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EFFECT OF BMI AND UNCONTROLLED HYPERTENSION ON LEFT VENTRICULAR DYSFUNCTION IN HYPERTENSIVE PATIENTS WITH PRESERVED EJECTION FRACTION

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Abstract

Introduction: Hypertension and elevated body mass index(BMI) are established independent predictors of cardiovascular morbidity and mortality.

Objective: The aim of this study was to compare the effects of BMI and uncontrolled hypertension on echocardiographically assessed parameters related to left ventricular dysfunction in of interest in hypertensive patients with preserved ejection fraction.

Methods: This prospective analytical cross-sectional study was conducted between 2024 and 2025 at the Public Clinical Hospital Tetovo, Republic of North Macedonia.A total of 92 patients aged ≥ 18 years with a clinical diagnosis of arterial hypertension and preserved ejection fraction (EF> 50%) were included.

Results: The presence of uncontrolled hypertension was significantly associated with disease duration >5 years (p=0.0013). No significant association was observed between controlled/uncontroled hypertension and BMI categories (p=0,2617). Overweight status was significantly associated with duration of hypertension >5 years (p=0.0177). No significant association was found between BMI categories and gender (p=0,6026). Regarding BMI categories, significantly worse echocardiographic parameters were observed in overweight and obese patients compared to those with normal weight,including RWT (p=0.0403), LVMI (p=0.0001), LAVI (p=0.0101), and TEI index (p=0.0301). GLS , EF and E/e'ratio were non-significantly worse in overweight and obese patients compared to normal-weight patients. Significantly worse GLS (p=0.00001) and TEI index (p=0.00005) values were observed in patients with uncontrolled hypertension compared to those with controlled arterial hypertension.No significant differences were found between controlled and uncontrolled hypertension groups regarding echocardiographic parameters EF, RWT, LVMI, LAVI and E/e'ratio.

Conclusion: Larger prospective cohort studies are needed to clarify casual relationships and to better understand the impact of controlling established and emerging risk factors.

Keywords: echocardiography; hypertension; left ventricular dysfunction; preserved ejection fraction; BMI, obesity

Introduction

Hypertension and high body mass index (BMI) are a significant public health problems in the countries around the world (1). Based on the results of multiple studies it has been proved that hypertension and high BMI are an important independent predictors of cardiovascular morbidity and mortality (1, 2, 3). World Health Organization (WHO) underline the importance of controlling hypertension as 31% of the world's population have CVD. Additionally, WHO dealt with high blood pressure as a severe problem and considered obesity as one of the most important risk factors to address (1, 4).

Hypertension is a primary cause of left ventricular (LV) dysfunction due to chronic pressure overload. Over a period of time, hypertension specially uncontrolled hypertension initially causes changes in the left ventricular mass leading to poor relaxation and elevated filling pressures, which may progress to systolic and diastolic dysfunction (1, 3, 5-6). The prevalence of overweight and obesity has been increasing throughout the world, also affecting 60% of European adults. High BMI is decisive risk factor in many chronic diseases such as hypertension, dyslipidemia, and diabetes mellitus type 2 (1,7). The link between obesity and hypertension is complex, considering that obesity-related hypertension is

closely associated with other diseases in the course of the obesity (8). Hypertension, and high BMI tremendously increases metabolic and hemodynamic demand, leading to adaptive alterations in cardiac structure and function (1,3). Adipose tissue, increased intravascular volume and greater sympathetic drive are several factors related to obesity which have been implicated in left ventricular changes like left ventricular hypertrophy and diastolic dysfunction (1). Compounding the problem is the fact that changes in left ventricular function have been reported not only in clinically asymptomatic patients, but even in those with normal ejection fraction and preserved global LV systolic function (9, 10, 11).

The early detection of individuals with existence of risk factor such as uncontrolled hypertension as well as overweight/ obesity is of priority importance. This is based on many authors hypothesized that mentioned risk factors significantly alter left ventricular functions even in those without clinically evident cardiovascular disease. Recent techniques help in the evaluation of functions of heart even in asymptomatic adults. Modern echocardiography is considered a validated and sensitive technique for measuring and classifying changes of the parameters of interest for LV structure and functions (12, 13, 14).

Goal

The study goal was to compare the effects of BMI and uncontrolled hypertension on echocardiographically assessed parameters of interest for left ventricular dysfunction in hypertensive patients with preserved ejection fraction.

Material and methods

Study population

This was a prospective analytical cross-sectional study conducted during a the period 2024 - 2025 at the Public Clinical Hospital Tetovo, Republic of North Macedonia. A total of 92 patients aged ≥ 18 years 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. Informed consent for participation was obtained from each patient, and the study was implemented with approval from the ethics committee of the University "St. Cyril and Methodius", Faculty of Medicine, Skopje.

Blood Pressure Measurement

Blood pressure was measured with a manual sphygmomanometer according to the 2021 guidelines of European Society of Hypertension (15). The arterial hypertension was defined as blood pressure values of <140/90 mmHg determined in an outpatient setting and occurring for an unknown reason in the majority of cases. In all participants, blood pressure measurements were obtained after resting for 5 min in a seated position, with 30 s intervals between cuff inflations. An average of three measurements were used. Care was taken to select the cuff size according to the participant's arm circumference. In all the experimental settings, the assessment was performed in a dedicated room, with an optimal room temperature, and respecting the privacy. Data on hypertension status (uncontrolled /controlled) was obtained through anamnesis and national electronic health system.

Anthopometric evaluation

Well-trained examiners, measured anthropometric indices with participants wearing light, thin clothing and no shoes. Body weight was measured through an analogue medical scale. Body height was measured using a standard stadiometer. Body weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively. BMI was defined as weight (kg) divided by the square of height (m^2). The BMI cutoffs recommended by the WHO were used. The classes of BMI reported by the WHO are: 18.5–24.9 kg/m^2 for normal, 25.0–29.9 kg/m^2 for overweight, and > 30 kg/m^2, for obesity.

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 slices (4D-ventricular, 3D-ventricular and 2D-ventricular).

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 together with measurements of the heart chambers. The accepted normal GLS value was (-17%). The increase/decrease of the negative GLS value meant the improvement / deterioration of the patient's condition respectively. 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 ventricul mass index/body surface area) with a normal value for women <95g/m2 and for men <115g/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 (average mitral-to-peak early diastolic annular) which, at a value in the interval between >15cm/s and <8cm/s, indicates diastolic dysfunction; and g) TEI index (myocardial performance index), higher values of which indicate worse cardiac function.

Statistical analysis

The software package SPSS for Windows, version 26 (SPSS, Chicago, IL, USA) was used for data analysis. 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 for normality assumptions of continuous variables. Mann Whitney U test and Kruskal-Wallis H test was used to test the significance of the difference between two and more independent numerical variables. A $p<0.05$ was considered statistically significant.

Results

Sample characteristics

The total of 92 patients were elaborated with male/ female ratio of 1.7:1. Average age of male was 55.96±9.33 years and of female was 56.97±6.47 years with no significant difference between genders related to age (p=0.9130). Characteristics of the study population according to the BMI classes are summarized in (Table 1).

With duration of arterial hypertension ≤5 / >5 years were 57 (61.96%) vs 35 (38.04%) patients respectively (p=0.0012). Controlled/ uncontrolled arterial hypertension had 46 (50%) patients each. With controlled/ uncontrolled hypertension were 36 (63.16%) vs. 21 (36.84%) patients respectively from the group with duration of hypertension ≤5 years and 10 (28.57%) vs. 25 (71.43%) patients respectively from the group with duration of hypertension >5 years. The presence of uncontrolled hypertension was significantly associated with its duration >5 years (p=0.0013). There was no significant association of controlled/uncontrolled hypertension with BMI classes (p=0,2617) (Table 1).

None of the patients was underweight, and half of them were either overweight or obese. The average BMI in the sample was 25.22±4.12 kg/m^2, with a min/max of 19.3 / 35.1 kg/m^2. In 50% of patients the BMI was ≤25.05 kg/m^2, and in 25% it was >28.1 kg/m^2 for Median IQR= 25.05 (21.3-28.1) kg/m^2. In the group with the duration of arterial hypertension ≤5 years, the proportion of patients with normal wight was the largest – 35 (61.40%). The overweight significantly associated with duration of hypertension >5 years (p=0.0177). No significant association was found between the BMI classes and gender (p=0,6026) (Table 1).

Diabetes mellitus was present in 49 (53.26%) of the study patients with unsignificant association with duration of hypertension ≤5/>5 years (p=0.1483) as well as with BMI classes (p=0,7663) (Table 1).

Table 1. Characteristics of the study population according to BMI classes

Parameters	Total	BMI classes††		
		Normal weight	Overweight	Obese
Gender				
Male	58 (63%)	27 (46,55%)	23 (39,66%)	8 (13,79%)
Female	34 (3755,88%)	19 (29,41%)	10 (30,30%)	5 (14,71%)
Total	92 (100%)	46 (50%)	33 (35,87%)	13 (14,13%)
Age (years)				
Age (years)	56,34±8,36	55,33±7,92	56,54±8,71	59,38±8,88
Controlled hypertension				
No	46 (50%)	23 (50%)	19 (41,30%)	4 (8,70%)
Yes	46 (50%)	23 (50%)	14 (30,43%)	9 (19,57%)
Duration of arterial hypertension				
≤ 5 years	57 (61,96%)	35 (61,40%)	15 (26,32%)	7 (12,28%)
>5 years	35 (38,04%)	11 (31,43%)	18 (51,43%)	6 (17,14%)
Diabetes				
No	43 (46,74%)	22 (51,16%)	14 (32,56%)	7 (16,28%)
Yes	49 (53,26%)	24 (48,98%)	19 (38,78%)	6 (12,24%)

† Data are given as number (percent) for gender, controled hypertension, duration of arterial hypertension, diabetes; for age means ± SD are reported.
†† None of the patients in the sample was underweight. BMI – Body mass index
*significant for p<0,05

Echocardiographic parameters

Echocardiographic parameters for all patients are listed in Table 2-3. All patients had preserved ejection fraction (EF) above 50%. The mean EF value in the entire study population was 64.43±3.62% with min/max values of 55/ 70% half of the patients with EF value ≥ 65 for Median IQR=65 (62-67). No significant difference was found between BMI classes related to EF (p=0,2164) (Table 2).

The average value of Global Longitudinal Strain (GLS) 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)]. With an abnormal GLS defined as a value greater than -17% were only 2 (2.17%) patients with uncontrolled arterial hypertension and with a duration of hypertension >5 years. Between BMI classes there was no significant difference related to GLS (p=2098) (Table 2 - 3).

Related to BMI classes, significantly worse values were determined for the echocardiographic parameters RWT (p=0.0403), LVMI (p=0.0001), LAVI (p=0.0101), and TEI index (p=0.0301) in patients with obesity or overweight compared to those with normal weight (Table 2). The values for GLS, EF and E/e'ratio in patients with obesity or overweight were non-significantly worse compared to those with normal weight (Table 2).

In terms of uncontrolled/controlled arterial hypertension, significantly worse values for GLS (p=0.00001) and TEI index (p=0.00005) were determined in patients with uncontrolled compared to controlled arterial hypertension. There was no significant difference between patients in the group with

controlled/ uncontrolled arterial hypertension in terms of echocardiographic parameters EF, RWT, LVMI, LAVI and E/e'ratio (Table 3).

Table 2. Selected echocardiographic parameters in relation to BMI classes

Parameters	Statistic						p
	N	Mean±SD	Min/Max	Percentiles			
				25th	50th (Median)	75th	
GLS - Global Longitudinal Strain (%)							
Normal weight	46	-20,03±1,35	-26,5/-17,9	-20,7	-19,9	-19,3	$X^2_{(2, N=92)}$ = 3,123; p=0,2098
Overweight	33	-19,55±1,75	-21,2/ -16,1	-20,7	-19,1	-18,4	
Obese	13	-19,98±0,96	-21,5/ -18,5	-20,5	-20,3	-18,9	
EF - Ejection fraction (%)							
Normal weight	46	65,15±3,29	57/ 70	63	65	68	$X^2_{(2, N=92)}$ = 3,061; p=0,2164
Overweight	33	63,60±3,96	55/ 70	61	64	67	
Obese	13	64,00±3,55	60/ 70	61	63	65	
RWT - Relative wall thickness (g/m^2)							
Normal weight	46	0,41±0,03	0,3/ 0,5	0,4	0,4	0,4	$X^2_{(2, N=92)}$ = 6,424; p=0,0403*
Overweight	33	0,43±0,02	0,4/ 0,5	0,4	0,4	0,4	
Obese	13	0,43±0,04	0,4/ 0,5	0,4	0,4	0,5	
LVMI - Left ventricul mass index/ BSA (g/m^2)							
Normal weight	46	112,93±13,38	92,4/ 148	101,7	112,3	121,4	$X^2_{(2, N=92)}$ =18,324; p=0,0001*
Overweight	33	114,85±10,09	97,8/ 129	106,0	115,7	123,8	
Obese	13	134,01±24,36	90,7 /146	110,2	134,4	146,0	
LAVI - Left atrial volumen (mL/m^2)							
Normal weight	46	22,83±3,30	17,8/ 29,1	19,8	22,8	23,9	$X^2_{(2, N=92)}$ =9,193; p=0,0101*
Overweight	33	25,81±3,95	16,8/ 37,0	23,8	24,9	28,7	
Obese	13	26,88±3,70	20,2/ 32,9	22,5	28,2	29,1	
E/e'ratio - Average mitral-to-peak early diastolic annular (cm/s)							
Normal weight	46	8,40±2,14	3,5/ 14,0	7,1	8,3	9,5	$X^2_{(2, N=92)}$ =2,259; p=0,3232
Overweight	33	8,53±1,41	4,8/ 10,9	7,5	8,4	9,5	
Obese	13	9,10±1,46	6,5/ 11,3	8,7	8,8	10,0	
TEI index - Myocardial performance index							
Normal weight	46	0,42±0,05	0,3/0,5	0,39	0,41	0,46	$X^2_{(2, N=92)}$ =7,005; p=0,0301*
Overweight	33	0,43±0,05	0,3/ 0,5	0,41	0,44	0,46	
Obese	13	0,45±0,06	0,3/ 0,5	0,41	0,44	0,51	
*сигнификантно за p<0,05							

Table 3. Echocardiographic parameters according to controlled / uncontrolled hypertension

Parameters	Statistics						p
	N	Mean±SD	Min/Max	Percentiles			
				25th	50th (Median)	75th	
GLS - Global Longitudinal Strain (%)							
неконтролирана	46	-18,80±0,80	-19,9/ 26,5	-16,1	-19,4	-18,9	Z=-8,09; p=0,00001*
контролирана	46	-20,90±1,21	-26,5/ -19,0	-21,0	-20,7	-20,3	
EF - Ejection fraction (%)							
неконтролирана	46	64,28±4,06	55/ 70	62	65	67	Z=(-0,007; p=0,9937
контролирана	46	64,59±3,14	60/ 70	62	65	67	
RWT - Relative wall thickness (g/m^2)							
неконтролирана	46	0,42±0,03	0,3/ 0,5	0,4	0,4	0,4	Z=-1,136; p=0,2559
контролирана	46	0,42±0,03	0,3/ 0,5	0,4	0,4	0,4	
LVMI - Left ventricul mass index/ BSA (g/m^2)							
неконтролирана	46	124,10±21,77	96/ 176	106	120,2	134,7	Z=-1,136; p=0,2558
контролирана	46	117,46±18,24	90,7/ 186	105	116,5	126,4	
LAVI - Left atrial volumen (mL/m^2)							
неконтролирана	46	26,31±3,21	19,8/ 32,9	23,5	26,9	28,7	Z=-0,937; p=0,3487
контролирана	46	25,54±4,57	16,8/ 37,0	22,0	26,6	28,8	
E/e'ratio - Average mitral-to-peak early diastolic annular (cm/s)							
неконтролирана	46	8,84±1,67	4,8/ 14,0	7,9	8,8	9,9	Z=-1,792; p=0,0731
контролирана	46	8,25±1,92	3,3/ 14,0	7,1	8,1	9,4	
TEI index - Myocardial performance index							
неконтролирана	46	0,45±0,05	0,3/ 0,5	0,4	0,5	0,5	Z=-3,479; p=0,00005*
контролирана	46	0,41±0,04	0,3/ 0,5	0,4	0,4	0,4	
*significant for p<0,05							

Discussion

High BMI and uncontrolled hypertension are one of the major risk factors for CVD, and by many authors has been proved that they can cause subclinical changes even in asymptomatic individuals. Left ventricle hypertrophy is an important marker of cardiovascular disease, either potential or in an established condition, has been given a lot of importance in clinical diagnosis and in planning of treatment (1). Our study elaborated the effects of BMI and uncontrolled hypertension on echocardiographically assessed parameters of interest for left ventricular dysfunction in hypertensive patients with preserved ejection fraction, and highlight several important aspects.

Uncontrolled arterial hypertension is a significant independent risk factor for global longitudinal left ventricular function (GLS), which emphasizes the importance of the need for continued blood pressure control to prevent cardiac damage. Patients with uncontrolled arterial hypertension face a significant risk of worsening GLS, suggesting that persistent high blood pressure may result in cardiovascular damage due to fibrosis and left ventricular hypertrophy (6, 16, 17). Our study also found

a significantly worse GLS values as well as TEI index in patients with uncontrolled compared to the one with controlled arterial hypertension. In some studies, uncontrolled hypertension has been shown to be an independent risk factor that acts to reduce negative GLS values in hypertension with preserved left ventricular ejection fraction (LVEF) (18). Few studies have concluded that sub-optimally treated hypertension results in steadily increasing LV end-diastolic pressures and later lead to diastolic heart failure, characterized by limited myocardial relaxation, preserved LVEF, and a significant annual mortality (1). This observation further emphasizes the need for rigorous blood pressure control to improve cardiac function and reduce the likelihood of cardiovascular events.

Hight BMI may cause a variety of changes in cardiac morphology that predispose patients to ventricular dysfunction. Also hight BMI is associated with an increased risk of heart failure (19). Previous studies have demonstrated that high BMI can induce left ventricular (LV) hypertrophy, enlargement, cardiac fibrosis, and diastolic dysfunction that eventually evolves to overt heart failure. In addition, elevated LV wall stress in obesity evokes the increases in myocardial oxygen consumption (19, 20). In our study we found significantly worse values for the echocardiographic parameters RWT, LVMI, LAVI, and TEI index in patients with obesity or overweight compared to those with normal weight.

Left ventricle hypertrophy is an important predictor of cardiovascular morbidity and mortality in obese and hypertensive patients. Considering the adverse outcomes which are associated with LVH, it becomes essential to diagnose it at an early stage. Among the various diagnostic tools, echocardiography is a relatively simple and a non-invasive test with a good predictive value. The positive lifestyle modifications such as dietary changes and proper control of hypertension with medication can help in regression of left ventricle hypertrophy. The echocardiographic screening of patients with high BMI and arterial hypertension for evaluation of potential cardiac dysfunction and early institution of treatment is important. Controlling BMI in obese patients may reduce the impairment to the left ventricular myocardial function. The subclinical impairment in LV systolic dysfunction in obese patients needs further exploration.

Conclusion

This study indicates risk factors such as uncontrolled arterial hypertension and high BMI association with GLS in hypertensive individuals with preserved ejection fraction. The findings should be used to identify high-risk patients and their timely intervention. The subclinical impairment in LV systolic dysfunction in obese patients needs further exploration. More precise data from the extensive cohort study is needed to explain the causal relationships and the effects of controlling known and possibly new risk factors.

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