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Impact of TAVI on Valvulo-Arterial Impedance and Systemic Arterial Distensibility in Patients with Severe Aortic Stenosis

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ABSTRACT

Background: Calcific aortic stenosis (AS) involves progressive valve narrowing and increased left ventricle (LV) afterload. Transcatheter aortic valve implantation (TAVI) offers an alternative to surgery for high-risk patients. Its effect on systemic arterial properties, including valvulo-arterial impedance (ZVa) and systemic arterial distensibility (SAD), is vital for improving outcomes.

Objective: To investigate the effects of TAVI on LV afterload, focusing on ZVa and SAD in patients with severe AS.

Patients and Methods: This analytic cross-sectional study included 50 patients with severe symptomatic aortic stenosis, who underwent TAVI. Comprehensive echocardiographic and hemodynamic assessments were performed before and six months post-TAVI at the Cardiology Department of Nasr City Hospital and Mansoura University Hospital.

Results: TAVI resulted in a significant reduction in both systolic blood pressure (SBP) ($p < 0.0001$) and diastolic blood pressure (DBP) ($p = 0.038$). Mean aortic gradient decreased markedly from 54.69 ± 15.64 to 8.45 ± 5.21 mmHg ($p < 0.0001$), while SV and stroke volume index (SVI) increased significantly (SV: 71.93 ± 10.31 to 97.19 ± 17.20 mL; SVI: 38.88 ± 5.60 to 51.66 ± 9.68 mL/m², $p < 0.0001$). Although ZVa showed a slight increase from 5.20 ± 1.04 to 5.56 ± 0.49 mmHg/mL/m² ($p < 0.0001$), SVR decreased significantly from 2.15 ± 3.32 to 1.14 ± 0.23 dyn/sec/cm ($p = 0.034$). SAD demonstrated substantial improvement, increasing from 0.66 ± 0.20 to 1.25 ± 0.31 mL/mmHg ($p < 0.0001$).

Conclusion: TAVI significantly improves systemic arterial distensibility, contributing to a more favourable hemodynamic profile in patients with severe AS.

Keywords: Aortic stenosis, TAVI, Valvulo-arterial impedance, Systemic arterial distensibility, Hemodynamics.

INTRODUCTION

Calcific degeneration of the aortic valve constitutes the most common primary valvular pathology in Western populations, with its prevalence anticipated to rise substantially in the forthcoming decades [1].

The management guidelines for aortic stenosis (AS) have evolved considerably with the advent of transcatheter aortic valve implantation (TAVI), which offers a viable alternative to the conventional gold-standard surgical replacement, particularly for individuals classified as high or intermediate surgical risks [2]. Within this framework, the discovery of biomarkers capable of enhancing patient stratification and guiding therapeutic decision-making is of paramount importance [3].

The safety and effectiveness of TAVI have been validated through the PARTNER trial and multiple registries, encompassing over 60,000 patients with symptomatic severe AS who were either at high surgical risk or deemed ineligible for surgery [4]. TAVI significantly improves clinical outcomes, enhances systolic LV performance, and optimizes aortic valve hemodynamics. Moreover, marked reductions in LV hypertrophy have been observed in patients undergoing TAVI for aortic stenosis. However, the extent of LV mass regression varies considerably between individuals following surgical aortic valve replacement (SAVR). Notably, older patients demonstrate a more limited reduction in LV mass and experience greater impairments in diastolic function compared to their younger counterparts post-replacement [5].

The long-term prognosis of patients who undergo aortic valve replacement is adversely affected by the prolonged presence of diastolic dysfunction and LV hypertrophy as a result of the procedure. The absence of a clear correlation between stenosis-dependent pressure overload relief and LV mass reduction following aortic valve replacement has prompted a further investigation of supplementary pathophysiological determinants of LV geometry and function [6].

For instance, the beneficial effects of aortic valve replacement on LV function and hypertrophy regression may be impeded by ongoing reduced systemic arterial compliance [7].

In elderly patients with calcific AS, systemic arterial compliance is often compromised due to coexisting arterial atherosclerosis and/or medial elastocalcinosis. The reduction in arterial compliance exacerbates LV afterload, further straining the heart. To assess the combined burden of both valvular and arterial loading on the LV, the valvulo-arterial impedance (Zva) metric has been employed [8].

Reductions in survival rates have been observed in the conservatively treated aortic stenosis

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population when Zva levels are significantly elevated. In many cases, patients who are candidates for TAVI have a significantly reduced systemic arterial compliance and an increased Zva, which can initially decrease following TAVI [9].

Therefore, the aim of this study was to investigate the effect of TAVI on LV after load specifically valvulo-arterial impedance and systemic arterial distensibility in patients with severe aortic stenosis.

PATIENTS AND METHODS

Study Design and Participants:

This analytic cross-sectional study was conducted at the Cardiology Department of Nasr City Hospital for Health Insurance and Hospitals of Mansoura University. It extended over 1.5 years from December 2021 to May 2023 and included 50 patients diagnosed with severe symptomatic aortic stenosis who were selected for TAVI.

Inclusion and Exclusion Criteria:

The study included patients of both sexes, aged over 18 years, with symptomatic and clinically significant aortic stenosis as per the ESC guidelines [10]. Patients were excluded if they had a Charlson comorbidity index of 5 or higher, high frailty, a life expectancy of less than 1 years, severely, active infections, or thrombi in the LV or aorta.

METHODS

Demographic data and examination:

The analysis included, patient demographics and history taking with recording of anthropometric measurements including weight, height, and BMI. Detailed clinical examination was conducted for each patient, which included general examination with recording of blood pressure parameters including DBP, SBP, MAP, and Pulse pressure. Local cardiac examination was also conducted.

Laboratory and Radiological Investigations:

Twelve lead ECG was done to all patients to assess rhythm, conduction abnormalities, and LV strain pattern (LVH criteria, Sokolow criteria) [11]. Comprehensive transthoracic echocardiographic examination was performed to all patients before and after 6 months of TAVI procedure using Vividiq Ultra Edition ultrasound system equipped with M5Sc XD clear matrix probe with simultaneous ECG signal to assess mean pressure gradient (MPG) and peak pressure gradient (PPG) across aortic valve, stroke volume, and indexed to body weight (SV=VTI x AVA).

CT Parameters

CT parameters for the evaluation of aortic valve anatomy and related structures were assessed using OsiriX MD v.9.0 software, following standardized imaging recommendations. The aortic annulus was analyzed for mean diameter, perimeter, and area **(Figure 1-I)**.

The height of the coronary ostia (LMCA and RCA) was measured from the annulus to the coronary arteries using a coronal view **(Figure 1-II)**. Aortic valve calcification was graded from 1 (no calcification) to 4 (heavily calcified) based on the extent of calcification **(Figure 1-III)**.

The presence of basal ventricular septal calcification was recorded as either 0 (no calcification) or 1 (presence of calcification) using coronal CT views **(Figure 1-IV)**. Additionally, the length of the membranous septum (MS) was defined as the distance between the aortic valve and the crest of the muscular IVS, measured in the coronal view **(Figure 1-V)**.

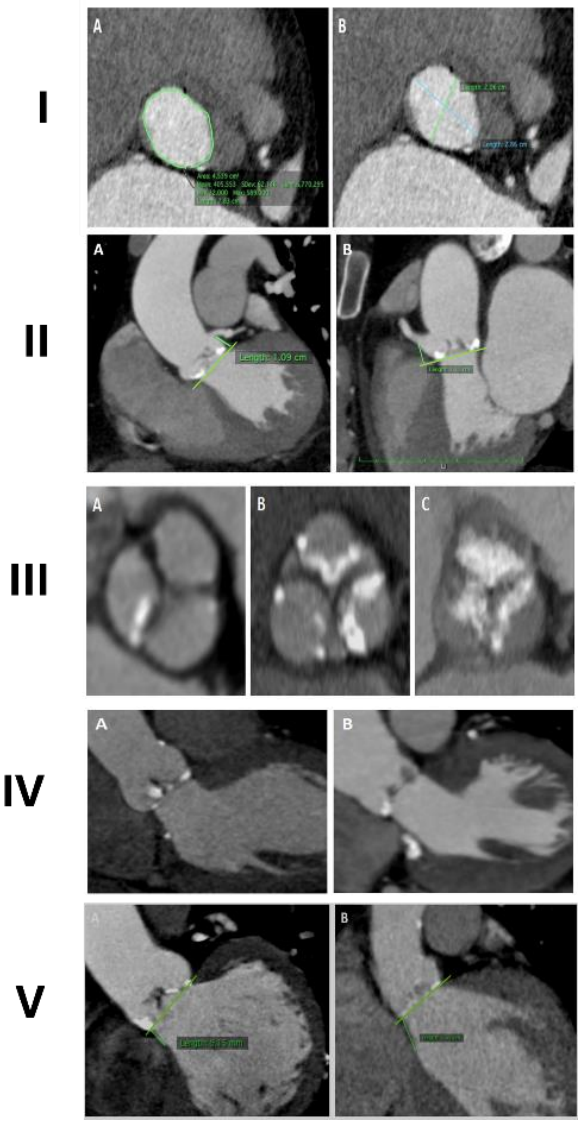

Figure 1: Different CT Parameters for the evaluation of aortic valve anatomy and related structures.

Hemodynamic assessment

Hemodynamic assessment was conducted including monitoring blood pressure to estimate the MAP using the formula MAP = DP + 1/3(SP – DP) and calculating pulse pressure as the difference between SBP and DBP. Stroke volume and stroke volume index were derived from echocardiographic data. Systemic arterial distensibility (SAD) was calculated using the formula SVI/Pulse pressure, while systemic vascular resistance (SVR) was estimated using (80 x mean BP) / cardiac output (COP). Valvuloarterial impedance (Zva) was calculated using the formula (SBP + mean aortic pressure gradient) / stroke volume index [12]. Follow-up was performed post-TAVI with measurement of the same variables at 6-months.

Ethical considerations:

The study was done after being accepted by the Research Ethics Committee, Faculty of Medicine, Mansoura University. All patients provided written informed consents prior to their enrolment. The consent form explicitly outlined their agreement to participate in the study and for the publication of data, ensuring protection of their confidentiality and privacy. This study was conducted in full compliance with the ethical principles outlined in the Declaration of Helsinki, established by the World Medical Association, for research involving human participants.

Data Management:

SPSS version 28 (IBM, Armonk, New York, USA) was utilized for data management and statistical analyses. The normality of quantitative variables was assessed using the Shapiro-Wilk test, supplemented by visual inspection methods. Quantitative data were expressed as means with standard deviations and ranges. Categorical variables were summarized as frequencies and percentages. The Mann-Whitney U test was employed to compare non-normally distributed quantitative variables, while the independent t-test was used to compare normally-distributed quantitative variables. Statistical significance was defined as a P-value less than 0.05, and all statistical tests were conducted as two-sided.

RESULTS

The demographic and baseline characteristics of the included cases (n = 50) show a balanced distribution of gender. The mean age was 77.29 ± 3.79 years. The calculated mean BMI was 29.27 ± 4.45kg/m². Blood pressure measurements showed that mean SBP was 144.6 ± 16.7 mmHg, while mean DBP was 81.8 ± 11.2 mmHg (**Table 1)**.

Table 1: Distribution of the included cases according to demographic data and their baseline characteristics (n = 50)

Sample characteristics	No.	%
Gender		
Male	21	42
Female	29	58
Age (year)		
Min.– Max.	66.0–83.0	
Mean ±SD.	77.29±3.79	
Weight (kg)		
Min.– Max.	60–110	
Mean ±SD.	81.22±12.94	
Height (cm)		
Min.– Max.	145.0–188.0	
Mean ±SD.	162.94±9.35	
BMI (kg/m²)		
Min.– Max.	21.7 – 40.0	
Mean ±SD.	29.27± 4.45	
BSA (m²)		
Min.– Max.	1.51 – 2.26	
Mean ±SD.	1.86 ± 0.17	
Systolic blood pressure (mmHg)		
Min.– Max.	120 – 180	
Mean ±SD.	144.6 ± 16.7	
Diastolic blood pressure (mmHg)		
Min.– Max.	60 – 110	
Mean ±SD.	81.8 ± 11.2	

BMI, body mass index; BSA, body surface area.

Both SBP and DBP decreased significantly postoperatively. The mean and peak aortic gradients also showed marked reductions. SV and SVI improved significantly. Although there was a slight increase in ZVa, SVR decreased significantly. SAD showed a substantial improvement **(Table 2)**.

Table 2: Various parameters before the procedure and at 6-months postoperatively

Parameters	Pre-operative, mean ± SD	6-month post-op, mean ± SD	p-value
SBP (mmHg)	144.6 ± 16.7	124 ± 10.1	**P< 0.0001***
DBP (mmHg)	81.8 ± 11.2	78.6 ± 7.83	**P= 0.038***
Mean aortic gradient (mmHg)	54.69 ± 15.64	8.45 ± 5.21	**p< 0.0001***
Peak aortic gradient (mmHg)	89.38 ± 22.78	16.08 ± 7.75	**p< 0.0001***
SV (mL)	71.93 ± 10.31	97.19 ± 17.20	**p< 0.0001***
SVI (mL/m^2)	38.88 ± 5.60	51.66 ± 9.68	**p< 0.0001***
ZVa (mmHg/ mL/m^2)	5.20 ± 1.04	5.56 ± 0.49	**p< 0.0001***
SVR (dyn/sec/cm)	2.15 ± 3.32	1.14 ± 0.23	**p= 0.034***
Systemic arteria distensibility (SAD) (mL/mmHg)	0.66 ± 0.20	1.25 ± 0.31	**p< 0.0001***

SBP: systolic blood pressure; DBP: Diastolic blood pressure; SV: stroke volume; SVI: stroke volume index; ZVa: valvulo-arterial impedance; SVR: systemic vascular resistance; SAD; systemic arterial distensibility. *: Statistically significant.

The Pearson correlation analysis showed no significant relationships between the preoperative LV mass index and any of the examined variables **(Table 3)**.

Table 3: Pearson correlation coefficient between preoperative LV mass index and other variables

Parameters	Pre-operative LV mass index	
	Pearson Correlation	Sig. (2-tailed)
Age	-0.42	0.770
Weight	-0.227	0.113
Height	-0.162	0.260
BMI	-0.251	0.80
BSA	0.151	0.294
SBP at 6 months postoperative	-0.014	0.925
DBP at 6 months postoperative	0.143	0.321
Mean aortic gradient at 6 months post – op	0.022	0.902
Peak aortic gradient at 6 months post – op	0.110	0.529
SV at 6 months postoperative	0.168	0.335
SVI at 6 months postoperative	0.278	0.106
ZVa at 6 months postoperative	-0.281	0.102
SVR at 6 months postoperative	-0.229	0.185
SAD at 6 months postoperative	0.282	0.100

BMI, body mass index; BSA, body surface area, DBP: Diastolic blood pressure; SBP: systolic blood pressure; SV: stroke volume; SVI: stroke volume index; ZVa: valvulo-arterial impedance; SVR: systemic vascular resistance; SAD; systemic arterial distensibility.

DISCUSSION

In individuals with AS, LV afterload is influenced by both the severity of valvular obstruction and the condition of the systemic arterial system. As observed within our study cohort, patients with AS frequently present with coexisting comorbidities such as hypertension, hyperlipidemia, diabetes, and atherosclerosis, all of which suggest potential modifications in the structural and functional properties of the systemic vasculature [13]. These factors contribute to a decline in arterial elasticity and/or an escalation in arteriolar resistance. As a result, the left ventricle in these individuals must contend with a dual burden: the valvular load associated with AS and the arterial load driven by diminished SAC and/or increased SVR [14]. In fact, extensive research has demonstrated that calcific AS should not be viewed in isolation as a mere valvular disorder but must instead be considered within the broader context of arterial hemodynamics [15]. This study aims to clarify how TAVI influences Zva and systemic arterial distensibility, with post-procedural changes that may affect LV function and patient outcomes.

TAVI has a significant impact on arterial hemodynamics and blood pressure response in patients with aortic stenosis. In patients with AS, the LV is subjected to heightened afterload due to the combined effects of systemic hypertension, valvular obstruction, and increased stiffness of the aortic wall [16].

The current study found that both SBP and DBP decreased significantly 6 months postoperatively. This can be attributed to several physiological changes. TAVI improves the function of the aortic valve by relieving the stenosis, thereby reducing the LVOT obstruction. This leads to a decrease in the pressure required to eject blood from the left ventricle, contributing to a lower SBP. The reduction in SBP can also be related to the improved hemodynamics and decreased left ventricular afterload, as the aortic valve gradient diminishes significantly after valve replacement, allowing for more efficient cardiac output. DBP improvement mechanism may involve improved arterial compliance following the procedure [17].

Similarly, **Giannini *et al.*** reported significant reduction in aortic diastolic pressure (from 62.4 ± 11.7 to 55.2 ± 13.8, p=0.0001) after TAVI [18]. Additionally, **Nemes *et al.*** reported reductions in both SBP and DBP at 3 weeks and 6 months after AVR compared to baseline [19]. In contrast to our findings, **Katsanos *et al.*** reported an increase in both SBP and DBP following TAVI. This increase could also reflect a compensatory response (recovery phenomena) to improved cardiac output following relief of AS especially that their monitoring was only one month post-op [8], whereas our findings may indicate a more pronounced reduction in systemic afterload 6 months post-procedure.

According to the present study, the mean and peak aortic gradients also showed marked reductions.

Additionally, SV and SVI improved significantly with a markable increase. LV is partially discharged following TAVI, and the short-term therapeutic efficacy is frequently evaluated by normalizing the mean pressure gradient and stroke volume index [8].

Similarly, **Giannini *et al.*** addressed enhancement of hemodynamic performance after TAVI. They reported after TAVI, immediate reductions in the transaortic peak pressure gradient (from 88.7 ± 24.2 to 15.7 ± 7.5, P < .0001) and mean pressure gradient (from 56.4 ± 16.8 to 8.5 ± 4.5, P < .0001) **[18]**. In line with our results, **Nemes *et al.*** reported that post-AVR, a significant and sustained decrease was found in peak and mean aortic gradients (from 90.5 ± 24.3 and 53.3 ±12.9 at baseline, to 15.0 ± 4.5 and 8.4 ± 2.4 at 6 months post AVR, respectively) **[19]**.

However, a more comprehensive evaluation of therapeutic success can be achieved by considering the reduction in valvular-arterial impedance, which incorporates markers of both valvular and arterial load, representing the global LV load. Reduction in ZVa has been associated with improved long-term therapeutic outcomes and LV remodeling in AS **[20]**. In our study, although there was a slight increase in ZVa, SVR decreased significantly and there was marked improvement in systemic arterial distensibility (SAD), reflecting a more compliant vascular system post-procedure. This suggests that, despite the minor increase in ZVa, the decreased SVR and enhanced SAD may contribute to an overall reduction in the workload on the heart, improving hemodynamic conditions in patients with severe AS.

Katsanos *et al.* conducted a thorough evaluation of the prognostic significance of Zva, systemic arterial compliance, and SVR following TAVI. Their findings revealed a significant reduction in Zva post-procedure, declining from 5.40 ± 1.52 mmHg/mL/m² at baseline to 4.13 ± 1.17 at one month and 4.35 ± 1.38 at one year (p < 0.001). In contrast, systemic arterial compliance demonstrated minimal variation, shifting from 0.57 ± 0.27 mL/m²/mmHg initially to 0.57 ± 0.28 at one month and 0.53 ± 0.27 at one year (p = 0.408). Additionally, SVR exhibited a notable decrease, dropping from 2194 ± 689 dyn/sec/cm^{-5} at baseline to 1971 ± 899 at one month and 1937 ± 822 at one year (p = 0.001) **[8]**.

Giannini *et al.* reported analogous findings in a cohort of 102 patients who underwent TAVI, observing marked reductions in Zva during the early postoperative phase. Additionally, their analysis demonstrated a temporary but significant enhancement in systemic arterial compliance, increasing from 0.69 ± 0.34 to 0.81 ± 0.43, accompanied by a decrease in systemic vascular resistance, which declined from 2.14 ± 0.89 to 1.83 ± 0.71 **[18]**.

Furthermore, **Vizzardi *et al.*** evaluated aortic distensibility post-TAVI in patients with severe AS. The study reported a significant enhancement in both peak and mean aortic valve gradients (p < 0.001 for both). Additionally, aortic distensibility showed progressive improvement (p = 0.032 within the first 6 months, p = 0.005 during the subsequent 6 months, and p = 0.003 from baseline to 12 months), while arterial stiffness exhibited a corresponding decline (p = 0.034, 0.090, and 0.001, respectively). These findings demonstrated that the elastic properties of the aorta undergo notable improvement at both 6 and 12 months post-TAVI, contributing to enhanced ventriculo-arterial coupling and improved left ventricular function **[2]**.

Nevertheless, this investigation is subject to certain limitations. Initially, the generalizability of the findings may be restricted by the sample size of 50 patients, which could conceivably impact the ability to detect subtle effects of TAVI on hemodynamic parameters. Additionally, the study's cross-sectional design only allows for observations at baseline and a single follow-up point six months post-TAVI, preventing analysis of long-term outcomes and potential late changes in valvulo-arterial impedance and systemic arterial distensibility.

CONCLUSIONS

TAVI significantly reduces systemic blood pressure and improves systemic arterial distensibility, contributing to a more favourable hemodynamic profile in patients with severe AS. Despite a slight increase in ZVa, the overall decrease in SVR and improvement in SAD suggest a beneficial impact on LV afterload.

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