

LEFT VENTRICULAR DYSFUNCTION IN HYPERTENSIVE PATIENTS WITH PRESERVED EJECTION FRACTION

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Abstract

Introduction: Due to its high prevalence, arterial hypertension is a significant public health problem, and the single greatest risk factor for heart failure (HF) at a population level.

Aim: The study goal was to evaluate the left ventricular dysfunction in patients with preserved EF and arterial hypertension with varying durations, in an attempt to detect latent impairment of LV systolic function.

Material and methods: An analytical cross-sectional study was conducted at the Public Health Clinical Hospital Tetovo, Republic of North Macedonia in the period 2024/2025. A total of 92 patients over 18 years of age with a diagnosis of arterial hypertension and preserved EF above 50% were selected.

Results: Out of 92 patients, 58 (63%) were males and 34 (37%) females. The average age was 56.34±8.36 years with a min/max of 40/68 years and 50% of patients aged ≤58 years, with no significant difference between the genders. Significantly worse values were found for the echocardiographic parameters GLS (p=0.0003), RWT (p=0.00005), LVMI (p=0.00001), E/e'ratio (p=0.0015) and TEI index (p=0.0002) in patients from the group with atrial hypertension >5 years compared to those with hypertension duration ≤5 years. GLS significantly correlated with hypertension control, duration of hypertension and diabetes. No significant correlation was found between GLS and gender, age, and BMI.

Conclusion: The implementation of larger cohort studies for evaluation of the left ventricular dysfunction in patients with preserved ejection fraction (≥50%) and arterial hypertension with different durations will support the detection of latent impairment of LV systolic function, will identify high-risk patients and will allow timely intervention.

Keywords: echocardiography; hypertension; left ventricular dysfunction; preserved ejection fraction

Introduction

Hypertension is recognized as a significant modifiable risk factor for cardiovascular diseases and other health complications, emphasizing the importance of effective management. Due to its high prevalence, arterial hypertension is a significant public health problem, and the single greatest risk factor for heart failure (HF) at a population level^[1,2]. According to the 2021

guidelines of the European Society of Hypertension, arterial hypertension is generally defined as a condition characterized by persistently elevated blood pressure, with specific thresholds set at systolic BP ≥ 140 mmHg and/or diastolic BP of ≥ 90 mmHg. Hypertension occurs for an unknown reason in the majority of cases^[2,3]. As a condition, arterial hypertension results in complications affecting major organs, including the heart, brain, eyes, kidneys, and peripheral arteries^[1,3]. The progression of hypertension to congestive heart failure is well established^[4,5]. Clinical manifestations of hypertensive heart disease refer to development of diastolic dysfunction, left ventricular (LV) hypertrophy, and heart failure with preserved ejection fraction. It goes from a reversible stage of left ventricular hypertrophy (LVH) and diastolic dysfunction to an irreversible stage of systolic dysfunction. Clinical evaluation and assessment of hypertension-mediated organ damage is an essential step in the proper management of the hypertensive patient in the latest guidelines^[3-6].

Ejection fraction is a major parameter for clinical assessment of cardiac function. It is frequently used to diagnose myocardial dysfunction and provide prognostic information for clinical treatment. However, studies by several authors indicate that despite preserved ejection fraction, significant abnormalities of myocardial deformation may be present, which may also be associated with an unfavorable prognosis^[7-9]. Additionally, Global Longitudinal Strain (GLS) allows for early detection of LV systolic dysfunction by highlighting the relationship between systolic and diastolic function of the left ventricle^[1,8]. Myocardial strain assessed by GLS and traditional hemodynamic parameters share common ground, which supports the benefits of assessing myocardial strain in patients with preserved ejection fraction^[1,3,7].

Besides clinical observation for early recognition of cardiac dysfunction, echocardiography is the most commonly used diagnostic tool with the ability to determine the presence of cardiac dysfunction in cases of mild myocardial dysfunction, even in the absence of heart structural changes^[10,11]. Echocardiography with an automated method (Speckle tracing) detects cardiac function abnormalities even in cases of mild myocardial dysfunction and the absence of structural changes in the heart^[10,11]. Systolic and diastolic function can be assessed, as well as myocardial fibrosis, helping to distinguish between left ventricular hypertrophy caused by hypertension and that resulting from other etiologies^[12].

Aim

The study goal was to evaluate left ventricular dysfunction in patients with preserved ejection fraction ($\geq 50\%$) and arterial hypertension with different duration, in an attempt to detect latent impairment of LV systolic function.

Material and methods

Study population

A prospective analytical cross-sectional study was conducted at the Public Clinical Hospital Tetovo, Republic of North Macedonia in a two-year period (2024-2025). According to the principle of availability (total sampling approach), 92 patients over 18 years of age, with a clinical diagnosis of arterial hypertension and preserved ejection fraction (EF) above 50% were selected. Exclusion criteria for participation in the study were the presence of heart failure, valvular disease, atrial fibrillation, cardiomyopathy, inflammatory diseases, coronary artery disease, chronic kidney disease and lung disease. Data on clinical parameters such as BMI, hypertension duration (≤ 5 years/ >5 years), hypertension status (controlled/ uncontrolled) and diabetes were obtained through anamnesis and national electronic health system. Informed consent for participation was obtained from each patient, and the study was implemented with approval from the Ethics Committee of the Faculty of Medicine, Ss. Cyril and Methodius University in Skopje.

Echocardiographic assessment

The Philips Epiq Elite, Rev,7.0.3 device was used for echocardiographic assessment. All patients underwent standard 2D echocardiography and analysis of the global longitudinal strain (GLS) of the left ventricle. Quantification of myocardial function of left ventricular GLS was performed from an apical approach with analysis of 3 cross sectional views (four chamber, three chamber and two chamber view).

The obtained images were analyzed with an automated method (Speckle tracing) for the longitudinal deformation of each cross-section individually and generating GLS from all 18 segments. The accepted normal GLS value for our machine was a negative value greater than -17%. The decrease of the negative GLS value means reduced myocardial deformation. Ejection fraction (EF) was measured by the 2D Simpson method using the Philips software and 2DK (Philips Software, a2DQ-auto 2D quantification) incorporated into the ultrasound device, as well as in the Q-lab version 15.3 program. EF>50% was accepted as normal.

The assessed parameters were: a) GLS (Global Longitudinal Strain) with a normal value greater than -17%; b) EF (ejection fraction); c) RWT (relative wall thickness) with a normal value ≤ 0.42 g/m²; d) LVMI (left ventricular mass index/body surface area) with a normal value for women <95 g/m² and for men <115 g/m²; e) LAVI (left atrial volume index – mL/m²) with a normal value ≤ 28 mL/m², mild=29-33 mL/m², moderate=34-39 mL/m², severe ≥ 40 mL/m²; f) E/e' ratio (E-wave velocity obtained by pulse Doppler and average e' value from tissue Doppler (TDI) of the lateral and septal value) greater than > 8 cm/s with additional parameters such as LAVI and tricuspid regurgitation velocity in determined diastolic dysfunction; g) TEI index (myocardial performance index), estimated by TDI, which is a measure of both systolic and diastolic functions of the heart. A value higher than 0.39 indicated cardiac dysfunction.

Statistical analysis

Data were analyzed with the software package SPSS for Windows, version 26 (SPSS, Chicago, IL, USA). Pearson Chi square test was used to determine the association between certain qualitative nominal/ordinal parameters. Difference test was used to compare proportions. Measures of central tendency (mean, median, minimum and maximum values) as well as measures of dispersion (standard deviation) were used to analyze the numerical echocardiographic parameters (GLS, EF, RWT, LVMI, LAVI, E/e' ratio, TEI index). Shapiro-Wilk W test was used to assess the normality of the frequency distribution of continuous variables. Mann Whitney U test was used to test the significance of the difference between two independent numerical variables. The association between selected parameters and GLS was determined using Spearman Rank Order Correlation. A p<0.05 was considered statistically significant.

Results

Sample characteristics

The study included 92 patients with male/ female ratio of 1.7:1. The average age was 56.34±8.36 years with a min/max age of 40 to 68 years, and 50% of patients aged ≤ 58 years, Median IQR= 58 (48.5-63.5). No significant difference between genders related to age was found (p=0.9130) (Table 1).

The duration of arterial hypertension in 57 (61.96%) of patients was ≤ 5 years, and in significantly smaller proportion of 35 (38.04%) patients the duration was >5 years (p=0.0012). Controlled and uncontrolled arterial hypertension was equally present in 46(50%) patients. Among patients with hypertension duration ≤ 5 years, 36(63.16%) had controlled hypertension vs. 21(36.84%) patients who had uncontrolled hypertension. In the group with hypertension duration >5 years, 10(28.57%) had controlled hypertension and 25(71.43%) had uncontrolled

hypertension. The presence of uncontrolled hypertension was significantly associated with its duration >5 years (p=0.0013) (Table 1).

Table 1. Sample characteristics according to selected parameters

Parameters	Statistic N (%)
<i>Gender</i>	
Male	58(63%)
Female	34(37%)
Total	92(100%)
<i>Age (years)</i>	
Male	55.96±9.33
Female	56.97±6.47
Total	56.34±8.36
<i>Duration of arterial hypertension</i>	
≤5 years	57(61.96%)
>5 years	35(38.04%)
<i>Controlled arterial hypertension</i>	
No	46(50%)
Yes	46(50%)
<i>BMI (kg/m²)</i>	
BMI	25.22±4.12
underweight	-
Healthy weight	46(50%)
Overweight	33(35.87%)
<i>Diabetes</i>	
No	43(46.74%)
Yes	49(53.26%)

*significant for p<0.05

The average BMI was 25.22±4.12 kg/m², with a min/max of 19.3 / 35.1 kg/m². In 50% of patients, the BMI was ≤25.05 kg/m², and in 25% it was >28.1 kg/m², for Median IQR= 25.05 (21.3-28.1) kg/m². In the group with arterial hypertension duration ≤5 years, the proportion of patients with normal BMI was largest –35(61.40%). There was a significant association (p=0.0177) between hypertension duration >5 years and overweight, which in this group was present in 18(51.43%) patients (Table 1).

Diabetes mellitus was present in 49 (53.26%) of patients in the sample, without a significant association with hypertension duration ≤5/>5 years (p=0.1483) (Table 1).

Echocardiographic findings and GLS

Echocardiographic findings of all patients are listed in Table 2. All patients had preserved ejection fraction (EF) above 50%. The mean EF value in the entire sample was 64.43±3.62% with min/max values of 55/ 70%, without significant difference between groups with hypertension duration ≤5/>5 years (p=0.8722) (Table 2).

The average GLS value in the entire sample was 19.86±1.47% with a min/max value of -26.5/ -16.1%, and half of the patients with a GLS value ≤-19.9%, for Median IQR=-19.9 [-20,7-(-18.9)]. Only 2 (2.17%) patients with an abnormal GLS defined as a value greater than -17% were with uncontrolled hypertension with a duration >5 years (Table 2).

Duration of arterial hypertension and echocardiographic findings

Significantly worse values were found for the echocardiographic parameters GLS (p=0.0003), RWT (p=0.00005), LVMI (p=0.00001), E/e'ratio (p=0.0015) and TEI index (p=0.0002) in patients from the group with arterial hypertension >5 years compared to those with arterial hypertension ≤5 years. EF and LAVI values in patients with duration of arterial

hypertension >5 years were non-significantly worse compared to those with arterial hypertension duration ≤5 (Table 2).

Table 2. Echocardiographic parameters according to duration of arterial hypertension

Parameters	N	Mean±SD	Statistics			P	
			Min/Max	25th	Percentiles 50 th (Median)		75th
<i>GLS - Global Longitudinal Strain (%)</i>							
≤5 years	57	-20.16±1.12	-24.2/-17.9	-20.8	-20.3	-19.4	Z=3.647; p=0.0003*
>5 years	35	-19.35±1.82	-26.5/-16.1	-20.0	-19.0	-18.1	
Total	92	-19.86±1.47	-26.5/-16.1	-20.7	-19.9	-18.9	
<i>EF - Ejection fraction (%)</i>							
≤5 years	57	64.59±3.46	57/ 70	62	65	67	Z=(-0.161; p=0.8722
>5 years	35	64.17±3.89	55/ 70	61	65	67	
Total	92	64.43±3.62	55/ 70	62	65	67	
<i>RWT - Relative wall thickness (g/m²)</i>							
≤5 years	57	0.41±0.03	0.3/ 0.5	0.39	0.41	0.42	Z=4.069; p=0.00005*
>5 years	35	0.44±0.03	0.4/ 0.5	0.42	0.44	0.46	
Total	92	0.42±0.03	0.3/ 0.5	0.40	0.42	0.44	
<i>LVMI - Left ventricular mass index/ BSA (g/m²)</i>							
≤5 years	57	112.80±13.89	90.7/ 146	101.7	108.7	121.6	Z=4.524; p=0.00001*
>5 years	35	133.71±22.37	101.7/ 186	118.6	131.0	148.0	
Total	92	120.75±20.25	90.7/ 186	106.0	118.6	131.2	
<i>LAVI - Left atrial volume (mL/m²)</i>							
≤5 years	57	25.78±3.92	16.8/ 32.9	22.5	26.7	28.7	Z=0.394; p=0.6935
>5 years	35	26.16±4.03	17.8/ 37.0	23.1	27.1	28.7	
Total	92	25.92±3.94	16.8/ 37.0	22.8	26.8	28.7	
<i>E/e'ratio - Average mitral-to-peak early diastolic annular (cm/s)</i>							
≤5 years	57	8.07±1.51	3.5/ 11.9	7.1	8.2	9.0	Z=3.173; p=0.0015*
>5 years	35	9.13±2.03	4.8/ 14.0	8.1	9.4	10.5	
Total	92	8.54±1.82	3.5/ 14.0	7.4	8.7	9.5	
<i>TEI index - Myocardial performance index</i>							
≤5 years	57	0.42±0.05	0.3/ 0.5	0.4	0.4	0.4	Z=3.719; p=0.0002*
>5 years	35	0.46±0.05	0.3/ 0.5	0.4	0.5	0.5	
Total	92	0.43±0.05	0.3/ 0.5	0.4	0.4	0.5	

*significant for p<0.05

Table 3. Correlation of selected parameters and GLS

Selected parameters	Spearman Rang Order Correlation - R GLS - Global Longitudinal Strain (%) †
Gender (male/ female)	R ₍₉₂₎ =0.147; p=0.1626
Age (years)	R ₍₉₂₎ =0.129; p=0.2199
Controlled hypertension (no/ yes)	R ₍₉₂₎ =-0.849; p=0.00001*
Duration of hypertension (≤5/ >5 years)	R ₍₉₂₎ =0.383; p=0.0002*
BMI	R ₍₉₂₎ =0.131; p=0.2113
Diabetes (no/ yes)	R ₍₉₂₎ =0.270; p=0.0091*

† normal value greater than -17%; *significant for p<0.05

Correlation of selected parameters and GLS

The analysis indicated: a) a significant strong linear negative correlation between controlled hypertension and GLS (%) (R₍₉₂₎=-0.849; p=0.00001), indicating that hypertension control was associated with significantly increased GLS values; b) a significant moderate linear positive correlation between hypertension duration and GLS (%) (R₍₉₂₎=0.383; p=0.0002), indicating that longer hypertension duration was associated with significantly decreased GLS values; and c) a significant weak linear positive correlation between diabetes and GLS

(%)($R_{(92)}=0.270$; $p=0.0091$), indicating that the presence of diabetes was associated with significantly decreased GLS values. There was no significant correlation between GLS and gender ($p=0.1626$), age ($p=0.2199$), and BMI ($p=0.2113$) (Table 2 and Figure 1).

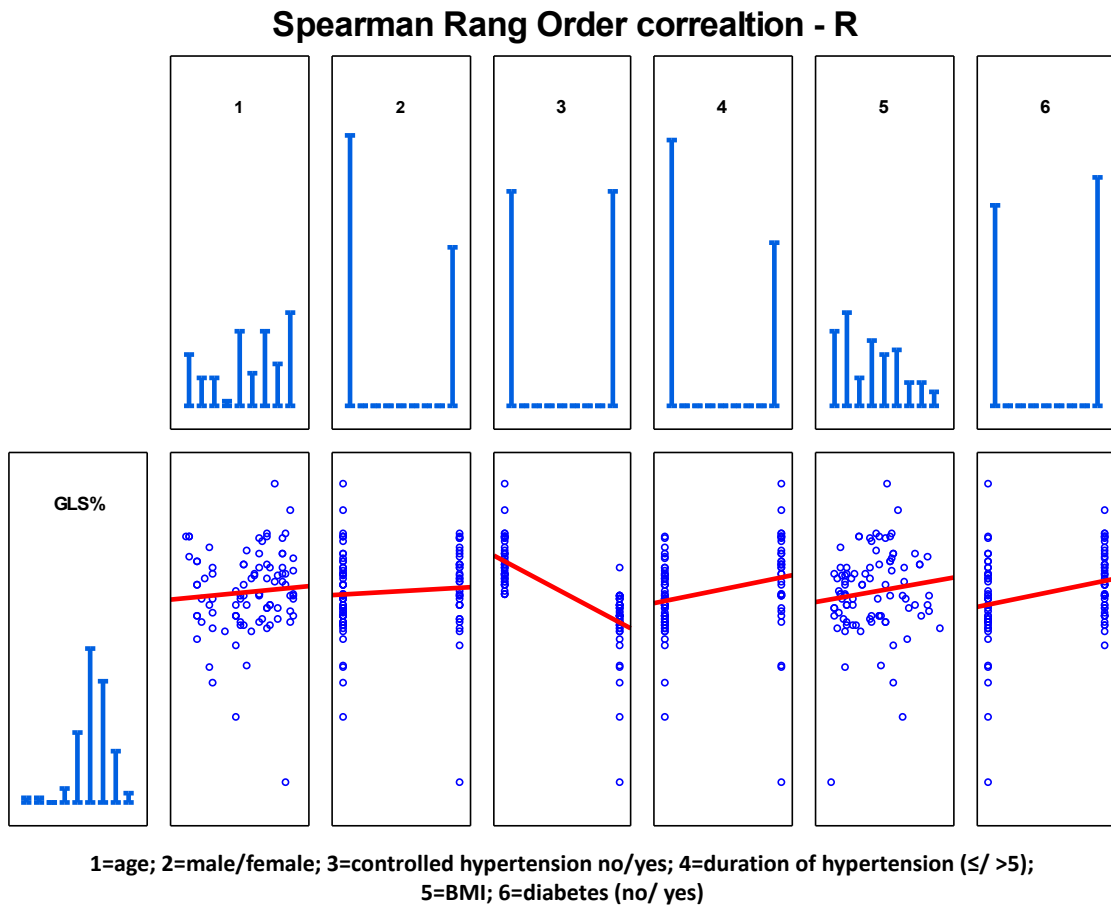


Fig. 1. Correlation of selected parameters and GLS

Discussion

Uncontrolled hypertension serves as an independent risk factor for global longitudinal left ventricular function (GLS), highlighting the essential need for continued blood pressure control to prevent cardiac damage. Patients with uncontrolled hypertension face a significantly higher risk of worsening GLS as well as the echocardiographic parameters (GLS, EF, RWT, LVMI, LAVI, E/e' ratio, TEI index), suggesting that persistent high blood pressure may result in cardiovascular damage due to fibrosis and left ventricular hypertrophy^[13,14]. In our study, significantly worse values of the echocardiographic parameters GLS, RWT, LVMI, E/e' ratio and TEI index were observed in patients with arterial hypertension with duration over 5 years compared to those with hypertension duration under 5 years. Also in our study, we determined a significant correlation between uncontrolled arterial hypertension and abnormal values of GLS. In some studies, uncontrolled hypertension has been indicated as an independent risk factor that acts to reduce negative values of GLS in hypertension with preserved left ventricular ejection fraction (LVEF). This observation further emphasizes the need for rigorous regulation of blood pressure to improve cardiac function and reduce the likelihood of cardiovascular problems^[15].

Some authors indicate a significant correlation between age and abnormal GLS values. This especially applies to people over 60 years of age, where a significantly higher incidence of GLS damage was observed. This is associated with negative changes due to aging, the

appearance of myocardial fibrosis, and reduced elasticity of the blood vessel walls^[1,16-18]. In our study, no significant correlation was found between GLS and the age of patients, which is in accordance with the results obtained in other studies^[19,20]. The inconsistency in the findings of different authors can be attributed to the assumption that age affects the reduction of GLS only in patients with cardiovascular conditions. Regardless of the difference in observations, the authors agree that timely identification of left ventricular dysfunction in people over 60 years of age is essential for reducing the risk of developing heart failure.

Diabetes is a significant risk factor for abnormal GLS values. Due to potential vascular and myocardial damage, patients with diabetes face an increased risk of left ventricular dysfunction. This is in line with previous studies indicating diabetes as an independent risk factor for diabetic cardiomyopathy, which leads to reduced myocardial contractile capacity even before the manifestation of clinical symptoms, especially in individuals with hypertension^[21,22]. Reduced GLS (cut-off value of -17.2) with preserved left ventricular ejection fraction was found in 43% of people with diabetes^[23]. In accordance with other authors, a significant correlation between diabetes and abnormal GLS values was observed in our study.

The role of GLS in the early detection of cardiac dysfunction in hypertensive patients with normal ejection fraction is a novel and promising strategy. GLS may detect decline in contractile function earlier than other measures, such as ejection fraction (EF), especially in the absence of structural changes such as left ventricular hypertrophy or ventricular enlargement^[1,5,6,24]. These research findings highlight that GLS serves as a valuable tool for monitoring the progression of cardiovascular disease in this specific patient population^[3-5].

Conclusion

This study demonstrated a significant deterioration of echocardiographic parameters associated with GLS in individuals with different durations of arterial hypertension who have preserved ejection fraction. Implementation of larger cohort studies for evaluation of the left ventricular dysfunction in patients with preserved ejection fraction ($\geq 50\%$) and arterial hypertension with different duration will support the detection of latent impairment of LV systolic function, will identify high-risk patients and will allow timely intervention.

Conflict of interest statement. None declared.

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