## Original Article

# *Isovolumic Relaxation Time as an Indicator of Diastolic Dysfunction in Hypertrophic Cardiomyopathy*

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## ABSTRACT

***Background:*** Hypertrophic cardiomyopathy (HCM) is clinically characterized by the presence of left ventricular hypertrophy in the absence of hypertension and valvular heart disease. Diastolic dysfunction is an important pathology in patients with HCM, and it is characterized by abnormal relaxation, increased left ventricular filling pressure, pulmonary congestion, and ultimately cardiac symptoms. The present study aimed to assess the isovolumic relaxation time (IVRT) in patients with HCM as an important indicator of diastolic dysfunction.

***Methods:*** Nineteen control subjects and 35 patients with HCM were included in the present study. Diagnosis was based on the confirmation of unexplained myocardial hypertrophy in the left ventricle by conventional echocardiography. The peak velocity of early (E) and late (A) filling, E-wave deceleration time (DT), and the E/A ratio were assessed using pulsed-wave Doppler (PWD) echocardiography at the tip of the mitral valve leaflets in the apical 4-chamber view. The IVRT was measured in the 4-chamber view via the PWD method. To that end, the filtering gain of the images was adjusted and the IVRT was estimated.

***Results:*** The mean age of the patients was 31±16 years. The IVRT more significantly increased in the patients with HCM than in the control group ($P<0.01$). The IVRT rose more significantly in the patients with no left ventricular outflow tract (LVOT) obstruction than in those with LVOT gradients (97±38 vs 82±29; $P<0.001$). The mean septal thickness was 24±7 mm in the patients with HCM, and increased septal thickness was significant in the patients who received implantable cardioverter defibrillators ($P<0.05$).

***Conclusions:*** The diastolic function was impaired in our patients with HCM. Moreover, the IVRT as a noninvasive index of the diastolic function was prolonged in those with HCM. ***(Iranian heart Journal 2018; 18(2): 44-49)***


**KEYWORDS:** Hypertrophic cardiomyopathy, Isovolumic relaxation time, Diastolic dysfunction

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Hypertrophic cardiomyopathy (HCM) is a primary myocardial disease in which hypertrophy occurs in the left ventricle (LV) independent of load. Hypertrophy occasionally occurs because of high blood pressure or pressure overload. Impaired relaxation in the LV is the hallmark of every type of hypertrophy, [1] and it eventually causes increased LV end-diastolic pressure as well as pulmonary congestion and edema, while the systolic function of the LV remains normal. [2-4]

In the wide range of HCM, physical examination is not the best diagnostic method inasmuch as most patients do not have left ventricular outflow (LVOT) obstruction and their examination is almost normal. Additionally, the initial suspicion in these people arises from their family history, abnormal ECG pattern, systolic murmur, or new symptoms during exercise. [5,6]

Histopathological features of HCM include myocardial fiber disarray, which causes impairment in myocardial relaxation and stiffness in the myocardium. [2,7,8]

The present study aimed to assess the isovolumic relaxation time (IVRT) in patients with HCM, which is regarded as an indicator of diastolic dysfunction in these patients.

## METHODS

### Patients

A total of 35 patients (20 women and 15 men) with HCM, at a mean age of 31±16 years, were included in the present study. Diagnosis was based on the confirmation of unexplained myocardial hypertrophy in the LV via conventional echocardiography. A normal sinus rhythm and an LV ejection fraction of at least 55% were detected in all the patients. All the medications taken by the patients were discontinued for at least 48 hours before the study. The control group comprised 19 patients at a mean age of 31±13 years with no history of cardiovascular disease but with normal physical examination, ECG, and echocardiographic findings.

### Echocardiography

Imaging was performed in the left lateral decubitus position using a VIVID 3 echocardiography device. The diameters of the atria and ventricles were measured in the standard views using 2D and the M-mode method. The LV volumes were measured according to the disc summation method. The transmitral LV filling signal was assessed manually by using pulsed-wave Doppler (PWD) echocardiography at the tip of the mitral valve leaflets in the apical 4-chamber view, and the following variables were assessed: peak velocity of early (E) and late (A) filling, E-wave deceleration time (DT), and the E/A ratio.

The gradient of the LVOT was assessed using continuous wave Doppler interrogation in the region below the aortic valve and by the assessment of the Doppler velocity profile, LVOT obstruction at rest was considered a gradient of equal to or greater than 30 mm Hg.

The IVRT is the interval between the closure of the aortic valve and the start of ventricle filling following mitral valve opening. To assess the IVRT in the 4-chamber view, the operator should turn the probe anteriorly so that the aortic valve and the outflow tract are in clear view. During PWD, the sample volume is placed between the aortic and mitral valves so that the aortic and mitral valve signals can be clearly assessed. Thereafter, the filtering gain of the images is adjusted and the IVRT is measured (Fig. 1).

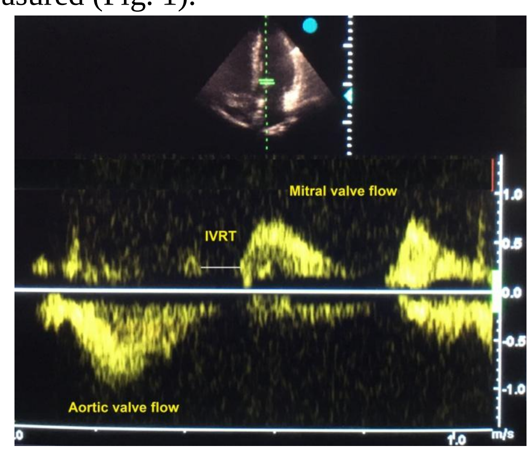


**Figure 1.** Pulsed-wave Doppler for the evaluation of the isovolumic relaxation time (IVRT)

## RESULTS

Of all the patients, 25 (72%) reported dyspnea, 27 (78%) palpitation, and 17 (48%) chest pain. Two patients reported a history of at least 1 episode of syncope. The demographic details and the physical examination data of both HCM and normal groups are shown in Table 1.

### Echocardiographic results for the patients with HCM and the control group

The IVRT increased more significantly in the patients with HCM than in the control group (*P*<0.01) and in the patients with LVOT gradients. The IVRT had a more significant rise in the patients with no LVOT obstruction than in the patients with LVOT gradients (97±38 vs 82±29; *P*<0.001). Moreover, the early diastolic flow velocity (E wave) was significantly lower and the late diastolic flow velocity (A wave) was higher in the patients without LVOT gradients (*P*<0.01 and *P*<0.05, respectively). The demographic details, clinical symptoms, and echocardiographic data in the 2 groups of patients, with and without LVOT gradients at rest, are shown in Table 2. The mean septal thickness was 24±7 mm in the patients with HCM, and increased septal thickness was significant in the patients who received implantable cardioverter defibrillators (*P*<0.05). The echocardiographic characteristics of the case and control groups are illustrated in Table 3.

**Table 1.** Demographic and physical examination data of both HCM and normal groups

| Characteristic/ Variable | HCM (n= 35) | Control (n = 19) |
|---|---|---|
| Age, y | 31±16 | 32±13 |
| Gender (male) | 57% | 58% |
| BMI, kg/m$^2$ | 23.6 | 23.2 |
| Dyspnea | 72% | - |
| Palpitation | 78% | - |
| Chest pain | 48% | - |

HCM, Hypertrophic cardiomyopathy; BMI, Body mass index

**Table 2.** Demographic and physical examination data and the IVRT of the patients with and without LVOT obstruction

| Characteristic/ Variable | LVOT Gradient ≥ 30 mm Hg (n= 11) | LVOT Gradient < 30 mm Hg (n = 24) | *P* value |
|---|---|---|---|
| Age, y | 30±14 | 32±17 | <0.001 |
| Gender (male) | 54.5% | 58.3% | |
| BMI, kg/m$^2$ | 23.9 | 23.3 | |
| Dyspnea | 69% | 75% | |
| Palpitation | 75% | 79% | |
| Chest pain | 54.5% | 58% | |
| IVRT | 82±29 | 97±38 | |

IVRT, Isovolumic relaxation time; LVOT, Left ventricular outflow tract; BMI, Body mass index

**Table 3.** Conventional echocardiographic parameters in the normal subjects and those with HCM

| | | Patients with HCM | | | | |
|---|---|---|---|---|---|---|
| Characteristic/ Variable | Control (n=19) | HCM (n=24) | *P* value | ICD + (n=6) | ICD – (n=18) | *P* value |
| LVEF, % | 60±5 | 60±10 | | 60±10 | 60±10 | |
| LVEDVI | 70±8 | 63±17 | | 53±15 | 65±12 | |
| Septal thickness, mm | 9±1 | 24±7 | | 27±8 | 21±6 | <0.05 |
| LA area, cm$^2$ | 17±3 | 19±5 | | 18±3 | 19±4 | |
| E/A ratio | - | 0.8±0.3 | | 0.8±0.3 | 0.8±0.3 | |
| DT, ms | - | 229±56 | | 215±49 | 235±59 | |
| IVRT, ms | 55±20 | 82±29 | <0.01 | 103±40 | 90±35 | |
| LVOT gradient, mm Hg | 0 | 15±5 | | 17±7 | 13±7 | |
| SAM, mm | 0 | 6 | | 1 | 5 | |

HCM, Hypertrophic cardiomyopathy; LVEF, Left ventricular ejection fraction; LVEDVI, Left ventricular end-diastolic volume index; LA, Left area; DT, Declaration time; IVRT, Isovolumic relaxation time; LVOT, Left ventricular outflow tract; SAM, Systolic anterior motion; ICD, Implantable cardioverter defibrillator

## DISCUSSION

HCM is a complex genetic disorder and a major cause of disability and mortality in all age groups. This disease has a medallion autosomal dominate trait. [5] Diastolic dysfunction of the hypertrophied LV is an important presentation of hypertrophic cardiomyopathy, and it causes clinical symptoms in patients. [7,9]

The present study aimed to investigate diastolic dysfunction in the LV using the IVRT in patients with HCM. Clinically, HCM is LV hypertrophy in the absence of hypertension and valve diseases. HCM with no cardiovascular causes occurs in almost 1:500 people in the general population.

Almost 25% of patients with HCM have a significant gradient of at least 30 mm Hg in the LVOT at rest. [5,6] In a study conducted by Betocchi et al [10] on 44 patients with HCM, the LV end-diastolic pressure and the left atrial end-diastolic pressure had significantly increased compared to those in the control group and the LV ejection fraction was higher in the patients with HCM, while the peak filling rate was the same in both groups. The authors also reported that the IVRT had a significant rise in HCM. In addition, diastolic dysfunction was observed in 82% of their patients with HCM, and passive diastolic function was impaired in 55%. Another interesting point in that study was that the IVRT was the same in both groups with and without LVOT obstruction, while in the patients with high LVOT gradients, the peak systolic pressure was higher. In fact, isovolumic relaxation disorder occurs due to such different reasons as subendocardial ischemia, changes in ventricular loading, [10] and an increase in the cytosolic calcium level. [11]

In the present study, the IVRT was higher in the patients with HCM, which agrees with the results obtained by Betocchi and colleagues; nonetheless, the IVRT was lower in the patients with LVOT obstruction than in those without LVOT gradients in our study.

In a study by Spirito et al, [3] impaired LV filling was demonstrated in HCM, but the important point was that not only patients with diffuse hypertrophy but also those with mild segmental LV hypertrophy had a regional diastolic abnormality. In fact, the cardiomyopathy process in these patients suggests that the filling disorder is not limited to the wall thickness, but there is abnormality in the myocardial tissue.

A study by Kato et al [8] on 36 patients with non-obstructive HCM showed that the peak negative mitral valve gradient provided important information about active relaxation and passive stiffness and could be an index for the follow-up of patients with increased ventricular mass in echocardiography. The authors also showed that reduced mass in LV hypertrophy led to a reduction in cardiac complications. In a study by Matsumura et al [12] on patients with HCM, the early diastolic mitral annular velocity (E') as assessed by tissue Doppler imaging exhibited a clear reduction and the E/E' ratio correlated with the New York Heart Association's function class and exercise capacity of the patients.

The importance of diastolic dysfunction in patients with HCM has highlighted the importance of using noninvasive methods such as echocardiography to assess the presence and severity of the diastolic function in this group of patients. [2,13]

Guodong et al, [14] investigating the early diastolic mitral annular velocity during exercise to identify the diastolic dysfunction in patients with HCM and normal ejection fractions, showed that a higher E/E' worsened the patients' prognosis and that after cardiopulmonary exercise testing, tissue Doppler imaging was an appropriate method for predicting exercise capacity in patients with HCM. There are various less dependent preload methods for demonstrating diastolic disorders in HCM, including early flow propagation velocity and early diastolic annular velocity, which can assist in estimating the ventricular filling pressure. [15-17]

## CONCLUSIONS

Previous studies have demonstrated diastolic dysfunction and increased LV end-diastolic pressure in HCM in different ways and through various echocardiographic techniques. Abnormalities in the IVRT can be deemed an indicator of LV diastolic dysfunction.

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