

Transcatheter aortic valve implantation in severe aortic stenosis does not necessarily reverse left ventricular myocardial damage: data of long-term follow-up

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Aims

Aortic stenosis (AS) is causing myocardial damage and replacement is mainly indicated based on symptoms. Non-invasive estimation of myocardial work (MW) provides a less afterload-dependent tool for assessing myocardial function. We sought to look at the impact of transcatheter aortic valve implantation (TAVI) on the myocardium at long-term follow-up and according to current indications.

Methods and results

We conducted an observational, cross-sectional, single-centre study. Patients were selected based on the validated indication for a TAVI. Standardized echocardiographies were repeated. A total of 102 patients were included. The mean age was 85 years, 45% were female, 68% had high blood pressure, and 52% had a coronary disease. One-fifth was suffering from low-flow–low-gradient AS. A follow-up was performed at 22 ± 9.5 months after the TAVI. No TAVI dysfunction was observed. Left ventricular (LV) ejection fraction was stable ($62 \pm 8\%$), and global longitudinal strain had improved (-14.0 ± 3.7 vs. $-16.0 \pm 3.6\%$, $P < 0.0001$). No improvement of the MW parameters was noticed (LV global work index 2099 ± 692 vs. 2066 ± 706 mmHg%, $P = 0.8$, LV global constructive 2463 ± 736 vs. 2463 ± 676 mmHg%, $P = 0.8$). Global wasted work increased [214 (149; 357) vs. 247 (177; 394) mmHg%, $P = 0.0008$].

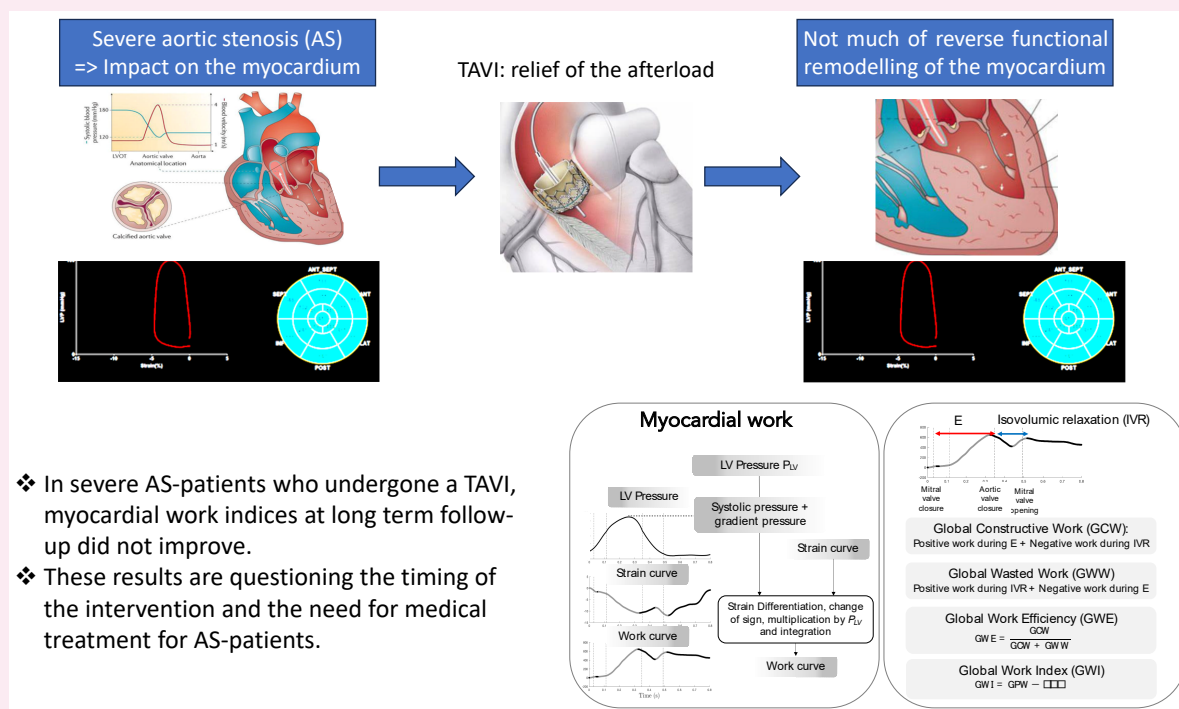
Conclusion

In a population of severe symptomatic AS patients who had undergone a TAVI, the non-invasive myocardial indices that assess the LV performance at long-term follow-up did not improve. These results are questioning the timing of the intervention and the need for more attention in the pharmacological management of these AS patients.

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Graphical Abstract



Keywords

aortic valve stenosis • myocardial damage • transcatheter aortic valve implantation • myocardial work • deformation imaging

Introduction

Despite many steps made forward in the understanding and management of aortic stenosis (AS), the optimal timing for valve replacement remains controversial.¹ A staging of AS severity is defined by guidelines, with a new definition of 'normal' left ventricular (LV) ejection fraction (EF).^{2,3}

One of the keys for ensuring symptom relief after treatment is the timing to refer these patients for aortic valve replacement (AVR).^{4,5} However, according to guidelines, intervention is recommended in symptomatic patients with severe high-gradient AS or in severe low-flow and low-gradient AS with reduced LVEF < 50% and evidence of flow reserve (Class I, Level B). Intervention should also be considered in symptomatic low-flow-low-gradient AS (Class IIa, Level C). Asymptomatic severe AS may be operated only in restrictive clinical situations.^{2,3}

Rest transthoracic echocardiography (TTE) is an important tool that provides pertinent information.⁶ This first-line exam gives prognostic information thanks to the degree of valve calcification, LV function, and wall thickness. It helps to detect other valve diseases or aortic pathology. ESC guidelines highlight the necessity of recording the TTE with the knowledge of the blood pressure (BP) values. LVEF and LV global longitudinal strain (GLS) are highly afterload pressure and difficult to interpret in severe aortic stenosis (SAS). Lately, new normal values for LVEF were defined,⁷ and myocardial work (MW) might be a better tool to assess the LV damages in SAS. Indeed, it relies on the registration of pressure-strain loops (PSLs) and it provides four quantitative parameters, these are fully describing the LV-performance, its efficiency and the wasted energy. The main LV ones are the global work index (LV GWI) and global work efficiency (LV GWE), itself calculated thanks to the global constructive (LV GCW) and wasted (LV GWW) MWs. The

feasibility of this model has been described in patients suffering from severe AS by Fortuni et al.⁸ and is well correlated with invasive measurement works. The method has then been validated as appropriate by Taconne et al.⁹

For this study, the primary objective was to assess the evolution of the four MW indices at long-term follow-up more than 1 year after transcatheter aortic valve implantation (TAVI) when compared with prior to TAVI, with the assumption that they will decrease due to afterload reduction and LV reverse remodelling. Secondary objectives were focused on clinical data with New York Heart Association (NYHA) improvement and its predictors, as well as conduction disturbances prevalence. Relevant sub-group analyses (sex, age, and stroke volume) were predefined too.

Methods

Study design

We conducted an observational, cross-sectional, single-referral centre study. Screening criteria were patients with a symptomatic aortic severe stenosis proved by rest echocardiography, in whom a percutaneous aortic replacement technique was decided and performed in the centre after Heart Team discussion and alive 6 months after the procedure. Loops of rest echocardiography prior to and the very next days after the percutaneous valve implantation were needed for a core lab review, including the calculation of MW. Exclusion criteria were limited to BP recording missing, insufficient image quality, aortic regurgitation more than mild on prior-to-TAVI echocardiography, or failure to perform the procedure because of technical reasons. Patients unable to be reassessed by echocardiography in our centre were excluded too.

Follow-up data were recorded during a specific appointment with the patient. The clinical data were collected as well as the non-invasive brachial BP and the rest electrocardiography (ECG). Also, the latest medications prescription, and blood sample results (including renal function, haemoglobin, and N-terminal prohormone of B-type natriuretic peptide levels). An inquiry was performed to assess the dyspnoea stage (according to the NYHA scale), chest pain, or any cardiovascular complication or rehospitalization since the TAVI procedure. When information was missing, general practitioners were called to get the most recent results.

All patient consents were authenticated as they gave them as participants of the France-TAVI register. Data collection was performed in accordance with the Declaration of Helsinki.

Echocardiographic acquisitions

All exams were recorded at the echocardiography laboratory of the centre and performed by trained sonographers using a commercially available ultrasound system (Vivid E95, E9, S70; General Electric Healthcare, Horten, Norway). Loops were recorded at rest in a leftward lying position, with the assessment of all the routine parameters according to the latest ESC recommendations.¹⁰ Sub-costal, long and short parasternal axes, as well as four, two, and three apical chambers were used. Assessment of the LV structure was done with routine measurements (end-diastolic diameter, thickness, mass index, indexed volumes) as well as its function (LVEF thanks to the Simpson Biplane method, GLS; diastolic parameters with mitral E-wave and A-wave, tissue Doppler at the mitral annulus, left atrial indexed volume estimation, and peak velocity of the tricuspid regurgitation).

For the aortic valve, trans-aortic mean and maximal pressure gradients were assessed by continuous Doppler. The estimated aortic valve surface was calculated thanks to the continuous equation using the LV outflow tract diameter, trans-aortic mean pressure gradient, and velocity–time integral aortic values. Other valvopathies were screened and quantified when present. Right ventricular function was also assessed with regular parameters [tricuspid annular plan systolic excursion (TAPSE), S'-wave at the tricuspid annulus, estimated systolic pulmonary artery pressure].

Non-invasive MW assessment

As previously described, the LV afterload pressure was estimated by the sum of the mean trans-aortic pressure gradient to the systolic brachial artery cuff pressure of the patient.¹¹ These data were then computed with LV GLS loops, recorded in four, two, and three apical chambers as recommended, with an optimized frame rate. Thanks to a 2D three-chamber view and continuous aortic pulse recording, markers were manually positioned to define aortic and mitral opening and closing times, and LV PSLs were then obtained. Finally, they were offline post-treated thanks to a specific semi-automated software (EchoPAC PC version 204, GE-Healthcare, Horten, Norway).

Thus, four main MW indices were used to model the LV performance, as already described in the literature.¹² The LV GWI (mmHg%) is a simple tool that estimates the amount of LV work contributing to ejection in systole, calculated as the area within the PSL from mitral valve closure to opening. To assess the LV performance not only during systole but also during the diastole, three other MW indices are useful. The LV GCW (mmHg%) integrates shortening during systole but also lengthening during diastole. The LV GWW (mmHg%) is the opposite of LV GCW, determined as the lengthening during systole and shortening during diastole (e.g. dyssynchrony, paradoxical myocardial lengthening or shortening, that does not contribute to useful work). LV GWE (%) is thus the division of LV GCW by the sum of LV GCW and LV GWW. After post-treatment, all parameters were exported from the software to be included in the database (Excel version 2302, Microsoft, Redmond, WA, USA).

Statistical analysis

With a single cohort of participants, clinical and paraclinical data were registered during the consultation meeting at long-term follow-up. The centre

database was used to compare the data to prior-to-TAVI ones. Continuous variables are presented as mean $\pm$ standard deviation or median with the first, third, or interquartile range (IQR), as appropriate. Categorical variables are in percentages. Changes were expressed as the mean relative change or annualized median relative change for continuous parameters. A Wilcoxon signed-rank statistic test assessed the null hypothesis for which the mean or median change was equal to zero. For categorical binary variables, a McNemar χ^2 test was computed.

We expected the GWI would decrease from 15% at long-term follow-up compared with prior to TAVI, based on the available data of the literature.¹³ Thus, the minimum number of subjects to be enrolled to perform the study with a statistical power of 90% and an alpha power of 5% was calculated at 75 patients (R soft, version 4.2.3 for Windows, Indianapolis, IN, USA).

Logistic regression modelling was used to explore the association between pre-specified predictors and NYHA improvement. Linearity assumption was assessed through splines in a general additive model. The fully conditional specification in multivariate imputation was performed by the chained equations method to impute values for a data set with an arbitrary missing pattern. We assumed that joint distribution exists for the data and generated 25 complete data sets (MI procedure, SAS 15.1; SAS Institute Inc., Cary, NC, USA). Analyses of imputations were obtained by using standard SAS procedures (i.e. PROC LOGISTIC). These results were combined in the MIANALYZE procedure to derive valid inferences.

Results

Population characteristics

In the timeframe from May 2020 to August 2021, 126 consecutive patients underwent a successful TAVI procedure at the centre and met the selection criteria. Twelve of them died during the study: one case of terminal heart failure, one case of acute TAVI thrombosis, one case of terminal stage of pulmonary fibrosis, and nine cases with undetermined diagnosis. Twelve others refused to participate in the study, mainly because of geographical distance from the centre. Thus, 102 patients were included in the main analysis (Figure 1).

Patient's baseline characteristics are summarized in Table 1. The mean age was 84.5 years, 45% were female, 67.6% had high BP, and 52% had a coronary disease. Less than one-third had a history of atrial fibrillation. One-fifth was previously suffering from low-gradient–low-flow AS (proved by dobutamine stress with an increased stroke volume $\geq 20\%$), with 10 of them having low-flow–low-gradient with preserved EF due to severe LV concentric remodelling. Proven underlying cardiac transthyretin amyloidosis reached 4.9%. Participants had regular cardiovascular treatment with more than half of them receiving beta-blockers, renin–angiotensin, and/or loop diuretics, similar to pre-TAVI and close follow-up. TAVI procedure details showed a high surgical risk with a mean Euroscore II at 8.5%. The balloon-expandable prosthesis was mainly used. Femoral access was privileged (92%) and only 4.9% were valve-in-valve procedures.

Table 2 shows the main echocardiographic parameters registered during the medical meeting. LVEF was preserved ($62 \pm 8\%$) and the left atrium was enlarged (47.8 ± 16.7 mL/m²). TAVI assessment showed satisfying parameters with a trans-aortic mean pressure gradient at 11.0 mmHg (9.00; 16.0). One-third of the patients experienced mild paravalvular aortic regurgitation, with any case of severe leaking. No case of patient-prosthesis mismatch was noticed.

Follow-up results

Long-term follow-up data were collected between January 2021 and April 2023 with pre-specified clinical and paraclinical parameters. Early follow-up echocardiography was performed 3 ± 7 days after TAVI and 22 ± 9.5 months after the procedure for long-term follow-up echocardiography. The mean BP was $148 \pm 21/76 \pm 11$ mmHg at

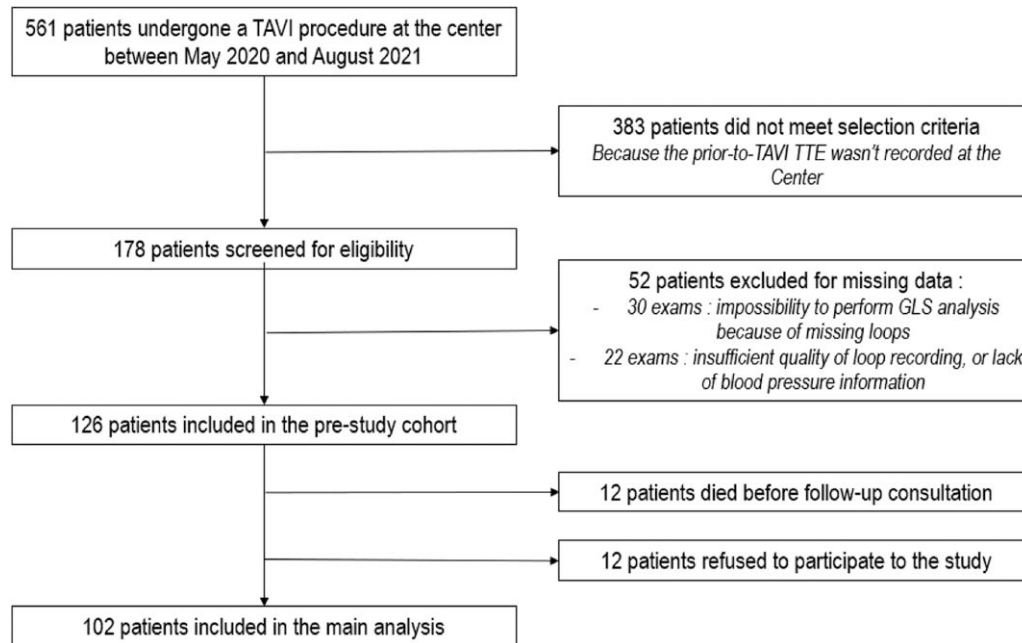


Figure 1 Flow chart.

long-term follow-up, higher than compared with the previous recordings ($129 \pm 19/69 \pm 11$ mmHg in pre-TAVI; $128 \pm 17/68 \pm 12$ mmHg at close follow-up) (Table 3). Occurring supraventricular arrhythmia during TTE was close to 16%, superposable to the rate of prior to TAVI and at close follow-up. Trans-aortic mean pressure gradient aortic values dropped down after intervention (11 vs. 52 mmHg, $P < 0.0001$). LVEF stayed preserved with no significant evolution (64.0% (56.0 ; 70.0) vs. 62.0% (59.0 ; 67.0), $P = 0.4128$). GLS gets improved ($-14.0\% \pm 3.71$ vs. $-16.0\% \pm 3.62$, $P < 0.0001$). Diastolic function remained unchanged. The peak of tricuspid regurgitation velocity was lower after the procedure (2.99 ± 0.48 vs. 2.76 ± 0.46 m/s, $P = 0.0096$) (see Supplementary data online, Table S4A).

Focusing on non-invasive MW assessment, the LV GWI value, approximating the amount of LV work contributing to ejection in systole, did not reduce at long-term follow-up when compared with prior to TAVI (2066 ± 706 vs. 2099 ± 692 mmHg%, $P = 0.8671$) (Table 3 and Supplementary data online, Table S3A). Looking at the percentage of LV work which is useful for contraction during systole but also relaxation in diastole, LV GWE values did not significantly decrease when compared with prior to TAVI [88.0% (83.0 ; 92.0) vs. $87.0 \pm 5.66\%$, $P = 0.7502$]. In detail, the LV GCW did not get improved (2463 ± 676 vs. 2463 ± 736 mmHg%, $P = 0.8076$). LV GWW even increased [247 (177 ; 394) vs. 214 (149 ; 357) mmHg%, $P = 0.0008$]. Results were similar in the different subgroups analysis according to gender. No difference was found according to high or low-flow low-gradient status (stroke volume indexed $<$ or > 35 mL/m²). But according to age, participants older than 85 years did not suffer from significant deterioration of their LV GWW values [0.30 , 95% confidence interval (CI) -0.08 – 0.68].

On secondary outcomes, clinical findings showed that severe dyspnoea dropped down quickly after the afterload release (38.2% of patients with NYHA III or IV prior to TAVI when compared with 1.0% right after). But this proportion increased at long-term follow-up meeting (11.9%). Logistic regression analysis was performed to identify predictors of NYHA improvement, but none of the studied parameters changed significantly. The occurrence of conduction disturbance with a complete bundle branch block was greater after the procedure

(40.2 vs. 23.5%). One-fifth of them led to the implantation of a permanent ventricular stimulation device. Cardiovascular events rate after TAVI procedure was low; relevant additional statistical analysis about prognosis was not valid. Seven ischaemic cerebral strokes were reported as well as 13 episodes of congestive heart. More than half of them led to hospitalization, and four of them to percutaneous correction of severe symptomatic mitral or tricuspid regurgitation (transcatheter edge-to-edge repairs).

Discussion

Main results

In a population suffering from severe AS who had undergone a successful TAVI procedure, LV MW did not significantly improve at long-term follow-up when compared with prior to TAVI. These findings are in accordance with the conclusions of G  n  reux *et al.*⁵ which highlighted that a significant amount of patients are insufficiently enhanced by the TAVI procedure.

Traditional echocardiographic tools are insufficient to accurately evaluate LV performance.⁶ LVEF evaluation is not sensitive enough for describing the change in LV function after TAVI.¹⁴ This result is not surprising as the LV adapts 'against' afterload. Specific parameters such as the LV ejection time (LVET) were described to calculate the immediate haemodynamic response after TAVI. But its invasive nature makes it less likely to be used in routine clinic.¹⁵ Other sensitive tools have been designed to detect the early stages of LV dysfunction. One of these is the LV GLS. This tool has, among others, shown its prognostic value with post-TAVI morbidity and mortality.¹⁶ In our study, we found a slight improvement at long-term follow-up. Nevertheless, GLS is still dependent to LV afterload. Even though some optimistic results have been previously reported, others failed to show improvement after AVR.^{17,18} Cardiac magnetic resonance has been developed too. Our results are in line with the ones describing the value of late gadolinium enhancement prior to intervention (in favour of replacement fibrosis) to predict the lack of significant improvement after release of the

Table 1 Baseline characteristics of the population

Label	Study participants (n = 102)
Standard data	
Age, years	84.3 ± 6.2
Female, %	53 (45.1)
Body mass index, kg/m ²	26.1 ± 5.1
Comorbidities	
Coronary disease, %	53 (52.0)
Diabetes mellitus, %	12 (11.8)
Hypertension, %	69 (67.6)
History of atrial fibrillation, %	31 (30.4)
Chronic obstructive pulmonary disease, %	8.0 (7.8)
Medications	
Beta-blocker, % (n = 99)	58 (56.9)
ACEI, ARB, or ARNI, % (n = 95)	56 (54.9)
Loop diuretics, % (n = 99)	56 (54.9)
Laboratories	
Haemoglobin, g/dL (n = 93)	12.8 [2.4]
NT-pro-BNP, pg/mL (n = 90)	548.0 [1163]
Renal clearance CKD-EPI, mL/min/1.73 m ² (n = 96)	83.0 [35.8]
Type of aortic stenosis	
Low-flow low-gradient aortic stenosis, %	20 (19.6)
Confirmed amyloidosis aTTR, %	5 (4.9)

Statistics are mean ± standard deviation, median (IQR), or number (%).

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; NT-pro-BNP, N-terminal prohormone of B-type natriuretic peptide; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; TTR, transthyretin.

afterload.¹⁹ T₁-mapping and extra-cellular volume are supposed to assess the reverse remodelling of the LV after SAS correction.²⁰ Interestingly, LV-strain apical sparing has been reported to be a relatively common finding in patients with severe AS who underwent TAVI, and its prevalence decreases after the afterload relief related to the intervention.²¹ It has not been that clear in our experience. The myocardial damage is not always reversible.¹⁹

Diastolic function remained unchanged in our study while improving in some others.²² The conclusions of Ayhan *et al.* showing an improvement after TAVI of all parameters related to right ventricular systolic function were not been found here.^{23,24} Our patients are more advanced if one considers the Euroscore, for instance (e.g. younger patients with a mean age close to 79 vs. 84.5 years in our study). We probably have a much higher prevalence of concentric LV-remodelling phenotype.²⁵ It has been shown to be associated with less change in the E/e' ratio after AS correction when compared with concentric remodelling seen at earlier AS stages.²²

In this context, non-invasive myocardial indices of function and anatomical LV remodelling have been developed and are of matter of interest.¹⁹ The meta-analysis of Truong *et al.* (13 data sets, 1665 patients) reported normal mean values for non-invasive MW in adult healthy subjects: LV GWI ±2.010 mmHg% [95% confidence interval (CI), 1.907–2.113 mmHg%]; mean LV GWE ±96.0% (95% CI, 96–96%);

Table 2 Echocardiographic data at long-term follow-up after TAVI

Label	TTE long-term follow-up after TAVI (n = 102)
LV structure and systolic function	
LV diastolic dimension, mm	46 ± 6.8
LV wall thickness, mm (n = 101)	11 [2]
LV mass index, g/m ² (n = 101)	107 [39]
LV end-diastolic volume index, mL/m ² (n = 101)	57 [19]
LV ejection fraction in SB, %	62 [8]
LV global longitudinal strain, %	−16 ± 3.6
LV diastolic function	
LA volume index, mL/m ² (n = 101)	47.8 ± 16.7
E/e' mean ratio (n = 97)	15.8 ± 5.6
Peak of tricuspid regurgitation, m/s (n = 92)	2.8 ± 0.5
Aortic valve parameters	
Peak of velocity, m/s	2.2 [0.7]
Trans-aortic mean pressure gradient, mmHg	11 [7]
Stroke volume indexed, mL/m ² (n = 101)	50.0 [13.0]
Estimated aortic surface area, cm ² (n = 101)	1.9 ± 0.6
Estimated indexed aortic surface area, cm ² /m ² (n = 101)	1.1 ± 0.3
Permeability index, % (n = 101)	0.4 [0.2]
Mild paravalvular aortic regurgitation, %	38 (37.3)
Other valves assessment	
Aortic regurgitation moderate to severe, %	0 (0.0)
Mitral regurgitation moderate to severe, %	2 (2.0)
Tricuspid regurgitation moderate to severe, %	8 (7.8)
RV function	
TAPSE, mm (n = 94)	22 ± 5
Estimated sPAP, mmHg (n = 91)	33 [14]

Statistics are mean ± standard deviation, median (IQR), or number (%).

TTE, transthoracic echocardiography; TAVI, transcatheter aortic valve implantation; LV, left ventricle; SB, Simpson biplane method; LA, left atrium; E/e', mean ratio stands for the ratio of early diastolic mitral inflow velocity to early diastolic mitral annulus velocity; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion; sPAP, systolic pulmonary artery pressure.

LV GCW ±2.278 mmHg% (95% CI, 2.186–2.369 mmHg%); LV GWW ±80 mmHg% (95% CI, 73–87 mmHg%).²⁶ Variability and reproducibility were good for the four parameters. Manganaro *et al.*²⁷ found also an accurate correlation of non-invasive MW indices with traditional 2 dimensional echocardiographic parameters of myocardial systolic function and myocardial strain. Those tools have been evaluated and validated in different clinical conditions, such as ischaemic heart disease, heart failure, valvular diseases, and cardiac resynchronization therapy.²⁸ Focusing on patients suffering from severe AS, our results partially match with the most recent publications.^{11,12} The study of De Rosa *et al.*¹³ built a robust protocol close to the one we used, but with a smaller group of patients where patients with left bundle branch block were excluded and with an echocardiographic follow-up limited to 1 year. They failed to show an improvement of LV GWE and

Table 3 Outcomes

Label	Prior to TAVI (n = 102)	Early follow-up (n = 102)	Long-term follow-up (n = 102)	Late change (P-value)
Primary outcomes				
Non-invasive myocardial work				
LV GWE, %	87.0 ± 5.66	85.0 ± 7.27	88.0 [83.0; 92.0]	0.7502
LV GWI, mmHg%	2099 ± 692	1455 ± 537	2066 ± 706	0.8671
LV GCW, mmHg%	2463 ± 736	1752 ± 556	2463 ± 676	0.8076
LV GWW, mmHg%	214 [149; 357]	222 [140; 326]	247 [177; 394]	0.0008*
Secondary outcomes				
Dyspnoea assessment				
NYHA stage III or IV, %	39 (38.2)	1 (1.0)	12 (11.9)	<0.0001**
Conduction disturbances				
Complete bundle branch block, %	11 (10.8)	22 (21.6)	21 (20.6)	0.0003
Including ventricular permanent stimulation, %	10 (9.8)	21 (20.6)	20 (19.6)	0.0067

Statistics are mean ± standard deviation, median (first quartile; third quartile), or percentage.
Primary outcomes P-value for a Wilcoxon signed-rank test statistic for the null hypothesis that the mean or median is equal to zero*.
Secondary outcomes P-value for McNemar χ^2 test**.
LV GWE, left ventricular global work efficiency; LV GWI, left ventricular global work index; LV GCW, left ventricular global constructive work; LV GWW, left ventricular global wasted work; NYHA, New York Heart Association Classification.

LV GWW, but found a significant LV GWI and LV GCW reduction after TAVI.¹³ Similar results were observed in our previous work.¹² If this trend was found in our study at close follow-up too, our results were not significant at long-term meeting. LV GWI and LV GCW switched back to their pre-TAVI values, and LV GWW even increased in our population. Hypotheses may be various. The main one was that our quantification of LV function was affected by insufficient BP control at long-term follow-up. This leads to a less pronounced LV afterload decrease when compared with the pre-operative period. This condition is leading to insufficient LV afterload decrease after TAVI that potentially has masked the improvement in GLS. In addition, the irreversible myocardial damage leads to a progressive increase in the disease process including myocardial fibrosis that exists in AS but also in heart failure with preserved EF. Also, the prevalence of ECG conduction disturbances (e.g. newly developed branch bundle block and/or permanent ventricular stimulation) is a trigger of LV-desynchrony. Reduced LV is then expected.²⁹ A substantial amount of patients had atrial fibrillation at the echocardiographic follow-up. That is a limit for the robustness of MW measurement. Finally, the low-flow–low-gradient AS was prevalent in our cohort. These are probably too severe to experience any significant LV remodelling after TAVI (19.6 vs. 13.7% in De Rosa et al.¹³).

Patients, we are dealing with, nowadays are suffering from more or probably too advanced AS stages of myocardial damage. We hypothesize that to significantly improve the outcome of TAVI patients, we should be able to get a significant LV remodelling. It should probably push for an earlier referring and an improved imaging assessment of these patients for an intervention in earlier stages.⁶

Predictors of prognostic cardiovascular status after severe AS correction are crucial, and the potential role of LV MW indices has been recently studied too. At baseline, some publications assert that LV GWI may be an independent predictor for heart failure leading to re-hospitalizations after TAVI.¹³ For mortality, Wu et al. found that LV GWI value following TAVI was independently associated with all-cause death, with a higher prognostic value compared with LVEF and GLS. This trend was even more significant for patients in the lower tertile of LV GWI (<1532 mmHg%) with a worse clinical risk profile. This

threshold seems likely as the 12 patients who died before inclusion in our work had weak LV GWI (mean value at 1074 mmHg%). The mean LV GWE value was reported to be constant up to 45 years of age and to decrease then after. Gender has been reported to impact on LV GWI, LV GWW, and LV GWE.²⁶ We performed specific sub-group analyses, and our primary outcomes were unchanged after adjustment on gender (lack of power could be advocated). In the sub-group of participants older than 85 years, we found no significant deterioration of their LV GWW values at long-term follow-up. The scope of this finding is still limited as these patients had already more impaired prior-to-TAVI LV GWW values [230 (142; 307) vs. 221 (127; 350)].

Strengths

Our study has several strengths. Our participant’s characteristics are fitting with the current epidemiology (mean age 84.5 years, 67.6% with high BP, 52% of coronary disease, 30.4% with a history of atrial fibrillation) of severe AS in referral centres.³⁰ We made the choice of a very limited amount of exclusion criteria to get the largest panel of profiles, including low-flow–low-gradient AS. In these, cardiac amyloidosis is associated with a need for the diagnosis and the treatment of both the AS and the amyloidosis.³¹ The impact of both on myocardial function is weakly reported up to now.¹³ Therefore, sub-group analyses on primary outcomes with participants having a low-flow stroke volume <35 mL/m² were performed, but their non-invasive myocardial parameters were not statistically different.

Limitations and perspectives

This work includes some limitations. First, our long-term follow-up MW indices may have been distorted by the BP values, as previously described.³² Measurements performed might have overestimated the pressure when compared with the one recorded during the hospitalization. This bias seems nevertheless difficult to control, as all the values were registered according to the standard recommendations (lying position with a prior rest period for at least 5 min). Brachial BP was controlled at the end of the medical evaluation.

The relationship between non-invasive MW and mortality after TAVI could have been of interest, as up to 33.9% of death after TAVR at 2-year follow-up has been reported in some elderly population.²⁵ But re-hospitalizations and mortality after TAVI was a rather infrequent condition in our study, leading to an underpowered statistical analysis to evaluate any impact of MW indices on clinical events prediction.

In a population of patients suffering from severe symptomatic AS, it may help to identify the ones who will really improve their symptoms after the TAVI. Severe AS is not limited to a valvular disease as it damages the LV myocardium too. Gonzales *et al.*³³ shown that LV hypertrophy represents early stages of adverse remodelling, and this condition is associated with a higher cardiovascular morbidity. On their side, Généreux *et al.*⁵ have proposed a classification in five stages of 'cardiac damage' among patients with AS. Their work showed that a specific evaluation is crucial to assess any LV damage (such as hypertrophy, severe diastolic or systolic dysfunction). Left atrial or mitral damage (e.g. left atrial enlargement, atrial fibrillation, moderate or severe mitral regurgitation) as well as right ventricular damage are matter of interest (e.g. pulmonary artery vasculature or tricuspid valve damage, and moderate or severe right ventricular dysfunction). When cardiac damage is present, only 15.6% of their participants reduced their cardiac damage stage after AVR. In our study, our participant suffered from advanced cardiac damage with 12.7% of right ventricular impairment (Stage 4) and 5% of pulmonary/tricuspid damage (Stage 3). Half of them suffered from left atrial or mitral damage (Stage 2) and only four participants had no echocardiographic cardiac damage (Stage 0). Those findings highlight the necessity to improve prognostic stratification and the selection of patients undergoing TAVR. This conclusion was shared by Gutierrez-Ortiz *et al.*³⁴ Multimodality imaging can also help to evaluate the LV remodelling response and improve risk stratification. This condition can be already present when the stenosis is still moderate.⁴ With this knowledge, some randomized controlled trials are ongoing to evaluate whether AVR can enhance outcomes in patients with moderate AS (TAVR UNLOAD Trial, NCT02661451).

Finally, routine cardiac medications have shown their potential benefit on LV reverse remodelling and thus reduce mortality at long-term follow-up after TAVR, such as statins. Angiotensin-converting enzyme inhibitor and angiotensin receptor blocker have been tested too, and may be even more efficient when prescribed prior to the procedure.^{35,36}

Conclusion

In a population of severe symptomatic AS patients who had undergone a TAVI, the non-invasive myocardial indices that assess the LV performance at long-term follow-up did not improve. These results are questioning the timing of the intervention and the need for more attention in the pharmacological management of these AS patients.

Supplementary data

Supplementary data are available at *European Heart Journal - Cardiovascular Imaging* online.

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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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