Assessment of the Left Ventricular Performance in Hypertensive Patients with Normal Coronary Angiography and Ejection Fraction: Insight by Two-Dimensional Speckle Tracking Echocardiography

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Abstract

Aim: To evaluate the validity of the longitudinal speckle tracking echocardiography (STE) in the detection of early changes in the performance of the left ventricle for hypertensive patients with normal ejection fraction (EF) and coronary angiography. **Patients and Methods:** A case-control study enrolled 50 patients and a randomly collected control group of 30, who consulted Ibn-Albitar Cardiac Center from November 2016 to the first September 2017. The patients had hypertension while the control did not. Both had normal coronary angiography, assessed by conventional echocardiography, two-dimensional STE, and anthropometric measures. **Results:** The mean age for the patients or cases was 52.48 ± 4.292 years, and their mean body mass index (BMI) was 30.10 ± 1.854 kg/m^2. They had been diagnosed with hypertension for a mean duration of 8.14 ± 3.326 years. All were on treatment; the mean left ventricular (LV) mass was 108.96 ± 19.469 (g/m^2) while the mean global longitudinal strain (GLS) was −16.720 ± 3.191. There was an approximately equal number of males and females among the cases: 24 (48.0%) and 26 (52.0%), respectively. Twenty-seven (54.0%) had LV hypertrophy (LVH), and only 4 (8.0%) cases had diastolic dysfunction with GLS −12. The mean age of the controls was 55 ± 4.792 years, and their BMI was 30.77 ± 2.063 kg/m^2. They had a mean LV mass of 92.50 ± 10.058 (g/m^2) and their GLS was slightly lower (more negative) than the cases, at −17.517 ± 2.222. Thirteen controls were males (43.3%) while 17 (56.7%) were females. Only 2 (6.7%) had diastolic dysfunction with GLS −14. GLS was significantly higher (less negative) in the cases with LVH compared to the controls: 15.278% compared to −17.517% respectively, with a mean difference of −2.238%. There was no statistically significant difference between controls and cases without LVH. **Conclusions:** The use of STE is beneficial in the detection of subtle changes in the LV of hypertensive patients with normal coronary angiography and normal EF.

Keywords: Echocardiography, Hypertension, left ventricular hypertrophy, normal coronary angiography, speckle tracking

Introduction

Hypertension, also known as elevation of blood pressure, is a long-term medical condition in which the blood pressure in the arteries is persistently raised. It is one of the most significant avoidable causes of premature mortality and morbidity in all countries (developed and developing).[1] According to the Framingham Study, hypertension is present in around 25% of heart failure patients.[2] In elderly patients, 68% of heart failure cases are related to hypertension.[3] Community-based studies have showed that hypertension probably leads to the failing of the heart in around 50-60% of patients. In patients with hypertension, the probability of heart failure is twice as high in men, and three times as high in women.

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Poor control of hypertension can be responsible for many variations in the muscle of the heart, coronary arteries, and the electricity of the heart. All of these variations can result in the formation of left ventricular hypertrophy (LVH), coronary artery disease (CAD), different conduction system diseases,

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and diastolic and systolic dysfunction of the heart. These are implications that occur clinically as chronic coronary syndrome or myocardial infarction, cardiac arrhythmia (especially atrial fibrillation), and congestive heart failure. It is of high importance to discover left ventricular (LV) impairment as early as possible to identify patients with a high probability of developing heart failure.[3]

This study was conducted to assess the validity of the longitudinal speckle tracking echocardiography (STE) in the detection of early changes in the performance of the LV in hypertensive patients with normal ejection fraction (EF) and coronary angiography.

Patients and Methods

This is a case-control study of enrolled 50 patients and 30 randomly collected controls, who consulted Ibn-Albitar cardiac center from November 2016 to the first September 2017. The patients had hypertension while the control group did not. Both had normal coronary angiography, which was performed for both groups. Both were also assessed based on a thorough history with the evaluation of risk factors, clinical examination, echocardiography, and anthropometric measures.

Exclusion criteria

1. Atrial fibrillation or multiple ventricular ectopic beats
2. Significant valvular heart disease
3. LV systolic dysfunction (less than EF = 50%)
4. Poor acoustic window or poor image acquisition
5. Diabetes
6. Chronic kidney disease
7. Known CAD.

Echocardiographic examination

The usual two-dimensional (2D) echocardiographic examinations were carried out using a Philips iE33 system (Bothell WA, USA) with an S5-1 transducer. Examinations contained calculations for the dimensions and EF for the left ventricle, and the analysis followed the American Heart Association recommendations. Speckle tracking strain was then studied by 2D greyscale harmonic images using an S5-1 transducer in multiple views (apical long-axis three-chamber, four-chamber, and two-chamber views using the left lateral position with ECG leads connected) for the analysis of segmental and global types of GLS. All images were taken at the rate of 60–100 frames/s. Three successive cycles of the heart were saved in digital format. A strain analysis was performed by using Philips Q. lab cardiac motion quantification. The aortic valve closing time was used as a reference value in the apical long-axis view for the four-chamber and two-chamber images. For every apical view, three endocardial points were recorded: one at the apex and the other two points at the base of the left ventricle, at the sides of the mitral annulus at the end of the systolic phase. Three lines were automatically formed by the software along the epicardial, mid-myocardial, and endocardial layers, following each myocardial layer by a speckle tracking algorithm. After that, the entire myocardial layer and region of interest were adjusted, and the tracking quality was validated throughout the cardiac cycle. An automated algorithm will provide the longitudinal strain with segments in a bull's eye configuration. GLS was defined as an average value of the 17 segmental longitudinal strains of the LV.

Results

This case-control study enrolled 50 cases complaining of systemic hypertension versus 30 controls with no systemic hypertension. The mean age for cases was 52.48 ± 4.292 years, and their mean body mass index (BMI) was 30.10 ± 1.854 kg/m^2. They had been diagnosed with hypertension for a mean duration of 8.14 ± 3.326 years, and all were on treatment. Mean LV mass was 108.96 ± 19.469 (g/m^2) while mean GLS was −16.720 ± 3.191 as shown in Table 1.

Males and females were approximately equal among the cases: 24 (48.0%) and 26 (52.0%) respectively. Twenty-seven (54.0%) had LVH, while only 4 (8.0%) cases had diastolic dysfunction. The mean age of the controls was 55 ± 4.792 years, and their BMI was 30.77 ± 2.063 kg/m^2. They had a mean LV mass of 92.50 ± 10.058 (g/m^2) and their GLS was slightly lower (more negative) than the cases, at −17.517 ± 2.222. Thirteen controls were males (43.3%) and 17 (56.7%) were females; only 2 (6.7%) had diastolic dysfunction. Age was significantly higher among the controls compared to the cases, with 2.52 years' difference, while LV mass was significantly lower in controls, with a difference of 16. 46 g/m^2. BMI was very close in both groups, with a difference of only 0.67 kg/m^2, which did not represent a significant statistical difference. Although GLS was higher (more positive) in the cases, the difference, which was only −0.797%, was not statistically significant.

Age and BMI did not show statistically significant differences between the cases, with or without LVH, and the controls. LV mass was higher in the cases with LHV (113.33 g/m^2) and cases without LVH (105.32 g/m^2), compared to LV mass in the controls (92.50 g/m^2), with a mean difference of 20.83 (g/m^2) and 12.82 (g/m^2), respectively.

GLS was significantly higher (less negative) in cases with LVH compared to controls,-15.278% compared to − 17.517%, respectively, with a mean difference of − 2.238% as in Table 2. There was no statistically significant difference between controls and cases without LVH, as the latter group stood at-17.980%, with a mean difference of only 0.463% as in Table 3.

Gender had no significant statistical association with hypertension, which indicated that the two samples were drawn from the same population as shown Table 4. The same applies to diastolic dysfunction with hypertension, but the GLS of this group was −12 (mean), while the GLS of the control was −14 for six cases of diastolic dysfunction (four from the case group and two from the control group) as shown in table 5. This might be attributed to the small number of cases and controls with diastolic dysfunction.

The correlation between GLS and other variables within cases showed that there was no correlation with age, BMI, or LV mass. There was only a poor positive correlation with the duration of hypertension, which indicated that, as the duration of hypertension increased, the GLS became higher (less negative) as found in table 6.

Regarding the assessment of predictors of LVH within cases, only GLS showed a significantly increased odds ratio of developing LVH as it increased (became less negative), with 1.604 times more risk. Again stating actual results may be more important than merely stating significance level. The odds ratio for having LVH was higher for males, 1.891 times more than females, as the latter benefited from a protective effect, odds ratio = 0.529. Other variables (age, BMI, and LV mass) hovered around as shown in table 7.

Discussion

For patients with hypertension, LV systolic function is ordinarily regarded as normal if the global EF and fractional shortening (FS) are normal. However, FS and EF just mean the global contractility of the cardiac function and do not take precisely localized abnormalities of the systolic function into consideration.[4] 2D speckle tracking is an aid to detect early hidden changes in the myocardium among hypertensive patients, despite normal parameters of global systolic function returned by the ordinary 2D echocardiography. GLS values decreased significantly in hypertensive patients with LVH in comparison with the control group. This is consistent with Huang *et al*., who showed that 2D-STE revealed an impairment of systolic longitudinal strain in all patients with hypertension, particularly those with LVH.[5]

Regarding the percentage of abnormal GLS results in both the cases and the controls, numerous studies determine the normal range of GLS. Based on the meta-analysis of Yingchoncharoen *et al*.,[6] the percentage of abnormal results among the cases was 80%, and 83% among the controls. However, using the HUNT study,[7] the percentage of abnormal results in the cases was 46%, with 33% in the controls. This could be explained by the high number of studies and wide range of mean and cutoff values.

The other explanation for these results is the small samples for both cases and controls, who underwent coronary angiography, which was normal. Most of them complained of chest pain, whether typical or atypical. The low values of GLS (more negative) could be due to microvascular disease or syndrome X (angina with normal coronary angiography). This is consistent with Yağmur *et al*., who found (significant) impairment of LV longitudinal myocardial systolic function detected by STE in patients with syndrome X, although normal 3D EF.[8] However, it is inconsistent with Amal *et al*., who detected that 23 of 60 patients (38.3%) in the hypertensive

Table 1: Comparison of age, body mass index, left ventricular mass, and global longitudinal strain between cases and controls

Variable	Mean			*P**
	Cases	Controls	Difference	
Age	52.48	55.00	2.52	0.017
BMI	30.10	30.77	0.67	0.140
LV mass	108.96	92.50	16.46	0.000
GLS	−16.720	−17.517	−0.797	0.223

*Independent sample *t*-test. LV: Left ventricular, LVH: LV hypertrophy, BMI: Body mass index, GLS: Global longitudinal strain

Table 2: Comparison of age, body mass index, left ventricular mass, and global longitudinal strain between cases with left ventricular hypertrophy and controls

Variable	Mean			*P**
	LVH	Controls	Difference	
Age	52.69	55.00	2.037	0.082
BMI	30.22	30.77	0.544	0.342
LV mass	113.33	92.50	20.83	0.000
GLS	−15.278	−17.517	−2.238	0.001

*Independent sample *t*-test. LV: Left ventricular, LVH: LV hypertrophy, BMI: Body mass index, GLS: Global longitudinal strain

Table 3: Comparison of age, body mass index, left ventricular mass, and global longitudinal strain between cases with no left ventricular hypertrophy and controls

Variable	Mean			*P**
	No LVH	Controls	Difference	
Age	51.96	55.00	3.04	0.022
BMI	30.20	30.77	0.567	0.251
GLS	−17.980	−17.517	−0.463	0.540

*Independent sample *t*-test. LV: Left ventricular, LVH: LV hypertrophy, BMI: Body mass index, GLS: Global longitudinal strain

Table 4: Relationship between sex and study groups according to global longitudinal strain

Variable	Cases, *n* (%)	Controls, *n* (%)	Significance
Sex			
Male	24 (48.0)	13 (43.3)	CC=0.045 (NS)*
Female	26 (52.0)	17 (56.7)	
Total	50 (100.0)	30 (100.0)	

*Chi-square test. NS: Non significant

Table 5: Relationship between diastolic dysfunction and study groups

Variable	Cases, *n* (%)	Controls, *n* (%)	Significance
Diastolic dysfunction			
Yes	4 (8.0)	2 (6.7)	CC=0.024 (NS)*
No	46 (92.0)	28 (93.3)	
Total	50 (100.0)	30 (100.0)	

*Chi-square test. NS: Not significant

Table 6: Correlation between global longitudinal strain and age, body mass index, duration of hypertension among case group

Variable	Age	BMI	Duration of hypertension
GLS			
*r**	0.170	0.040	0.363
P	NS	NS	0.009

**r*: Pearson correlation coefficient

Table 7: Risk stratification for predictors of left ventricular hypertrophy

Variable	OR		*P**
	Mean	CI	
Age	0.943	0.824-1.078	0.388
BMI	0.924	0.680-1.254	0.611
LV mass	0.962	0.916-1.010	0.118
GLS	1.604	1.191-2.159	0.002
Male	1.891	0.613-5.833	0.268
Female	0.529	0.171-1.631	

*Binary logistic regression. OR: Odds ratio, CI: Confidence interval, BMI: Body mass index, GLS: Global longitudinal strain, LV: Left ventricular, LVH: LV hypertrophy

group suffer from subclinical LV systolic dysfunction, defined as GLS less negative than −19.1%. Only three of 30 of controls (10%) in Amal *et al*. study had subclinical LV dysfunction. The study was on hypertensive patients and the control group did not have hypertension; neither of them underwent coronary angiography.

Diastolic function was normal in most cases and controls, without statistically significant GLS. This is inconsistent with the usual finding that links hypertension with Grade 1 diastolic dysfunction, as in Slama *et al*.[9] and is due to the present study using new guidelines for the diagnosis of diastolic dysfunction (ASE 2016). It is consistent with a study carried out by McFarlane *et al*.,[10] as a high number of patients were repeatedly classified to a different diastolic function grade. There was a sharp decrease in the percentage of patients classified as having indeterminate diastolic function (51% in 2009 against 21% in 2016). According to the 2016 guidelines, a high percentage of patients were determined to have a normal diastolic function (37% vs. 24%). However, the GLS values of both the case group and the controls revealed six cases, all of them abnormal despite the small number. This is consistent with Wang *et al*.[11] who stated that 2D speckle tracking is highly dependent on the relaxation of the left ventricle and can predict the filling pressure with reasonable accuracy, particularly among normal EF patients. It is also consistent with Kimura *et al*.,[12] who argued that speckle tracking derived E/E' (SR-ST) could be used as a replacement of the increased filling pressure measurement for the LV. In ICU patients, E/E '(SR-ST) revealed a better association with PCWP and higher accuracy for the diagnosis than the tissue Doppler approach.

Conclusions

The use of STE is beneficial in the detection of subtle changes of LV performance among patients with hypertension and normal coronary angiography, normal EF, and presenting LVH. This, therefore, requires the intensification of hypertension treatment and the follow-up of the LV.

Abnormal GLS findings in patients with chest pain and normal coronary angiography can help in the diagnosis of coronary microvascular angina.

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Conflicts of interest

There are no conflicts of interest.

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