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Myocardial work and risk stratification in patients with severe aortic valve stenosis referred for transcatheter aortic valve replacement

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ABSTRACT

Background: Transcatheter aortic valve replacement(TAVR) has shown clear survival benefits in severe aortic valve stenosis(AS). However, patients unable to recover left ventricle function remain at risk with poor long-term survival. This single-center prospective study aims to analyze the supplementary benefits of myocardial work (MW) assessment for baseline risk stratification in patients with severe AS referred for TAVR.

Methods: A total of 110 patients with severe AS referred for TAVR were included in the study. Baseline ECG data, transthoracic echocardiographic(TTE) images and blood samples were obtained. The TTE examination was repeated one day and one month after valve replacement. The primary outcome of the study was a composite endpoint consisting of all-cause mortality and HF hospitalization.

Results: During a mean follow-up period of 521 ± 343 days, 29patients(26.4 %) reached the composite endpoint. Baseline troponins, NT-proBNP, sST2, GWI and GCW showed statistically significant differences between groups. Patients with a baseline GWI<2323 mmHg% (sensitivity 0.63 and specificity 0.76)had significantly worse outcome following TAVR. A basic predictive model included QRS-length, TAPSE, LAVI and E/e'. The addition of biomarkers did not yield any further advantages whereas incorporating the GWI cut-off value of 2323 mmHg% significantly enhanced the predictive value. Although there were no significant changes in LVEF and GLS, all patients exhibited a significant reduction in GWI and GCW immediately after TAVR.

Conclusion: Our findings provide evidence for the enhanced usefulness of MW analysis in the initial risk stratification of patients with severe AS referred for TAVR. Specifically, a baseline GWI<2323 mmHg% demonstrates an independent predictor associated with increased incidence of all-cause mortality and HF hospitalization following TAVR.

1. Introduction

Aortic valve stenosis (AS) is the most common valve disease observed among the elderly population in Europe [1,2]. Transcatheter aortic valve replacement (TAVR) has shown significant survival benefits and is recommended for older patients who are at high risk or unsuitable for surgery [3,4]. However, the longstanding high pressure in the left ventricle (LV) can lead to irreversible myocardial damage. As a result, patients may not recover normal LV function after the intervention leading to a worsened prognosis and decreased survival rates. Consequently, there is an urgent need for a meticulous patient risk stratification system to guide disease management.

In 2017, Généreux et al.[5] developed a classification system consisting of five stages to categorize severe AS based on the extent of associated extra-valvular cardiac damage or dysfunction. Each stage is associated with an increased risk of mortality within 1 year, ranging from 4 % in stage 0 to 25 % in stage 4. More recently, the role of myocardial work (MW) has also been validated in AS patients [6,7]. This advanced echocardiographic tool analyzes the LV myocardial performance by incorporating afterload through pressure-strain loops [8,9].

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Given the abrupt drop in afterload experienced by patients with severe AS after TAVR, MW analysis has emerged as a promising area of research in this patient population. Previous studies have demonstrated that MW parameters are not only independently associated with heart failure (HF) symptoms [10] but also with post-TAVR outcomes [11,12]. However it is important to note that MW assessment was not included in the Généreux et al. classification of AS, which consist of five stages: Stage 0 – No extra-aortic valve damage; Stage 1 – LV damage as defined by the presence of LV hypertrophy (LV mass index $\geq$ 95 g/m^2 for women, $\geq$115 g/m2 for men), elevated LV filling pressures (E/e'$\geq$14) or LV systolic dysfunction (LV ejection fraction $\leq$ 50 %); Stage 2 – Left atrial or mitral valve damage/dysfunction as defined by the presence of enlarged left atrium (LA volume index $\geq$ 34 mL/m2), the presence of atrial fibrillation, or the presence of at least moderate mitral regurgitation; Stage 3 – Pulmonary artery vasculature or tricuspid valve damage/dysfunction as defined by the presence of systolic pulmonary hypertension (systolic pulmonary arterial pressure $\geq$ 60 mmHg or the presence of at least moderate tricuspid regurgitation; Stage 4 – Right ventricle damage as defined by the presence of at least moderate dysfunction (either tricuspid annulus systolic velocity S'$\leq$9.5 cm/s, tricuspid annular plane systolic excursion $\leq$ 17 mm or stroke volume index $\leq$ 30 ml/m^2).

This single-center prospective study was designed to assess the prognostic significance of baseline characteristics in severe AS patients referred for TAVR. In particular, we focused on evaluating the additional value of MW parameters in risk stratification of these patients at baseline. Furthermore, we investigated the longitudinal changes in LV function and performance immediately following TAVR and during long term follow-up.

2. Methods

2.1. Patient selection and data collection

Between July 2020 and October 2023, all patients with symptomatic or asymptomatic severe AS referred for TAVR at Onze Lieve Vrouw Hospital in Aalst (Belgium) were screened for inclusion. Exclusion criteria comprehended patients who had previously undergone aortic valve replacement, had a mitral valve prosthesis, cardiac amyloidosis, moderate or severe mitral valve stenosis or pacemaker dependency. Patients who did not give consent or had inadequate echocardiographic image quality were also excluded. This study was conducted in accordance with the Declaration of Helsinki (1975) and was approved by the local Ethics Committee of the OLV Hospital Aalst. Informed consent was obtained from all subjects involved.

Data regarding signs and symptoms of HF, medical treatment, comorbidities, and cardiovascular risk factors were extracted from the patients' clinical records. Each patient underwent an electrocardiogram (ECG), blood pressure (BP) measurement and transthoracic echocardiographic (TTE) imaging and blood collection at the time of inclusion, one day before the intervention (baseline). The TTE examination was then repeated one day (post-TAVR) and one month (follow-up) after valve replacement. All patients were followed for a minimum of three months after TAVR.

Blood samples were analyzed to determine the plasma level of selected cardiac biomarkers including high-sensitivity troponin (Trop HS) [13], N-terminal pro-B-type natriuretic peptide (NT-proBNP) [14], and soluble suppression of tumorigenicity 2 (sST2) [15].

2.2. Echocardiographic data acquisition and measurements

A comprehensive TTE was performed using a Vivid S70 ultrasound system which was equipped with M4S transducers (GE Vingmed Ultrasound, Horten, Norway). Two-dimensional (2D), color, pulsed and continuous wave Doppler images were obtained from parasternal and apical views adhering to current recommendations. The TTE examinations were performed with patients in the left lateral decubitus position at rest [16]. The peak aortic jet velocity and the LV outflow tract (LVOT) velocity–time integral were estimated using the continuous and pulsed wave Doppler recordings from the apical 5-chamber view. The velocity–time integral measured on the pulsed-wave Doppler recordings of the LV outflow tract was used to calculate the stroke volume index (SVi). The aortic valve area (AVA) was calculated using the continuity equation, which involved the velocity time integrals of the LVOT and aortic valve (AV), and was then indexed for body surface area (BSA). The mean and peak transvalvular pressure gradients were calculated using the Bernoulli equation [17]. In the parasternal long-axis view, the end-diastolic and end-systolic volume were measured, and the LV mass was calculated and indexed for BSA. The LV ejection fraction (LVEF), the LA volume and LA volume index (LAVI) were calculated using the Simpson's biplane method in the 2- and 4-apical views and indexed for BSA. In the apical 4-chamber view, pulsed wave Doppler at the mitral valve was used to assess LV diastolic function and filling pressures, while tissue Doppler was used at the mitral annulus. The Proximal Iso-velocity Surface Area method was employed to evaluate mitral valve regurgitation. The right ventricular pressure was calculated based on the peak velocity of the tricuspid regurgitant jet. Consequently the systolic arterial pulmonary pressure (sPAP) was estimated by adding the right atrial pressure determined by the inspiratory collapse of the inferior vena cava [18]. The right ventricular function was evaluated by measuring tricuspid annular plane systolic excursion (TAPSE) using M−mode in the apical 4-chamber view [19]. *Myocardial Work calculation*

The optimized 2-, 3- and 4-chamber apical view images of the LV were digitally stored in cine-loop format at high frame rates (55–75 frame per second) for subsequent offline calculation of MW parameters using dedicated software (EchoPac, GE Vingmed Ultrasound, Horten, Norway). Semi-automated 2D speckle tracking was employed to analyze the three apical views to evaluate the global longitudinal strain (GLS) and obtain the LV bull's-eye with the segmental strain values. If necessary, the myocardium contour and region of interest width were manually adjusted by the operator according to the patient anatomy. LV systolic pressure was estimated using echocardiography by adding the mean aortic transvalvular gradient to the aortic systolic pressure obtained from cuff measurement at the time of examination [10]. The timing of aortic and mitral valve events was visually determined from the apical 3-chamber view. To construct non-invasive pressure-strain loops of the LV, strain values, echocardiography-derived LV systolic pressure and valve events were integrated. The global work index (GWI), efficiency (GWE) as well as global constructive (GCW) and wasted work (GWW) were computed using previously described methods [20].

2.3. Statistical analysis

The primary outcome of the study was a composite endpoint of all-cause mortality and HF related hospitalization. Baseline characteristics were compared between groups (Group A: patients who did not meet the study composite endpoint, Group B: patients who reached the study composite endpoint) using independent *t*-test for continuous variables. The Chi-square test was performed to analyze association of the categorical variables with the study composite endpoint. The prognostic value of these characteristics was assessed through univariate and multivariate Cox analysis. Additionally, the Receiver Operating Characteristic (ROC) method was employed to analyze MW parameters with the calculation of the Area Under the Curve (AUC) to determine the optimal cut-off value that maximizes sensitivity and specificity. Patients were subsequently categorized according to this threshold and the survival rates were calculated using the Kaplan-Meier method with the long rank (Mantel-Cox) test for intergroup difference. Significant longitudinal changes in LVEF, GLS and MW parameters were analyzed using paired samples *t*-test.

Continuous data were presented as mean ± SD while categorical

data were presented as frequencies and percentages (n, %). SPSS software version 23.0 (IBM, Armonk, New York) was used for statistical analyses. A two-sided p value < 0.05 was considered statistically significant.

The intra- and interobserver variability analysis was performed for LVEF, GLS and MW parameters. Briefly, ten patients were randomly selected for each analysis. Intra-observer variability was performed by the sonographer repeating measurements on off-line data with a time interval of at least three months. Interobserver variability was performed by repeating measurements from the same images by 2 independent expert sonographers blinded to the patient's clinical data and each other's results. Intra- and interobserver variability were calculated by intraclass coefficient (ICC) and the standard error of measurements.

3. Results

3.1. Baseline characteristics and outcome

A total of 110 patients diagnosed with severe AS who were referred for TAVR were enrolled in the study. The baseline characteristics of the patients are displayed in **Supplemental Table 1**. Over a mean follow-up period of 521 ± 343 days after procedure, the combined endpoint was reached by a total of 29 patients (26.4 %): 22 patients died (20 %), whereas 12 patients were hospitalized due to HF (11 %).

Patients in Group B, who died or were hospitalized for HF, displayed a relatively higher prevalence of AS stage 3 or 4, NYHA class 3, atrial fibrillation, and severe dyspnea compared to patients in group A, who did not meet the endpoint. Additionally, this group exhibited a higher prevalence of smoking history, severe tricuspid or mitral valve regurgitation and diuretic intake. Baseline QRS duration, Trop HS, NT-proBNP, sST2, GWI, GCW, TAPSE, E/A, LA volume, LAVI, septal e' and E/e', mean E/e' and systolic pulmonary artery pressure (sPAP) all showed statistically significant differences between the two groups. Furthermore, all these parameters, apart from sST2 and sPAP, appeared to be associated with outcome based on the univariate Cox analysis (Table 1).

3.2. Baseline myocardial work parameters as predictors of outcome

Among the MW parameters, only baseline GWI and GCW were found to be significantly different between patients groups A and B. In the ROC curve analysis both variables had an AUC of 0.657 (Fig. 1***A***). A baseline GWI of 2323 mmHg% was established as the cut-off for categorizing patients with a sensitivity of 0.63 and specificity of 0.76. Survival analysis demonstrated a significant association between a lower, GWI<2323 mmHg% and worse outcome following TAVR (Fig. 1***B***).

Based on the variables from the AS staging system developed by Généreux et al., a prognostic model was constructed to incorporate cardiac biomarkers and MW parameters for predicting outcomes following TAVR. The specific outcomes considered in the model were all-cause death or HF hospitalization. The baseline variables included were QRS length, TAPSE, LAVI, and mean E/e' (Table 2). The addition of NT-proBNP, Trop HS or sST2 to the initial model did not yield any discernible advantages. However, the model showed significant improvement when incorporating the baseline GWI cut-off value of 2323 mmHg%.

3.3. Longitudinal changes in myocardial work parameters

Serial MW measurements were compared at three time points: baseline, one day after intervention and at one month follow-up in each group (**Supplemental Table 2**). Furthermore, patients from group A and B, with negative or positive composite endpoint respectively, were compared to each other (**Supplemental Table 3**).

Whereas patients in group A demonstrated a considerable improvement in LVEF and GLS, patients in group B did not exhibit such

Table 1
Clinical parameters, ECG values, serum biomarkers' levels and TTE measurements in patients with negative *vs* positive endpoint. Univariate cox analysis of variables showing significant intergroup difference at baseline. (Group A: patients who did not meet the study composite endpoint, Group B: patients who reached the study composite endpoint).

	ALL (110)	**Group A (81)**	**Group B (29)**		**Univariate Cox Analysis**	
	Mean ± SD	*Mean ± SD*	*Mean ± SD*	*p value*	*χ2*	*p value*
General Characteristics						
Age *years*	83 ± 6	83 ± 6	82 ± 6	0.36		
BSA m^2	1.4 ± 0.2	1.4 ± 0.2	1.4 ± 0.2	0.81		
SBP *mmHg*	143 ± 25	146 ± 25	136 ± 23	0.06		
DBP *mmHg*	83 ± 89	85 ± 103	76 ± 11	0.42		
PR *ms*	176 ± 38	174 ± 36	184 ± 44	0.33		
QTc *ms*	426 ± 29	423 ± 27	433 ± 34	0.12		
QRS *ms*	106 ± 41	100 ± 23	123 ± 69	**0.01**	8.16	<0.01
Prolonged QRS *n(%)*	19 (17.3)	14 (17.3)	5 (17.2)	0.99		
Afib *n(%)*	10 (9.3)	6 (7.5)	4 (14.3)	0.31		
Cardiac Biomarkers						
Trop HS *ng/l*	36.4 ± 38.7	31.5 ± 37.2	49.8 ± 40.3	**0.04**	4.78	0.03
NT-proBNP *ng/l*	2460 ± 3875	1924 ± 3006	3931 ± 5418	**0.02**	4.58	0.03
sST2 *ng/l*	30.7 ± 14.5	28.3 ± 12.0	36.7 ± 18.4	**0.03**	3.76	0.05
Echocardiographic Parameters						
LV EDV *ml*	93 ± 42	90 ± 37	101 ± 55	0.27		
LV ESV *ml*	43 ± 30	40 ± 27	51 ± 38	0.16		
LV mass *mg*	215 ± 61	210 ± 56	231 ± 70	0.12		
LVEF *%*	51 ± 10	51 ± 10	49 ± 11	0.33		
E max *m/s*	0.9 ± 0.3	0.9 ± 0.3	1.0 ± 0.3	0.19		
A max *m/s*	1.0 ± 0.4	1.0 ± 0.3	0.9 ± 0.4	0.34		
E/A	1.1 ± 0.9	1.0 ± 0.7	1.5 ± 1.4	**0.02**	7.24	<0.01
E/e' mean	17.2 ± 7.6	16.2 ± 7.0	20.3 ± 8.5	**0.02**	5.03	0.03
LA vol *ml*	78 ± 29	73 ± 24	91 ± 36	**<0.01**	10.9	<0.01
LAVI ml/m^2	45 ± 17	43 ± 14	52 ± 20	**0.03**	7.42	<0.01
TAPSE *mm*	22 ± 5	23 ± 5	20 ± 6	**0.03**	5.37	0.02
TR Vmax *m/s*	2.8 ± 0.9	2.7 ± 0.9	2.9 ± 0.7	0.23		
TR Pmax *mmHg*	32 ± 16	30 ± 15	37 ± 18	0.07		
sPAP *mmHg*	38 ± 16	35 ± 15	44 ± 18	0.04	3.47	0.06
Aortic Valve Parameters						
LVOT *mm*	19 ± 5	20 ± 5	19 ± 4	0.53		
AVA cm^2	0.6 ± 0.3	0.6 ± 0.3	0.7 ± 0.3	0.85		
AV Vmax *m/s*	4.3 ± 0.6	4.4 ± 0.6	4.3 ± 0.7	0.45		
AV Pmean *mmHg*	50 ± 15	51 ± 16	47 ± 15	0.36		
AV Pmax *mmHg*	77 ± 22	77 ± 22	74 ± 23	0.51		
SVi ml/m^2	49 ± 17	50 ± 17	46 ± 17	0.35		
Advanced Echocardiographic parameters						
GLS *%*	−15.7 ± 5.8	−16.2 ± 6.2	−14.2 ± 4.4	0.07		
GWI *mmHg%*	2381 ± 785	2485 ± 775	2091 ± 750	**0.02**	4.78	0.03
GCW *mmHg%*	2940 ± 942	3061 ± 928	2604 ± 913	**0.03**	4.78	0.03
GWW *mmHg%*	239 ± 191	236 ± 206	247 ± 145	0.77		
GWE *%*	91 ± 6	91 ± 6	89 ± 6	0.08		

A: late diastolic peak velocity, Afib: atrial fibrillation, AV: aortic valve, AVA: aortic valve area, BSA: body surface area, DBP: diastolic blood pressure, e': early diastolic tissue velocity, E: early diastolic peak velocity, EDV: end diastolic volume, ESV: end systolic volume, GCW: global constructive work, GLS: global longitudinal strain, GWE: global work efficiency, GWI: global work index, GWW: global wasted work, LA vol: left atrium volume, LAVI: left atrium volume index, LV: left ventricle, LVEF: left ventricle ejection fraction, LVOT: left ventricle outflow tract, NT-proBNP: N-terminal pro-B-type natriuretic peptide, Pmax: peak pressure gradient, Pmean: mean pressure gradient, SBP: systolic blood pressure, SD: standard deviation, sPAP: peak systolic pulmonary artery pressure, sST2: soluble suppression of tumorigenicity 2, SVi: stroke volume index, TAPSE: tricuspid annular plane systolic excursion, TR: tricuspid valve regurgitation, Trop HS: high sensitive troponins, Vmax: peak velocity.

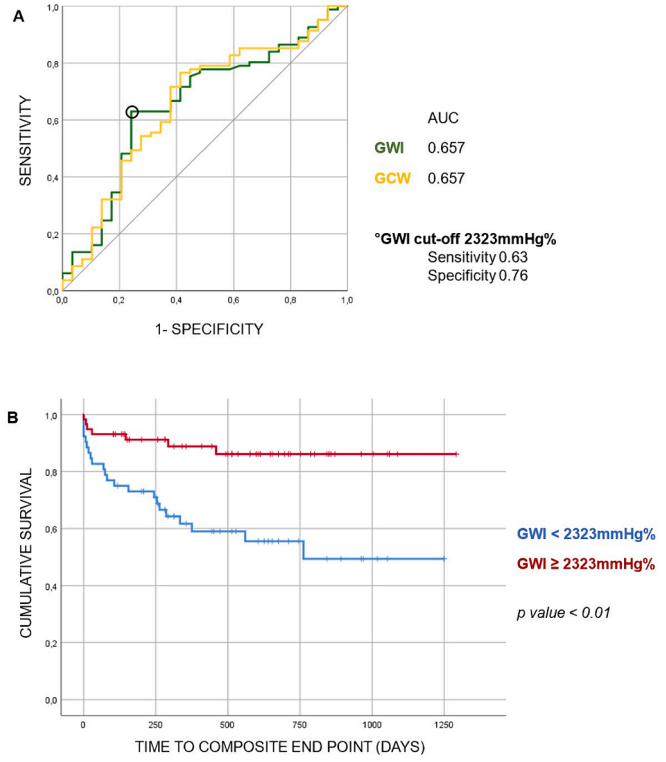

Fig. 1. *ROC curve analysis* ***(A)*** *of GWI (green) and GCW (yellow).* Kaplan-Meier plot **(B)** for survival rates analysis in patients with baseline GWI≥2323 mmHg% (red) *vs* baseline GWI<2323 mmHg% (blue).

improvement at one month follow-up.

Although both groups showed a significant decline in GWI and GCW immediately after TAVR, only patients in group A demonstrated significant change in GWI at follow-up when compared to baseline (Fig. 2). Both GWI and GCW were significantly lower at baseline and one day after intervention in group B with respect to group A. However, the differences between both groups were not statistically significant at one month follow-up.

GWW demonstrated an initial decline following the intervention in all patients, only statistically significant in group A, however no further reduction was observed in the long-term follow-up. Furthermore, a gradual enhancement in GWE was observed across all patients although this improvement did not reach statistical significance.

Finally, the intra- and interobserver variability for LVEF, GLS and MW parameters are reported in **Supplemental Table 4**.

4. Discussion

The main findings of this study can be summarized as follows. Firstly, baseline MW parameters, specifically GWI and GCW demonstrate a significant correlation with TAVR outcome. Secondly, a GWI below 2323 mmHg% at the baseline may serve as a valuable tool for identifying patients at higher risk and can provide additional predictive value for TAVR outcomes. Lastly, when compared to measures such as LVEF and GLS, MW analysis proves to be more sensitive for assessing longitudinal changes in cardiac function in patients with severe AS undergoing TAVR.

Previous studies have suggested that the LVEF is not sensitive enough to detect early left ventricular dysfunction in patients with severe AS [21,22]. More recent studies have shown that even asymptomatic patients with subtle impairment in left ventricle function may benefit from early aortic valve replacement [23]. Our study also highlights that there is no difference in baseline LVEF between patients with favorable or unfavorable outcome after TAVR, indicating that ventricles with "low-normal" LV function face a significant afterload challenge, which could be linked to a poorer prognosis. These ventricles may be more prone to decompensation with sudden changes in afterload compared to other ventricles. These findings support the idea that the concept of a "normal LVEF" in severe AS is not valid, and emphasize the need for new parameters to effectively characterize the extent of (subclinical) left ventricular dysfunction.

It is noteworthy that the variables we found to be lower at baseline in patients with unfavorable outcome, strongly coincide with the variables included in the AS staging proposed by Généreux et al [5]. This correlation is not surprising as a higher AS stage has shown to be associated with worse outcome. Additionally, we have observed significantly higher serum levels of Trop HS and NT-proBNP along with significantly lower values of GWI and GCW among patients with a less favorable outcome (group B). These findings provide evidence that, despite the similarities in standard measurements of LV systolic function, such as GLS and EF, in both cohorts, MW analysis reveals subtle differences in

Table 2
Multivariate Cox analysis of selected variables to build a predictive model for all-cause death and HF hospitalization after TAVR including MW assessment.

Basic model			**Basic model + NT-proBNP**			**Basic model + NT-proBNP+GWI<2323 mmHg%**		
	X²	***p value***		***X²***	***p value***		***X²***	***p value***
Model score	22.3	<0.01	***Model score***	22.5	<0.01	***Model score***	39.9	<0.01
Variables	***HR***		***Variables***	***HR***		***Variables***	***HR***	
QRS	1.005	0.06	QRS	1.005	0.06	QRS	1.007	0.03
TAPSE	0.937	0.08	TAPSE	0.927	0.08	TAPSE	0.978	0.42
LAVI	1.021	0.08	LAVI	1.021	0.08	LAVI	1.036	0.07
E/e' mean	1.079	<0.01	E/e' mean	1.0.86	<0.01	E/e' mean	1.081	0.04
			NT-proBNP	1.000	0.59	NT-proBNP	1.000	0.44
			vs basic model		0.58	GWI<2323 mmHg%	0.183	0.01
						vs previous model		<0.01
						vs basic model		0.02

GWI: global work index, HR: hazard ratio, LAVI: left atrium volume index, NT-proBNP: N-terminal pro-B-type natriuretic peptide, TAPSE: tricuspid annular plane systolic excursion.

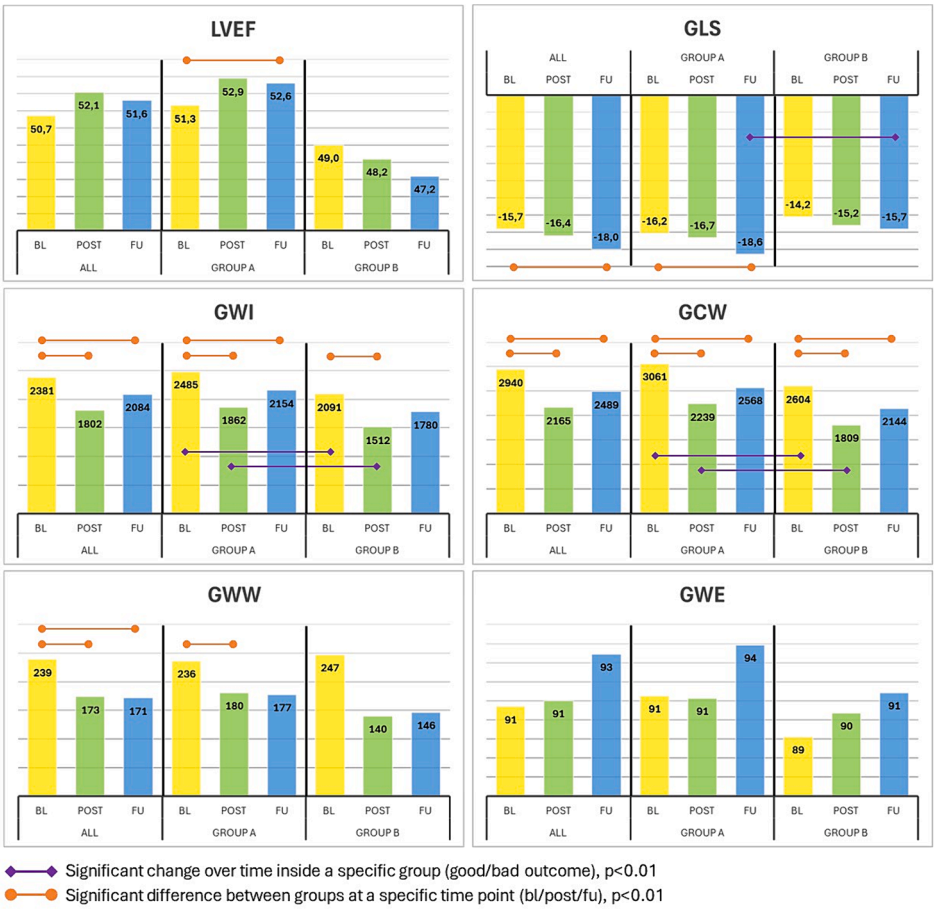

Fig. 2. Measurements of LVEF, GLS and MW parameters in the whole study population (ALL) and per study group (NEG: negative endpoint, POS: positive endpoint) at baseline (BL, yellow), one day (POST, green) and one month (FU, blue) after TAVR. (Group A: patients who did not meet the study composite endpoint, Group B: patients who reached the study composite endpoint).

LV performance otherwise unnoticed. The lower GWI and GCW baseline values indicate increased myocardial stress and impaired myocardial performance in patients with poorer outcome following TAVR. These parameters, unlike other echocardiographic measurements of LV function such as GLS or EF, are able to detect these subtle abnormalities in contractile function.

Of note patients in group B displayed a substantially longer QRS duration, which was associated with outcome, and a higher incidence of atrial fibrillation. Both characteristics could potentially impact the parameters of MW analysis [24]. However, we did not observe any significant association between QRS duration or atrial fibrillation and MW parameters. This may be attributed to the limited number of patients exhibiting these abnormalities. Consequently, further research is required to establish a potential impact of atrial fibrillation and QRS prolongation on MW analysis in AS patients.

As GWI corresponds to the translation of myocardial energy into mechanical energy, depressed values reflect impaired LV contractile function and thus compromised cardiac performance [20]. Different cutoff values for GWI have been proposed for diagnosing or predicting outcomes in multiple pathologies. In the study conducted by Wang et al [25], a GWI value below 750 mmHg% was found to be significantly associated with an increased risk of all-cause mortality and HF hospitalization in patients with reduced ejection fraction. In cardio-oncology, lower GWI at baseline was related to a higher risk for developing cancer treatment related cardiac dysfunction, irrespectively of LVEF and GLS baseline values [26]. Additionally, Guo et al [27] reported that a regional MW index below 1623.7 mmHg% could serve as a differentiating factor between ischemic and non-ischemic segments in individuals with coronary artery disease.

Although the prognostic value of MW parameters in AS patients undergoing TAVR has been studied previously [12], baseline cutoff values for risk stratification are still lacking in clinical practice. Our results suggest that a GWI of < 2323 mmHg% at baseline might be useful in identifying patients at high risk after TAVR intervention. The abnormally increased LV pressure in AS patients is an important variable in MW calculation and probably the reason for this remarkable high GWI threshold as it is combined with a whether or not decreased strain.

In the longitudinal analysis of LV function, the observed decrease in GCW along with an increase in GLS after TAVR aligns with the results reported by Jain et al [6]. However, our study, which includes a third evaluation at one month follow-up, reveals that GLS experiences a gradual recovery instead of an immediate one after TAVR whereas GCW increases after the initial decline following the intervention. The longitudinal evolution in GCW can be explained by the subsequent changes in its components. Initially, the valve replacement results in a dramatic decrease in afterload which causes a substantial reduction in GCW. Consequently, the normal LV loading condition is restored directly while the recovery of LV myocardial contractility takes longer. Subsequently, there is a gradual increase in GLS without any significant change in afterload resulting in a corresponding rise in GCW. Interestingly, all patients showed similar longitudinal changes in LV function. However, only the changes observed in patients with favorable outcome (group A) were statistically significant. This suggests that patients who are unable to sufficiently recover LV function after TAVR have a poorer prognosis and lower chances of survival in the long term. Importantly, GWI and GCW, but not LVEF and GLS, were significantly worse at baseline and

could help in the earlier detection of the patients at risk as suggested by De Rosa et al [11].

In conclusion, our results provide evidence for enhanced use of MW analysis in the initial risk stratification of patients with severe AS who are referred for TAVR. We observed that a baseline GWI<2323 mmHg% is correlated with increased rates of all-cause mortality and HF hospitalization following TAVR intervention. Moreover, longitudinal MW analysis facilitates the identification of patients who truly benefit from TAVR and further research is warranted to evaluate the impact of TAVR on LV performance through serial MW assessment.

4.1. Limitations

This study has several limitations that should be acknowledged. Firstly, MW assessment is an advanced and sophisticated technique that relies heavily on the acquisition of high-quality echocardiographic images. However, obtaining such images in daily clinical practice can be challenging. Secondly, the longitudinal analysis of the study was hampered by the loss of follow-up of patients referred from other hospitals. This limitation prevented the researchers from obtaining a complete picture of the long-term outcomes. Finally, MW is a relatively new method and there is still a lack of clear and robust reference values, specifically for patients with severe AS. This lack of standardized reference values limits the ability to interpret MW measurements in the context of severe AS. Lastly, this study was limited by its small sample size and single-center design. These factors may introduce bias and limit the generalizability of the findings. Therefore, large scale studies are warranted to validate these results and establish a more comprehensive understanding of the application of MW in severe AS as well as its prognostic value after TAVR.

CRediT authorship contribution statement

Ana Moya: Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Elayne Kelen de Oliveira:** Writing – review & editing, Validation. **Leen Derule:** Writing – review & editing, Data curation. **Monika Beles:** Writing – review & editing, Methodology, Formal analysis. **Dimitri Buytaert:** Formal analysis, Data curation. **Marc Goethals:** Visualization, Investigation. **Sofie Verstreken:** Visualization, Investigation. **Riet Dierckx:** Visualization, Investigation. **Jozef Bartunek:** Visualization, Investigation. **Ward Heggermont:** Visualization, Investigation. **Eric Wyffels:** Visualization, Investigation. **Marc Vanderheyden:** Writing – review & editing, Methodology, Visualization, Investigation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2024.101474.

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