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Original article

Pulse Wave Velocity of Arterial Doppler /Longitudinal Strain as a Novel Marker for Ventricular-Arterial Coupling in Hypertensive Patients

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Abstract

Background: Hypertension is a leading risk factor for cardiovascular diseases, primarily due to its adverse effects on ventricular-arterial (VA) coupling and subsequent target organ damage (TOD). This study investigates the utility of carotid-femoral pulse wave velocity (PWV) and global longitudinal strain (GLS) as novel markers for VA coupling in hypertensive patients. **Methods:** In a single-center observational analytical case-control study, 200 participants, comprising 150 hypertensive patients and 50 non-hypertensive healthy controls, were enrolled. Comprehensive assessments, including echocardiography, pulse wave velocity, and myocardial performance estimation were conducted. Comparing the PWV/GLS ratio to the conventional Ea/Ees ratio, the novel index of VA coupling was evaluated. **Results**: Hypertensive patients showed significant alterations in VA coupling parameters compared to controls. The PWV was notably higher in patients (11.1 ± 1.2 vs. 7.7 ± 0.8, $p < 0.001$), as was the Ea/Ees ratio (0.6 ± 0.1 vs. 0.48 ± 0.12, $p < 0.001$). Significant variations were observed in the PWV/GLS ratio among the groups (-0.66 ± 0.09 vs. -0.39 ± 0.04, $p < 0.001$), indicating altered VA coupling. ROC analysis demonstrated the superior predictive value of PWV/GLS for TOD, with AUCs significantly higher than those of Ea/Ees across various markers of TOD (IMT, diastolic dysfunction, LV mass index, and GLS). Multivariate logistic regression adjusted for confounders confirmed PWV/GLS as a significant predictor of TOD ($p < 0.001$). **Conclusion:** The PWV/GLS ratio emerges as a novel and superior marker for assessing ventricular-arterial coupling and predicting target organ damage in hypertensive patients, compared to the traditional Ea/Ees ratio.

Keywords: Pulse Wave Velocity; Arterial Doppler; Longitudinal Strain; Ventricular-Arterial Coupling; Hypertensive Patient.

Introduction

Ventricular-arterial coupling (VAC) pertains to the dynamic correlation between the heart and the systemic vasculature. The interaction between these two factors is crucial for the optimal functioning of the cardiovascular system. The body's capacity to modulate systemic blood pressure (BP), regulate cardiac output, and respond suitably to variations in preload, afterload, and heart rate is contingent upon the characteristics of the heart and the vasculature into which blood is ejected by the left ventricle (1).

Hypertension is linked to the rigidification of major arteries and the left ventricle. A transient reduction in the volume of blood ejected from the LV can occur due to elevated arterial pressure that opposes this process. To counterbalance that reduction, an autoregulation mechanism activated, and the LV pump function is elevated to a more energy level (the Frank-Starling mechanism). Consequently, an increase in LV stiffness results from the heart's response to increased afterload (2, 3).

Echocardiographic evaluation of the arterial elastance (EA) to the left ventricular elastance (EES) ratio is extensively employed as an indicator of ventricular-arterial coupling. This ratio is valuable as it offers insights into the mechanical efficiency and performance of the ventricular-arterial system. Nevertheless, it is critical to acknowledge that pressure-volume analyses have certain constraints, and the term "ventricular-arterial coupling" incorporates a multitude of physiological facets, a considerable number of which are not accounted for in the pressure-volume plane (4).

In hypertensive individuals, arterial stiffness may increase alongside LV myocardial stiffness, potentially leaving a relatively unchanged EA/EES ratio. Notwithstanding this, an elevated systolic blood pressure may be correlated with a specific increase in stroke volume (SV) among these patients, particularly subsequent to physical exertion (5).

In recent decades, there has been a notable emergence of more dependable indicators of ventricular and arterial performance among individuals with hypertension. Carotid-femoral pulse wave velocity (PWV) is specifically associated with cardiovascular events in this population category and is regarded as the optimal and most reliable measure of aortic stiffness. likewise, there has been extensive studies on global longitudinal strain (GLS) in hypertension patients, suggesting that it could serve as an a preliminary indicator of subclinical LV contractile dysfunction in this population (6-8).

Therefore, the current research aimed to evaluate the value of carotid-femoral pulse wave velocity/global longitudinal

strain as a marker for arterial-ventricular interaction in predicting target organ damage in hypertensive patients, compared to arterial elastance/left ventricular elastance ratio, which is a standard marker of arterial-ventricular interaction.

Patients and methods

Study Design:

The study, an analytical case-control investigation with an observational approach, was conducted at the Cardiology Department of Benha University Hospital, taking place from January 2021 to June 2023, and was confined to a single center. The study involved 200 participants divided into two groups: hypertensive patients (150 individuals) and non-hypertensive healthy subjects (50 individuals).

The study was conducted following the approval from the Faculty of Medicine's Research Ethics Committee at Benha University (MS 18-3-2021). Informed written consent was obtained from the patients.

Inclusion Criteria: Hypertensive patients were diagnosed based on repeated SBP values ≥140 mmHg, diastolic BP values ≥90 mmHg, or a history of antihypertensive medications. Additionally, participants needed to be above 18 years old.

Exclusion Criteria: Participants with diabetes, ischemic heart disease, significant valvular heart disease, conduction abnormalities (such as left bundle branch block and arrhythmias like atrial fibrillation), poor echogenic window, chronic pulmonary disease, or renal dysfunction were excluded from the study.

Methods:

Complete demographic data, including age, gender, and cardiovascular risk factors, were collected. Physical examination focused on systolic and diastolic blood pressure and heart rate. Resting 12-lead ECG was performed to assess rhythm and the presence of left ventricular hypertrophy. Echocardiographic assessments were performed using a Philips Epic 7C system equipped with a 5S probe and a 5.5 transducer, alongside a concurrent ECG signal. Patients underwent examination in the left lateral decubitus posture. All echocardiography data were acquired and stored for offline analysis. Quantification of left ventricular volumes (end-systolic, end-diastolic, and stroke volume), as well as LVEF, was conducted utilizing Simpson's method of discs.

LV mass was determined using Devereux "cube" formula (0.8 x (1.04 x [(LVEDD + IVSD + PWD)3 – (LVEDD)3]) + 0.6) (9). By multiplying the systolic arterial pressure to volume curve by 0.9 × SBP/SV, the arterial elastance (Ea) was determined (1). This formula was employed due to the linear correlation observed between SV and end-systolic arterial pressure, under the

assumption that zero SV corresponds to zero arterial pressure (10).

The calculation of systolic arterial pressure was performed by multiplying the brachial systolic pressure by 0.9. Stroke volume (SV) was assessed using echocardiography, focusing on measurements of the diameter of the LV outflow tract and the velocity time integral. The ratio representing arterial-ventricular coupling, known as Ea/Ees, was obtained from the ratio of the LV end-systolic volume to SV. Ea was determined by dividing the end-systolic pressure (ESP) by SV, and Ees was calculated as ESP divided by the end-systolic volume (ESV) (11).

Given that ESP represents the end-systolic pressure, SV signifies the stroke volume, and ESV denotes the end-systolic volume, the formula for EA/EES can be articulated as (ESP/SV)/(ESP/ESV). Simplifying by removing ESP from the equation results in EA/EES equating to ESV/SV (12).

At the tips of the mitral valve, the sample volume for the pulsed wave Doppler was positioned to ascertain the E/A ratio. An E/A ratio of 0.8 or less is deemed abnormal (13).

Tissue Doppler imaging (TDI) was utilized to measure myocardial velocities, positioning the sample volume at the mitral annulus's medial and lateral points in the apical four-chamber view, aimed at assessing the early diastolic velocity, E'. Values of E' velocity at or below 9 cm/sec were deemed to be abnormal (14).

The determination of left ventricular GLS involved the manual delineation and adjustment of the endocardial border in the apical 4, 2, and 3 chamber views during the end stages of systole. Patients who could not provide satisfactory quality for more than two segments were excluded from the study. Automatic analysis was performed on longitudinal strain curves, and the average peak strain value from all three views was measured (15).

Carotid intima-media thickness Carotid:

Carotid IMT was assessed using ultrasound imaging of the carotid artery. Scans were conducted while patients were lying down with their necks slightly extended. The IMT was assessed at six locations within both carotid arteries: near the common carotid artery, at the carotid bulb, and beyond the carotid bifurcation in the internal carotid artery, with three readings averaged for each location. The average IMT across all six areas was calculated for each individual to establish the average IMT value. An IMT measurement above 0.9 mm was classified as abnormal (16).

Aortic stiffness and arterial ventricular coupling:

Simultaneous assessment of carotid and femoral waveforms is beyond reach, yet individual normalization with the electrocardiogram (ECG) is achievable

through gating techniques. Utilizing an ECG-synchronized Philips L12-3 broadband linear array transducer, the assessment commenced with positioning the patient horizontally and pinpointing the carotid artery just above the collarbone (1-2 cm before it branches) via B-mode. Subsequent to this, Doppler flow waveforms were aligned with the ECG readings. A similar approach was employed for the common femoral artery located in the groin region. We conducted three separate captures for each artery, with every capture documenting two to three beats. Digital calipers were used to calculate the transit time (TT) by measuring the duration from the onset of the QRS complex's R wave to the beginning of the waveform. We recorded the heart rate three times and averaged these measurements. The speed was deduced from the length spanned between the carotid and femoral artery points (17).

The AV coupling index, which was recently proposed, was calculated using the PWV/GLS ratio, which is the ratio of arterial rigidity (as measured by PWV) to myocardial performance (as estimated by GLS). Subsequently, this index was compared to the widely employed Ea/Ees ratio, a calculation facilitated by echocardiography, as previously stated.

Statistical analysis

Data analysis and management were executed using IBM's SPSS software, version 28, located in Armonk, New York, USA. The distribution of the quantitative data was assessed through the Kolmogorov-Smirnov test, the Shapiro-Wilk test, and visual inspection methods. Depending on the results of these evaluations, quantitative results were presented as mean values and standard deviations, reflecting their distribution's normalcy. Categorical variables were depicted using counts and percentages. The analysis compared quantitative variables across different groups using the independent t-test, while categorical variables were analyzed through the Chi-square test or Fisher's exact test, as appropriate. Receiver Operating Characteristic (ROC) analysis was conducted for Ea/Ees and PWV/GLS to assess their predictive power for target organ damage, including calculation of the area under the curve (AUC) along with 95% confidence intervals, optimal threshold values, and diagnostic effectiveness. Both univariate and multivariate logistic regression analyses were performed for Ea/Ees and PWV/GLS to determine their ability to predict target organ damage, with odds ratios and 95% confidence intervals being reported. Statistical significance was determined by two-sided tests, with a P-value threshold of less than 0.05 indicating significant results.

Results

General & clinical characteristics

Electrocardiogram (ECG) findings showed a significant difference between the studied groups ($P < 0.001$), with

normal sinus rhythm (NSR) present in 73.3% of patients compared to 100% of controls and left ventricular hypertrophy (LVH) observed in 26.7% of patients but absent in controls. Furthermore, systolic, diastolic, and mean arterial pressures were significantly higher in patients, with mean values of 153 ± 6 mmHg, 95 ± 3 mmHg, and 114 ± 3 mmHg, respectively, compared to 121 ± 8 mmHg, 74 ± 7 mmHg, and 90 ± 7 mmHg in controls (P < 0.001 for all). In contrast, variables such as age (P = 0.222), sex (P = 0.505), smoking status (P = 0.354), and body surface area (BSA) (P = 0.571) did not show statistically significant differences between the two groups.

Table 1.

The average IMT was notably higher in patients (1.06 ± 0.1) compared to controls (0.55 ± 0.1), with a highly significant p-value of <0.001. Similarly, ESV and EDV were significantly greater in patients (39.5 ± 7.9 and 105.1 ± 13.7, respectively) than in controls (31.2 ± 5.6 and 96.3 ± 8.1, respectively), both with p-values of <0.001. EF, E/A ratio, septal e', and lateral e' velocities also differed significantly between the groups, with patients showing lower EF and E/A and reduced septal and lateral e' velocities, all with p-values of <0.001.

Table 1.

Additionally, the study found a significant prevalence of diastolic dysfunction in patients compared to controls, with 44.7% of patients in Grade I and 30.7% in Grade II, whereas all controls were normal (P < 0.001). Other significant differences included the Left Atrium (LA) volume index and LV mass index, which were higher in patients (33.4 ± 2.1 and 110.5 ± 8.7, respectively) compared to controls (27.7 ± 2.7 and 70 ± 8.3, respectively), both with p-values of <0.001. GLS was also significantly different, being lower in patients (-17 ± 1) compared to controls (-20 ± 1), with a p-value of <0.001. In contrast, SV did not show a significant difference between patients and controls (P = 0.62).

Table 1.

PWV was considerably higher in patients (11.1 ± 1.2) compared to controls (7.7 ± 0.8), with a p-value of <0.001. Additionally, Ea was also significantly greater in patients (2.12 ± 0.28) than in controls (1.66 ± 0.27), with a p-value of <0.001.

Table 1.

The ratio of Ea/Ees showed a significant difference between the groups. Patients exhibited a higher Ea/Ees ratio (0.6 ± 0.1) compared to controls (0.48 ± 0.12), with a p-value of <0.001. Moreover, the ratio of Pulse Wave Velocity to Global Longitudinal Strain (PWV/GLS) was significantly different between patients and controls (-0.66 ± 0.09 vs. -0.39 ± 0.04, respectively), with a p-value of <0.001.

Table 1.

Ea/Ees according to target organ damage

Patients with TOD in the form of increased Intima-Media Thickness (IMT) exhibited a lower Ea/Ees ratio (0.59 ± 0.1) compared to those without this condition (0.71 ± 0.05), with a p-value of <0.001. For diastolic dysfunction (DD) as a form of TOD, the Ea/Ees ratio was significantly lower in affected patients (0.58 ± 0.1) compared to those without DD (0.68 ± 0.08), with a p-value of <0.001. Similarly, those with increased Left Atrial Volume Index (LAVi) as TOD had a lower Ea/Ees ratio (0.56 ± 0.12) than those without (0.64 ± 0.08), with a p-value of <0.001. **Table 2.**

Furthermore, patients with an elevated Left Ventricular (LV) mass index as a form of TOD also had a lower Ea/Ees ratio (0.59 ± 0.1) compared to those without increased LV mass (0.7 ± 0.1), with a p-value of <0.001. Lastly, the presence of TOD in the form of altered Global Longitudinal Strain (GLS) was associated with a lower Ea/Ees ratio (0.6 ± 0.1) compared to those without GLS changes (0.71 ± 0.03), with a p-value of <0.001. **Table 2.**

Patients with TOD in the form of increased Intima-Media Thickness (IMT) had a notably different PWV/GLS ratio (-0.68 ± 0.08) compared to those without this form of TOD (-0.5 ± 0.06), with a p-value of <0.001. **Table 2.**

Similarly, for DD as a form of TOD, the PWV/GLS ratio was significantly altered in affected patients (-0.69 ± 0.07) compared to those without DD (-0.58 ± 0.09), with a p-value of <0.001. For patients with increased Left Atrial Volume Index (LAVi) as TOD, the PWV/GLS ratio was -0.68 ± 0.07, compared to -0.65 ± 0.1 in those without LAVi, with a p-value of 0.034. **Table 2.**

In cases with elevated LV mass index as TOD, the PWV/GLS ratio was considerably lower in affected patients (-0.69 ± 0.07) compared to those without increased LV mass (-0.52 ± 0.05), with a p-value of <0.001. Lastly, the presence of TOD in the form of altered GLS was associated with a different PWV/GLS ratio (-0.67 ± 0.08 for TOD present vs. -0.48 ± 0.04 for TOD absent), with a p-value of <0.001. **Table 2**

ROC analyses for Ea/Ees and PWV/GLS ratios to predict target organ damage

ROC analyses were done for Ea/Ees and PWV/GLS to predict target organ damage based on IMT. For Ea/Ees, the AUC was 0.855, with a 95% CI ranging from 0.757 – 0.952 (P < 0.001). The optimal cutoff value was determined to be ≤0.69, yielding a sensitivity of 89.3%, specificity of 70%, NPV of 31.8%, PPV of 97.7%. **Figure 1-A**. For PWV/GLS, the AUC was higher (0.957), with a 95% CI ranging from 0.911 – 1.0 (P < 0.001). The best cutoff point was > 0.61, at which sensitivity, specificity, PPV, and NPV were 77.1%, 100%, 100%, and 23.8%, respectively. **Figure 1-B.**

ROC analyses were done for Ea/Ees and PWV/GLS to predict target organ damage based on diastolic dysfunction. For Ea/Ees, the AUC was 0.817, with a 95% CI ranging from 0.736 – 0.898 (P < 0.001). The best cutoff was ≤ 0.61, at which specificity, sensitivity, PPV, and NPV were 94.6%, 63.7%, 97.3%, and 46.1%, respectively. **Figure 1-C**. For PWV/GLS, the AUC was higher (0.891), with a 95% CI ranging from 0.815 – 0.968 (P < 0.001). The best cutoff point was > 0.63, at which sensitivity, specificity, PPV, and NPV were 85%, 94.6%, 98%, and 67.3%, respectively. **Figure 1-D.**

ROC analyses were performed on Ea/Ees and PWV/GLS ratios to assess their ability to forecast target organ damage, utilizing LAVi as a benchmark. In the case of Ea/Ees, the AUC recorded was 0.693, with the 95% CI extending from 0.604 to 0.782, demonstrating significant results (P < 0.001). The optimal threshold identified was ≤ 0.59, at which the measures of sensitivity, specificity, PPV, and NPV were 63.9%, 78.2%, 73%, and 70.1%, in that order **Figure 1-E**. Regarding the PWV/GLS ratio, it exhibited a somewhat lower AUC of 0.594, with a 95% CI between 0.501 and 0.687 (P = 0.047), suggesting moderate predictive accuracy. The most effective cutoff value was determined to be > 0.63, at which the sensitivity reached 83.3%, specificity stood at 51.3%, PPV at 61.2%, and NPV at 76.9% **Figure 1-F.**

ROC evaluations were performed on the Ea/Ees and PWV/GLS ratios for their ability to anticipate target organ damage, with the LV mass index as the criterion. For Ea/Ees, the AUC reached 0.856, and the 95% CI was calculated to be between 0.734 and 0.978, indicating significant predictability (P < 0.001). The optimal threshold identified was ≤ 0.7, resulting in a sensitivity of 96.9%, specificity of 75%, PPV of 96.2%, and NPV of 78.9% **Figure 1-G**. For the PWV/GLS ratio, the AUC exhibited a superior value of 0.979, with its 95% CI stretching from 0.959 to 0.999, showcasing strong statistical significance (P <0.001). The most effective cutoff value determined was > 0.58, yielding a sensitivity of 96.2%, a specificity of 100%, a PPV of 100%, and NPV of 80% (Table 9, Figure 12-B) **Figure 1-H.**

ROC analyses were done for Ea/Ees and PWV/GLS to predict target organ damage based on GLS. For Ea/Ees, the AUC was 0.872, with a 95% CI ranging from 0.797 – 0.948 (P = 0.011). The best cutoff was ≤ 0.66, at which sensitivity, specificity, PPV, and NPV were 74%, 100%, 100%, and 9.5%, respectively. **Figure 1-I**. For PWV/GLS, the AUC was higher (0.971), with a 95% CI ranging from 0.940 – 1.0 (P = 0.001). The best cutoff point was > 0.53, at which sensitivity, specificity, PPV, and NPV were 92.5%, 100%, 100%, and 26.7%, respectively (Table 10, Figure 13-B). **Figure 1-J.**

Prediction of target organ damage

Univariate and multivariate regression analyses were conducted for the Ea/Ees and PWV/GLS ratios to evaluate their predictive accuracy for target organ damage. In the univariate analysis, both ratios were identified as significant indicators. Specifically, for intima-media thickness greater than 0.9, Ea/Ees showed an OR of 0.71 with a 95% CI between 0.572 and 0.882 (P = 0.002), while PWV/GLS exhibited an OR of 2.035 with a 95% CI from 1.403 to 2.955 (P < 0.001). For diastolic dysfunction, Ea/Ees had an OR of 0.761 with a 95% CI of 0.673 to 0.859 (P < 0.001), and PWV/GLS had an OR of 1.514 with a 95% CI of 1.308 to 1.754 (P < 0.001). In predicting left atrial volume index greater than 34, Ea/Ees presented an OR of 0.864 with a 95% CI of 0.804 to 0.929 (P < 0.001), and PWV/GLS showed an OR of 1.083 with a 95% CI of 1.004 to 1.167 (P = 0.039). Lastly, for left ventricular mass greater than 100, Ea/Ees had an OR of 0.705 with a 95% CI of 0.593 to 0.837 (P < 0.001), and PWV/GLS revealed an OR of 2.658 with a 95% CI of 1.736 to 4.071 (P < 0.001).

Table 3.

Multivariate analysis, adjusted for age, gender, smoking, BSA, and mean arterial pressure revealed that only PWV/GLS was a significant predictor for TOD based on IMT > 0.9 (OR = 1.997, 95% CI = 1.215 - 3.285, P = 0.006), diastolic dysfunction (OR = 1.394, 95% CI = 1.145 – 1.697, P <0.001), and LV mass index > 100 (OR = 3.754, 95% CI = 1.442 - 9.77, P = 0.007)

Table 3.

Table 1: General and clinical characteristics between the studied groups

		Patients (n = 150)	**Controls (n = 50)**	**P-value**
Age (years)	Mean ±SD	50 ±9	52 ±7	0.222
Sex				
Males	n (%)	92 (61.3)	28 (56)	0.505
Females	n (%)	58 (38.7)	22 (44)	
smoking	n (%)	59 (39.3)	16 (32)	0.354
Body surface area	Mean ±SD	1.9 ±0.15	1.89 ±0.17	0.571

ECG				
NSR	n (%)	110 (73.3)	50 (100)	**<0.001***
LVH	n (%)	40 (26.7)	0 (0)	
Systolic blood pressure	Mean ±SD	153 ±6	121 ±8	**<0.001***
Diastolic blood pressure	Mean ±SD	95 ±3	74 ±7	**<0.001***
Mean arterial pressure	Mean ±SD	114 ±3	90 ±7	**<0.001***
Average IMT	Mean ±SD	1.06 ±0.1	0.55 ±0.1	**<0.001***
ESV	Mean ±SD	39.5 ±7.9	31.2 ±5.6	**<0.001***
EDV	Mean ±SD	105.1 ±13.7	96.3 ±8.1	**<0.001***
SV	Mean ±SD	65.6 ±7.9	65 ±6.8	0.62
EF	Mean ±SD	62.4 ±4.2	67.2 ±4.9	**<0.001***
E/A	Mean ±SD	1 ±0.3	1.43 ±0.3	**<0.001***
Septal e	Mean ±SD	6.7 ±1.2	8.6 ±1.4	**<0.001***
lat e	Mean ±SD	9.4 ±1.3	11.6 ±1.1	**<0.001***
Diastolic dysfunction				
Normal	n (%)	37 (24.7)	50 (100)	**<0.001***
G I	n (%)	67 (44.7)	0 (0)	
G II	n (%)	46 (30.7)	0 (0)	
LA volume index	Mean ±SD	33.4 ±2.1	27.7 ±2.7	**<0.001***
LV mass index	Mean ±SD	110.5 ±8.7	70 ±8.3	**<0.001***
GLS	Mean ±SD	-17 ±1	-20 ±1	**<0.001***
PWV	Mean ±SD	11.1 ±1.2	7.7 ±0.8	**<0.001***
Ea	Mean ±SD	2.12 ±0.28	1.66 ±0.27	**<0.001***
Ea/Ees	Mean ±SD	0.6 ±0.1	0.48 ±0.12	**<0.001***
PWV/GLS	Mean ±SD	-0.66 ±0.09	-0.39 ±0.04	**<0.001***

*Significant at P < 0.05; SD: Standard Deviation NSR: Normal sinus rhythm; LVH: left ventricular hypertrophy; IMT: Intima-Media Thickness; SD: Standard Deviation; ESV: End-Systolic Volume; EDV: End-Diastolic Volume; SV: Stroke Volume; EF: Ejection Fraction; E/A: Ratio of Early to Late Ventricular Filling Velocities; Septal e: Septal E' Velocity; lat e: Lateral E' Velocity; G I: Grade I Diastolic Dysfunction; G II: Grade II Diastolic Dysfunction; LA: Left Atrium; LV: Left Ventricular; GLS: Global Longitudinal Strain; PWV: Pulse Wave Velocity; Ea: Effective Arterial Elastance; Ees: End-Systolic Elastance; PWV/GLS: Ratio of Pulse Wave Velocity to Global Longitudinal Strain.

Table 2: Ea/Ees and PWV/GLS according to target organ damage in hypertensive patients

	Ea/Ees		**PWV/GLS**	
TOD	**Mean ±SD**	**P-value**	**Mean ±SD**	**P-value**
IMT > 0.9				
Yes	0.59 ±0.1	**<0.001***	-0.68 ±0.08	**<0.001***
No	0.71 ±0.05		-0.5 ±0.06	
Diastolic dysfunction				
Yes	0.58 ±0.1	**<0.001***	-0.69 ±0.07	**<0.001***
No	0.68 ±0.08		-0.58 ±0.09	
LAVi > 34				
Yes	0.56 ±0.12	**<0.001***	-0.68 ±0.07	**0.034***
No	0.64 ±0.08		-0.65 ±0.1	
LV mass index > 100				
Yes	0.59 ±0.1	**<0.001***	-0.69 ±0.07	**<0.001***

No	0.7 ±0.1		-0.52 ±0.05	
GLS < -18				
Yes	0.6 ±0.1	**<0.001***	-0.67 ±0.08	**<0.001***
No	0.71 ±0.03		-0.48 ±0.04	

*Significant at P < 0.05; TOD: Target Organ Damage; IMT: Intima-Media Thickness; SD: Standard Deviation; PWV/GLS: Ratio of Pulse Wave Velocity to Global Longitudinal Strain; LAVi: Left Atrial Volume Index; LV: Left Ventricular; GLS: Global Longitudinal Strain.

Table 3: Univariate and multivariate analyses for Ea/Ees and PWV/GLS to predict target organ damage

	Crude		**Adjusted**	
TOD	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
IMT > 0.9				
Ea/Ees	0.71 (0.572 - 0.882)	**0.002***	0.925 (0.714 - 1.198)	0.553
PWV/GLS	2.036 (1.403 - 2.955)	**<.001***	1.997 (1.215 - 3.285)	**0.006***
Diastolic dysfunction				
Ea/Ees	0.761 (0.673 - 0.859)	**<.001***	0.965 (0.828 - 1.125)	0.651
PWV/GLS	1.514 (1.308 – 1.754)	**<.001***	1.394 (1.145 - 1.697)	**<.001***
LAVi > 34				
Ea/Ees	0.864 (0.804 - 0.929)	**<.001***	0.953 (0.866 - 1.048)	0.321
PWV/GLS	1.083 (1.004 - 1.167)	**0.039***	0.995 (0.888 - 1.115)	0.93
LV mass > 100				
Ea/Ees	0.705 (0.593 - 0.837)	**<.001***	0.883 (0.7 - 1.115)	0.297
PWV/GLS	2.658 (1.736 - 4.071)	**<.001***	3.754 (1.442 - 9.77)	**0.007***

*Significant at P < 0.05; OD: Target Organ Damage; IMT: Intima-Media Thickness; Ea/Ees: Ratio of Effective Arterial Elastance to End-Systolic Elastance; PWV: Pulse Wave Velocity; GLS: Global Longitudinal Strain; LAVi: Left Atrial Volume Index; LV: Left Ventricular; OR: Odds Ratio; CI: Confidence Interval.

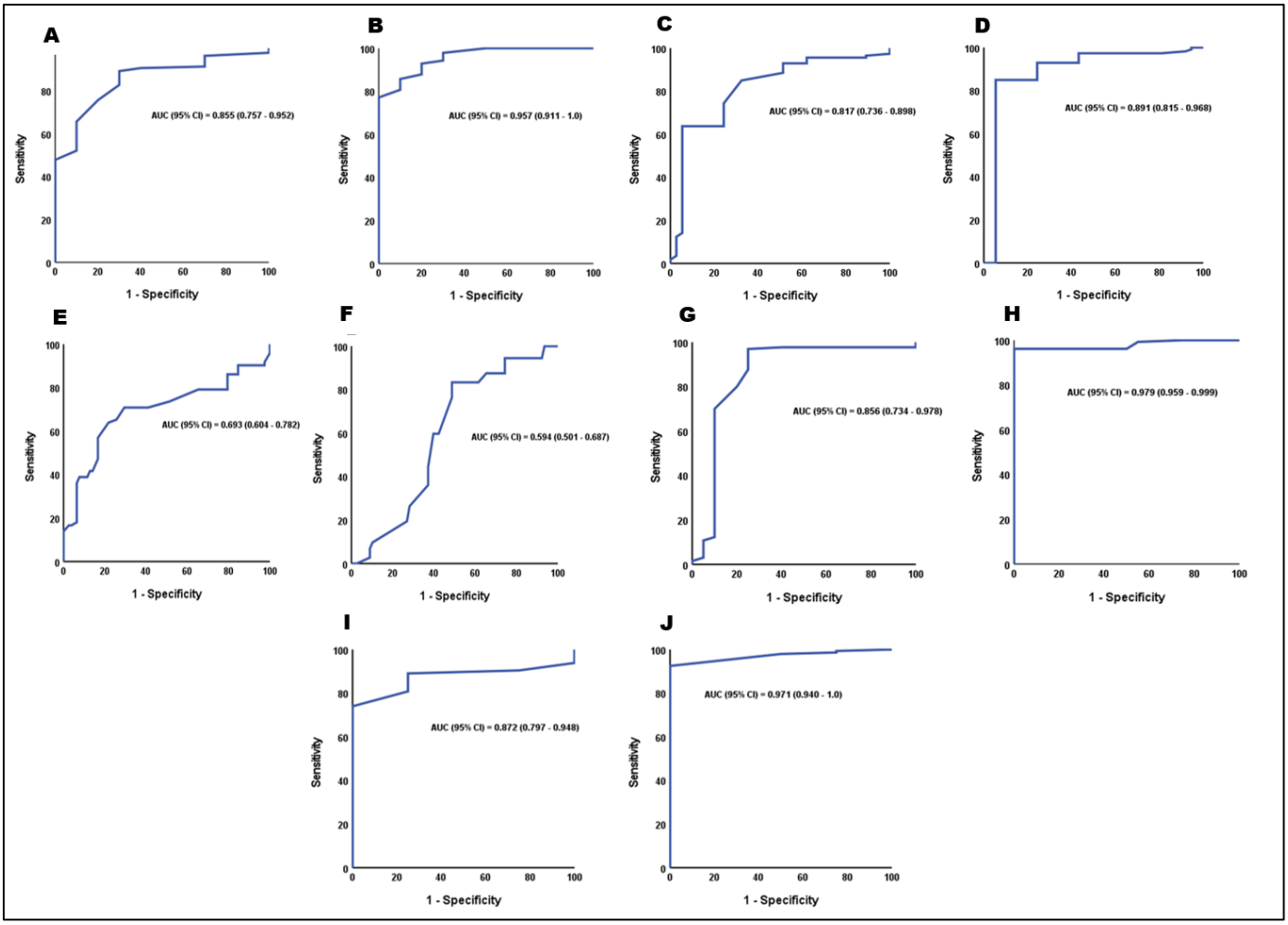

Figure 1: ROC analyses for a) Ea/Ees; b) PWV/GLS ratios to predict target organ damage based on IMT; c) Ea/Ees; d) PWV/GLS ratios to predict target organ damage based on diastolic dysfunction; e) Ea/Ees; f) PWV/GLS ratios to predict target organ damage based on LAVi; g) Ea/Ees; h) PWV/GLS ratios to predict target organ damage based on LV mass index; i) Ea/Ees; j) PWV/GLS ratios to predict target organ damage based on GLS.

Discussion:

In studies aligning with ours, a study. explored the association between carotid-femoral PWV/GLS ratio and vascular and cardiac damage in 299 untreated hypertensive patients, suggesting it may be a superior marker to the traditional arterial elastance/left ventricular elastance index. They found significant differences in systolic, diastolic, and mean blood pressure between hypertensives and controls, with no age, sex, body surface area, or smoking status differences (1). In a similar vein, another study. assessed the efficacy of the PWV/GLS ratio in conjunction with other cardiac and vascular parameters in hypertensive patients, dividing 135 subjects into hypertensives with and without coronary

artery disease and healthy controls. They observed significant systolic blood pressure differences but no variance in diastolic blood pressure or heart rate. Additionally, they reported significant differences in GLS values, cardiac volumes, and diastolic dysfunction indicators (E, A, E/A ratio, E/e' ratio) across groups, with hypertensives showing worse outcomes. IMT was also higher in hypertensive patients, especially those with coronary artery disease (18).

It was found significant differences in cardiovascular health markers between hypertensive patients and controls. IMT was notably higher in patients on both the left (0.81 vs. 0.69 mm) and right (0.89 vs. 0.70 mm) sides, with average IMT also elevated (0.85 vs. 0.70 mm), all with p-values <0.001. Additionally, hypertensives had increased Left Ventricular End-Systolic Diameter (30.0 vs. 28.2 mm), Left Ventricular Mass (160 vs. 136 grams), and left atrial volume (54 vs. 48 mL), alongside lower Global Longitudinal Strain (−18.8 vs. −21.0) indicating worse cardiac function, with significant p-values (1). It was reported higher aortic stiffness in hypertensives, with Pulse Wave Velocity (PWV) higher in both HT+CAD (9.90) and HT (9.70) groups compared to controls (7.85), significant differences in PWV/GLS ratio, and elevated E/e' ratio indicating diastolic dysfunction (p-values <0.001). Similarly, Ikonomidis et al. highlighted increased PWV (11.0 vs. 9.3 m/sec), arterial elastance (Ea) (2.2 vs. 1.8 mm Hg/L per m^2), Ea/Ees ratio, and PWV/GLS ratio in hypertensives, suggesting worse vascular and cardiac health (p-values <0.001 to 0.009) (1, 18)17).

Our study demonstrated significant correlations between target organ damage and both Ea/Ees and PWV/GLS ratios, showing that higher markers of cardiovascular risk (including IMT, diastolic dysfunction, LAVi, LV mass index, and altered GLS) are associated with lower Ea/Ees ratios and altered PWV/GLS ratios. Similarly, Holm et al. (19) found that higher PWV/GLS ratios correlate with increased cIMT and LV mass index in a young cohort. Seed et al. (20) also highlighted the PWV/GLS ratio's stronger correlation with subclinical target organ damage compared to the Ea/Ees ratio in hypertensives. Ikonomidis et al. suggested the PWV/GLS ratio as a promising marker for early detection of disease progression in hypertension, unlike the Ea/Ees ratio, which showed no significant link to target organ damage (1). A research provided rare evidence of an association between Ea and IMT despite a generally weak relationship with arterial stiffness measures (21).

In the current study, ROC analyses evaluated the predictive performance of Ea/Ees and PWV/GLS ratios for various target organ damages. Across IMT, diastolic dysfunction, LAVi, LV mass index, and GLS-related damages, PWV/GLS consistently showed higher AUCs (ranging from 0.594 to 0.971)

compared to Ea/Ees (AUCs ranging from 0.693 to 0.872), showing its superior predictive ability across these parameters. For IMT and diastolic dysfunction, PWV/GLS notably outperformed Ea/Ees with AUCs of 0.957 versus 0.855 and 0.891 versus 0.817, respectively, and showing significant superiority in predicting LV mass index and GLS-related damages with AUCs of 0.979 and 0.971, respectively, compared to Ea/Ees (AUCs of 0.856 and 0.872).

In support of this, it was demonstrated that in hypertensive patients, the PWV/GLS ratio was significantly associated with LV wall thickness. The discriminatory power of the PWV/GLS ratio in predicting altered VA coupling was moderate. A threshold of -0.054 was established using the ROC curve to detect altered ventricular-arterial coupling. These findings provide further evidence for the intricate connection between arterial stiffness, diastolic dysfunction, and LV remodeling (18).

Univariate and multivariate analyses assessed the predictive capacity of Ea/Ees and PWV/GLS ratios for TOD. At the univariate level, both ratios were significant predictors of TOD across various parameters: IMT > 0.9, diastolic dysfunction, LAVi > 34, and LV mass > 100. However, in the multivariate analysis, adjusted for age, gender, smoking, BSA, and mean arterial pressure, only PWV/GLS emerged as a significant predictor for TOD based on IMT > 0.9, diastolic dysfunction, and LV mass index > 100 (ORs ranging from 1.394 to 3.754, $P < 0.001$ to $P = 0.007$).

Ikonomidis et al. found significant associations of PWV/GLS with IMT, CFR, E/A, and TDI E' in both normal subjects and hypertensive patients. The multivariate analysis in their study associated PWV/GLS with IMT > 0.9, CFR ≤ 2.5, E/A ≤ 0.8, and TDI E'≤9 cm/sec, showing the predictive value of PWV/GLS for these markers in hypertensive patients. In hypertensive individuals, after adjusting for gender, age, and brachial blood pressure, the PWV/GLS ratio was significantly associated with higher carotid IMT and indicators of LV diastolic dysfunction (E/A ratio and tissue Doppler imaging E'). Additionally, initial analyses showed its association with increased LV volume and LA mass. (1).

Among hypertensives, it is apparent that the progression of ventricular and aortic stiffness results in a reduction of the PWV/GLS index, a ratio that exclusively accepts negative values. PWV (nominator) increases with aortic tree stiffness, whereas subclinical LV dysfunction results in elevated (abnormal) GLS values (which, by definition, acquire only negative values) and further reduces the ratio.

Conversely, within the identical clinical context, elevated levels of E_a and E_{es} produce a comparatively consistent E_a/E_{es} ratio, with the E_a increase serving as the main trigger. The early identification of subclinical disease

progression through the PWV/GLS ratio could significantly contribute to the observed correlation with target organ damage, including IMT. Our findings are reinforced by the correction made for numerous parameters that are recognized to impact AV coupling. While the univariate predictor of LV mass was PWV/GLS, in the multivariate model it did not exhibit any association with LAV or LV mass. This lack of association can likely be attributed to the substantial impact of MAP (1).

Conclusion

In conclusion, innovative approaches like the PWV/GLS ratio could potentially offer a more effective indication of VAC compared to the conventional echocardiographic Ea/Ees ratio when it comes to forecasting damage to target organs. This improved predictive ability may stem from the PWV/GLS ratio's inclusion of gold standard techniques for evaluating aortic rigidity and LV performance. Such methods could be instrumental in tracking the early onset of damage across various organs in individuals with hypertension and assessing the effectiveness of various antihypertensive treatments.

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