations was calculated (sinus, STJ, tubular ascending aorta). This multisegmental approach was adopted in the present study, as it considers the typical variation of aortic width (small STJ, wide SoV and tubular ascending aorta) that has been described in previously published echocardiographic,²¹ computed tomography,¹⁹ and MRI studies.¹⁸ The individual determination of ascending aortic dimension at different anatomic levels might be more accurate as single measurements, e.g. at STJ, and considers the fact that pressure recovery occurs at a longer distance distal to the aorta. Only small variations in PR parameters were found in the current study between different positions of measurement in the ascending aorta. Nevertheless, incidence of PR (measured by iPR) might be overestimated using measurements at the narrower STJ.

Comparison of echocardiographic and CMR measurements

In the present study, echocardiographic measurements were compared with CMR measurements at 3CV, as this view is most comparable with echocardiographic parasternal long-axis view, and CMR diameters at STJ were found to be similar to echocardiographic values. Data comparing aortic root measurements between CMR and echocardiography are relatively sparse. Whereas one study reported no significant differences,²² another study found that 2D-TTE measurements were smaller compared with CMR values.²³ The different result from the present study might be explained by the fact that echo values were compared with coronal oblique MRI measurements, and not with 3CV.²³

Clinical relevance of PR by assessment of aortic stenosis severity

In accordance with previously published data,⁷ the absolute extent of pressure recovery was increased, but the clinically relevant pressure recovery was decreased, with increasing degree of aortic stenosis severity measured by peak velocity. However, the absolute extent of PR was smaller compared with the present study, and only 16.8% of patients showed clinically relevant pressure recovery.⁷ These differences may be explained by the higher degree of aortic stenosis severity in the present patient population, with mean v_{\max} of 4.34 ± 0.83 m/s versus 3.08 ± 0.54 m/s.

The strong association between clinically relevant pressure recovery and aortic size has been postulated by former echocardiographic works. For example, Bahlmann et al.⁸ stated that clinically relevant pressure recovery occurs only in patients with an aortic size that is in a lower normal range or smaller, and this may explain the higher incidence of clinically relevant PR in the present patient cohort.

Clinical relevance of PR by prediction of outcome

Pressure recovery concepts predict aortic valve events, however, the most interesting clinical question of total mortality and hospitalization for heart failure seems not to be improved by PR assessment.⁷ The clear trend shown in the present relatively small patient population ($n = 25$) for a predictive value concerning all-cause mortality warrants further analyses in larger patient cohorts. Age is known to be a strong predictor for mortality, whereas sex is not.

Limitations

The results of the present study may be limited by several factors. First, the extent of PR is not only dependent on severity of

aortic stenosis and width of the ascending aorta, but also further influencing factors, such as shape and geometry of the stenosis,²⁴ and eccentricity of flow jet distal to the stenosis.²⁵ Neither of these influencing parameters were registered in the present study. Regarding the latter, the recently available technique of 4D-flow analysis might allow the direct quantification of energy loss by flow turbulences,^{26,27} and even allows determination of the exact level of where energy loss takes place.²⁸ Secondly, the aortic root was measured only in oblique views, as the present authors believe that orthogonal measurements in different time-points of the cardiac cycle are disturbed by craniocaudal movements of the aortic root due to ventricular contraction,¹⁸ and a self-navigation for systolic movements of the aortic valve was not available in the present study setting.²⁹ Thirdly, the study investigated a relatively small sample of patients ($n = 25$), and a portion of the patients died of causes other than chronic heart failure during follow-up. Additionally, there was no accessible data to measure whether reclassification had any impact on daily routine (e.g. patients did not undergo surgery or transcatheter aortic valve replacement and were treated conservatively). Further prospective studies with larger patient numbers are necessary to determine the effect of PR reclassification in patient handling.

Conclusion

The presented hybrid approach (flow values by echocardiography and diameters by CMR) allows estimation of PR by CMR and resulted in a maximal downward classification-rate, from severe to moderate aortic stenosis severity, in 20% of patients. Larger coverage of the ascending aorta using CMR compared with echocardiography may explain the higher degree of

downward classification in CMR versus echocardiography.

The prediction of overall mortality by functional data, such as ELI, has great potential and warrants further multicentre prospective studies.

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Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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