Evaluation of functional indices of left ventricular wall layers using layer-specific strain analysis in normotensive and hypertensive patients

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Abstract

Background: In systemic hypertension, left ventricular remodeling results in an increase in ventricular wall thickness due to augmented ventricular afterload. Most studies on myocardial function in hypertensives are performed using imaging techniques in which the evaluation of myocardial wall thickness is performed without separating the LV myocardial triple layers from the endocardium to the pericardium. The specific myocardial function of each layer or layer-specific in both segmental and global form can also be examined using left ventricular strain analysis. The purpose of the present study was to evaluate the functional indices of each layer of the left ventricular myocardium using layer-specific strain analysis and also to evaluate the relationship between ventricular structural remodeling with the functional changes of the ventricle in each layer of the myocardium in hypertensive and normotensive individuals. Methods: Eighty eight patients (46.6% were normotensive and 53.4% were hypertensive) underwent two-dimensional echocardiography and longitudinal and circumferential strain indices were analyzed in all three layers . All parameters evaluated in terms of diastolic dysfunction were compared between two groups. Results: In patients with diastolic dysfunction, GLS and GCS strains significantly decreased in epicardial and mid myocardial layers in hypertensive patients, but these changes did not revealed in those without diastolic dysfunction. Conclusion: Decreases in GLS and GCS indices of the ventricular wall in mid myocardium and epicardial layers are predictable in the context of hypertension, and these changes in strain are evident in patients with ventricular diastolic dysfunctio

INTRODUCTION

Although many long-term benefits for the treatment and control of hypertension such as reduced risk of stroke, renal failure or myocardial infarction have been well documented, an important part of the need for hypertension control is related to prevent left ventricular hypertrophy and thus to reduce its adverse consequences. Left ventricular hypertrophy and its associated ventricular wall abnormalities are mainly the result of an excessive overload and chronic response to ventricular wall injury and are thus considered as an important risk factor in hypertensive patients. In the Framingham Heart Study, even the presence of borderline hypertension in the elderly has been associated with increased left ventricular wall thickness and subsequent ventricular diastolic filling defect (1). Patients with moderate arterial hypertension may also experience a wide range of changes in ventricular mass, from normal ventricular mass to severe hypertrophy. In addition, left ventricular remodeling may have an eccentric or concentric form, independent of the hypertension intensity. Since hypertension does not always lead to left ventricular hypertrophy, simultaneous evaluation of both cardiac indices such as hypertension and assessment of left ventricular wall stress condition is essential. Diagnosis and detection of left ventricular hypertrophy is very important because the risk of cardiac mortality and morbidity in these patients will be approximately two to four times higher than

patients with normal left ventricular mass (2,3).

Another important issue about the incidence and detection of left ventricular hypertrophy in the context of hypertension is to evaluate this event through various imaging modalities, especially focusing on changes in left ventricular wall function which can be detected by ventricular strain analysis . First, it should be remembered that secondary left ventricular hypertrophy is a major pathological finding of hypertension coupled with histological changes in the ventricular wall, such as stimulation of fibroblast growth, incidence of interstitial fibrosis, and ultimately structural remodeling in the left ventricular wall (4,5). Therefore, strong evidence suggests that in secondary left ventricular hypertrophy due to essential hypertension, shrinkage of the left ventricle volume is associated with increased diastolic filling and decreased coronary blood flow reserve and ultimately ventricular wall hypertrophy. In particular, evaluation of diastolic filling by Doppler echocardiography would be very valuable (6).

Another important point regarding the effect of hypertension on the left ventricle is the induction of reverse remodeling to the incidence of heart failure (7,8). This change increase both the size of the cardiomyocytes and the accumulation of fibrosis in the extracellular matrix. These pathological changes will eventually have heterogeneous effects on the left ventricular wall (9,10). The left ventricular myocardial layers contain myocardial fibers with distinctive features such that the longitudinal fibers in the subendocardial layer gradually switch to the circumferential format in the middle layer and eventually recapitulate in the subepicardial layer (11). Two-dimensional speckle tracking echocardiography allows the quantitative evaluation of local strain deformities (12,13). The change in left ventricular strain in a cardiac cycle has a close relationship with the structural status of ventricular myofibers (12). Among these features, longitudinal strain is of particular interest because its clinical significance is extremely high in patients with heart failure as well as in hypertensive patients (14,15). Some studies have shown that the status of longitudinal left ventricular strain changes has a strong relationship with the physical and functional capacity of patients as well as the prognosis of patients (15-17). However, what still remains to be a fundamental question is how in the context of hypertension, changes in the left ventricular wall strain will be particularly relevant to varying degrees of left ventricular hypertrophy.

MATERIALS AND METHODS

This cross-sectional study was conducted on patients in two hypertensive and normotensive groups with left ventricular ejection fraction (LVEF) greater than 50% without evidence of ischemic heart disease or congestive heart failure. All patients with valvular disorders, different types of arrhythmias, as well as a history of renal failure or diabetes mellitus were excluded.

Echocardiographic measurement

All patients underwent two-dimensional echocardiography according to standardized procedures on EPIC (Philips Ultrasound Machine), 2-dimensionally guided tracings recorded during at least 4 consecutive cycles and longitudinal and circumferential strain indices in all three endocardial layers(epicardium, mid myocardium, endocardium) were measured offline. Strain measurements were reevaluated in a second review by an expert echocardiologist and data agreement was acceptable :pearson correlation of GCS indices=0.774, pearson correlation of GLS indices=0.523 .All parameters evaluated in terms of diastolic dysfunction were compared in two groups. Normal diastolic function was defined as E/A = 1 to 2 or declaration time = 150 to 200msec.

The results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by absolute frequencies and percentages for categorical variables. Normality of data was analyzed using the Kolmogorov-Smirnoff test. Quantitative variables were also compared with t test, or Mann U test. For the statistical analysis, the statistical software SPSS version 16.0 for windows (SPSS Inc., Chicago, IL) was used. P values of 0.05 or less were considered statistically significant.

RESULTS

A total of 88 patients were included in this study. The mean age of patients was 45.30 ± 11.50 years,

ranging from 21 to 82 years. In terms of sex distribution, 37 cases (42.0%) were male and 51 cases (58.0%) were female. All patients were non-diabetic. Overall, 41 (46.6%) were normotensive and 47 (53.4%) were hypertensive. The prevalence of diastolic dysfunction was estimated to be 41 (46.6%) considering E/A <1.0 or declaration time>250 msec.

In a subgroup of patients with diastolic dysfunction, among all echocardiographic parameters, the hypertensive patients had significantly higher mean left ventricular mass index , higher mean interventricular septal (IVS) thickness, as well as higher mean posterior wall (PW) thickness. Hypertensive group had significantly lower mean global longitudinal strain (GLS) in mid myocardial and epicardial layers, as well as lower mean global circumferential strain (GCS) in these layers (Table 1). In the group without diastolic dysfunction (Table 2), we found significantly higher mean left ventricular mass index, higher mean IVS thickness, as well as higher mean PW thickness, but without any significant difference in global longitudinal and circumferential strain indices between hypertensive and normotensive subgroups.

DISCUSSION

Left ventricular remodeling caused by hypertension is a well-known phenomenon that can be evaluated by echocardiographic techniques. In recent decades, new echocardiographic techniques such as Speckle Tracking Echocardiography have made it possible to evaluate mechanical changes of the left ventricle in the context of hypertension. The evaluation of the strain index as an important part of the evaluation of the ventricular wall in various layers of the ventricle in these patients has received much attention. In this regard, evaluation of the left ventricular strain, especially the longitudinal strain in the triple layers of the ventricular wall, was a stronger predictor of cardiovascular morbidity and morbidity than the LVEF index. Given that hypertensive heart disease is one of the important risk factors for the development of heart failure and impaired cardiac systolic and diastolic function even in cases with normal LVEF, careful determination of ventricular strain changes in various layers in the presence of hypertension is essential. In particular, the impact of hypertension in the background of ventricular diastolic dysfunction on ventricular wall dimensionality remains to be elucidated. What we focused on in the present study was to evaluate and compare strain changes in the triple layers of the ventricular wall in hypertensive and normotensive patients in the presence or absence of left ventricular diastolic dysfunction.

In this study, patients were classified into hypertensive and normotensive groups; then both GLS and GCS indices were evaluated in three layers of endocardial,mid myocardial and epicardial ventricular walls. The presence of ventricular diastolic dysfunction as a confounding factor in the effect of hypertension on ventricular strain was considered important. The important finding of this study was the significant effect of hypertension on the reduction of GLS and GCS in mid myocardial and epicardial layers in the presence of left ventricular diastolic dysfunction. In other words, first, the presence of diastolic dysfunction in the reduction of left ventricular wall strain in the context of hypertension seems to be essential as a trigger factor; therefore, in cases of preserved diastolic function, left ventricular wall strain involvement may not be very noticeable. Second, there was no evidence of any decrease in endocardial layer strain and therefore no endocardial layer involvement; it is possible that our sample cases were mostly in the early stages of hypertention with lesser chronicity and better medically controlled disease and if this study was performed in different patient group with poorly controlled hypertention , or patients with longer history and advanced stages of disease ,would have shown that uncontrolled hypertension may eventually lead to endocardial layer strain reduction later in the disease course. Overall, it can be concluded that proper control of hypertension in patients with a history of hypertension, especially in the context of left ventricular diastolic dysfunction, will lead to improved left ventricular wall function and thus improved prognosis.

Impaired strain in various layers of the left ventricular wall in the background of hypertension has been studied and confirmed in various studies, although the stimulatory effect of diastolic dysfunction in such disorder has been indicated in few studies. In Tadic et al study (18), GLS was significantly lower in hypertensive men than in normotensive patients. The major factor in the development of left ventricular remodeling following hypertension was the effect of sex hormones and its associated biohormonal systems. The results of the above study were similar to ours, but these changes were not limited to a specific gender. Diastolic dysfunction

was also a triggering factor in our study. In Navarini et al study (19), there was no difference between the hypertensive and the normotensive groups in terms of left ventricular volume and LVEF. GLS values in the two groups were -15.1 and -18.5, GCS values were -15.2 and -19.9, and GRS values were + 44.0 and + 63.4, respectively indicating a difference between the two groups that was consistent with our study. In Tadic et al study (20), and quite unlike our study, a decrease in left ventricular strain in hypertensive patients was restricted to the endocardial layer, although in our study, the presence of diabetes was also considered as an exclusion indicator while this has not been the case in their study. In a study by Craciunescu et al (21) and similar to our study, both GLS and GCS were significantly lower in the group with uncontrolled hypertension than in patients with controlled hypertension. In a study by Nagata et al (22), the GLS and GLS values in the endocardial layer were higher than in the other layers, and this may justify strain retention in the context of hypertension in the endocardial layer. In Kim et al study (23), the evaluation of strain in each layer showed a decreasing endocardial gradient toward the epicardium in both groups with and without hypertension, but there was a significant difference between the two groups in all three layers. In a study by Sharif et al (24), patients with diastolic dysfunction experienced a relative decrease in GLS in all three myocardial layers compared to patients without diastolic dysfunction, which was consistent with the findings of our study. Toufan M et al study(25) demonstrated that in HFNEF patients with diastolic dysfunction; the global, basal, mid and apical PSLSs(The global peak systolic longitudinal strain) were significantly lower compared to control group. They observed a significant positive correlation between the global PSLS and the septal e' ,as well as a negative correlation between the global PSLS and the E/e'ratio. Results also revealed negative correlations between the IVRT and the global PSLS .Similar results were observed in our study in which diastolic dysfunction was substantial factor in the left ventricular wall strain decrement in hypertensive patients . all these studies demonstrate that strain imaging can uncover some degree of systolic dysfunction despite a preserved LVEF indicated by conventional echocardiography.What can be emphasized as a final result is that prolonged and uncontrolled hypertension with intensification of cardiomyocyte growth as well as cardiomyocyte fibrosis secondary to inflammatory and growth factors secretion can induce left ventricular hypertrophy and thereby reduction of strain indices in the layers, especially mid myocardial and epicardial layers. Of course, the role of ventricular diastolic dysfunction is very important in determining these changes.

CONCLUSION

As a final conclusion, a decrease in GLS and GCS indices of mid myocardial and epicardial ventricular wall layers is predictable in the context of hypertension, and this is significantly evident in patients with ventricular diastolic dysfunction. It seems that more studies on larger sample patients with more chronic and advanced hypertention as well as considering patients' drug history as variable, are required to achieve the most confident conclusion.

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Table 1: Echocardiography parameters in patients with diastolic dysfunction

Parameter	With hypertension	Without hypertension	P value
Mean E velocity	0.64 ± 0.17	0.64 ± 0.13	0.963
Mean E/A ratio	0.82 ± 0.16	0.80 ± 0.18	0.777
Mean declaration time	204.17 ± 56.49	171.75 ± 53.40	0.155
Mean E' velocity	7.92 ± 3.5	9.79 ± 3.00	0.156
Mean E/E' ratio	7.83 ± 2.43	6.19 ± 2.13	0.076
Mean EDD	4.22 ± 1.54	4.34 ± 0.48	0.825
Mean PW	1.16 ± 0.21	0.87 ± 0.08	0.001
Mean IVS	1.17 ± 0.23	0.86 ± 0.12	0.001
Mean BSA	1.81 ± 0.27	1.78 ± 0.14	0.763
Mean LV mass Index	107.09 ± 29.30	66.22 ± 12.26	0.001
Mean endocardial GLS	-15.79 ± 2.71	-14.45 ± 10.35	0.506
Mean mid myocardial GLS	-14.42 ± 2.35	-16.14 ± 2.47	0.046
Mean epicardial GLS	-12.43 ± 5.66	-15.23 ± 2.69	0.043
Mean endocardial GCS	-24.40 ± 9.80	-29.30 ± 5.08	0.140
Mean mid myocardial GCS	-17.90 ± 2.99	-20.16 ± 5.40	0.023
Mean epicardial GCS	-10.60 ± 3.19	-14.25 ± 4.29	0.008

Table 2: Echocardiography parameters in patients without diastolic dysfunction

Parameter	With hypertension	Without hypertension	P value
Mean E velocity	0.81 ± 0.17	0.75 ± 0.14	0.187
Mean E/A ratio	1.31 ± 0.30	1.47 ± 0.97	0.517
Mean declaration time	180.50 ± 31.10	155.81 ± 43.84	0.054
Mean E' velocity	10.29 ± 3.00	12.16 ± 2.81	0.054
Mean E/E' ratio	8.16 ± 2.51	6.75 ± 2.55	0.090
Mean EDD	4.60 ± 0.31	4.64 ± 0.43	0.768
Mean PW	1.03 ± 0.19	0.84 ± 0.10	0.001
Mean IVS	1.01 ± 0.17	0.84 ± 0.10	0.001
Mean BSA	1.97 ± 0.31	1.93 ± 0.16	0.585
Mean LV mass Index	86.50 ± 22.51	67.33 ± 15.42	0.001
Mean endocardial GLS	-17.01 ± 1.60	-18.30 ± 3.26	0.248
Mean myocardial GLS	-15.77 ± 1.48	-17.17 ± 1.73	0.069
Mean epicardial GLS	-14.35 ± 1.63	-15.41 ± 1.94	0.068
Mean endocardial GCS	-25.25 ± 16.68	-28.53 ± 3.31	0.293
Mean myocardial GCS	-17.83 ± 9.33	-18.27 ± 8.16	0.868
Mean epicardial GCS	-12.40 ± 4.21	-12.94 ± 2.76	0.599