ESC HEART FAILURE
ESC Heart Failure 2022; **9**: 1721–1730
Published online 29 March 2022 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.13846

ORIGINAL ARTICLE

Acute haemodynamic impact of transcatheter aortic valve implantation in patients with severe aortic stenosis

Francesca Graziani[1], Pio Cialdella[2], Rosa Lillo[3], Gabriella Locorotondo[1], Lorenzo Genuardi[1], Gessica Ingrasciotta[1,2], Stefano Cangemi[1,2], Marialisa Nesta[1], Piergiorgio Bruno[1,2], Cristina Aurigemma[1], Enrico Romagnoli[1], Michele Calabrese[1], Nicole Giambusso[1], Antonella Lombardo[1,2], Francesco Burzotta[1,2]* and Carlo Trani[1,2]

[1]*Department of Cardiovascular Medicine, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy; and* [2]*Università Cattolica del Sacro Cuore, Rome, Italy;* [3]*Department of Emergency Medicine, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy*

Abstract

Aims There are limited data about the intraprocedural haemodynamic study performed immediately before and after transcatheter aortic valve implantation (TAVI) in patients with severe aortic stenosis (AS). We aimed to evaluate the acute haemodynamic impact of TAVI in patients with severe AS and to investigate invasive and non-invasive parameters predicting all-cause mortality.

Methods and results A total of 245 consecutive AS patients (43% male, mean age 80.3 ± 7.3 years) undergoing TAVI were enrolled. Intraprocedural left heart catheterization (LHC) and echocardiogram before and after TAVI were performed. The clinical endpoint was the death for any cause. LHC after TAVI revealed significant changes in aortic and left ventricular (LV) pressures, including indexes of intrinsic myocardial contractility and diastolic function such as positive dP/dT (1128.9 ± 398.7 vs. 806.3 ± 247.2 mmHg/s, $P < 0.001$) and negative dP/dT (1310.7 ± 431.1 vs. 1075.1 ± 440.8 mmHg/s, $P < 0.001$). Post-TAVI echo showed a significant reduction in LV end-diastolic ($P = 0.036$) and end-systolic ($P < 0.001$) diameters, improvement in LV ejection fraction (from 55 ± 12% to 57.2 ± 10.5%, $P < 0.001$), and pulmonary artery systolic pressure (42.1 ± 14.2 vs. 33.1 ± 10.7 mmHg, $P < 0.001$). After a mean follow-up time interval of 24 months, 47 patients died. Post-TAVI significant aortic regurgitation at echocardiography was the only independent predictor of mortality (hazard ratio 5.592, confidence interval 1.932–16.184, $P = 0.002$).

Conclusions Left heart catheterization performed immediately before and after prosthesis release offers a unique insight in the assessment of LV adaptation to severe AS and the impact of TAVI on LV, catching changes in indexes of intrinsic contractility and myocardial relaxation. Aortic regurgitation assessed by echocardiography was the only independent predictor of mortality in patients undergoing TAVI.

Keywords TAVI; Aortic stenosis; Haemodynamic; Cardiac catheterization; Personalized medicine

Received: 20 September 2021; Revised: 26 December 2021; Accepted: 4 February 2022
**Correspondence to: Francesco Burzotta, Institute of Cardiology, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, L.go A. Gemelli 1, 00168 Rome, Italy. Tel: +39-06-30154187; Fax: +39-06-3055535. Email: francescoburzotta@gmail.com*

Introduction

Aortic stenosis (AS) is the most common heart valve lesion, with an incidence rate of severe AS of ~4% to 7% per year among people ≥65 years of age.[1] For decades, the only available treatment for severe AS has been surgical aortic valve replacement (SAVR), which significantly improves survival, symptoms, and quality of life.[2] However, as much as 30–40% of patients are deemed unsuitable for SAVR.[3] Lately, the traditional treatment paradigm for patients with severe AS has been challenged by the development of transcatheter aortic valve implantation (TAVI) procedure.[4–9] TAVI

profoundly changed the management of patients judged at prohibitive surgical risk, including those with severe heart failure (HF). Patients with AS and HF benefit from this procedure in terms of symptom alleviation, and a post-TAVI favourable prognosis has been observed, particularly in patients with HF with preserved or mildly reduced ejection fraction (EF) compared with patients with HF and reduced EF.[10] TAVI leads to cardiac reverse remodelling, although there are conflicting results about the regression of left ventricular (LV) hypertrophy as well as about the improvement of LV systolic and diastolic function.[11–14]

There are limited data regarding the invasive haemodynamic evaluation of patients undergoing TAVI and even less about the prognostic role of the haemodynamic study performed immediately before and after prosthesis deployment.[15–20] Most of the available invasive studies focused on right heart catheterization,[17–20] and the few studies performed with left heart catheterization (LHC) focused on the role of residual aortic regurgitation (AR) as predictor of long-term mortality.[21,22]

The aims of our study were (i) to assess the acute effect of TAVI on LV haemodynamics as well as the early impact on echocardiographic parameters and (ii) to identify the stronger predictor of all-cause mortality after TAVI.

Methods

Study design

The present study is a clinical retrospective study that reports data prospectively collected in a large registry that includes all consecutive patients undergoing TAVI in our centre.

We retrospectively selected consecutive patients who underwent TAVI between January 2016 and March 2019 at our institution. The study population included symptomatic patients with severe AS defined according to guidelines.[8] The exclusion criteria were TAVI performed for pure AR and valve-in-valve procedures.

Transcatheter aortic valve implantation procedure

The management of patients with AS in our centre is routinely performed according to internal guidelines (in the institutional clinical pathway dedicated to patients with heart valve diseases: https://www.policlinicogemelli.it/servizi-paziente/percorsi-assistenziali/valvulopatia/).[23] All TAVIs were conducted according to a procedural plan performed on the basis of computed tomography (CT) scan. For each patient, the CT scan was revised by at least two operators to assess the potential suitability for TAVI implantation. Transfemoral approach was considered the preferred option, other accesses being considered in the case of absence of suitable aorto–iliac–femoral anatomy due to insufficient lumen size, extreme tortuosity, and/or severe atherothrombosis. All TAVIs were performed following the manufacturer's best practice recommendations. Details of the transfemoral TAVI technique have been recently published.[24]

Pre-transcatheter aortic valve implantation and post-transcatheter aortic valve implantation evaluation

Each patient underwent a thorough clinical and echocardiographic evaluation before the procedure according to the standard practice of our centre, and all patients were referred for TAVI on the basis of formal, multidisciplinary, Heart Team discussion. Clinical data and procedure details were prospectively entered into a dedicated database that allowed previously to assess the impact of EuroSCORE on coronary interventions[25] and the safety of trans-radial procedures.[26] Patients' surgical risk was graded according to the Society of Thoracic Surgeons (STS)-predicted operative mortality at the time of Heart Team consultation. TAVI risk was graded according to the STS/American College of Cardiology Transcatheter Valve Therapy[27] using the online TAVI in-hospital mortality risk calculator (https://tools.acc.org/tavrrisk/#!/content/evaluate/). In-hospital clinical outcomes were prospectively recorded because the continuous monitoring of in-hospital clinical outcomes for TAVI is part of our institutional clinical pathway dedicated to patients with heart valve diseases. The study was in compliance with the Declaration of Helsinki, and all patients signed a dedicated informed consent to the study procedure, which included the authorization to database insertion and clinical follow-up assessment.

In the pre-TAVI evaluation, the following data were collected:

- *Clinical data*: age, sex, weight, height, body surface area, body mass index, cardiovascular risk factors, medical history, major co-morbidities, and New York Heart Association (NYHA) functional class. The assessment of patients' symptomatic status and physical examination were carefully performed by experienced teams of physicians from our specialized heart valve clinic. HF was defined according to the current European Society of Cardiology guidelines definition.[28]
- *Laboratory tests*: blood cell count, electrolytes, liver function, serum creatinine, and estimated glomerular filtration rate were obtained by the Chronic Kidney Disease Epidemiology Collaboration formula.
- *A standard 12-lead electrocardiogram*.
- *Complete echocardiography*: all patients underwent echocardiographic assessment within 24 h before the

scheduled procedure and a second evaluation within 2–5 days after TAVI.
- *Computed tomography*: all patients underwent CT for work-up and pre-procedural planning before TAVI for the selection of prosthesis type sizing as well as for the evaluation of vascular access site. Clinical follow-up was available for all the patients enrolled, and data were obtained by telephone or in an outpatient visit to assess vital status.

All the echocardiograms were performed by experienced physicians (F. G., G. L., and A. L.) from our heart valve clinic. Images were acquired with patients at rest in the left decubitus position using commercially available ultrasound systems (Toshiba Artida, Toshiba, Tokyo, Japan; Philips Epiq 7, Philips Medical Systems, Andover, Massachusetts, USA) equipped with 3.5 MHz or M5S transducers. Two-dimensional, colour, pulsed-wave (PW), and continuous-wave Doppler data were obtained in parasternal and apical views. Apical two-chamber and four-chamber views were used for quantification of LV end-diastolic and end-systolic volumes, and LVEF was calculated using Simpson's biplane method. LV dimensions and wall thicknesses were measured on M-mode recordings of the parasternal long-axis view. All acoustic windows were explored in order to obtain the best ultrasound beam alignment for Doppler recording of the aortic valve (AV): aortic mean and peak gradients were evaluated using continuous-wave Doppler with the simplified Bernoulli equation. AS was assessed using a multi-parametric approach as suggested by the European Association of Cardiovascular Imaging (EACVI)/American Society of Echocardiography (ASE) guidelines.[29,30]

Heart chamber dimension classification, as well as LV mass index (LVMi) for men and women, and the grading of diastolic dysfunction and associated valvular heart disease were all carried out in accordance with the most recent EACVI/ASE guidelines.[29,30]

Regarding diastolic function assessment, pertinent echocardiographic variables were obtained as follows: early flow peak velocity (E), E-wave deceleration time (DT), and peak velocity during atrial systole (A) were measured from trans-mitral flow patterns obtained between the mitral leaflets using PW Doppler in the apical four-chamber view. Early diastolic annular velocity (e′) of the lateral and septal LV wall was measured by PW tissue Doppler imaging. Left atrial volume was calculated using Simpson's rule. Pre-procedural LV diastolic dysfunction was classified into three grades (I, II, and III) based on 2016 ASE/EACVI Recommendations for Evaluation of Left Ventricular Diastolic Function by Echocardiography.[31]

Finally, we applied the staging classification recently proposed by Généreux *et al*.[32] for the characterization of the extent of cardiac damage among patients with severe AS.

Aortography and LHC were performed before and after valve deployment. LHC was performed using two 5F or 6F diagnostic catheters positioned in the left ventricle (through the main TAVI access site) and in the ascending aorta (through the radial or femoral ancillary arterial access). LV and aortic pressure–time curves were simultaneously recorded and stored on our Hemodynamic Recording System (Mac-Lab, GE Medical Systems Informa Technologies, Milwaukee, Wisconsin, USA). The values of systolic and diastolic pressures were collected, and, after data processing, systolic and diastolic intervals and pressure gradients between the LV and the aorta were calculated. *Figure 1* shows an example of LHC (with the evaluated parameters before and after TAVI). AR index was calculated as previously described[33] before and after TAVI and the AR index ratio[34] derived for each patient.

Statistical analysis

Categorical variables were expressed as percentages and analysed by χ^2 or Fisher's exact test as appropriate. Continuous variables were expressed as mean ± standard deviation and/or median [inter-quartile range] and compared using the paired *t*-test or the non-parametric Wilcoxon test, as appropriate. Normality of distribution of continuous variables was assessed by Kolmogorov–Smirnov test. Kaplan–Meier curves were constructed for mortality. Comparison of the variables between patients who survived and those who died was performed. To assess the independent predictors of survival, a Cox regression univariate and multivariate analysis model was realized. Variables with a *P* value lower than 0.1 in the univariate analysis were included in the backward stepwise multivariate analysis. Differences were considered significant with $P < 0.05$. Data were analysed using IBM SPSS Statistics Version 24.0 software (IBM, Armonk, NY, USA).

Results

Out of the 267 patients who underwent TAVI during the period considered, 245 patients undergoing TAVI for severe AS of the native valve were selected and constituted the study population.

Baseline clinical characteristics of the patients are summarized in *Table 1*. Mean age was 80.3 ± 7.3 years, and 140 (57%) patients were female. As much as the 87% of the entire population was hypertensive, and 31% had type II diabetes. More than 60% of patients (153; 63%) had overt HF, being in NYHA Class III–IV. The majority of patients had preserved LVEF (EF $\geq$ 50%), 33 (13.4%) had HF with reduced EF (EF $\leq$ 40%), and 33 (13.4%) had mildly reduced EF (EF $<$ 50% but $>$40%). Seventy-eight patients (32%) have been previously hospitalized for HF. Pre-TAVI atrial fibrillation was documented in 34 patients (13.8%). Almost half of the population (103; 42%) had a history of coronary artery disease, 30 patients (12%) had previous cardiac surgery, 56 patients (23%) were affected by peripheral vascular disease,

DOI: 10.1002/ehf2.13846

Figure 1 Example of left heart catheterization with the evaluated parameters before and after transcatheter aortic valve implantation. LV, left ventricular.

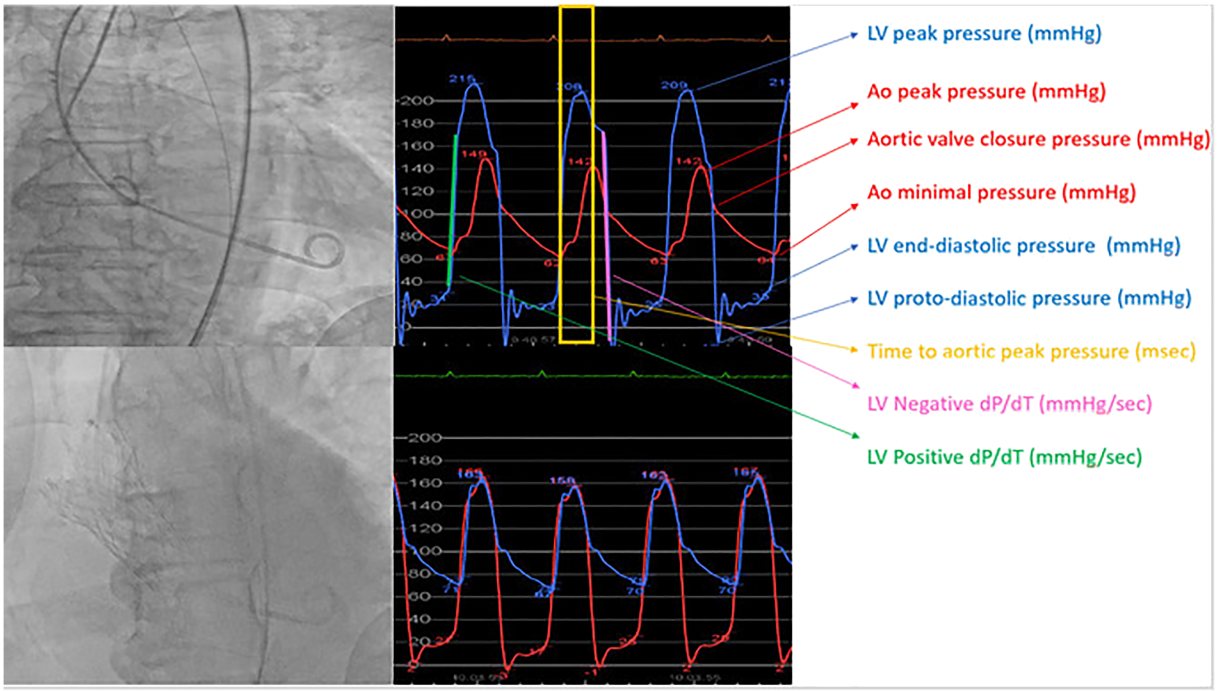


Table 1 Clinical characteristics of the study population

Variables	Study population (n = 245)
Age (years), mean ± SD	80.3 ± 7.3
Male, *n* (%)	105 (43%)
Cardiovascular risk factors	
Diabetes mellitus, *n* (%)	76 (31%)
Arterial hypertension, *n* (%)	214 (87%)
Dyslipidaemia, *n* (%)	156 (64%)
Smoker, *n* (%)	87 (36%)
Obesity (BMI ≥ 30), *n* (%)	55 (22%)
Co-morbidities	
Atrial fibrillation, *n* (%)	34 (13.8%)
Previous hospitalization for HF, *n* (%)	78 (32%)
Renal failure (serum creatinine >1.2 mg/dL), *n* (%)	19 (8%)
COPD, *n* (%)	63 (26%)
Peripheral vascular disease, *n* (%)	56 (23%)
Previous MI > 3 months, *n* (%)	20 (8%)
Previous PCI, *n* (%)	71 (29%)
Previous cardiac surgery, *n* (%)	30 (12%)
Clinical presentation	
NYHA Class III–IV, *n* (%)	153 (63%)
Pre-procedural risk	
STS score (%), mean ± SD	5.3 ± 2.4
TAVI score (%), mean ± SD	3.9 ± 2.2

BMI, body mass index; COPD, chronic obstructive pulmonary disease; HF, heart failure; MI, myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; SD, standard deviation; STS, Society of Thoracic Surgeons; TAVI, transcatheter aortic valve implantation.

and 63 (26%) suffered from chronic obstructive pulmonary disease.

Mean STS score was 5.3 ± 2.4, and TAVI score was 3.9 ± 2.2. Of the 245 TAVI, 202 (83%) were performed by femoral access: 129 (53%) right femoral and 73 (30%) left femoral. Axillary access was used in four cases (1.6%) and aortic in two patients (0.8%). Trans-apical TAVI was 37 (15%). In most cases (78.7%), self-expandable valves were used. Specifically: CoreValve was used in 187 (76.3%), Edwards SAPIEN 3 in 52 (21.2%), and Portico in 6 (2.4%).

The TAVI procedure was successful in 244/245 patients (99.6%). In one case, only the procedure was not completed because of the occurrence of ascending aortic rupture so that conversion to urgent SAVR was successfully performed. After TAVI, 26 (10.6%) patients needed a permanent pacemaker implantation.

Haemodynamic parameters obtained before and after the procedure are reported in *Table 2*. LHC data were incomplete/missing in eight patients due to insufficient quality traces.

As expected, AV peak and mean gradient significantly decreased after TAVI ($P < 0.001$), as well as AV closure pressure ($P = 0.001$) and time to aortic peak pressure ($P < 0.001$), while aortic peak pressure increased ($P < 0.001$). The relief of abnormal afterload after the deployment of the prosthesis

Table 2 Haemodynamic parameters before and after TAVI

Variables	Before TAVI	After TAVI	*P value*
LV pressures			
LV peak pressure (mmHg), mean ± SD	198.3 ± 36.5	164.2 ± 32.2	<0.001
LV proto-diastolic pressure (mmHg), mean ± SD	5.6 ± 9.5	8.2 ± 7.8	0.001
LV end-diastolic pressure (mmHg), mean ± SD	26.2 ± 9.2	27.4 ± 8.2	0.107
Aortic pressures			
Aortic peak pressure (mmHg), mean ± SD	139.3 ± 31.6	158.4 ± 32.7	<0.001
Aortic valve closure pressure (mmHg), mean ± SD	123.6 ± 30.9	113.3 ± 26.0	0.001
Aortic minimal pressure (mmHg), mean ± SD	61.5 ± 13.6	62.2 ± 12.3	0.538
Ventricular–aortic systolic gradients			
AV peak gradient (mmHg), mean ± SD	59.2 ± 29.4	5.8 ± 13.1	<0.001
AV mean gradient (mmHg), mean ± SD	60.5 ± 21.5	6.2 ± 4.5	<0.001
Time intervals and time-derived measures			
Time to aortic peak pressure (ms), mean ± SD	285.2 ± 37.6	221.2 ± 44	<0.001
LV negative dP/dT (mmHg/s), mean ± SD	1310.7 ± 431.1	1075.1 ± 440.8	<0.001
LV positive dP/dT (mmHg/s), mean ± SD	1128.9 ± 398.7	806.3 ± 247.2	<0.001
Post-TAVI aortic regurgitation			
Aortic regurgitation index ratio		1.0 ± 0.6	
Moderate-to-severe aortic regurgitation at aortography, *n* (%)		17 (6.9%)	

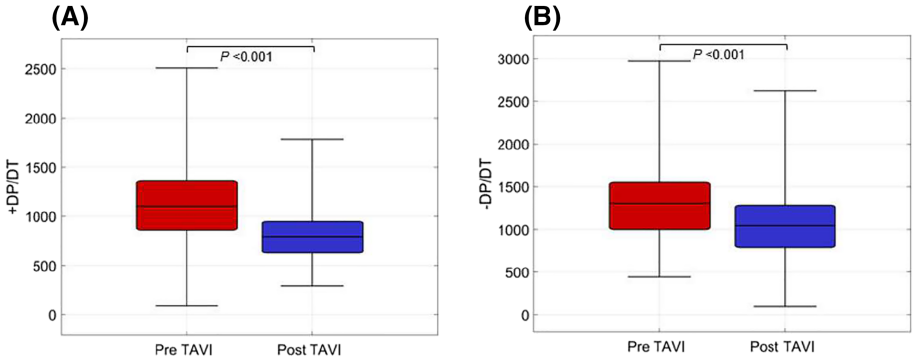
AV, aortic valve; LV, left ventricular; SD, standard deviation; TAVI, transcatheter aortic valve implantation.

was followed by a significant reduction of LV peak pressure ($P < 0.001$) and LV positive dP/dT ($P < 0.001$, *Figure 2A*). While end-diastolic pressure did not significantly change after the procedure ($P = 0.107$), negative dP/dT decreased after TAVI ($P < 0.001$, *Figure 2B*) and LV proto-diastolic pressure increased ($P = 0.001$).

Echocardiographic characteristics before and after TAVI are presented in *Table 3*. At baseline, mean LVEF was 55 ± 12% and 20 (8%) patients showed severe LV systolic dysfunction (LVEF ≤ 30%). The mean gradient across the AV was 52 ± 14.4 mmHg. The mean calculated AV area was 0.7 ± 0.2 cm^2. Mean LVMi was 145.4 ± 37.8 g/m^2. Assessment of diastolic function was available in 151 patients (61.6%): only one patient had normal diastolic function, and Grade I diastolic dysfunction was found in 42 patients (27.8%), Grade II in 88 (58.3%) patients, and Grade III in 20 (13.2%) patients. According to the Généreux classification, most patients were in Stage 2 (69%), followed by Stages 3 (19%), 1 (8%), and 4 (4%).

After TAVI, as expected, mean aortic gradient decreased (from 52 ± 14.4 to 8.9 ± 4.8 mmHg, $P < 0.001$), but, more interestingly, there was a significant reduction in LV diameters and volumes (respectively: LV end-diastolic diameter from 48.4 ± 7.5 to 47.4 ± 6.9 mm, $P = 0.036$; LV end-systolic diameter from 33 ± 8.6 to 30.1 ± 8.1 mm, $P < 0.001$; and LV end-diastolic volume index from 54.6 ± 18.4 to 51.7 ± 17.5 mL/m^2, $P = 0.017$; *Figure 3A*) and a significant improvement in LV systolic function with increase in post-procedural LVEF (from 55 ± 12% to 57.2 ± 10.5%, $P < 0.001$; *Figure 3B*). In particular, patients with worse pre-TAVI systolic function showed significant improvement in LVEF compared with patients with preserved pre-procedural LVEF (ΔLVEF respectively 6% vs. 1.6%, $P < 0.001$). Moreover, pulmonary artery systolic pressure decreased significantly [pulmonary artery systolic pressure (PASP) from 42.1 ± 14.2 to 33.1 ± 10.7 mmHg, $P < 0.001$; *Figure 3C*].

Figure 2 Impact of transcatheter aortic valve implantation (TAVI) on haemodynamic parameters: box plot with median and inter-quartile ranges of (A) positive dP/dT and (B) negative dP/dT values before vs. after TAVI.



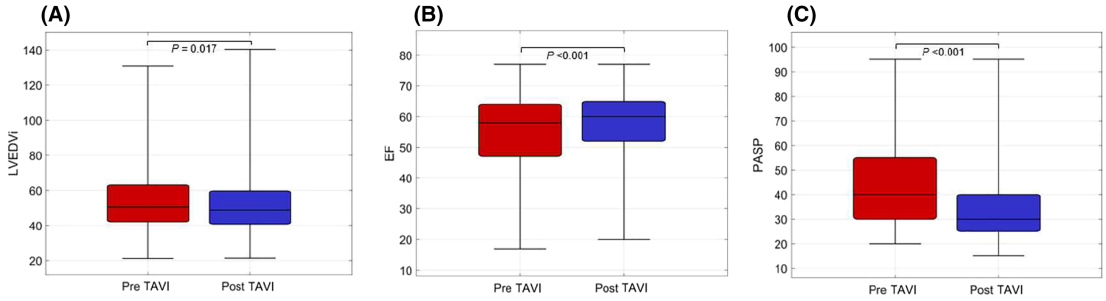
DOI: 10.1002/ehf2.13846

Table 3 Echocardiographic characteristics before and after TAVI

Variables	Before TAVI	After TAVI	*P* value
AV mean gradient (mmHg), mean ± SD	52 ± 14.4	8.9 ± 4.8	<0.001
LVEDD (mm), mean ± SD	48.4 ± 7.5	47.4 ± 6.9	0.036
LVESD (mm), mean ± SD	33 ± 8.6	30.1 ± 8.1	<0.001
LVEDVi (mL/m^2), mean ± SD	54.6 ± 18.4	51.7 ± 17.5	0.017
LVEF (%), mean ± SD	55 ± 12	57.2 ± 10.5	<0.001
PASP (mmHg), mean ± SD	42.1 ± 14.2	33.1 ± 10.7	<0.001
Grade III diastolic dysfunction, *n* (%)	20 (13%)	20 (13%)	0.869
TAPSE (mm), mean ± SD	20.3 ± 4	19.5 ± 3.4	0.004
Moderate-to-severe mitral regurgitation, *n* (%)	16 (6.3%)	7 (3.5%)	0.05
Moderate-to-severe tricuspid regurgitation, *n* (%)	13 (5%)	8 (4%)	0.372
AS stage according to Généreux *et al.*			<0.001
Stage 1, *n* (%)	20 (8%)	18 (7.3%)	
Stage 2, *n* (%)	169 (69%)	207 (85%)	
Stage 3, *n* (%)	47 (19%)	15 (6%)	
Stage 4, *n* (%)	9 (4%)	5 (2%)	

AS, aortic stenosis; AV, aortic valve; LVEDD, left ventricular end-diastolic diameter; LVEDVi, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; PASP, pulmonary artery systolic pressure; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion.

Figure 3 Impact of transcatheter aortic valve implantation (TAVI) on echocardiographic parameters: box plot with median and inter-quartile ranges of (A) left ventricular end-diastolic volume index (LVEDVi), (B) left ventricular ejection fraction (EF), and (C) pulmonary artery systolic pressure (PASP) values before vs. after TAVI.



Interestingly, TAVI procedure was found to significantly impact on Généreux's classification: as shown in *Table 3*, after TAVI, the Généreux classification stages significantly changed ($P < 0.001$), and this change was mainly driven by a major reduction of Stage 3 patients. We found no major differences in diastolic function indexes before and after TAVI; none of the patients with Grade III diastolic dysfunction before TAVI showed an improvement after the procedure. A borderline statistical significance was reached for the decrease of patients with moderate-to-severe mitral regurgitation (before vs. after TAVI: 6.3% vs. 3.5%, $P = 0.05$). Neither of the patients with atrial fibrillation before TAVI showed spontaneous restoration of the sinus rhythm nor anyone underwent cardioversion.

According to echocardiography, the severity of post-TAVI AR was as follows: none in 141 (57.6%), mild in 86 (35.1%), and moderate to severe in 18 (7.3%) patients.

After a mean follow-up time interval of 24 months (range 3–50 months), 47 patients died.

Table 4 shows the results of survival Cox regression analyses for clinical, echocardiographic, and haemodynamic variables, in order to investigate possible predictors of mortality.

At univariable analysis, male sex [hazard ratio (HR) 2.1, confidence interval (CI) 1.209–3.923, $P = 0.01$] and smoke (HR 1.3, CI 1.008–1.817, $P = 0.04$) were significantly associated with mortality, together with moderate-to-severe AR assessed with echocardiography (HR 2.9, CI 1.298–6.545, $P = 0.010$). NYHA class ($P = 0.994$) and previous hospitalization for HF ($P = 0.464$) were not significantly associated with mortality, while a trend was observed for atrial fibrillation (HR 2.0, CI 0.919–4.468, $P = 0.08$).

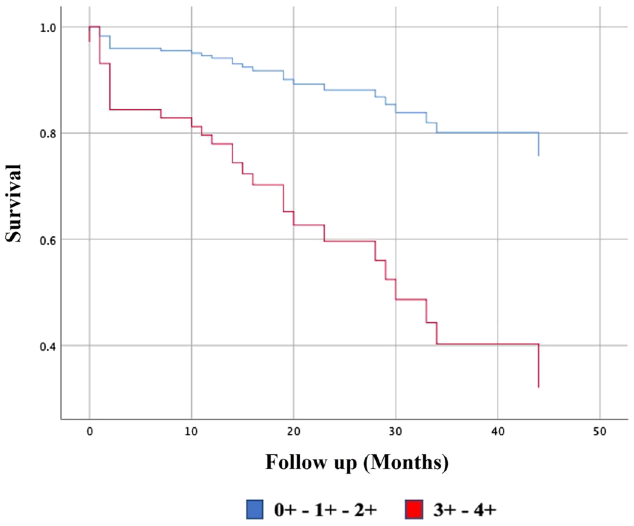
At multivariate analysis, moderate-to-severe AR after TAVI was the only independent predictor of mortality (HR 5.592, CI 1.932–16.184, $P = 0.002$, *Figure 4*), while pre-TAVI aortic peak pressure (HR 0.978, CI 0.966–0.991, $P = 0.001$) and post-TAVI LV peak systolic pressure (HR 0.980, CI 0.963–0.998, $P = 0.027$) were found to be weakly associated with reduced mortality (*Table 4*).

Table 4 Univariate and multivariate predictors of death

	Univariate analysis		Multivariate analysis	
	P value	HR (95% CI)	*P* value	HR (95% CI)
Pre-TAVI parameters				
Aortic peak pressure[a]	<0.001	0.977 (0.966–0.988)	0.001	0.978 (0.966–0.991)
Post-TAVI parameters				
LV peak systolic pressure[a]	0.047	0.986 (0.973–1.000)	0.027	0.980 (0.963–0.998)
LV positive dP/dT[a]	0.044	1.002 (1.000–1.003)	0.001	1.003 (1.001–1.005)
Moderate-to-severe aortic regurgitation[b]	0.010	2.9 (1.298–6.545)	0.002	5.592 (1.932–16.184)

CI, confidence interval; HR, hazard ratio; LV, left ventricular; TAVI, transcatheter aortic valve implantation.
[a]Assessed at left heart catheterization.
[b]Assessed at echocardiography.

Figure 4 Kaplan–Meier curves for survival showing that moderate-to-severe aortic regurgitation (3+ and 4+) assessed with echocardiography had the strongest association with mortality.



Discussion

The present study analysed invasive data obtained from LHC before and soon after TAVI as well as early echocardiographic changes after the procedure, offering a unique insight in the pathophysiology of severe AS and the impact of TAVI. Moreover, we investigated the prognostic significance of haemodynamic and echocardiographic parameters before and after TAVI.

Our relevant findings are as follows: (i) global haemodynamics, afterload, and contractility change *immediately* after TAVI; (ii) an early LV remodelling is appreciable at echocardiography after TAVI; and (iii) post-TAVI significant AR at pre-discharge echocardiography is the only independent predictor of mortality after an interval of 24 months.

Despite several studies aiming to compare non-invasive (echocardiographic and cardiac magnetic resonance) pre-TAVI and post-TAVI data have been performed, poor data are available on the role of the haemodynamic assessment performed immediately before and after prosthesis deployment in patients with severe AS.[15,16,35,36]

The few studies available on this topic have mainly focused on the variations of LV end-diastolic pressure (LVEDP).[36] In our study, LVEDP did not show any significant change after TAVI, while LV proto-diastolic pressure increased. Previous studies showed that, after deployment of the prosthesis, the LVEDP tends to reduce significantly (>5 mmHg).[36] However, other studies reported that immediately after TAVI, LVEDP may even increase.[15] This may be explained by the fact that during TAVI procedure, rapid ventricular pacing (RVP) is required to produce a transient decrease in cardiac and catheter motion. The transient cycle of hypotension and low cardiac output induced by repeated RVP may cause LVEDP elevation; moreover, deterioration in coronary perfusion induced by RVP[15] may have been partly responsible for the temporary myocardial stunning and the non-reduction in LVEDP observed in our study. Finally, the administration of intravenous fluid infusion and iodinated contrast agent during procedure could have had a role in the lack of reduction of LVEDP. Even if LVEDP did not change significantly, we observed a decrease of negative dP/dT, an intrinsic index of diastolic function.

We performed a comprehensive assessment of haemodynamic changes after TAVI, including LV systolic function, so far poorly understood. Beyond the expected reduction of AV peak and mean gradient, driving the reduction of LV peak pressure, several parameters significantly changed after the procedure. Interestingly, positive dP/dT, an index of myocardial contractility, decreases after TAVI. We can speculate that patients with AS and preserved LVEF use efficiently the contractile reserve in order to overcome the increased afterload; once the key pathophysiological element of the AS is fixed, that is, the increased valvular load, indexes of intrinsic contractility decrease as well as those of myocardial relaxation (i.e. negative dP/dT). Our results are in line with the recent findings of Seppelt *et al*.[16] They performed (in a pilot study on eight patients) an invasive LV pressure volume loop analysis and found impaired systolic and diastolic function in the early phase after TAVI, even if ventricular–arterial coupling

data suggested an early improvement of global cardiovascular energy efficiency. Moreover, at multivariate analysis, we found that higher values of pre-TAVI aortic peak pressure and post-TAVI LV peak systolic pressure were weakly associated with reduced mortality.

Several previous studies demonstrated that the acute relief of the increased afterload by TAVI leads to immediate improvement of cardiac function assessed with echocardiography, followed by reverse heart remodelling with regression of LV volume and mass as well as improvement of LV systolic and diastolic function.[11,37–39] In line with previous findings, we found major LV remodelling in the early post-TAVI echo, with significant reduction in LV diameters and volumes together with significant improvement in LV systolic function, expressed as an increase in post-procedural LVEF. In particular, patients with worse pre-TAVI systolic function are those who benefit the most in terms of LVEF recovery. We observed an immediate reduction of PASP after TAVI, together with a slight reduction of tricuspid annular plane systolic excursion, whose values however stayed within normal range. Interestingly, Généreux staging classification, a well-recognized tool to objectively characterize the extent of cardiac damage associated with AS, significantly changed after TAVI, reflecting the early cardiac remodelling and pulmonary pressure reduction soon after the procedure. When investigating the prognostic significance of LHC and echocardiographic data before and after TAVI, we found that the only significant independent predictor of mortality was significant AR assessed at pre-discharge echocardiography. This finding is in line with previous studies.[21,22,40] Indeed, in a multicentre registry by Zahn *et al*.[40] on 1444 patients treated with TAVI, one of the strongest predictors identified as *modifiable* was residual AR $\geq$ II°. However, other variables independently associated with mortality were identified, among which atrial fibrillation and prior decompensation. The differences found with Zahn *et al*. could rely on the different size of the study population; the larger sample size likely allowed them to identify more than one independent predictor of prognosis. However, we confirmed the prognostic role of post-TAVI AR, and in light of these considerations, patients with moderate-to-severe AR (3+ and 4+) pre-discharge must be considered high-risk group, who would probably benefit of a closer follow-up and personalized therapeutic management.

Limitations of the study

Some limitations of the study should be acknowledged: first, its retrospective observational single-centre design with wide follow-up range. This might have had an impact on results, which need to be confirmed in larger studies. Second, despite the collection of systematic haemodynamic data, some variables were not collected (such as pharmacological treatment including hypertensive drugs and diuretics), and we cannot exclude that they might have had an impact. Moreover, right heart catheterization was not performed.

Conclusions

Left heart catheterization performed immediately before and after prosthesis release offers a unique pathophysiology insight in the assessment of LV adaptation to severe AS and the acute impact of TAVI.

Our data suggest that patients with AS and preserved LVEF use efficiently the contractile reserve in order to overcome the increased afterload; once the key pathophysiological element of the AS is fixed, that is, the increased valvular load, indexes of intrinsic contractility, as well as those of myocardial relaxation, decrease.

Aortic regurgitation is the only independent predictor of mortality in patients undergoing TAVI.

Conflict of interest

F.B., C.T., E.R., and C.A. received speaker's fees from Abbott, Medtronic, and Abiomed. The other authors have no conflicts of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Durko AP, Osnabrugge RL, Van Mieghem NM, Milojevic M, Mylotte D, Nkomo VT, Pieter Kappetein A. Annual number of candidates for transcatheter aortic valve implantation per country: current estimates and future projections. *Eur Heart J* 2018; **39**: 2635–2642.
2. Kvidal P, Bergström R, Hörte LG, Ståhle E. Observed and relative survival after aortic valve replacement. *J Am Coll Cardiol* 2000; **35**: 747–756.
3. Iung B, Cachier A, Baron G, Messika-Zeitoun D, Delahaye F, Tornos P, Gohlke-Bärwolf C, Boersma E, Ravaud P, Vahanian A. Decision-making in elderly patients with severe aortic stenosis: why are so many denied surgery? *Eur Heart J* 2005; **26**: 2714–2720.
4. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR,

Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S, PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010; **17**: 1597–1607.

5. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Williams M, Dewey T, Kapadia S, Babaliaros V, Thourani VH, Corso P, Pichard AD, Bavaria JE, Herrmann HC, Akin JJ, Anderson WN, Wang D, Pocock SJ, PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med* 2011; **364**: 2187–2198.
6. Leon MB, Mack MJ, Hahn RT, Thourani VH, Makkar R, Kodali SK, Alu MC, Madhavan MV, Chau KH, Russo M, Kapadia SR, Malaisrie SC, Cohen DJ, Blanke P, Leipsic JA, Williams MR, McCabe JM, Brown DL, Babaliaros V, Goldman S, Herrmann HC, Szeto WY, Genereux P, Pershad A, Lu M, Webb JG, Smith CR, Pibarot P, PARTNER 3 Investigators. Outcomes 2 years after transcatheter aortic valve replacement in patients at low surgical risk. *J Am Coll Cardiol* 2021; **77**: 1149–1161.
7. Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Søndergaard L, Mumtaz M, Adams DH, Deeb GM, Maini B, Gada H, Chetcuti S, Gleason T, Heiser J, Lange R, Merhi W, Oh JK, Olsen PS, Piazza N, Williams M, Windecker S, Yakubov SJ, Grube E, Makkar R, Lee JS, Conte J, Vang E, Nguyen H, Chang Y, Mugglin AS, Serruys PW, Kappetein AP, SURTAVI Investigators. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2017; **376**: 1321–1331.
8. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, Capodanno D, Conradi L, De Bonis M, De Paulis R, Delgado V, Freemantle N, Gilard M, Haugaa KH, Jeppsson A, Jüni P, Pierard L, Prendergast BD, Sádaba JR, Tribouilloy C, Wojakowski W, ESC/EACTS Scientific Document Group. ESC/EACTS Scientific Document Group; ESC Scientific Document Group. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J* 2021 Aug 28:ehab395.
9. Popma JJ, Deeb GM, Yakubov SJ, Mumtaz M, Gada H, O'Hair D, Bajwa T, Heiser JC, Merhi W, Kleiman NS, Askew J, Sorajja P, Rovin J, Chetcuti SJ, Adams DH, Teirstein PS, Zorn GL 3rd, Forrest JK, Tchétché D, Resar J, Walton A, Piazza N, Ramlawi B, Robinson N, Petrossian G, Gleason TG, Oh JK, Boulware MJ, Qiao H, Mugglin AS, Reardon MJ, Evolut Low Risk Trial Investigators. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. *N Engl J Med* 2019; **380**: 1706–1715.
10. Fischer-Rasokat U, Renker M, Liebetrau C, Weferling M, Rolf A, Doss M, Möllmann H, Walther T, Hamm CW, Kim WK. Outcome of patients with heart failure after transcatheter aortic valve implantation. *PLoS ONE* 2019; **14**: e0225473 PMID: 31770401; PMCID: PMC6879149.
11. Dobson LE, Musa TA, Uddin A, Fairbairn TA, Swoboda PP, Erhayiem B, Foley J, Garg P, Haaf P, Fent GJ, Malkin CJ, Blackman DJ, Plein S, Greenwood JP. Acute reverse remodelling after transcatheter aortic valve implantation: a link between myocardial fibrosis and left ventricular mass regression. *Can J Cardiol* 2016; **32**: 1411–1418.
12. Kamperidis V, Joyce E, Debonnaire P, Katsanos S, van Rosendael PJ, van der Kley F, Sianos G, Bax JJ, Ajmone Marsan N, Delgado V. Left ventricular functional recovery and remodeling in low-flow low-gradient severe aortic stenosis after transcatheter aortic valve implantation. *J Am Soc Echocardiogr* 2014; **27**: 817–825.
13. Treibel TA, Kozor R, Schofield R, Benedetti G, Fontana M, Bhuva AN, Sheikh A, López B, González A, Manisty C, Lloyd G, Kellman P, Díez J, Moon JC. Reverse myocardial remodeling following valve replacement in patients with aortic stenosis. *J Am Coll Cardiol* 2018; **71**: 860–871.
14. Fairbairn TA, Steadman CD, Mather AN, Motwani M, Blackman DJ, Plein S, McCann GP, Greenwood JP. Assessment of valve haemodynamics, reverse ventricular remodelling and myocardial fibrosis following transcatheter aortic valve implantation compared to surgical aortic valve replacement: a cardiovascular magnetic resonance study. *Heart* 2013; **99**: 1185–1191.
15. Toyota K, Ota T, Nagamine K, Koide Y, Nomura T, Yamanaka F, Shishido K, Tanaka M, Saito S. Effect of transcatheter aortic valve implantation on intraoperative left ventricular end-diastolic pressure. *J Anesth* 2016; **30**: 1051–1055.
16. Seppelt PC, De Rosa R, Mas-Peiro S, Zeiher AM, Vasa-Nicotera M. Early hemodynamic changes after transcatheter aortic valve implantation in patients with severe aortic stenosis measured by invasive pressure volume loop analysis. *Cardiovasc Interv Ther* 2020.
17. Sultan I, Fukui M, Bianco V, Brown JA, Kliner DE, Hickey G, Thoma FW, Lee JS, Schindler JT, Kilic A, Gleason TG, Cavalcante JL. Impact of combined pre and postcapillary pulmonary hypertension on survival after transcatheter aortic valve implantation. *Am J Cardiol* 2020; **131**: 60–66.
18. Schewel D, Schewel J, Martin J, Voigtländer L, Frerker C, Wohlmuth P, Thielsen T, Kuck KH, Schäfer U. Impact of transcatheter aortic valve implantation (TAVI) on pulmonary hyper-tension and clinical outcome in patients with severe aortic valvular stenosis. *Clin Res Cardiol* 2015; **104**: 164–174.
19. O'Sullivan CJ, Wenaweser P, Ceylan O, Rat-Wirtzler J, Stortecky S, Heg D, Spitzer E, Zanchin T, Praz F, Tüller D, Huber C, Pilgrim T, Nietlispach F, Khattab AA, Carrel T, Meier B, Windecker S, Buellesfeld L. Effect of pulmonary hypertension hemodynamic presentation on clinical outcomes in patients with severe symptomatic aortic valve stenosis undergoing transcatheter aortic valve implantation: insights from the new proposed pulmonary hypertension classification. *Circ Cardiovasc Interv* 2015; **8**: 1–13.
20. Levy F, Bohbot Y, Sanhadji K, Rusinaru D, Ringle A, Delpierre Q, Smaali S, Gun M, Marechaux S, Tribouilloy C. Impact of pulmonary hypertension on long-term outcome in patients with severe aortic stenosis. *Eur Heart J Cardiovasc Imaging* 2018; **19**: 553–561.
21. Tamburino C, Capodanno D, Ramondo A, Petronio AS, Ettori F, Santoro G, Klugmann S, Bedogni F, Maisano F, Marzocchi A, Poli A, Antoniucci D, Napodano M, De Carlo M, Fiorina C, Ussia GP. Incidence and predictors of early and late mortality after transcatheter aortic valve implantation in 663 patients with severe aortic stenosis. *Circulation* 2011; **123**: 299–308.
22. Athappan G, Patvardhan E, Tuzcu EM, Svensson LG, Lemos PA, Fraccaro C, Tarantini G, Sinning JM, Nickenig G, Capodanno D, Tamburino C, Latib A, Colombo A, Kapadia SR. Incidence, predictors, and outcomes of aortic regurgitation after transcatheter aortic valve replacement: meta-analysis and systematic review of literature. *J Am Coll Cardiol* 2013; **61**: 1585–1595.
23. Pavone N, Burzotta F, Bruno P, Spalletta C, Farina P, Cammertoni F, Nesta M, Chiariello GA, Grandinetti M, De Belvis AG, Marzetti E, Angioletti C, Pasquini A, Mazza A, Iafrancesco M, Trani C, Lombardo A, Massetti M. Heart valve critical pathway and heart valve clinic: novel benchmarks for modern management of valvular heart disease. *Crit Pathw Cardiol* 2021; **20**: 126–133.
24. Burzotta F, Aurigemma C, Romagnoli E, Shoeib O, Russo G, Zambrano A, Verdirosi D, Leone AM, Bruno P, Trani C. A less-invasive totally-endovascular (LITE) technique for trans-femoral transcatheter aortic valve replacement. *Catheter Cardiovasc Interv* 2020; **96**: 459–470 Epub 2020 Jan 11. PMID: 31925991.
25. Romagnoli E, Burzotta F, Trani C, Siviglia M, Biondi-Zoccai GG, Niccoli G, Leone AM, Porto I, Mazzari MA, Mongiardo R, Rebuzzi AG, Schiavoni G, Crea F. EuroSCORE as predictor of in-hospital mortality after percutaneous coronary intervention. *Heart* 2009; **95**: 43–48.

26. Burzotta F, Trani C, Mazzari MA, Tommasino A, Niccoli G, Porto I, Leone AM, Tinelli G, Coluccia V, De Vita M, Brancati M, Mongiardo R, Schiavoni G, Crea F. Vascular complications and access crossover in 10,676 transradial percutaneous coronary procedures. *Am Heart J* 2012; **163**: 230–238.
27. Edwards FH, Cohen DJ, O'Brien SM, Peterson ED, Mack MJ, Shahian DM, Grover FL, Tuzcu EM, Thourani VH, Carroll J, Brennan JM, Brindis RG, Rumsfeld J, Holmes DR Jr. Development and validation of a risk prediction model for in-hospital mortality after transcatheter aortic valve replacement. *JAMA Cardiol* 2016; **1**: 46–52.
28. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, Burri H, Butler J, Čelutkienė J, Chioncel O, Cleland JGF, Coats AJS, Crespo-Leiro MG, Farmakis D, Gilard M, Heymans S, Hoes AW, Jaarsma T, Jankowska EA, Lainscak M, Lam CSP, Lyon AR, McMurray JJV, Mebazaa A, Mindham R, Muneretto C, Francesco Piepoli M, Price S, Rosano GMC, Ruschitzka F, Kathrine Skibelund A, ESC Scientific Document Group. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: developed by the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure of the European Society of Cardiology (ESC). With the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail* 2022; **24**: 4–131.
29. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU. 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**: 233–270.
30. Baumgartner H, Hung J, Bermejo J, Chambers JB, Edvardsen T, Goldstein S, Lancellotti P, LeFevre M, Miller F Jr, Otto CM. Recommendations on the echocardiographic assessment of aortic valve stenosis: a focused update from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. *J Am Soc Echocardiogr* 2017; **30**: 372–392.
31. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, Edvardsen T, Flachskampf FA, Gillebert TC, Klein AL, Lancellotti P, Marino P, Oh JK, Alexandru Popescu B, Waggoner AD, Houston, Texas; Oslo, Norway; Phoenix, Arizona; Nashville, Tennessee; Hamilton, Ontario, Canada; Uppsala, Sweden; Ghent and Liège, Belgium; Cleveland, Ohio; Novara, Italy; Rochester, Minnesota; Bucharest, Romania; and St. Louis, Missouri. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2016; **17**: 1321–1360.
32. Généreux P, Pibarot P, Redfors B, Mack MJ, Makkar RR, Jaber WA, Svensson LG, Kapadia S, Tuzcu EM, Thourani VH, Babaliaros V, Herrmann HC, Szeto WY, Cohen DJ, Lindman BR, McAndrew T, Alu MC, Douglas PS, Hahn RT, Kodali SK, Smith CR, Miller DC, Webb JG, Leon MB. Staging classification of aortic stenosis based on the extent of cardiac damage. *Eur Heart J* 2017; **38**: 3351–3358.
33. Sinning JM, Hammerstingl C, Vasa-Nicotera M, Adenauer V, Lema Cachiguango SJ, Scheer AC, Hausen S, Sedaghat A, Ghanem A, Müller C, Grube E, Nickenig G, Werner N. 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**: 1134–1141.
34. Sinning JM, Stundl A, Pingel S, Weber M, Sedaghat A, Hammerstingl C, Vasa-Nicotera M, Mellert F, Schiller W, Kovac J, Welz A, Grube E, Werner N, Nickenig G. 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**: 700–711.
35. Kiramijyan S, Koifman E, Magalhaes MA, Ben-Dor I, Didier R, Jerusalem ZD, Kumar S, Tavil-Shatelyan A, Rogers T, Steinvil A, Gai J, Torguson R, Satler LF, Pichard AD, Waksman R. Intraprocedural invasive hemodynamic parameters as predictors of short- and long-term outcomes in patients undergoing transcatheter aortic valve replacement. *Cardiovasc Revasc Med* 2018; **19**: 257–262.
36. Gonçalves A, Marcos-Alberca P, Almeria C, Feltes G, Rodríguez E, Hernández-Antolín RA, Garcia E, Maroto L, Fernandez Perez C, Silva Cardoso JC, Macaya C, Zamorano JL. Acute left ventricle diastolic function improvement after transcatheter aortic valve implantation. *Eur J Echocardiogr* 2011; **12**: 790–797.
37. Chen J, Nawaz N, Fox Z, Komlo C, Anwaruddin S, Desai N, Jagasia D, Herrmann HC, Han Y. Echocardiographic determinants of LV functional improvement after transcatheter aortic valve replacement. *Catheter Cardiovasc Interv* 2016; **87**: 1164–1172.
38. Lindman BR, Stewart WJ, Pibarot P, Hahn RT, Otto CM, Xu K, Devereux RB, Weissman NJ, Enriquez-Sarano M, Szeto WY, Makkar R, Miller DC, Lerakis S, Kapadia S, Bowers B, Greason KL, McAndrew TC, Lei Y, Leon MB, Douglas PS. Early regression of severe left ventricular hypertrophy after transcatheter aortic valve replacement is associated with decreased hospitalizations. *JACC Cardiovasc Interv* 2014; **7**: 662–673.
39. Kasapkara HA, Ayhan H, Sarı C, Aslan AN, Süygün H, Başтuğ S, Durmaz T, Keleş T, Bozkurt E. Impact of transcatheter aortic valve implantation on the left ventricular mass. *Cardiol J* 2015; **22**: 645–650.
40. Zahn R, Werner N, Gerckens U, Linke A, Sievert H, Kahlert P, Hambrecht R, Sack S, Abdel-Wahab M, Hoffmann E, Zeymer U, Schneider S, German Transcatheter Aortic Valve Interventions—Registry investigators. Five-year follow-up after transcatheter aortic valve implantation for symptomatic aortic stenosis. *Heart* 2017; **103**: 1970–1976 Epub 2017 Jul 6. PMID: 28684438.