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Hypertension impact on myocardial longitudinal strain assesed by dobutamine stress echocardiography in patients with anterior thoracic pain and non-significant coronary arteries

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Abstract

Pharmacological stress echocardiography (SE) in hypertensive patient with anterior thoracic pain (ATP) may reveal alteration of myocardial deformation, despite non-significant coronary artery disease (CAD). The objective of our study is to highlight the impact of hypertension (HT) on the myocardial strain under stress echocardiography in patients with normal epicardial coronary arteries but with angina. We evaluated myocardial deformation by global longitudinal strain (GLS) expressed through GLS18 segments, at each stage of dobutamine stress echocardiography. Patients with ATP at presentation, but without significant CAD at coronary angiography assessment were selected. The group of patients included was: 44 patients with mean age 54 years (9.5 years standard deviation), 63% women, 70% hypertensive patients. We obtained the following results: at the maximum dose of 40 mcg/Kg/min dobutamine we observed an alteration of GLS in the hypertensive versus non hypertensive patients (p=0.038), although at rest and low dose dobutamine there were no significant differences of myocardial strain among hypertensive vs non-hypertensive patients. Hypertension induced changes may be explained by impaired coronary microcirculation.

Keywords: CAD, chest pain, coronary microcirculation, global longitudinal strain, dobutamine stress echocardiography, microvascular dysfunction, permeable coronary arteries, hypertension

Introduction

Management of patients with ATP and normal coronary arteries is a challenge. Classical, to highlight the microvascular angina it must be fulfilled the triad: typical effort angina, ECG stress test or a positive imagistic stress test, and non-obstructive coronary artery disease [1,2].

Cardiovascular risk factors such as: hypertension, hyperglycemia/insulin resistance and cigarette smoking are all conditions of oxidative stress related to endothelial dysfunction in microvascular angina [3]. Another pathophysiological mechanism would be the increased

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sympathetic drive in these patients. A clinical study on patients with Syndrome X showed an autonomic imbalance expressed by a sympathetic activity. These patients subsequently showed a higher incidence of systemic hypertension during follow-up [4].

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Microvascular dysfunction can occur secondary to hypertension and diabetes in patients with no significant coronary artery disease (CAD) leading to contractile myocardial abnormalities detectable by global deformation analysis. Uncomplicated hypertension or diabetes mellitus can be considered risk factors for coronary microvascular dysfunction, as they are for coronary atherosclerosis [5].

The important health issue of hypertension has a major impact on morbidity and mortality and can lead to target organ damage [6]. For instance, in Romania, according to SEPHAR II study, the prevalence of hypertension is 40.4%, from which 59.1% of hypertensive patients were treated and 25% of them were therapeutically controlled [7].

In hypertension, the structure and function of the microcirculation may be altered in several ways: endothelial dysfunction, vascular wall remodeling and capillary density reduction [8].

Patients with concentric remodeling commonly have hypertension and a high probability of microvascular CAD [9]. Cannon et al [10] found reduced coronary vasodilator reserve in one third of hypertensive patients although they had no left ventricular hypertrophy.

The objective of our study is to highlight the impact of hypertension on the myocardial strain under dobutamine stress echocardiography in patients with non-significant CAD but with angina symptoms.

Material and method

We evaluated myocardial deformation using global longitudinal strain (GLS) expressed through GLS 18 segments using standard protocol of dobutamine stress echocardiography, assessing GLS 18 at rest, at each stage of dobutamine, at the maximum load of 40 mcg/Kg/min dobutamine and finally in the recovery phase. We selected patients who presented ATP during clinical presentations but with non-significant CAD at coronary angiography assessment.

Study protocol

Our study group was selected from patients with ATP presented to the ER. Patients with nonspecific ECG changes, no myocardial enzyme elevation and no wall-motion abnormalities in resting conditions were assessed by dobutamine stress echocardiography in the first 24 hours. We included in our study only patients with angina symptoms and/or ECG changes but no wall motions abnormalities during stress, and with non-significant CAD at coronary angiography (stenosis < 50%) .

Patients with acute myocardial infarction with or without ST segment elevation, those with unstable angina, significant valvulopathy (quantified as moderate-severe), global or segmental systolic dysfunction were excluded.

Finally, were included in the study a total of 44 patients.

Dobutamine stress echocardiography examination

Transthoracic stress echocardiographic study was performed using Vivid E9 XD clear equipment (General Electric Vingmed Ultrasound, Horten, Norway) with a 3.5 MHz transducer. GLS was analyzed using 2D Speckle Tracking Echocardiography (2D STE) with Automatic Functional Imaging (AFI) technique. The obtained data were processed off-line on the workstation EchoPAC (BT 12 General Electric Vingmed Ultrasound, Horten, Norway) by an experienced observer.

Standard protocol was used with automatic intravenous infusion of dobutamine at doses progressively increased, in 3 minutes increments, starting with 5mcg

Table 1. Statistical results on mean square, degree of freedom df, test value F, p, η^2 partial and observed power, statistical significance is reached at p <0.05.

Factors	Type III Sum of Squares	df	Mean Square	F	p	η^2 partial	Observed Powera
Dobutamine load	37.106	2	18.553	2.732	0.074	0.092	0.518
Dobutamine load & HT	18.885	2	9.443	1.391	0.258	0.049	0.286
Error(factor)	366.677	54	6.790				

/ kg / min, increasing to 10, 20, 30, up to a maximum 40 mcg / kg / min. If no end-point was reached, atropine was added to dobutamine (40 mcg / kg / min) in doses of 0.25 mg up to 1 mg. Image acquisition was done at baseline, at 20 mcg / kg / min, at 30 mcg / kg / min at 40 mcg / kg / min and during recovery, with 60-80 FPS for 2DSTE analysis. The test was done to achieve the target heart rate, namely 85% of the heart rate calculated using the formula: 220-age (years). The test was considered positive if the patient experienced at least one of the following: ATP, ECG changes, segmental wall motion abnormalities. Analysis of myocardial deformation parameters was done off-line for each stress level.

The segmental longitudinal strain (LS) was measured for each of the 18 segments of the LV, GLS was defined as the average of the 18 segments LS (GLS 18).

Statystical Analysis

Statistical analysis was performed using SPSS software package. Data were presented as percentages for qualitative variables and as mean ± standard deviation (SD) for quantitative variables. The differences between variables were assessed with the Student t test for quantitative variables and the Pearson's correlations for qualitative variables. Statistical significance was defined at the level of p<0.05.

We used the analysis of variance uni-factorial ANOVA, bi-factorial and mixed factorial to study the GLS differentiated by the presence of hypertension.

Results

Forty-four patients were studied, 63% women, mean age 54+/-9.5 years, 70% hypertensive patients.

The following results were obtained:

Using multivariance analysis ANOVA for repeated measures, the different dobutamine loading doses have not represented a significant factor for GLS 18 variation, for F=2.74; df=2; p=0.074. According with η2partial=0.092, the different dobutamine loading doses explain only 9.2% from GLS 18 variation. The presence of hypertension as a factor in GLS 18 variation during dobutamine stress test did not show statistical significance (F=1.39; df =2; p=0.26 >0.05) (Table 1).

Comparative analysis for each dobutamine dose stage identified a significant difference in the average deformation GLS 18 for 40 mcg/Kg/min dobutamine dose in the presence of hypertension (Fig 1).

At the maximum loading dose of 40 mcg/Kg/min dobutamine, the mean level of deformation in hypertensive patients (-18.58%) is statistically significant lower than non-hypertensive subjects (-22%), t=2.81, p=0.038 (Fig 2). The combination of the 2 factors: hypertension and loading dobutamine doses shows a 15% variation of GLS 18 % expressed by η^2 partially = 0.15. The observed difference of 3.42% with a standard error of 1.57% indicates a 95% confidence interval C.I. between 0.2% and 6.65% (Table 2).

Discussion

Among the parameters of myocardial deformation, GLS is one of the most studied. There are numerous studies, which have shown that GLS is not only decreased in patients with coronary artery disease [11–13], but also in patients with hypertension and hypertensive heart disease [13,14], hypertrophic cardiomyopathy[15] and diabetes [16].

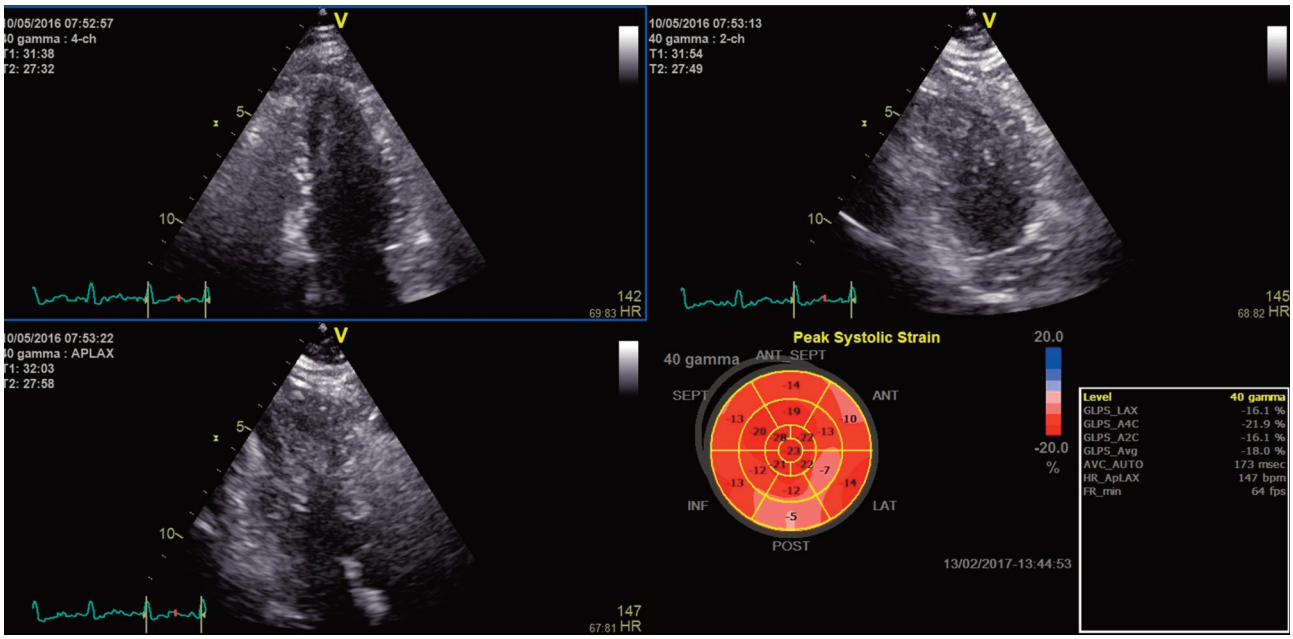

Fig. 1. Hypertensive patient with anterior thoracic pain and permeable coronary arteries: Bulls-eye figures of global longitudinal strain (GLS) values in the LV.

In contrast to the above mentioned studies, which showed an alteration of the rest GLS in hypertensive patients, we did not find a significant difference of GLS 18 between hypertensive and non-hypertensive patients in the rest phase and during loading dobutamine dose. In our study the different dobutamine loading doses did not represent a significant factor for GLS 18 variation, F=2.74, df =2, p=0.074. Also according with η^2partial=0.092, the different dobutamine loading doses explain only 9.2% of GLS 18 variation. These outcomes could be attributed to the small number of subjects included.

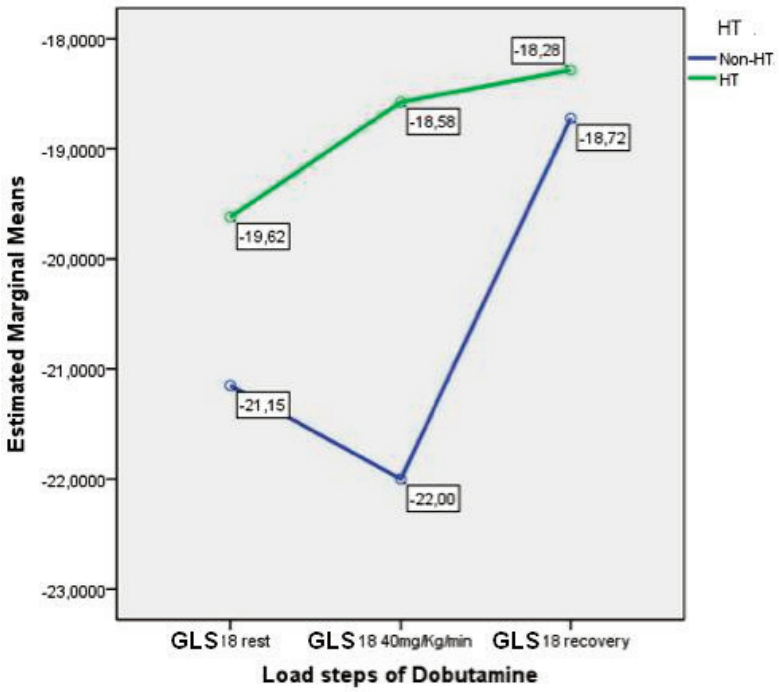

Fig.2. GLS 18 variation depending on dobutamine loading doses (rest; 40 mcg/kg/min; recovery) related on HT presence/absence

Table 2. It shows the mean ± std deviation, the confidence interval of the mean C.I. 95%, with lower and upper bound and the observed power, η^2 coefficient * 100 (%) indicates the proportion of deformation parameter variation explained by the presence / absence of hypertension. Observed power of the test * 100 (%) indicates the level of confidence that the difference is due to a real difference. Statistical significance is reached at p <0.05 of GLS18 variation explained by HT presence/absence.

Dependent Variable	Parameter	Dif. Mean	Std. Error	t	p	95% Confidence Interval		η2 partial	Observed Power
						Lower Bound	Upper Bound		
GLS18 40mcg/Kg/min	Non-HT/ HT	-3.42	1.570	-2.180	0.038	-6.65	-0.201	0.150	0.56

We identified a significant difference of GLS 18 only at the maximum loading dose of 40 mcg/Kg/min dobutamine, GLS 18 was -18.58% in hypertensive patients, versus -22% in non-hypertensive patients, p= 0.038. Also the combination of the 2 factors: hypertension and loading dobutamine doses showed a 15% variation of GLS 18 expressed by η^2 partially = 0.15. We would have expected to see an alterations of GLS 18 at lower doses of dobutamine during the stress test. The peak dose showed to be more sensitive in our case, although its accuracy has been questioned by some authors [17]. One of the problems raised for this technique during dobutamine stress echocardiography, especially when reaching the maximum doses, was related to the number of frames per seconds, which are considered insufficient by some authors. [18, 19]. Another possible concerned raised was regarding the translational and rotational movements of the heart, which at high frequencies could be out of the plane, leading to the introduction of errors in the calculation of the parameters of the myocardial deformation by 2D method [20].

A possible explanation for the observed differences of GLS 18, at maximum loading dobutamine dose, between hypertensive and non-hypertensive patients could be related to the presence of microvascular disease, and may be caused by an alteration in increasing coronary blood flow during stress conditions. Hypertension is a well-known risk factor for microvascular disease [3, 21].

Regarding distribution by gender, our study showed a higher proportion of female patients (63%), which is in accordance with others studies [22]. Predominance of women with ATP and non-obstructive CAD suggested a female-specific disorder. In WISE study (The Women's Ischemia Syndrome Evaluation) the authors showed that microvascular disease is responsible for the persistent angina symptoms and is a female-specific disorder. [23]. Estrogen deficiency causing endothelial dysfunction, may be one of the explanations for this gender distribution [3]. But the gender differences are more complex, not very well understood and further research are necessary [1].

The limitations of our study are related to the relatively small number of patients included in the study. Another limitation that could be taken into account is associated with the STE dependency on the dimensional image quality that must have a high spatial resolution for good subendocardium boundary delimitation, limiting its use to patients with optimal acoustic window.

During dobutamine SE, in particular when reaching the maximum dose, the movement of the heart at high frequencies out of the plane induces errors in the calculation of the parameters of the myocardial deformation by 2D-STE [20].

Conclusions

Although at rest and during dobutamine stress test loading doses there were no notable differences of GLS 18, at maximum dobutamine loading dose we observed significant alterations of GLS 18 among hypertensive patients.

In the future GLS could become a useful tool in the evaluation of hypertensive patients. Larger prospective studies are necessary for determining the prognostic value of this parameter in the hypertensive population. Alteration of GLS may be an early sign of target-organ damage and of microvascular dysfunction.

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Conflict of interests

There are no conflicts of interests

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