Razavi Int J Med. 2017 June; 5(2):e42876.
doi:10.30483/rijm.2016.118362
Published online 2017 April 29.
Research Article

Diastolic Function Changes during Stress Echocardiography in Hypertensive Patients

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Received 2016 May 23; **Accepted** 2017 February 15.

Abstract

Background: Some hypertensive patients experience dyspnea with exercise due to rise in filling pressures. So, exercise is helpful to determine left ventricular filling tension.

Objectives: This study aims to evaluate the effect of dobutamine stress echocardiography on diastolic function in hypertensive patients with normal ejection fraction.

Methods: In this study, 30 hypertensive patients (52.7 ± 3.6 years) and 30 sex and age matched healthy controls (50.8 ± 7.6 years) were examined. Exclusion criteria were patients with coronary artery disease, significant valvular heart disease, hypertrophic cardiomyopathy, left ventricular systolic dysfunction (EF (ejection fraction) < 50%), atrial fibrillation and bad echogenic view. We performed complete echocardiography and dobutamine stress echocardiography with pulsed wave Doppler tissue imaging at rest and during peak stress to measure primary mitral inflow diastolic wave rate (E), late mitral inflow diastolic wave rate (A), E/A ratio, primary diastolic myocardial wave rate (E′) and late diastolic myocardial wave velocity (A').

Results: At rest, E' was significantly lower in patients than controls (8.2 ± 1.6 vs 14.7 ± 2.6 P value < 0.001) and E/E (early mitral inflow diastolic wave rate/early myocardial diastolic wave rate) was significantly higher in patients (7.6 ± 1.2 vs 4.8 ± 1.0 P value <0.001). At peak stress, E/A ratio was significantly lower in patients (P < 0.001) while E/E′ was significantly higher in patients than controls (8.3 ± 2.1 vs 4.7 ± 0.7 P value < 0.001).

Conclusions: Dobutamine stress echocardiography with Doppler tissue study is effective in the evaluation of hypertensive patients with dyspnea on exertion with normal resting echocardiography.

Keywords: Hypertension, Diastolic Function, Dobutamine Stress

1. Background

Hypertension is one of the common, identifiable, and reversible risk factors for myocardial infarction, stroke, heart failure, atrial fibrillation, aortic dissection, and peripheral arterial disease (1, 2). Left ventricular diastolic dysfunctions is a common problem in hypertensive patients, especially if left ventricular hypertrophy is present, even with normal systolic function (3).

In almost all patients with essential hypertension without ischemic heart disease, systolic and diastolic function of left ventricular is normal at rest but it may respond abnormally during exercise and the patient experiences dyspnea on exertion. This event may show impaired left ventricular diastolic filling at stress and this is named lack of diastolic reserve (4).

Impaired diastolic reserve is defined as normal or impaired relaxation (stage 1 diastolic dysfunction) with normal filling pressure at rest that is converted to advanced stage of diastolic dysfunction with elevated filling pressure and symptom of dyspnea under stress (4).

In subjects with normal myocardial relaxation, E and E' rates increase proportionally with stress and exercise, and the E/E' ratio remains firm or is decreased (4). Nevertheless, in patients with impaired myocardial relaxation, the enhancement in E' with exercise is less than that of mitral E rates, such that the E/E' ratio enhances and E/E' was shown to relate significantly to LV (left ventricular) filling load pending stress, when Doppler echocardiography was acquired simultaneously with cardiac catheterization (5).

A precise and noninvasive modality that is used for the finding of ischemic heart disease (IHD) is Dobutamine stress echocardiography (DSE). Using doppler tissue imaging (DTI), reduction in the peak annular rates in systole and diastole with dobutamine has been demonstrated with known IHD (6, 7).

Dobutamine stress echocardiography is most helpful in hypertensive patients with unknown dyspnea on exertion who have mild diastolic dysfunction and normal filling load at rest. In those patients, E/E' ratio increases with stress (5).

2. Methods

2.1. Patient Selection

We calculate sample size according to $\alpha = 0.05$ and $\beta = 0.2$ with regard to compare the two means. Thirty hypertensive patients (14 males and 16 females) with mean age (52.7 ± 3.6) years were enrolled in the study who were referred to our clinic in Mashhad University of Medical Science and 30 age and sex matched patients were considered as the control group. All participants were provided with informed consent and the study protocol was approved by our institute commission. Hypertension was known as a prior blood pressure recording on 2 separate occasions of > 140 mmHg systolic or > 90 mmHg diastolic or the continuing prescription of antihypertensive cure (8).

Patients with documented CAD, significant valvular heart disease, cardiomyopathies, chronic renal failure, left ventricular systolic dysfunction (EF < 50%), AF (atrial fibrillation) and bad echogenic view were excluded.

2.2. Conventional Echocardiography

Echocardiographic evaluation was done by using the commercially available Vivid 6, (general electric healthcare) equipped with a 1.7 - 4 MHz phased-array transducer. Echocardiographic imaging was obtained in the parasternal long- and short-axis, and apical two-, three- and four-chamber views using standard transducer positions (LV end-diastolic and end-systolic diameters, septal and posterior wall thickness and ejection fraction) were measured in accordance with the recommendations of the American society of echocardiography (9).

A 1 - 2 mm pulsed Doppler sample volume was placed at the mitral valve tip, and mitral flow rates from 5 to 10 cardiac cycles were recorded from the apical window. The mitral inflow rates were traced and the following variables were attained: peak rate of primary diastolic wave rate (E), late diastolic wave rate (A) and E/A ratio.

Doppler tissue imaging of mitral annulus was acquired from the apical 4-chamber view. A 1.5-mm sample volume was placed at the lateral annulus. Analysis was applied for the assessment of systolic wave rate (S'), primary diastolic wave rate (E'), late diastolic wave rate (A'), E'/A' ratio and E/E' ratio that were computed at rest (10, 11).

2.3. Protocol of Dobutamine Stress

48 hours prior to the study, Beta-adrenergic blocking drugs were stopped. Dobutamine was infused at doses of 5, 10, 20, 30 and 40 μg/kg/min for every 3 minutes. A 12-lead electrocardiogram, blood pressure, and two-dimensional (2D) echocardiograms were taken at baseline, at low dose dobutamine, peak dobutamine, and at improvement.

Transmitral flow was used to measure early diastolic wave velocity (E), late diastolic wave velocity (A) and E/A ratio at peak dose using DTI lateral mitral annular velocities; systolic wave ratio (S'), early diastolic wave velocity (E'), late diastolic wave rate (A'), E'/A' and E/E' ratio were measured at peak dose of dobutamine.

The dobutamine stress test was stopped when 85% of the maximal predicted heart rate was achieved, or earlier if the patient had progressive or severe chest pain, dangerous ventricular arrhythmia, systolic blood pressure > 240 mmHg, symptomatic hypotension or systolic blood pressure < 80 mmHg or life-threatening side effects.

2.4. Statistical Analysis

Using statistical package for the social science software (SPSS) version 19, data from the patients and controls group were collected and analyzed with Independent -Sample T test. The level of significance is 95%. So, P value less than 0.05 was considered a non-significant result and that less than 0.001 was considered a highly significant result.

3. Results

Patients with hypertension had mean age of 52.7 ± 3.6 compare to control group with mean of 50.8 ± 7.6 (P value = 0.41). In patients with hypertension, we had 14 males and 16 females, in control group 11 males and 19 females (P value = 0.34). In patients with hypertension, E' and E'/A' were significantly lower while E/E' ratio was significantly higher than control group (Table 1 and Table 2).

At peak stress, Hypertensive patients have significantly higher A (late mitral inflow diastolic wave velocity) and prominently lower E/A ratio than control group.

Hypertensive patients in TDI have significantly lower E' and A' at peak stress than control group. On the other hand, both E'/A' ratio and E/E' ratio were significantly higher in hypertensive patients than control (Table 3).

All conventional echo measurements were significantly higher at peak stress than at rest in hypertensive patients (P value < 0.001).

Table 1. Echocardiographic Parameter of Patients and Control Groups at Rest

	Patients No. = 30	Controls No. = 30	P Value
EF%	59.6 ± 2.7	61.5 ± 2.3	0.24
E	69.6 ± 9.4	72.4 ± 3.3	0.14
A	74.3 ± 10.3	72.3 ± 6.6	0.54
E/A	0.94 ± 0.15	0.98 ± 0.14	0.16
S'	8.4 ± 0.9	8.7 ± 1.1	0.08
E'	8.2 ± 1.6	14.7 ± 2.6	< 0.001
A'	10.1 ± 2.3	11.0 ± 3.4	0.22
E'/A'	0.97 ± 0.26	1.35 ± 0.49	< 0.001
E/E'	7.6 ± 1.2	4.8 ± 1.0	< 0.001

Table 2. Comparison Between Echocardiographic Data of Patients and Control Groups at Peak Stress

	Patients No. = 30	Controls No. = 30	P Value
EF%	71.3 ± 1.9	72.2 ± 1.6	0.33
E	78.1 ± 15.6	82.3 ± 8.9	0.39
A	97.3 ± 12.3	86.5 ± 11.5	0.005
E/A	0.78 ± 0.11	0.96 ± 0.17	0.001
S'	13.2 ± 1.9	13.9 ± 1.8	0.11
E'	9.6 ± 2.3	16.5 ± 3.2	< 0.001
A'	11.2 ± 1.7	14.3 ± 3.5	0.001
E'/A'	0.88 ± 0.26	1.30 ± 0.35	< 0.001
E/E'	8.3 ± 2.1	4.7 ± 0.7	< 0.001

Table 3. Comparison Between Resting and Stress Echo Data in the Patients Group

	Resting	Peak Stress	P Value
EF%	59.6 ± 2.7	71.3 ± 1.9	< 0.001
E	69.6 ± 9.4	78.1 ± 15.6	0.03
A	74.3 ± 10.3	97.3 ± 12.3	< 0.001
E/A	0.94 ± 0.15	0.78 ± 0.11	< 0.001
S'	8.4 ± 0.9	13.2 ± 1.9	< 0.001
E'	8.2 ± 1.6	9.6 ± 2.3	0.39
A'	10.1 ± 2.3	11.2 ± 1.7	0.002
E'/A'	0.97 ± 0.26	0.88 ± 0.26	0.12
E/E'	7.6 ± 1.2	8.3 ± 2.1	0.16

In hypertensive patients, there was a highly prominent increase in systolic wave velocity (S') (P value < 0.001) and a significant increase in late diastolic wave velocity (A') by DTI (P value < 0.05) at peak stress compared to rest.

E/E' was higher at peak stress compared to rest in patients with hypertension but it did not reach a prominent value (P value > 0.05).

In echocardiography; ejection fraction, E (early mitral inflow diastolic wave rate) and A (late mitral inflow diastolic wave rate) were significantly higher at peak stress than at rest in control groups (P value < 0.001) as showed in Table 4.

The comparison between resting and stress echo data in the control group by tissue Doppler revealed that there was a highly significant increase in systolic wave velocity (S') and late diastolic wave velocity (A') (P value < 0.001) at peak stress than at rest. Similarly, there was a prominent increase in early diastolic wave velocity (E') (P value < 0.05) at peak stress. E/E' was lower at peak stress than at rest in control group but it did not reach a statistically significant value (P value > 0.05).

4. Discussion

The most prevalent reason of diastolic dysfunction is chronic hypertension. Left ventricular hypertrophy and increased connective tissue thickness are the result of diastolic dysfunction, which influence cardiac compliance. The diastolic pressure-volume curve will have an acute slope in the left ventricular hypertrophy. It means that slight activity can cause a significant increase in left ventricular end-diastolic pressure (12, 13).

The symptoms such as dyspnea due to increase in left ventricular diastolic pressure (LVDP), which are observed in diabetic and hypertensive patients, are independent of exertional ischemia (14-16).

Ejection fraction in patients with diastolic heart failure is maintained (17-20). Even with the existence of probable myocardial structural disease, normal resting diastolic filling could be achieved (21).

It has been demonstrated that by using Doppler techniques, LVDP is measured in resting situations (22). It has been shown that there is a relationship between the ratio of primary diastolic transmitral rate to tissue rate (E/E') and LVDP. Increase in LVDP is demonstrated by E/E' more than 15. When E/E' is evaluated during physical activity, it could provide more data of the effect of physical activity on LVDP (23).

In this study the patients were divided into two groups (30 patients with hypertension and 30 patients in control group). All patients had normal ejection fraction. Then heart diastolic function was evaluated by conventional Echocardiography and DTI in both rest position and peak dobutamine stress test. Then we assessed the diastolic dysfunction in patients with hypertension.

DTI is utilized for the evaluation of mitral annulus rate at lateral wall. Some studies recently mentioned that lateral tissue Doppler signals (E/E' and E'/A') have a close relationship with LV filling pressure, especially in patients with reserved EF. Therefore, in these patients, the use of lateral tissue Doppler signals is supported (24).

In this study, it is demonstrated that there is no significant difference at primary diastolic wave rate (E), late diastolic wave rate (A) and E/A ratio in patients with hypertension compared to control group. This result is matched with the study of Verdecchia et al. They reported no significant difference in E, A and E/A ratio between hypertensive patients and control group (25).

We also found no significant difference in late diastolic velocity of the mitral annulus (A) between the two groups.

Ommen et al. showed a remarkable lower E' in hypertensive patients which was a different result from our study. Reduction in early diastolic velocity (E') is demonstrated in inadequate relaxation situation, where increase in LV filling pressure causes E to decrease (23).

Resting E/E' ratio was significantly higher in hypertensive patients than controls. Nagueh et al. concluded that E/E' is helpful as a tool for assessing LV filling pressures that combines the efficacy of transmitral driving pressure and myocardial relaxation and it is identified as the best parameter for diagnosis when compared to other doppler measures (24-29).

Ommen et al. found that E/E' ratio had a better correlation with invasively measured LVDP than did other Doppler variables for all levels of diastolic function and they concluded that E/E' ratio could be used as the initial measurement for the estimation of LV filling pressures, particularly in those patients with preserved systolic function (23).

Regarding diastolic function, there was a significant decrease in E/A ratio at peak stress in patients than controls; this was similar to Hildo et al. who revealed that E/A ratio decreased at peak stress in hypertensives than controls (30).

In our study, E/E' ratio showed a significant increase in hypertensive group at peak stress than at rest. This can be explained as subjects with normal myocardial relaxation, E and E' rates enhance proportionally, and E/E' ratio remains firm or decreases. However, in patients with impaired myocardial relaxation, enhancement in E' with exercise is much less than that of mitral E rate so that E/E' ratio enhances. In that regard, when Doppler echocardiography was acquired simultaneously with cardiac catheterization, E/E' was shown to relate significantly to LV filling load during exercise (1).

Malcolm et al. concluded that E/E' correlates with invasively evaluated LVDP during exercise. It can be used to reliably recognize patients with measured LVDP during exercise and decreased exercise capacity. This increase in filling load is an identified phenomenon in a significant proportion of patients complaining of dyspnea and supports a cardiac cause of dyspnea (31).

Table 4. Comparison Between Resting and Stress Echo Data in the Control Group

	Resting	Peak Stress	P Value
EF%	61.5 ± 2.3	72.2 ± 1.6	< 0.001
E	72.4 ± 3.3	82.3 ± 8.9	0.003
A	72.3 ± 6.6	86.5 ± 11.5	< 0.001
E/A	0.98 ± 0.14	0.96 ± 0.17	0.16
S'	8.7 ± 1.1	13.9 ± 1.8	< 0.001
E'	14.7 ± 2.6	16.5 ± 3.2	0.01
A'	11.0 ± 3.4	14.3 ± 3.5	< 0.001
E'/A'	1.35 ± 0.49	1.30 ± 0.35	0.08

5. Conclusion

Dobutamine stress doppler tissue imaging is very useful in hypertensive patients with preserved left ventricular systolic function presented by exertional dyspnea. Diastolic dysfunction can be revealed in these hypertensive patients by increased E/E′ ratio at stress echocardiography.

Acknowledgments

The authors thank Mashhad University of Medical Sciences.

Footnote

Financial Disclosure: We have no Financial Disclosure

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