

## Original Article

# *Relationship between Syncope and Sudden Cardiac Death in Patients with Hypertrophic Cardiomyopathy and Left Ventricular Mass Index Calculated by Magnetic Resonant Imaging*

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### Abstract

**Study background and objective:** Hypertrophic cardiomyopathy (HCM) is the most common genetic cardiovascular disorder and is estimated to have affected one out of every 500 people. The symptoms of HCM can be diagnosed from early childhood and include dyspnea on exertion, chest pain, pre-syncope, and syncope resulting from the left ventricular (LV) outflow tract obstruction, LV systolic and diastolic dysfunction, and ventricular and supraventricular arrhythmia.

**Material and methods:** We assessed the effect of the LV mass index on syncope and sudden death in 60 HCM patients who were more than 16 years of age and referred to Rajaie Cardiovascular, Medical and Research Center between 2009 and 2012. The patients were studied using magnetic resonance imaging.

**Findings:** The study results indicated that the patients were on average  $45.53 \pm 16.85$  years old. The *t*-test showed that gender exerted no influence on the following variables: palpitations; family history; maximum thickness of the LV wall; sudden death; and syncope. In contrast, the age variable had a meaningful effect on the maximum thickness of the LV wall, LV mass, and LV mass index. There was no significant relationship between the LV mass index and sudden cardiac death.

**Conclusions:** Our results were indicative of a negative and significant relationship between age and all of the aforementioned variables. Also, there was no significant relationship between the LV mass index and sudden cardiac death. (*Iranian Heart Journal 2015; 16 (1):12-19*)

**Keywords:** ■ LV mass index; ■ Syncope; ■ Sudden cardiac death; ■ Cardiomyopathy, Hypertrophic; ■ Magnetic Resonance Imaging

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Nowadays, cardiovascular diseases are so prevalent that defining a clear distinction of their boundaries is unlikely. In this respect, hypertrophic cardiomyopathy (HCM) has been pinpointed as a crucial problem and it is regarded as one of the sudden death causes around the world. HCM is a complicated cardiac condition, and 250 people in every 100000 are diagnosed with this disease. It is accompanied with symptoms such as an increase in the heart muscle thickness, left ventricle (LV) stiffness, mitral valve variations, and heart cell variations. HCM can occur at any age.<sup>10</sup> Studies have shown that abnormal genes make individuals prone to HCM. Indeed, most of the individuals involved are found to have a family history of the disease.<sup>29</sup> The increase in the thickness of the heart muscle generally takes place in the interventricular septum immediately beneath the aortic valve, which may cause a closure or a reduction in the blood flow from the LV to the aorta. In this case, the ventricles should contract more intensely in order to deliver blood. HCM also can cause the thickening of the other parts of the heart muscle such as the apex, right ventricle (RV), and the entire LV.<sup>9</sup> In HCM the order and the organization of the heart muscle cells are disarranged, and this will eventually result in cardiac arrhythmias. Many of the individuals with this disease tend to live a normal life and they do not display any signs and symptoms or are partially symptomatic. Nonetheless, in those whose heart performance becomes disrupted, the symptoms are predominant. These signs can emerge at any age, with syncope and sudden cardiac death (SCD) accounting for the most serious of them.<sup>28</sup> Therefore, an appropriate treatment requires a direct determination of the risk factors leading certain patients with HCM to SCD. When accompanied by tachycardia or ventricular arrhythmia, HCM can lead to SCD substantively. High-risk patients will benefit from an implantable cardioverter-defibrillator. Unaccounted sudden death can be the first clinical emergence of

HCM. A significant indicator of the clinical emergence and expression of HCM is LV hypertrophy, but the relationship between the LV volume and the occurrence of the SCD has not been clearly identified. Most of the patients (about 60%) suffer sudden death when they are sedentary or doing low-intensity activities; nevertheless, around 40% of them die while doing intense physical activities or post-activity.

In the present study, we sought to measure the LV mass index in HCM patients via magnetic resonance imaging (MRI) and to assess the amount of the LV mass index in HCM patients with syncope or sudden death with a view to offering suggestions and recommendations based on the findings for the prevention of syncope and sudden death due to HCM.

### Materials and Methods

This retrospective research was performed to obtain data on individuals through medical history and questionnaires. Since the studied samples were patients diagnosed with HCM and that the measurement of the LV mass index was done using MRI, Rajaie Cardiovascular, Medical and Research Center was chosen as the study environment after consultations with the professors and experts of the center. This research-educational center boasts decades of first-rate services under the aegis of Iran University of Medical Sciences and is widely regarded as a center of excellence in the realm of cardiovascular diseases. As regards research, this center methodically registers all its patients' data and provides the necessary environment for researchers to have access to patients referring for treatment or follow-up.

The study sample included adult men and women above the age of 16 referring to Rajaie Cardiovascular, Medical and Research Center. All the patients included were diagnosed with HCM and fulfilled the study inclusion criteria. The inclusion criteria comprised having a family history of sudden

death, being young but having experienced frequent syncope incidents, experiencing an abnormal and unusual increase in the blood pressure in response to physical activity, having been diagnosed with a rapid heart rate accompanied by arrhythmia, and having intensive heart symptoms in tandem with the weak performance of the heart. The patients who did not consent to continue the study at any stage were excluded from the present study.

For the survey of the LV mass index via MRI, the following indices were assessed:

maximal LV wall thickness; maximal LV thickness  $\geq 30$  mm; LV mass (g); LV mass index ( $\text{g}/\text{m}^2$ ); LV end-diastolic volume (ml); LV end-diastolic volume index ( $\text{ml}/\text{m}^2$ ); LV end-systolic volume (ml); LV end-systolic volume index ( $\text{ml}/\text{m}^2$ ); ejection fraction (%); LV mass/volume ratio; and post-contrast delayed enhancement.

The minimum age of the study cohort was 16 years, and the percentage of the patients with any of the variables and their relations with the sudden death and syncope were obtained. The information in the current study was collected through a retrospective study as well as the analysis of the patients' files and MRI results. The studied variables in the current study include quantitative continual independent and dependent variables and demographic characteristics. The statistical analyses to determine any relationship and the degree of the relationship between the variables were conducted using the SPSS software.

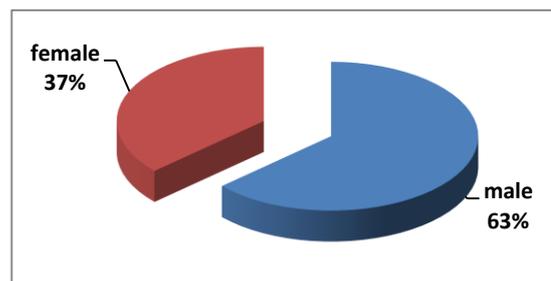
Traditionally, the diagnosis of HCM was dependent on clinical examinations and transthoracic echocardiography along with the determination of such characteristics as the LV hypertrophy, systolic anterior movement of the mitral valve (SAM), and the LV outflow tract obstruction. In a large number of clinical states, echocardiographic technical limitations and incongruent phenotypic expression render such evaluation difficult. Accordingly, the introduction of cardiovascular magnetic

resonance (CMR) has been heralded as a useful supplement to transthoracic echocardiography.<sup>8</sup> Indeed, CMR per se is deemed a unique resolution potential possessing a limitless capacity for imaging with high spatial and temporal resolution.<sup>7,1</sup>

The patients' MRI was reported by cardiology and radiology experts, unaware of the study methodology and samples. All the study indices were extracted similar to this method. There were some limitations in the implementation of this study insofar as some patients were fearful of undergoing MRI, some failed to give consent, and some had metal implants.

### Findings

At the inception of the research, the study subjects were surveyed. Generally, the study population consisted of 60 HCM patients, including 22 females with a frequency percentage of 36% and 38 males with a frequency percentage of 63.3%. The frequency results of the study subjects are as follows:



**Figure 1.** Frequency percentage of the study subjects in the two groups based on gender

The study subjects were divided into three groups based on their age: the patients 16-30 years of age (young); those 30-60 years of age (middle-aged); and the ones above 60 years of age (old). The results showed that 21.7% of the subjects were in the young group, 58.3% in the middle-aged group, and 20% in the old group. The frequency percentage of the individuals with HCM in the middle-aged group was higher than that in the other groups. The results are illustrated in Table 1.

**Table 1.** Frequency percentage of the study groups based on age

Age	Frequency	Percentage	Validity Percentage	Cumulative Percentage
12-30	13	21.7	21.7	21.7
30-60	35	58.3	58.3	80
60<	12	20	20	100
Total	60	100	100	

The results showed that the study subjects had a mean age of 45.53±2.17 years, body surface area mean of 1.78m<sup>2</sup>±0.29, LV mass mean of 187.41±94.18 gr, LV mass index mean of 105.10±62.21 gr/m<sup>2</sup>, LV end-diastolic volume of 126.55±39.86 ml, LV end-diastolic volume

index mean of 71.41±22.85 ml/m<sup>2</sup>, LV end-systolic volume of 52.29±33.86 ml, LV end-systolic volume index mean of 29.59±20.90 ml/m<sup>2</sup>, and LV wall thickness mean of 20.83±7.11 mm. Table 2 depicts the results.

**Table 2.** Mean of the study variables

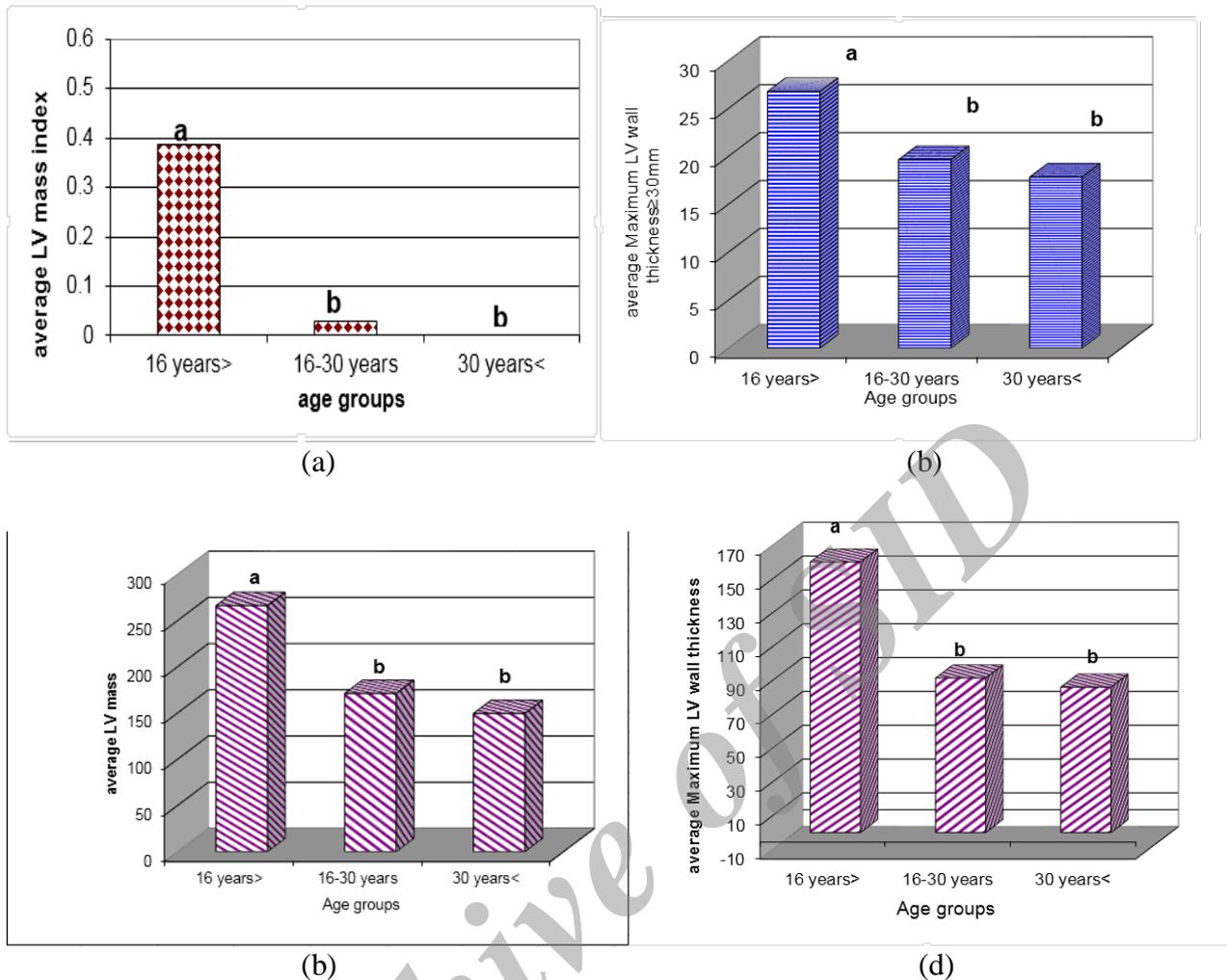
Variable	Mean/SD	
Age	45.53 ± 2.17	
Gender	Male	22
	Female	38
BSA	1.78 ± 0.29	
LVM	187.41 ± 94.18 g	
LVMI	105.10 ± 62.21 gr/m <sup>2</sup>	
LV end-diastolic volume	126.55 ± 39.86 cc	
LV end-diastolic volume index	71.42 ± 22.85 cc/m <sup>2</sup>	
LV end-systolic volume	52.29 ± 33.86 cc	
LV end-systolic volume index	29.59 ± 20.90 cc/m <sup>2</sup>	
LV wall thickness	20.83 ± 7.11 mm	
EF	58.65 ± 15.98 %	

BSA, Body surface area; LV, Left ventricle; LVM, Left ventricular mass; LVMI, Left ventricular mass index; EF, Ejection fraction

To compare the means of the study data, the Duncan test was employed in the present study. The results of the comparisons of the means of maximum LV thickness, maximum LV thickness >30 mm, LV mass, and LV mass index between the three age groups demonstrated significant differences. The most pronounced difference was between the young age group (16-30) on the one hand and the other two groups, i.e. the middle-aged (30-60) and old (>60) groups. In other words, the older HCM individuals grow, the lesser their maximum LV thickness, maximum LV

thickness > 30 mm, LV mass, and the LV mass index will become. The results obtained from the Duncan test are depicted in Figure 2.

The intervariable relationships were surveyed in the present study. The relationships between the study variables and sudden death were surveyed using the regression analysis (Table 3). The results obtained are suggestive of the absence of any relationship between sudden death and the study variables.



**Figure 2.** Results of the comparisons of the means of the study variables between the age groups via the Duncan test

**Table 3:** Results obtained from the variable correlations

Variable	B	P Value	95% C.I. for EXP(B)	
			Lower	Upper
Family history	-0.80	0.28	0.05	2.41
Palpitation	0.46	0.70	0.15	16.17
Syncope	1.23	0.26	0.40	29.73
Maximum LV wall thickness	-4.99	0.13	·	4.55
PCDE	-0.04	0.97	0.08	11.93
Maximum LV wall thickness $\geq$	0.16	0.15	0.94	1.46
LVM	0.01	0.68	0.96	1.03
LVMI	0.02	0.44	0.97	1.08
Constant	-5.99	0.14		

LV, Left ventricle; LVM, Left ventricular mass; LVMI, Left ventricular mass index;  
PCDE, Post contrast enhancement

## Discussions and Conclusions

Our results showed no significant relationship between sudden death and syncope. Previous research has revealed that the majority of HCM patients who die abruptly are

asymptomatic (or they exhibit few symptoms) and that most of them are anonymous and undiagnosed from a clinical point of view.<sup>4</sup> A major global health concern, SCD may happen in an instant with a heart sign or without any signs and symptoms due to

sudden cardiac dysfunction (heart arrest). Patients with unjustifiable syncope exhibit greater risk for sudden death than patients without syncope; however, older patients with controllable syncope attacks show no higher risk.<sup>3</sup>

The LV hypertrophy seems to be a crucial indicator of the clinical expressions of HCM, but the relationship between the LV volume and sudden cardiovascular death has yet to be fully elucidated. The LV mass is of vital importance in the management of HCM as well as systematic hypertrophy and other diseases.<sup>5</sup> In the present study, therefore, the LV mass index was surveyed and the results indicated no significant relationship between the LV mass index and sudden death and syncope. Previous studies have reported that the post-mortem examination of HCM patients having died suddenly shows a significant increase in the LV mass and thickness.<sup>25, 11, 24,30</sup> In such studies on HCM patients, the LV wall thickness shows a significant increase and the likelihood of the progression of hypertrophy to SCD in eight times that in control groups.<sup>28</sup> On the other hand, even a weak degree of hypertrophy is not free of sudden death risk:<sup>27, 23</sup> HCM patients without LV thickening are also prone to SCD.<sup>13, 14, 17</sup> Be that as it may, the relationship between the development of hypertrophy and being prone to sudden death is perhaps statistical.

Generally speaking, the individuals' age, followed by maximum LV thickness > 30 mm, had the greatest relationship with SCD. In the Emad et al. study (2010), there were no clear and well-determined cases in the entire study.

In SCD, the victim's medications and presence of non-sustained ventricular tachycardia in Holter monitoring can play a role. Consequently, one of the drawbacks of the current study can be the lack of the evaluation of the aforementioned conditions. We would, therefore, recommend that in HCM patients, all the prognostic and predictive factors of SCD along with CMR

findings be evaluated in a more complete research.

Given that gender plays a significant role in the clinical expression, prognosis, and intensity of cardiovascular diseases, it was included as a variable in the present study. Our results showed no significant relationship between the two genders in terms of variables such as palpitation, familial history, SCD, and syncope. In contrast, there are studies in the existing literature reporting a correlation between female gender and the rate of recovery or exacerbation of the disease.<sup>20, 21</sup>

Our results illustrated that an increase in age was allied to a decrease in the LV wall thickness, LV mass, and LV mass index. It has been previously reported that HCM is the most common genetic condition of the heart and that it is strongly related to SCD in young individuals.<sup>4</sup> Furthermore, HCM is a common cause of SCD in young individuals involved in competitive sports. Although adults below the age of 35 tend to show a higher prevalence of SCD, it has not been indicated that the other age groups are free from risk. SCD can happen in any type of activity, be it during sleep or during severe sporting activities. It is one of the most common genetic cardiovascular diseases correlating with sudden death in the young.<sup>12,</sup>

<sup>16</sup> A large number of studies have shown that SCD and HCM are common in children and young adults in the age range between 12 and 35 years<sup>1,22,9,8,6,26,27,15</sup> and that it can occur in elderly people even those who do not exhibit any signs or symptoms.<sup>27</sup> In addition, HCM is one of the most common causes of SCD in the young.<sup>18,19</sup> Most of the individuals with HCM do not exhibit any signs and their first expression can be SCD.<sup>7-2</sup>

The results obtained in the present study showed that a familial history of palpitation was of no relationship with the other parameters evaluated. In this regard, recent research has demonstrated that a familial history of SCD, albeit a non-independent factor, can predispose the individual to SCD.<sup>3</sup>

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