Journal of
HYPERTENSION RESEARCH
www.hypertens.org/jhr

Original Article

J Hypertens Res (2019) 5(2):99–106

Left ventricular dysfunction in hypertensive patients with atrial fibrillation and preserved ejection fraction

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Received: April 17, 2019, Accepted: June 5, 2019

Abstract

Atrial fibrillation(AF) may affect left ventricular function, causing abnormal diastolic filling and variable degrees of systolic abnormality to tachycardia-induced cardiomyopathy. We tried to find the influence of AF on left ventricular function in a group of hypertensive patients with preserved ejection fraction. This study included 108 prospectively enrolled subjects with essential hypertension(HTN), without any other important comorbidity and with preserved ejection fraction (LVEF>50%). 67 patients without any history of arrhythmia formed group one (group HTN) and 41 subjects with a recent AF episode, but in sinus rhythm at the enrollment, group two (group HTN and AF). We performed a standard echocardiography, evaluating LV mass, LV ejection fraction, diastolic function and LA maximal volume. Using the current recommendations of speckle tracking method, global longitudinal strain of left ventricle was analyzed. In arrhythmia group, we observed a longer history of HTN diagnosis (62.2 versus 40.4months, p=0.04) and most of the patients in this group had a more severe form of HTN (grade 3 HTN for 48.8 % patients). LV ejection fraction was in the range normal for all patients but for patients with AF the values were lower (58.44% versus 60.75% in HTN group, p=0.02). Also, the longitudinal strain of left ventricle (GLS) was lower in group2 in comparison with group1, suggestive for a mild myocardial dysfunction(-16.71% in group 2 versus -18.85% in group1, p=0.02). We found a greater diastolic dysfunction in AF patients based on mitral E/A ratio(p=0.04) and smaller values of A' septal and lateral velocity (p<0.0001 and p=0.002) in this group. Even paroxysmal or persistent types of AF can cause an incipient form of LV systolic dysfunction and diastolic dysfunction in asymptomatic hypertensive patients with preserved left ventricular ejection fraction.

Keywords: hypertension, atrial fibrillation, left ventricular dysfunction

Introduction

Hypertension(HTN) and atrial fibrillation(AF) are two prevalent conditions, that are closely linked. High blood pressure is one of the strongest risk factor for development of AF, probably because of the structural and functional remodeling of left atrium(LA)(1)(2). Diastolic dysfunction leads to elevated filling pressures and atrial remodeling, predisposing to AF. Also, there is increasing evidence that atrial fibrillation per se can cause a deterioration of left ventricular(LV) diastolic and systolic

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functions(3)(4)(5). The irregularity of the rhythm of AF can generate a decrease in cardiac output and an exacerbation of LV dysfunction, leading to tachycardia mediated cardiomyopathy that can be diagnosed even in subclinical early stages(6)(7).

Material and Methods

Study Population

Patients with high blood pressure(BP) without any other significant pathology and with preserved ejection fraction(EF), that were referred to the Echocardiography Laboratory of The Clinical Emergency Hospital of Bucharest between 2012-2013 and 2016-2017 were prospectively enrolled in this study. Secondary HTN, thyroid dysfunction, diabetes mellitus or any significant heart disease (moderate or severe valvulopathies, cardiac pacing, pulmonary hypertension, EF<50%) except left ventricular hypertrophy due to HTN were exclusion criteria. Also, patients with low quality echocardiographic views were excluded, for an accurate echocardiographic study.

One hundred eight patients were finally included, separated in two groups: the first group consisted of hypertensives without any history of arrhythmia (sixty seven patients), the second group comprised forty one patients with high blood pressure and a recent episode of atrial fibrillation (paroxysmal or persistent, but converted to sinus rhythm in the last month). Interview, physical examination and echocardiography were performed in all patients.

Echocardiographic Study

Echocardiography imaging was performed according to guidelines from the EAE(8) using a Vingmed Vivid 7 or a Vivid E9 unit, with the possibility of offline analysis of the recordings. Cardiac chamber size, LVEF, LV mass and LA dimensions were evaluated. LV ejection fraction was measured using the modified biplane Simpson's rule. Two methods were used for calculating LV mass: the classic liniar method and the 2D area-length method. LV mass was indexed to body surface area(LVMi). Pulsed-wave Doppler at the tip of mitral valve leaflets was used to measure early(E) and late(A) diastolic filling velocities, E/A ratio. Peak early and late diastolic mitral annular septal and lateral velocities

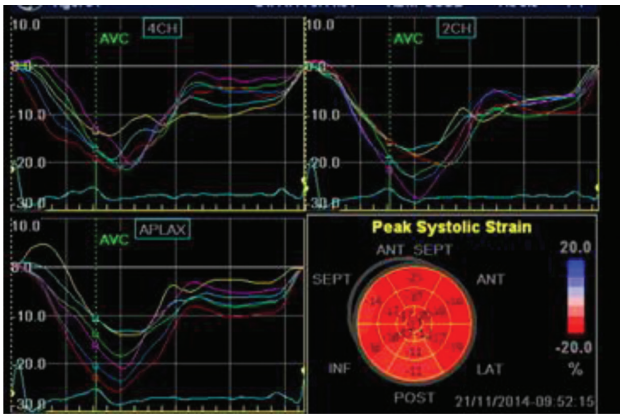

Figure 1. Assessment of global longitudinal strain of left ventricle using speckle tracking method (strain curves in each of the three apical views and bullseye)

were measured(E's, E'l, A's, A'l), averaged(E'a) and E/E'a was calculated. The timing of mitral and aortic valve opening and closure were defined by pulsed wave Doppler tracings of mitral inflow and LV outflow.

2D speckle tracking imaging was used to study LV deformation from the three apical views. Endocardial borders were manually traced on one frame in each view and the software automated generated tracking patterns of acoustic markers(speckles) throughout the cardiac cycle. Myocardial strain was assesses by the change in position of the speckles compared to the initial position. Global systolic strain was calculated by averaging the peak systolic values derived from the resulting 18 segments (6 segments in each of the three apical view). A positive value indicated myocardial lengthening and a negative value indicating shortening.

Statistical analysis

Analyses were performed using the SPSS(Statistical Package for the Social Sciences) software, release 22. Continuous variables are expressed as mean ± standard deviation(SD). Categorical data are summarized as frequencies and percentages. Inter and intraobserver reproducibility was assessed by calculating variability coefficients. Comparisons were performed using the Student's test for paired data and categorical data were analyzed by Chi square test or Fisher's exact test, when appropriate. The relationship between continuous variables was

assessed using Anova test. A P value<0.05 was considered statistically significant.

Results

Baseline characteristics

In both groups, female gender was preponderant (58.2% in group1 and 51.2% in group2). In arrhythmia group, we observed a longer history of HTN diagnosis(62.2 versus 40.4months, p=0.04) and most of the patients in this group had a more severe form of HTN(grade 3 HTN for 48.8 %patients), while in HTN group 28.4% presented a HTN grade 3. Most of the patients were treated, but with uncontrolled values of BP(just 40.3% in group 1 and 43.9% in group2 had controlled BP). Table 1 summaries general characteristics of the two groups.

The echocardiographic parameters are displayed in table 2 and 3.

Table 1. Baseline characteristics.

	HTN N=67	HTN and AF N=41	P
Age(years)	57.2±1.52	68.02±19	0.001
Gender			
• Female	39(58.2%)	21(51.2%)	NS
• Male	28(41.8%)	20(48.8%)	
BSA, m^2	1.89 ±0.03	1.92± 0.02	NS
BMI, kg/m^2	29.19±0.61	28.87±0.68	NS
Dyslipidemia	35(52.2%)	24(58.5%)	NS
Smoking-non smoker	42(20.9%)	21(51.2%)	NS
former smoker	12(17.9%)	10(24.4%)	
active smoker	13(19.4%)	10(24.4%)	
Systolic BP	148.23±2.3	143.93±2.44	NS
Diastolic BP	86.61±1.81	81.39±2.04	NS
HR(bpm)	74±5.4	66±5.1	NS
HTN history(months)	40.4±6.4	62.2±9.2	0.04
HTN grade			
• Grade 1	16(23.9%)	4(9.8%)	NS
• Grade 2	32(47.8%)	17(41.5%)	NS
• Grade 3	19(28.4%)	20(48.8%)	0.05
Antihypertensive treatment	57(86.1%)	38(93.7%)	NS
Controlled BP	27(40.3%)	18(43.9%)	NS
AF type			
• paroxysmal	–	14(34.1%)	
• persistent	–	27(65.9%)	
First AF episode	–	22(50.5%)	
Anticoagulation treatment	–	39(95.2%)	

Data are presented as mean+-standard deviation for numerical data and percentage for categorical data; N: total number from the group; NS:statistically nonsignificant(p>0.05); BSA=body surface area; BP=blood pressure; BMI: body mass index; HTN: hypertension; AF: atrial fibrillation

Table 2. Left ventricular size and systolic dysfunction

	HTN N=67	HTN and AF N=41	P
LVEDV(ml)	85.65±2.42	90.66±3.11	NS
LVESV(ml)	33.67±1.14	37.92±1.56	0.028
LV liniar mass(g)	209.99±10.73	233.05±12.81	NS
Indexed LV liniar mass(g/m^2)	109.87±4.21	120.78±6.83	NS
LV area-length mass(g)	194.03±6.97	220.17±7.08	0.016
Indexed LV area-length mass(g/m^2)	95.36±2.79	108.19±3.44	0.008
Relative wall thickness	0.45±0.11	0.45±0.14	NS
LV ejection fraction(%)	60.75±0.57	58.44±0.79	0.02
GLS LV(%)	–18.85±0.31	–16.71±0.35	0.02

Data are presented as mean+-standard deviation for numerical data and percentage for categorical data; N: total number from the group; NS:statistically nonsignificant(p>0.05); LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolic volume; LV: left ventricle; GLS: global longitudinal strain; HTN: hypertension; AF: atrial fibrillation

Table 3. Left diastolic dysfunction and atrial size

	HTN N=67	HTN and AF N=41	P
E(m/s)	0.69±0.21	1.28±0.45	NS
A(m/s)	0.76±0.02	0.68±0.05	NS
Mitral E/A ratio	0.9±0.02	1.8±0.51	0.04
E's(m/s)	0.08±0.1	0.07±0.02	NS
E'l(m/s)	0.26±0.14	0.10±0.004	NS
E'a(m/s)	0.21±0.11	0.08±0.1	NS
A's(m/s)	0.10±0.002	0.08±0.004	<0.0001
A'l(m/s)	0.10±0.003	0.08±0.004	0.002
E/E'a(m/s)	8.45±0.62	8.2±0.93	NS
LA maximal volume	65.81±2.62	94.67±3.93	<0.0001
Indexed LA maximal volume	34.82±1.22	49.3±2.35	<0.0001

Data are presented as mean+-standard deviation for numerical data and percentage for categorical data; N: total number from the group; NS:statistically nonsignificant(p>0.05); LA: left atrial; HTN: hypertension; AF: atrial fibrillation

LV mass calculated through both methods was smaller in HTN group, but only the area-length method had statistical significance. LV ejection fraction was in the range normal for all patients but for patients with AF the values were lower (58.44% versus 60.75% in HTN group, p=0.02). Also, the longitudinal strain of left ventricle(GLS) was lower in group2 in comparison with group1, suggestive for a mild myocardial dysfunction(-16.71% in group 2 versus -18.85% in group1, p=0.02).

We found a greater diastolic dysfunction in AF patients based on mitral E/A ratio(p=0.04) and smaller values of A' septal and lateral velocity(p<0.0001 and p=0.002) in this group.

Table 4. Univariate correlates for GLS

	r	P
Systolic BP	0.108	0.282
Diastolic BP	0.004	0.96
Dyslidemia	0.468	0.628
Smoking status	2.5	0.087
HTN grade	1.44	0.242
BMI	0.106	0.29
E/A ratio	0.05	0.637
E/E'a ratio	0.21	0.07
LVEDV	0.149	0.142
LVESV	0.349	0.0001
LAVI	0.234	0.04
LVEF	–0.528	0.0001

BP: blood pressure; HTN: hypertension; BMI: body mass index; LVEDV: left ventricle end-diastolic volume; LVESV: left ventricle end-systolic volume; LAVI: left atrial volume indexed; LVEF: left ventricular ejection fraction

Indexed LA maximal volume was greater in atrial fibrillation group, with high statistical significance between the two groups(34.82ml/ms in group1 versus 49.3ml/ms in group2).

Determinants of GLS for all patients are summarized in Table 3. LVEF was negatively associated with GLS (r=-0.528, p=0.0001), whereas LVESV(r=0.349, p=0.0001), LAVI(r=0.234, p=0.04), indexed LVMass area-length (r=0.298, p=0.023) were positively associated with GLS in univariate analysis.

Also, we found statistically differences between patients with different types of AF: paroxysmal or persistent AF, for GLS(-17.8 versus -16.5, F=2.9, p=0.04), LVEF(59% versus 57%, F=3.6, p=0.03) and E/E'a(10 versus 12, F=3.3, p=0.04). Patients with persistent AF had a lower LVEF and lower GLS and a higher E/E'a ratio. As we expected, E/Ea' ratio was increasing with HTN grade(7.4±0.5 for grade1, 8.3±0.41 for grade2, 9.5±0.7 for grade3, F=5.7, p=0.006).

Discussion

It is well known that persistent high blood pressure initiates a compensatory mechanism of left ventricular hypertrophy, in order to decrease myocardial parietal stress. The geometrical remodeling of the LV represents an important step in identifying a subclinical pathology with prognostic significance(9)(10). In our research, almost 2/3 of the patients had concentric ventricular hypertrophy at the time of enrollment (66.6% in group 1 and 67.2% in group2). Relative wall thickness was found similar between the two groups, but LV mass was higher in the group with atrial fibrillation (with statistical significance for LV mass calculated by area-length formula). The explanation can be the long history of hypertension in this group (62 month versus 40.4 months) and a higher percentage of grade 3 hypertension patients.

Hypertensive patients with impaired diastolic function depend on filing by atrial contraction. After onset of AF, the loss of atrial contraction contribution and the rapid, irregular rate mandate elevated atrial pressures to maintain cardiac output, aggravating the diastolic dysfunction(11). In our study, though in group 2 the patients were converted to sinus rhythm and had a controlled HR,

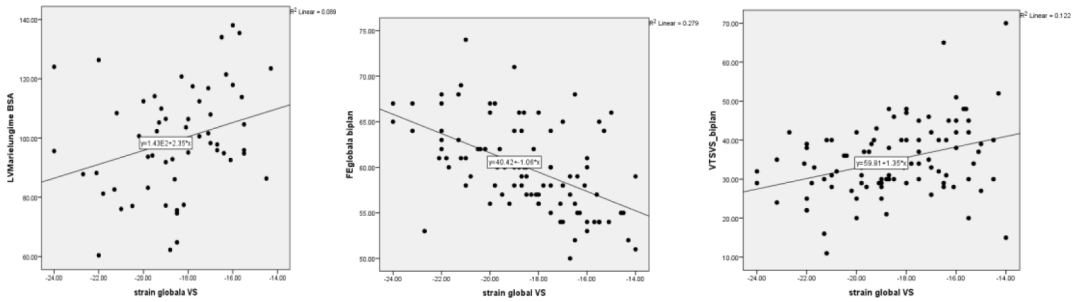

Figure 2. Correlation between GLS and a)LVESV, b)indexed LV mass area-length, c)LVEF

they presented a more advanced form of diastolic dysfunction, based on E/A ratio and had also lower A' septal and lateral velocities (that can be explained by persistent atrial stunning, after conversion but can be also secondary to atrial remodeling). E/E'a has been validated in the evaluation of outcome in patients with atrial fibrillation(12). In our study E/E'a did not help in identifying a more severe LV diastolic dysfunction between the two groups, but correlated with HTN grade(for entire group).

Atrial fibrillation causes a loss of the atrial mechanical contraction, that may influence hemodynamic performance and cause LV systolic dysfunction(13)(14). The irregular arrhythmia associated mostly with tachycardia can lead to a form of ventricular cardiomyopathy, that is usually recognized late, when the ejection fraction is reduced(15). The mechanisms responsible for tachycardia-induced cardiomyopathy are not clearly understood. In animal models, there have been evidence of myocardial energy depletion, abnormalities of calcium regulation and extracellular matrix remodeling(16). In present study, were enrolled only patients with preserved ejection fraction (LVEF over 50 percent) and all the subjects were evaluated in sinus rhythm(we excluded hypertensives with permanent atrial fibrillation). In group 2 we found a smaller ejection fraction and a higher GLS in comparison to group 1, even if the absolute values were in the range of normal, suggesting an incipient form of myocardial abnormality. There were also differences of LVEF and GLS between patients with paroxysmal atrial fibrillation and persistent atrial fibrillation. Patients with recent history of persistent AF had a more affected systolic and diastolic LV function(lower LVEF, lower GLS and higher E/E'a ratio) in comparison with subjects with paroxysmal AF.

Studies have shown a good correlation between global longitudinal strain and LVEF, GLS being an accurate method for quantifying global LV function(17). GLS is a more sensitive measure of early systolic abnormality and a predictor of cardiovascular outcome(18)(19). 2D strain assessment allows reliable distinction between active contraction and passive motion and can be used also in AF rhythm, but due to beat-to beat variability assessment post-conversion in sinus rhythm is preferred(20). GLS was significantly correlated with diastolic LV function in the study conducted by Galderisi(21). In our study, GLS did not correlate with diastolic dysfunction, but was associated with left atrial volume, LV mass and with other parameters of systolic dysfunction(LVEF and LVESV).

The prognosis of AF-induced cardiomyopathy has not been defined, but in some studies the survival in patients with mild form of LV dysfunction(LVEF>45%) was comparable to the survival of age- and sex matched controls and was better than in patients with persistent and more severe LV dysfunction(22).

Study Limitation

The small sample size in both groups and the heterogeneity of the hypertensives (all classes of hypertension, that were treated with different drug combinations) represent limitations of this study.

Between the two groups there was a statistically significant difference of the age of the population. Even we tried to compensate this finding by age-matching all the parameters, the increased age in the AF group comparing to the other group might have influenced the results.

We performed speckle tracking analysis of LV longitudinal strain, without measurements of radial, circumferential strain and LV twist. Though, longitudinal strain is the most sensitive and reproducible method among all strain measurements(23 24) and is affected earlier by disease.

Conclusion

Even paroxysmal or persistent types of AF can cause an incipient form of LV systolic dysfunction in asymptomatic hypertensive patients with preserved left ventricular ejection fraction. Also, a higher degree of diastolic dysfunction was observed in hypertensive patients with atrial fibrillation, using E/A ratio and lower A velocities.

Acknowledgment

This work was supported by CREDO Project - ID: 49182, financed by the National Authority of Scientific Research and Innovation, on behalf of the Romanian Ministry of European Fundsthrough the Sectoral Operational Programme "Increasing of Economic Competitiveness", Priority Axis 2, Operation 2.2.1 (SOP IEC -A2-0.2.2.1-2013-1) cofinanced by the European Regional Development Fun

Conflict of interest

The authors confirm that there are no conflicts of interest

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