Indian Heart Journal 72 (2020) 421–426

Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Original Article

Aortic pulse wave velocity and its relationship with transaortic flow and gradients in patients with severe aortic stenosis undergoing aortic valve replacement

Shraddha Ranjan [a], Hardeep Kaur Grewal [a], Ravi R. Kasliwal [a], Naresh Trehan [b], Manish Bansal [a, *]

[a] Department of Cardiology, Medanta-The Medicity, Gurgaon, India
[b] Department of Cardiothoracic Surgery, Medanta-The Medicity, Gurgaon, India

ARTICLE INFO

Article history:
Received 5 May 2020
Accepted 21 June 2020
Available online 27 June 2020

Keywords:
Low-flow aortic stenosis
Low-gradient aortic stenosis
Paradoxical low-flow low-gradient aortic stenosis
Arterial stiffness
Valvulo-arterial impedance

ABSTRACT

Background: Low-flow, low-gradient severe aortic stenosis (LFLGAS) is a common clinical entity and is associated with poor prognosis. Increased left ventricular (LV) afterload is one of the mechanisms contributing to low LV stroke volume index (SVi) in these patients. Aortic stiffness is an important determinant of LV afterload, but no previous study has evaluated its relationship with LVSVi in patients with AS.

Methods: Fifty-seven patients (mean age 66 ± 8 years, 71.9% men) with severe AS [aortic valve area (AVA) < 1.0 cm^2] undergoing aortic valve replacement (AVR) were included in this study. Echocardiographic parameters of AS were correlated with carotid-femoral pulse wave velocity (cfPWV), a measure of aortic stiffness, derived using PeriScope® device.

Results: Mean AVA was 0.63 ± 0.17 cm^2 with mean and peak transvalvular gradient 56.5 ± 18.8 mmHg and 83.2 ± 25.2 mmHg, respectively. Nearly half (26 of 57, 45.6%) of the subjects had SVi <35 mL/m^2, indicative of low-flow severe AS. These subjects had lower AVA, lower aortic valve gradient, and LV ejection fraction. CfPWV was numerically lower in these subjects [median 1467 (interquartile range 978, 2259) vs 1588 (1106, 2167)] but the difference was not statistically significant ($p = 0.66$). However, when analyzed as a continuous variable, cfPWV had significant positive correlation with SVi (Pearson's r 0.268, $p = 0.048$) and mean aortic valve gradient (Pearson's r 0.274, $p = 0.043$).

Conclusions: In patients with severe AS undergoing AVR, aortic stiffness measured using cfPWV is not a determinant of low-flow state. Instead, an increasing cfPWV tends to be associated with increasing transvalvular flow and gradient in these patients.

1. Introduction

Conventionally, aortic stenosis (AS) is considered severe if the aortic valve area (AVA) is < 1.0 cm^2 and the aortic valve mean pressure gradient (MPG) ≥40 mmHg.[1–3] However, it is now well-known that nearly one-third of the patients with AVA <1.0 cm^2 have MPG <40 mmHg.[4,5] This is termed as low-gradient severe AS (LGAS). In many of these cases, esp. if AVA is < 0.8 cm^2, the inappropriately low gradient is due to reduced transvalvular flow, an entity known as low-flow, low-gradient, severe AS (LFLGAS). Several studies have demonstrated that LFLGAS is associated with poor prognosis, which can be improved by timely surgical or transcatheter aortic valve replacement (AVR).[6–14] This has led to considerable interest in understanding pathophysiology and natural history of LFLGAS.

Several different mechanisms have been proposed to explain reduced transvalvular flow in patients with LFLGAS.[4] Impaired left ventricular (LV) ejection fraction (EF) is an obvious cause, but low-flow situation can occur even with preserved LVEF. Small size LV cavity, subclinical LV systolic dysfunction and increased LV afterload have been suggested to cause this paradoxical reduction in LV stroke volume.[4] Indeed, acute lowering of systemic blood pressure (BP) has been shown to increase transvalvular flow and gradients,

* Corresponding author.
E-mail address: manishaiims@hotmail.com (M. Bansal).

https://doi.org/10.1016/j.ihj.2020.06.010

supporting the role of increased afterload in producing low-flow situation.[15–17]

To quantify the impact of increased afterload on AS hemodynamics, valvulo-arterial impedance (ZVa) has been proposed as a simple and clinically useful parameter.[4,18] It is calculated by dividing the sum of systolic BP and MPG by LV stroke volume index (SVi). Previous studies have shown that the patients with elevated ZVa have greater likelihood of LFLGAS and have poorer prognosis.[18,19] However, despite these evidences, ZVa is not sufficient to explain the role of LV afterload in causing LFLGAS. The relationship between LFLGAS and elevated ZVa may merely reflect the fact that both MPG and SVi are included in the calculation of ZVa. This may also explain its association with poor prognosis. Therefore, a more direct assessment of systemic arterial stiffness- an important determinant of LV afterload- and its impact on SVi and AS gradients is required to better understand the pathophysiology of LFLGAS. Unfortunately, very limited data is available about arterial stiffness in AS and no previous study has evaluated its relationship with LVSVi.[20–22] The present study was therefore sought to study the effect of arterial stiffness on LVSVi and aortic valve gradients in patients with severe AS.

2. Methods

2.1. Study population

This was a prospective study conducted at a tertiary care hospital in North India. All consecutive patients undergoing AVR for severe AS who met the following inclusion criteria were included in this study- 1) AVA < 1.0 cm^2, 2) no other valve lesion of more than mild severity, 3) and age > 50 years. The patients with previous cardiac surgical or interventional procedure and those with lower limb arterial occlusive disease were excluded from the study. Occlusive lower limb arterial disease was defined based on symptoms of lower limb claudication, documented > 50% stenotic lesion(s) in lower limb arteries or history of previous lower limb vascular procedure.

Relevant clinical details including height, weight, heart rate, BP, etc. were recorded. All subjects underwent a complete transthoracic echocardiographic examination and assessment of systemic arterial stiffness. A written informed consent was obtained from all the patients prior to their enrollment in the study. The study was approved by the institutional review board and the local independent ethics committee.

2.2. Transthoracic echocardiography

The echocardiographic examination was performed using a commercially available ultrasound system (Vivid E9, GE Vingmed Ultrasound AS, Horten, Norway), using a 2.5–4.0 MHz transducer. The scanning was performed by a single experienced operator, with the patients in the left lateral position.

Standard echocardiographic measurements were obtained following the recommendations of the American Society of Echocardiography.[3,23,24] LV end-diastolic volume, end-systolic volume, and EF were calculated from the apical four- and two-chamber views using the Simpson's biplane method. Tissue Doppler imaging was used for measuring early diastolic mitral annular velocity (e'); average of the septal and lateral e' was used for analysis.

Aortic valve gradient was recorded from the acoustic window that provided the highest velocity and gradient. AVA was derived using the continuity equation. For this, LV stroke volume was first calculated as the product of LV outflow area (obtained from the parasternal long-axis view) and the LV outflow velocity-time integral (obtained from the apical five-chamber view). Dividing LV stroke volume by aortic valve velocity-time integral yielded AVA. As was the study design, all the subjects had AVA <1.0 cm^2, which is the threshold for defining severe AS. The patients who had MPG <40 mmHg were considered to be having LGAS. The flow-status was assessed using SVi (stroke volume indexed to body-surface area); a value of <35 mL/m^2 was defined as 'low flow'.[3] Stroke volume was also divided by the ejection time to calculate transaortic flow rate.

The ZVa was calculated using the following equation-

$$ZVa = (\text{aortic valve MPG} + \text{systolic BP})/\text{LVSVi}$$

A value of > 4.5 $mmHg/ml/m^2$ generally indicates high valvulo-aortic impedance.[4]

Speckle-tracking echocardiography was used for estimating LV global longitudinal strain (GLS). For this, the standard gray-scale images obtained from the apical two-, three- and four-chamber views were used and analyzed offline on a dedicated workstation (EchoPAC PC, version 12.0.0, GE Medical). Once all the three images are analyzed, the software automatically calculates GLS which is the average of the peak systolic longitudinal strain of all the 18 LV myocardial segments (six segments in each view). GLS is denoted with a 'minus sign' and a more negative value indicates better GLS. The normal value of GLS is in the range of -18-20% or more negative.[25] The image analysis was performed by the same operator who had performed echocardiography and was blinded to arterial stiffness data.

2.3. Arterial stiffness assessment

The assessment of arterial stiffness was performed using the PeriScope® device (Genesis Medical Systems Pvt Ltd, Hyderabad, India) which has been shown to have high degree of reproducibility and accuracy for this purpose.[26,27] This device is based on oscillometric method and records ECG-gated pressure waveforms from both arms and ankles simultaneously. From these pressure waveforms, the in-built software automatically calculates pulse wave velocity (PWV) for different vascular segments. Of these, the carotid-femoral PWV (cfPWV) is the most validated measure of aortic stiffness and the same was used in this study as well. Although the value of cfPWV varies according to age, gender, and ethnicity, a value of >10–12 m/s generally indicates increased aortic stiffness.[28,29]

The test was performed immediately after echocardiographic examination. After 10 min of supine rest, four BP cuffs, connected to the PeriScope® device, were tied around both arms and ankles. ECG electrodes were also applied on wrists and ankles. The machine then automatically inflated and deflated all the cuffs simultaneously, while recording pressure waveforms from all the four sites. From these pressure waveforms, cfPWV was automatically calculated and used for the analysis.

2.4. Statistical analysis

Standard statistical tools such as mean ± standard deviation, median with interquartile range (IQR), and counts with proportions were used for describing various characteristics of the study population. Comparisons between the patient groups based on mean gradient and SVi were made using Chi-square test for categorical variables and independent-samples *t*-test or Mann–Whitney *U* test for continuous variables. Correlations among different parameters were assessed using Pearson's correlation coefficient. Two-sided *p*-value < 0.05 was considered statistically significant. All the analyses were performed using SPSS version 20.0.

3. Results

A total of 57 subjects were included in this study. Mean age of the subjects was 66 ± 8 years and 41 (71.9%) were men. Average heart rate was 76 ± 15 beats/min and the BP was 137 ± 18 mmHg systolic and 77 ± 10 mmHg diastolic. Coronary artery disease was present in 17 subjects (29.8%).

3.1. Echocardiographic findings and arterial stiffness measurements in the study population

Table 1 describes echocardiographic findings in the entire study population. Mean AVA was 0.63 ± 0.17 cm^2 with mean and peak transvalvular gradients 56.5 ± 18.8 mmHg and 83.2 ± 25.2 mmHg, respectively. Average LVEF was in the normal range but GLS was reduced (−13.5 ± 4.0%). ZVa and cfPWV were elevated (Table 1).

3.2. High-versus low-gradient AS

In our study, 11 subjects (19.3%) had LGAS (Table 2). There was no difference in age, BP, LVEF, AVA, SVi and transaortic flow rate between the subjects with low or high aortic valve MPG. However, the proportion of the subjects with low SVi (<35 mL/m^2) was much higher in the group with LGAS (72.7% vs 39.1%, *p* value 0.044). ZVa and cfPWV were not different between the two groups, although cfPWV was numerically higher in the subjects with high gradient (Table 2).

3.3. Low-flow versus normal-flow AS

Nearly half (26 of 57, 45.6%) of all the subjects had SVi <35 mL/m^2, indicative of low-flow severe AS (Table 3). These subjects were more likely to be women and had faster heart rates, as compared to those with normal SVi. They also had lower AVA, aortic valve MPG, transaortic flow rate and LVEF. However, GLS was not different between the two groups. ZVa was significantly elevated in the subjects with low SVi. In contrast, cfPWV was numerically higher in patients with normal SVi, though the difference was not statistically significant (Table 3).

3.4. Correlation among echocardiographic parameters and PWV

SVi and AVA had significant positive correlation with each other and significant negative correlation with ZVa and GLS. SVi also showed modest positive correlation with cfPWV (Table 4, Fig. 1). The MPG had significant positive correlation with SVi and cfPWV but did not correlate with AVA, ZVa or GLS.

Table 1
Echocardiographic and arterial stiffness parameters in the study population.

Parameter	Values
Aortic valve pressure gradient	
Mean, mmHg	56.5 ± 18.8
Peak, mmHg	83.2 ± 25.2
Aortic valve area, cm^2	0.63 ± 0.17
Stroke volume index, mL/m^2	37.8 ± 11.0
Transaortic flow rate, mL/sec	232.1 ± 68.6
Left ventricular end-diatsolic volume, mL	77.3 ± 21.2
Left ventricular ejection fraction, %	55.3 ± 14.1
Early diastolic mitral annular velocity, cm/sec	6.0 ± 2.0
ZVa, mmHg/mL/m^2	5.6 ± 1.9
Global longitudinal strain, %	−13.5 ± 4.0
Carotid-femoral pulse wave velocity, cm/sec	1566 (1053, 2232)

All values are presented as mean ± standard deviation, except carotid-femoral pulse wave velocity which is presented as median with interquartile range.
ZVa-valvulo-arterial impedance.

4. Discussion

The present study shows that in patients undergoing AVR for severe AS, 'low-flow' state is common and is associated with lower aortic valve gradient, AVA and LVEF. Although the GLS and cfPWV did not show any significant difference when the patients were categorized based on the flow status, SVi had a negative correlation with GLS and a positive correlation with cfPWV. The cfPWV also had a positive correlation with aortic valve MPG.

4.1. Hemodynamic subsets of severe AS

Conventionally, AS is considered severe if the AVA is < 1.0 cm^2 and the aortic valve MPG ≥40 mmHg.[1-3] However, it is now well-known that nearly one-third of the patients with AVA <1.0 cm^2 have MPG <40 mmHg, which is known as LGAS.[4,5] Since many of these patients are generally not advised intervention, the prevalence of LGAS among those undergoing AVR is likely to be much lower. In our study, we found that almost 20% subjects had LGAS, which is thus consistent with the current evidence.

Reduced LVSVi is one of the important mechanisms underlying low gradients in LGAS. Indeed, low SVi is reported in nearly half of all patients with severe AS, some of whom present with high gradients whereas the remaining have LGAS.[4,14] Consistent with this, in our study too, we found 45% prevalence of low SVi. The low SVi in severe AS may either be due to reduced LVEF or may occur even with preserved LVEF, an entity known as paradoxical LFLGAS. Studies have shown that regardless of the mechanism, LFLGAS is associated with adverse prognosis, which is often worse than that of classical normal flow, high-gradient severe AS.[6,10,12,14] The outcome of LFLGAS patients can be improved significantly by timely intervention and therefore, recognition of this entity is crucial.[7–9,11,14]

4.2. Mechanisms of reduced LV stroke volume in paradoxical LFLGAS

Small LV cavity size is an important cause of reduced SVi[30] and therefore, paradoxical LFLGAS occurs commonly in elderly women with hypertrophied, small-size left ventricles.[2,4] Subclinical LV systolic dysfunction manifesting as reduced GLS is another proposed mechanism for reduced SVi in these patients.[31–33] In our study, we also found that reduced SVi was more common in women and that a negative correlation existed between GLS and LVSVi.

Increased LV afterload is yet another important mechanism underlying reduced SVi and valve gradients in AS.[15,34–36] Uncontrolled hypertension with raised systolic BP is known to cause underestimation of aortic valve gradients by reducing SVi.[15] Acute reduction of systolic BP with sodium nitroprusside increases SVi and MPG.[16,17] For this reason, it is recommended that in patients with LFLGAS with uncontrolled hypertension, echocardiographic assessment of AS severity should be reperformed after normalization of BP.[2,3]

Several different parameters have been used to quantify LV afterload in patients with severe AS.[18,20–22,34,37] The most commonly used among these are ZVa, effective arterial elastance and total arterial compliance. It has been demonstrated that the patients with low-flow, severe AS have increased ZVa and effective arterial elastance whereas total arterial compliance is reduced.[16,18] Furthermore, it has also been shown that elevated ZVa is associated with a higher risk of adverse events, including higher overall morality.[18] In our study, we also found a strong negative correlation between ZVa and LVSVi. However, it is noteworthy that SVi is included in the calculation of all the three parameters mentioned above, which may partly explain their relationship with SVi.

Table 2
Clinical, echocardiographic and arterial stiffness parameters in the study groups based on mean aortic valve gradient.

Parameter	Mean gradient <40 mmHg ($n = 11$)	Mean gradient ≥40 mmHg ($n = 46$)	p value
Age, years	69.3 ± 11.1	65.2 ± 6.9	0.13
Male gender, n (%)	10 (90.9)	31 (67.4%)	0.12
Heart rate, beats/min	73 ± 10	77 ± 14	0.44
Blood pressure			
Systolic, mmHg	139 ± 23	137 ± 17	0.68
Diastolic, mmHg	74 ± 10	77 ± 10	0.27
Aortic valve pressure gradient			
Mean, mmHg	33.3 ± 4.3	62.1 ± 16.5	<0.001
Peak, mmHg	53.5 ± 8.7	90.3 ± 22.4	<0.001
Aortic valve area, cm^2	0.67 ± 0.17	0.62 ± 0.17	0.37
SVi, mL/m^2	33.0 ± 7.4	39.0 ± 11.4	0.10
Subjects with reduced SVi[a], n (%)	8 (72.7%)	18 (39.1%)	0.044
Transaortic flow rate, mL/sec	202.6 ± 37.1	239.1 ± 72.8	0.13
Left ventricular end-diatsolic volume, mL	72.4 ± 21.0	78.6 ± 21.3	0.39
Left ventricular ejection fraction, %	53.1 ± 16.4	55.9 ± 13.6	0.56
Early diastolic mitral annular velocity, cm/sec	5.7 ± 1.4	6.1 ± 2.1	0.54
ZVa, $mmHg/mL/m^2$	5.4 ± 1.2	5.6 ± 2.0	0.79
Subjects with high ZVa[b], n (%)	8 (72.7%)	30 (65.2%)	0.64
Global longitudinal strain, %	−14.2 ± 4.1	−13.3 ± 4.0	0.51
Carotid-femoral pulse wave velocity, cm/sec	1033 (919, 2075)	1612 (1146, 2256)	0.10

All values are presented as mean ± standard deviation or actual numbers with percentages, except carotid-femoral pulse wave velocity which is presented as median with interquartile range.
SVi-stroke volume index; ZVa-valvulo-arterial impedance.
[a] Reduced SVi defined as SVi < 35 mL/m^2.
[b] High ZVa defined as ZVa ≥ 4.5 $mmHg/mL/m.^2$.

Aortic PWV is a well-established measure of systemic arterial stiffness, which is an important determinant of LV afterload. Non-invasively estimated cfPWV is the most validated and clinically the most used measure of systemic arterial stiffness.[28,29] It increases with ageing and is also elevated in patients with hypertension, chronic kidney disease, atherosclerotic vascular disease, etc. CfPWV has strong prognostic value and is therefore recommended as a potential tool for risk stratification, esp. in patients with hypertension.[28,29]

A few previous studies have evaluated aortic PWV in relation to AS. Bruschi et al reported elevated cfPWV in patients with AS undergoing AVR (surgical or transcatheter).[22] The cfPWV increased with increasing aortic valve MPG. In another study using invasive measurement of aortic stiffness, aorto-femoral PWV strongly correlated with MPG and the extent of aortic valve calcification.[20] However, in these studies, PWV was used as a marker of atherosclerosis and not as a measure of systemic afterload. Since degenerative AS shares its pathogenesis with atherosclerosis, the relationship between elevated PWV and higher aortic valve MPG was thought to reflect a more advanced atherosclerotic process and a more severe AS. These studies unfortunately overlooked the fact that low MPG might not necessarily reflect less severe AS. Since neither SVi nor AVA were reported in these studies, the true relationship between aortic PWV and AS severity could not be determined.

In our study, we have for the first time, evaluated the impact of increased aortic PWV on LVSVi and aortic valve gradients in severe AS. Although we had hypothesized that a higher PWV, by

Table 3
Clinical, echocardiographic and arterial stiffness parameters in the study groups based on left ventricular stroke volume index.

Parameter	Stroke volume index <35 mL/m^2 ($n = 26$)	Stroke volume index ≥35 mL/m^2 ($n = 31$)	p value
Age, years	65.1 ± 7.1	66.7 ± 8.6	0.43
Male gender, n (%)	15 (57.7)	26 (83.9%)	0.028
Heart rate, beats/min	82 ± 16	71 ± 11	0.003
Blood pressure			
Systolic, mmHg	142 ± 20	134 ± 16	0.10
Diastolic, mmHg	78 ± 11	76 ± 9	0.36
Aortic valve pressure gradient			
Mean, mmHg	49.3 ± 14.6	62.6 ± 19.9	0.006
Peak, mmHg	73.3 ± 19.3	91.5 ± 26.7	0.006
Mean gradient <40 mmHg, n (%)	8 (30.8)	3 (9.7%)	0.044
Aortic valve area, cm^2	0.52 ± 0.13	0.71 ± 0.16	<0.001
Stroke volume index, mL/m^2	28.3 ± 4.7	45.8 ± 7.9	<0.001
Transaortic flow rate, mL/sec	181.2 ± 32.5	275.7 ± 61.0	<0.001
Left ventricular end-diatsolic volume, mL	74.1 ± 17.6	80.3 ± 24.0	0.29
Left ventricular ejection fraction, %	50.5 ± 16	59.9 ± 10.5	0.013
Early diastolic mitral annular velocity, cm/sec	6.0 ± 2.6	6.0 ± 1.4	0.98
ZVa, $mmHg/mL/m^2$	7.0 ± 1.9	4.4 ± 0.6	<0.001
Subjects with high ZVa[a], n (%)	26 (100)	12 (38.7)	<0.001
Global longitudinal strain, %	−12.7 ± 4.6	−14.2 ± 3.3	0.16
Carotid-femoral pulse wave velocity, cm/sec	1467 (978, 2259)	1588 (1106, 2167)	0.66

All values are presented as mean ± standard deviation or actual numbers with percentages, except carotid-femoral pulse wave velocity which is presented as median with interquartile range.
ZVa-valvulo-arterial impedance.
[a] High ZVa defined as ZVa ≥ 4.5 $mmHg/mL/m.^2$.

Table 4
Correlation among various clinical, echocardiographic and arterial stiffness measurements.

Parameter		Systolic BP	Stroke volume index	Aortic valve MPG	Aortic valve area	Zva	GLS	cfPWV
Systolic BP	R	1	−0.139	**−0.271**	−0.016	**−0.39**	−0.144	0.122
	p value	–	0.304	**0.041**	0.904	**0.003**	0.285	0.374
Stroke volume index	R	−0.139	1	**0.453**	**0.636**	**−0.819**	**−0.277**	**0.268**
	p value	0.304	–	**<0.001**	**<0.001**	**<0.001**	**0.037**	**0.048**
Aortic valve MPG	R	**−0.271**	**0.453**	1	−0.190	−0.116	0.140	**0.274**
	p value	**0.041**	**<0.001**	–	0.158	0.391	0.299	**0.043**
Aortic valve area	R	−0.016	**0.636**	−0.190	1	**−0.689**	**−0.351**	0.114
	p value	0.904	**<0.001**	0.158	–	**<0.001**	**0.008**	0.41
ZVa	R	**−0.39**	**−0.819**	−0.116	**−0.689**	1	**0.304**	0.002
	p value	**0.003**	**<0.001**	0.391	**<0.001**	–	**0.022**	0.99
GLS	R	−0.144	**−0.277**	0.140	**−0.351**	**0.304**	1	0.036
	p value	0.285	**0.037**	0.299	**0.008**	**0.022**	–	0.80
cfPWV	R	0.122	**0.268**	**0.274**	0.114	0.002	0.036	1
	p value	0.374	**0.048**	**0.043**	0.41	0.99	0.80	–

BP-blood pressure, cfPWV-carotid-femoral pulse wave velocity; GLS-global longitudinal strain; MPG-mean pressure gradient; r-Pearson correlation coeffcieint; ZVa-valvulo-arterial impedance. All correlations with P-values <0.05 are highlighted in bold.

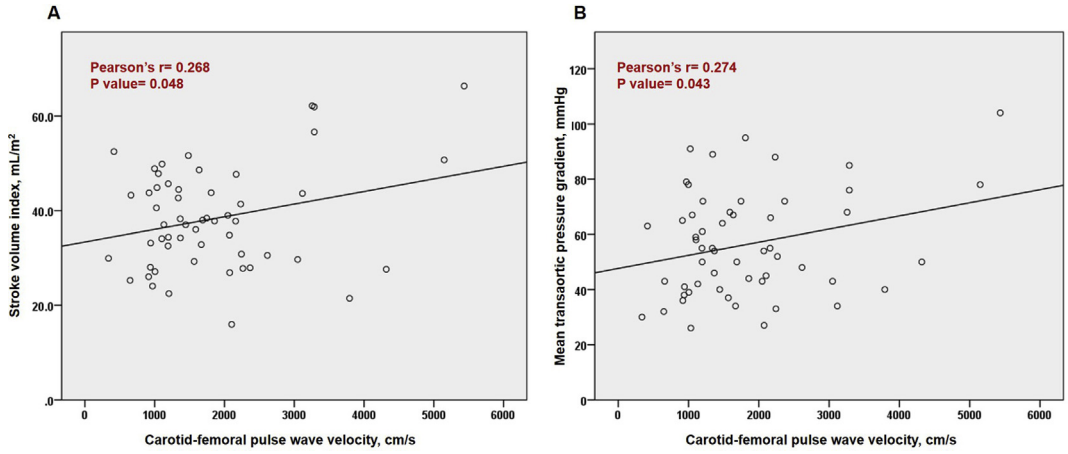

Fig. 1. Scatter plot showing correlation between carotid-femoral pulse wave velocity and left ventricular stroke volume index (A) and aortic valve mean gradient (B).

increasing LV afterload, would be associated with a lower SVi and lower MPG, our findings were opposite of this. We found that cfPWV was increased in patients with higher SVi and MPG. These findings, though in line with the previous studies, argue against the role of cfPWV as a measure of LV afterload, at least in patients with severe AS. It appears that aortic PWV is primarily a measure of the pulsatile component of the arterial afterload and not that of the resistive (pressure) component. In that scenario, our findings would suggest that a higher SVi might be responsible for driving a faster conduction of the arterial pulse wave along the vascular tree, instead of the reverse being true (i.e. a higher PWV resulting in increased afterload and impeding LV ejection). The correlation between cfPWV and MPG as seen in our study as well as the earlier studies cited above can also be explained by the same mechanism as MPG is directly dependent on SVi. However, at the same time, the contribution of atherosclerosis in this relationship can also not be excluded and warrants further evaluation in larger studies. Nonetheless, for the time-being, it seems clears that the aortic PWV increases with transaortic flow/gradient, regardless of the underlying mechanistic explanations.

4.3. Strengths and limitations

As discussed above, severe AS is a very heterogenous entity. To minimize this heterogeneity, we included only the subjects with clearly defined severe AS (i.e. AVA 1.0 cm^2) who were undergoing AVR. Similarly, aortic PWV is also affected by several different factors, with age being the most important determinant. Age also significantly influences the etiology of AS and AS hemodynamics. Non-calcific severe AS is common in young individuals whereas calcification is ubiquitous in elderly patients, regardless of AS etiology. To overcome these issues, we included only those subjects who were above 50 years of age. As a result, the mean age of our subjects was 66 years and almost all had calcific severe AS. Additionally, no correlation was observed between age and cfPWV in our study which suggested that the effect of age on cfPWV was indeed nullified.

Despite these strengths, our study had several limitations that merit attention. Although our sample size was larger than the previous studies on this subject, it was still inadequate to robustly assess the relationship between PWV and various determinants of AS hemodynamics. Second, as we had included only those patients who were undergoing AVR, it is likely that we missed many patients with LGAS who were not considered eligible for intervention. This is reflected in the fact that only 19% of our subjects had MPG <40 mmHg. However, it is important to note that the prevalence of 'low-flow' was high in our study population and was consistent with the existing literature.[4,14] Third, the information about ongoing background therapy, which could have influenced arterial stiffness, was not available. We acknowledge this limitation but would like to emphasize that our goal was to evaluate the instantaneous relationship between peripheral arterial stiffness and LV

stroke volume and transaortic gradients. It is therefore less likely that the ongoing background medical therapy would have significantly altered the interpretation of the study findings. Finally, due to logistic reasons, we could not study the relationship between echocardiographic parameters and cfPWV after the valve surgery. As a result, we could not determine whether low SVi did indeed contribute to lower cfPWV in our patients.

5. Conclusions

The present study shows that in patients with severe AS undergoing aortic valve replacement, aortic stiffness as measured using cfPWV is not a determinant of low-flow state. Instead, an increasing cfPWV tends to be associated with increasing transvalvular flow and gradient in these subjects.

Grants and funding

None.

Declaration of competing interest

All authors have none to declare.

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