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First-degree atrioventricular block in hypertrophic cardiomyopathy patients: an easy and worthy prognostic marker?

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Abstract

Hypertrophic cardiomyopathy (HCM) is the most common inherited cardiac disease. Recently, a connection has been observed between the presence of first-degree atrioventricular block (FDAVB) and cardiovascular outcomes, although the pathophysiology of this association remains poorly understood. Considering the period 2000-2023, we retrospectively included HCM patients at sinus rhythm at the first appointment and sought possible interactions of FDAVB (defined as PR interval >200 ms) with different clinical and imaging variables and with the occurrence of cardiovascular events, including atrial fibrillation (AF). A total of 97 patients were included, of whom 57 (58.8%) were men, with a mean age of 51±19 years, and 14 (14.4%) had FDAVB. During a median of 4.29 (P25 1.92, P75 7.67) years of follow-up, 35 cardiovascular events occurred, including 13 *de novo* diagnoses of AF, 8 hospitalizations due to heart failure, 8 new-onset strokes, 4 myocardial infarctions, and 2 implantations of cardio defibrillators in secondary prevention; no HCM-related death occurred. We did not find any association between outcomes and the presence of FDAVB. The role of FDAVB as a prognostic marker in HCM patients requires further investigation. We found that FDAVB patients were older, more frequently reported dyspnea, had a larger QRS duration, a higher E/e' ratio, and lower maximal left ventricle wall thickness by magnetic resonance (p<0.05). After multivariable analysis, FDAVB was independently associated with a higher echocardiographic E/e' ratio (p=0.039) (odds ratio=1.588). This is the first paper to document an independent association between FGAVB and a higher E/e' ratio in HCM patients.

Key words: hypertrophic cardiomyopathy, first degree atrioventricular block, atrial fibrillation, outcomes, E/e' ratio.

Introduction

Hypertrophic cardiomyopathy (HCM) is the most common monozygotic inherited cardiomyopathy, affecting 1:500 to 1:200 of the general population, mainly associated with autosomal dominant mutations in proteins of the contractile myofilaments of cardiac sarcomere and Z-disc. The pathophysiology of HCM is complex, involving morphofunctional alterations in cardiomyocytes and intercellular junctions, microvascular coronary disease, silent myocardial ischemia and systemic inflammation, ultimately resulting in myocardial hypertrophy and fibrosis. These alterations collectively contribute to an elevated risk of arrhythmic events and diastolic dysfunction in HCM patients [1-5].

Atrial fibrillation (AF) emerges as the most common arrhythmia in HCM patients, with a

multifactorial etiology. Fibrosis-related reentry circuits play a significant role, along with left atrial (LA) hypertrophy and dilation due to high left ventricle (LV) filling pressure, diminished ventricular relaxation, mitral regurgitation, and outflow tract obstruction. AF is associated with major cardiovascular events, including higher mortality, among HCM patients [6-9].

The clinical expression of HCM is highly heterogeneous, spanning from an asymptomatic state or a benign course to severe cardiovascular events such as advanced heart failure and sudden cardiac death. Stratifying the risk of life-threatening events and guiding the management of HCM accordingly remains a challenge [3,10,11].

Traditionally considered as benign and lacking prognostic relevance for cardiovascular events, first-degree atrioventricular block (FDAVB), defined as the prolongation of the PR interval exceeding 200 milliseconds (ms), has recently been recognized in numerous studies as a significant predictor of future adverse cardiac outcomes in diverse populations, both in healthy individuals and those with different cardiac diseases [12-21].

Recently, Higuchi et al were the first to document in a cohort of HCM patients an association of FDAVB with a higher prevalence of HCM-related death, AF and heart failure hospitalizations. However, the understanding of how FDAVB can predict adverse cardiovascular events remains limited. [22].

In this study, our objective was to further explore the associations of FDAVB with clinical and imaging characteristics and focusing on outcomes, particularly the development of AF, in a HCM patient cohort.

Materials and Methods

Study design

This retrospective cohort study involved an initial population of 108 patients with hypertrophic cardiomyopathy (HCM) monitored at the Myocardiopathy Consultation of the Cardiology Department at Centro Hospitalar e Universitário São João in Oporto, Portugal, spanning from April 2000 to January 2023. Patients were included based on a diagnosis of HCM, established by evidence of non-dilated left ventricle hypertrophy with a wall thickness 15 mm in transthoracic echocardiogram, in the absence of any other cardiac or systemic conditions justifying loading conditions [10,11].

From the initial sample of 108 patients, 11 were excluded due to the presence of atrial fibrillation (AF) at the time of the first appointment electrocardiogram (ECG). One patient had a missing value for the PR interval and was only included in the descriptive statistics. Patients were categorized based on the presence of first-degree atrioventricular block (FDAVB).

Data information

We collected clinical, 12-lead electrocardiogram (ECG), Holter ECG monitoring, transthoracic echocardiogram (TTE) and Magnetic Resonance Imaging (MRI) data, from the informatics system.

The initial evaluation encompassed the first clinical assessment, during which an ECG was performed. Data related to TTE, MRI, and Holter monitoring were extracted from the respective exams conducted closest to the date of the initial consultation. Outcomes were assessed from the first appointment until January 2023.

Relevant electrocardiogram and echocardiographic definitions

The duration of intervals on the ECG was automatically determined at acquisition and then manually confirmed. We utilized the ECG from the first appointment date to diagnose the presence of first-degree atrioventricular block (FDAVB) in our population, defining FDAVB as a PR interval greater than (>) 200 ms.

The echocardiographic ratio of the E peak velocity to the average E´ peak velocity, employing Tissue Doppler imaging, was calculated using the mean values of both e´ at the septal and lateral sides of the mitral annulus

Outcomes definitions

In our study, we considered as outcomes: cardiovascular death (including sudden cardiac death (SCD), heart failure-related death and stroke-related death), implantable cardioverter-defibrillator (ICD) placement for secondary prevention of SCD, ventricular appropriate ICD shocks, *de novo* AF, hospitalization due to heart failure, myocardial infarction and new onset stroke.

Statistical analysis

Categorical variables were presented as absolute frequencies (n) and relative frequencies (%). Mean with standard deviation or median with percentiles (P) 25 and 75 were used for continuous variables, accordingly to their distribution.

When testing a hypothesis about continuous variables, parametric Independent Samples t-test or nonparametric test Mann-Whitney were used as appropriate, taking into account normality assumptions and the number of groups compared. When testing a hypothesis about categorical variables a chi-square test and Fisher's exact test were used, as appropriate. In order to have a more thorough understanding of the factors associated with increased PR interval (dependent variable), bivariate and multivariate logistic regression modeling was used. Model goodness-of-fit was assessed using the Hosmer–Lemeshow statistic and discriminative power was

evaluated by receiver-operator curve (ROC) curve analysis. The significance lever used was 0.05. Statistical analysis was performed using the software Statistical Package for the Social Sciences v. 27.0.

Results

Baseline hypertrophic cardiomyopathy patients' characteristics

Ninety-seven HCM patients were included, consisting of 57 men (58.8%) with a mean age of 51±19 years. Forty-four patients (45.4%) had a family history of HCM and 41 (42,2%) had a positive genetic test with a mutation on MYBPC3, MYH7, TNNT2 or other genes in 13 (31,7%), 12 (29,3%), 9 (22.0%) and 7 (17.1%) patients, respectively. Additionally, 28 (28.9%) patients had a familiar history of sudden death.

The median PR duration at first visit was 160 (P25 – 145, P75 - 187) ms and 14 (14,4%) patients had FDAVB at the first evaluation. No patient had an implanted pacemaker. At TTE, 90 (92,7%) had normal left ventricle systolic function, while 5 (5,2%) and 2 (2,1%) had mild and moderate systolic dysfunction, respectively; all patients had normal right ventricle systolic function. Median E/e' ratio was 8,99 (P25 7,35 – P75 11,00) and median septal thickness was 16 (P25 – 13, P75 – 19) mm; basal or after Valsalva obstructive gradients were present in 7 (7,2%) patients. On MRI, 63 (64,9%) patients had presence of late gadolinium enhancement in at least one segment. On Holter monitoring, 6 (6,2%) patients showed episodes of non-sustained ventricular tachycardia, and 3 (3,1%) had paroxysmal atrial fibrillation.

Follow-up

During a median follow-up of 4,29 (P25 – 1.92, P75 – 7.67) years, two patients died from oncological causes; no cardiovascular death nor appropriate ICD shock were documented. A total of 35 cardiovascular events were recorded: 13 patients hadh *de novo* AF (3 diagnosis on Holter monitoring and 10 through ECG performed at a medical contact), 8 hospitalizations due to heart failure, 8 new onset strokes, 4 myocardial infarctions and 2 ICD implantations for secondary prevention.

Comparisons between patients with and without first-degree atrioventricular block

Among the fourteen patients with FDAVB, the majority were men (64.3%), with a median age of 67 years at the time of the first consultation. Clinical characteristics of FDAVB and non-FDAVB groups of patients are summarized in Table 1.

In bivariate analysis, significant differences were found in age at diagnosis (FDAVB patients were older, with median age of 67 vs 55 years old in the non-FDAB group, p=0.005), dyspnea (more frequent in the FDAVB group of patients - 28.6% vs 6.1% on the non-FDAVB group,

p=0.008), QRS duration (larger in the FDAVB group, with median 121 ms vs 99 ms in non-FDAVB group, p = 0.022), echocardiographic E/e` ratio (greater in the FDAVB group, with a median value of 11.vs 8.3 in non-FDAVB group, p = 0.039) and left ventricle maximal septal thickness (LVMWT) at MRI (greater in the FDAVB group, with a median of 16 mm vs 13 mm in non-FDAVB, p=0.011).

In multivariable logistic analysis, we found an association between a higher E/e` ratio and the presence of FDAVB, OR = 1.588, p = 0.041. No relation was stablished with other variables namely maximum LV wall thickness and QRS interval duration (Table 2).

No association was found between the presence of LGE and the E/e' ratio (median E/e'ratio of 6,4 in the LGE group and median 3,5 in the group with no LGE, p=0,456).

First-degree atrioventricular block and outcomes

We did not find any association between FDAVB and the occurrence of at least one outcome – 24 (29,2%) patients in the group of non-FDAVB vs 3 (21,4%) patients in the FDAVB had at least one event (p=0.751). The same was found for AF - in the group of non-FDAVB there were 12 (14.6%) de novo AF diagnosis, vs 1 (7.1%) in the FDAVB group (p=0.684) (Table 3). Dividing the patients accordingly to the development of AF during follow-up, there was no statistically difference regarding the PR interval - patients who had *de novo* AF had a median PR of 170 (P25 – 134, P75 – 180) ms and patients who did not had median PR of 160 (P25 – 91, P75 – 187), p=0.202.

Discussion

First-degree atrioventricular block and outcomes

In our cohort of HCM patients, no relation was found between the presence of FDAVB and the new onset of atrial fibrillation or other cardiovascular events during follow-up, contrarily to the findings of Higuchi et al. [22] The limited size of our population and the subsequent scarcity of events might have influenced the obtained results, potentially overlooking a possible association.

In the latter paper, the authors advanced two possible explanations for the documented association – 1) FDAVB leads to inappropriate atrioventricular coupling with pressure and volume overload, potentially contributing to the dilation of left atrium, which is a risk factor for atrial arrhythmogenesis and for sudden cardiac death [23-25]; 2) FDAVB might be a manifestation of advanced structural and electrical remodeling in a HCM heart, with higher risk of arrhythmia and death. The higher frequency of LA dilation in the FDAVB group substantiated the first hypothesis; the other alternative explanation was not as supported, as there was no difference of left ventricle dimensions, left ventricle ejection fraction, nor E/e'ratio

between FDAVB and non-FDAVB groups, and there was no data regarding fibrosis.

In our sample of patients, the duration of PR interval in FDAVB and non-FDAVB was similar compared to the one in the referred study, but contrary to it, no significant difference was found regarding LA dimensions and the presence of FDAVB. Whether this lack of association could elucidate why FDAVB failed to predict outcomes in our cohort of patients remains uncertain.

However, despite the substantial body of literature indicating FDAVB as a predictor of cardiovascular events across diverse populations (including healthy individuals of different ethnicities, patients with coronary disease, arrhythmogenic right ventricular cardiomyopathy, acute heart failure, among others) – [12-21], there are still neutral findings in some studies [26-27]. Indeed, even within an HCM population, a prior study by Claeys et al. examining ECG-derived risk factors for SCD, did not establish a link between FDAVB and SCD [28].

Additional research is essential to evaluate the potential link between the presence of FDAVB and outcomes in HCM patients.

First-degree atrioventricular block and hypertrophic cardiomyopathy findings

We found an association between the presence of FDAVB and age, which could merely represent the physiological process of age-related degeneration in the conduction system. An association of FDAVB and a larger QRS interval on ECG was also documented. In theory, both the aging degeneration and more advanced remodeling occur in the entireconduction system, including not only the AV node, but also the bundle branches. Delcrè SD et al showed that the severity of ECG abnormalities in HCM patients, involving a total of 9 criteria, including QRS duration, is directly related to the degree of phenotypic expression by CMR (both LV mass index and presence/extent of LGE) [29]. This association of FDAVB and larger QRS duration could be explained by a higher degree of remodeling and fibrosis of the electric system of the HCM patients. It is noteworthy that no differences were documented between the group with FDAVB and the group of patients with normal PR regarding cardiovascular medications, particularly beta-blockers.

Surprisingly, we documented that FDAVB patients had a lower LVMWT at MRI compared to non-FDAVB patients. While it is established that higher LVMWT is genotype dependent and an important variable for SCD score risk in HCM patients, there seems to be no consistent relationship with the presence of FDAVB – Higushi et al. [10,22,30]. Nonetheless, it is important to highlight the role of FDAVB as a red flag for hypertrophy phenocopies, as Fabry cardiomyopathy and amyloidosis [31]. One possible explanation for FDAVB and lower LVMWT is that more remodeled hearts could have a less hypertrophic and more fibrotic phenotype. Interestingly, although there was no difference of LGE presence in both groups,

identifying replacement fibrosis, we did not have data on interstitial fibrosis (through Myocardial T1 mapping) [32]. Additional investigation is needed on this topic.

First-degree atrioventricular block and E/e' ratio

The ratio between early diastolic transmitral flow (E) and mean early diastolic mitral annular velocity (e`), depicted as E/e`, is a well-established marker of left ventricular diastolic dysfunction, a parameter that correlates well with left ventricle end-diastolic pressure [33-34]. Impaired LV diastolic function is a major finding in HCM patients and is attributed to myocardial hypertrophy, myofibers disarray, and fibrosis; as well as sarcomeric contraction impairment and silent ischemia. A thickened and noncompliant LV results in under relaxation and abnormal diastolic filling, promoting LA remodeling and AF, both prognosis markers in HCM. [3,9,10].

Badran et al. discovered that the E/e' ratio is a significant predictor of all-cause mortality in HCM patients. Those with an E/e' > 13.5 exhibited the poorest cardiovascular outcomes, facing over twice the risk of events compared to individuals with an E/e' < 6.5 [35].

In our study, we found that HCM patients with FDAVB had a higher median E/e` ratio compared to those without FDAVB and, probably as consequence, more dyspnea. To the best of our knowledge, this is the first time that the association of FDAVB and E/e'ratio has been documented in a cohort of HCM patients, and it remained significant after adjustment to confounders QRS duration and LVMWT, markers of dyssynchrony and degree of morphological alterations. The crucial question is whether this association of FDAVB and higher E/e' solely reflects underlying advanced structural and electrical remodeling or if there could be a direct harmful impact of FDAVB on cardiac diastolic function.

Supporting the first hypothesis is the fact that FDAVB patients were older with larger QRS duration; on the other hand, we did not found differences considering the LA dimensions nor the presence of LGE between FDAVB and non-FDAVB patients. Accordingly to Adis et al, we observed no association between the presence of LGE and the E/e` ratio. Nevertheless, this observation might have overlooked interstitial fibrosis, a significant contributor to HCM pathophysiology [36].

With the abnormal delay of electric conduction within the atrioventricular node, FDAVB can alter the synchronization between atrial contraction and ventricular relaxation. This asynchrony can potentially result in inadequate ventricular filling since its atrial contribution becomes impaired, leading to diastolic dysfunction over time. In non-compliant HCM left ventricles, the contribution to ventricular filling through rapid diastolic filling phase is reduced while that from atrial systole is increased. Therefore, patients with HCM and FDAVB, may experience additionally compromised atrial kick, further exacerbating diastolic dysfunction,

and potentially explaining a lower E/e'ratio [37,38].

It is relevant to note that e` measurement can be attained by different methods and has inter-operator variability, with implications in different studies results. The E/e' ratio is also affected by some physiological factors such as age, gender and ethnicity [39].

Though the identified association between FDAVB and E/e'ratio in HCM patients may lack direct clinical implications, it does open the door to a new area of investigation worth exploring, as FDAVG obtained through a simple EKG may assist in detecting early stages of asymptomatic diastolic dysfunction.

Limitations

This is an observational retrospective single centre study, with its inherent limitations. It included a small number of patients, with a shorter follow-up time and fewer events, when compared with previous studies. It is worth noting that findings attained in echocardiogram, as the E/e` ratio, are operator dependent and those were different between patients, given the retrospective nature of the study. All these considerations must be considered when interpreting the obtained results. On the other hand, it is the first study about FDAVB in a cohort of Portuguese HCM patients, with collection of important clinical and multi-imaging data, and the first to document a relation between FDAVB and E/e'ratio.

Conclusions

In our HCM cohort of patients, FDAVB was independently associated with E/e' ratio, a surrogate of diastolic dysfunction. As so, it may help to identify HCM patients at pre-clinical phase, when subtle changes in LV filling appear.

Contrary to previous literature, no association was found with outcomes. FDAVB is a controversial parameter of worse prognosis in HCM patients. There are still few studies that analyzed this issue in HCM patients and should be a topic of further investigation in the future, with prospective large scale and multicenter studies.

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Table 1. Clinical characteristics and data from electrocardiogram, transthoracic echocardiogram, magnetic resonance imaging and 24h-Holter of first-degree atrioventricular block (FDAVB) group and non-FDAVB group.

	Non-FDAVB group (n=82)	FDAVB group (n=14)	P value
Age at the first consult, median (P25-P75)	55 (32-65)	67 (66-67)	**0.005[3]**
Gender - male, n (%):	48 (58.5%)	9 (64.3%)	0.686[1]
Symptoms, n (%)			
Tiredness	22 (26.8%)	6 (42.9%)	0.223[1]
Dyspnea	5 (6.1%)	4 (28.6%)	**0.008[1]**
Thoracic pain	17 (20.7%)	3 (21.4%)	>0.999[2]
Palpitations	14 (17.1%)	0 (0.0%)	0.211[2]
Syncope	6 (7.3%)	0 (0.0%)	0.588[2]
Family history of sudden death n (%)	23 (28.0%)	4 (28.6%)	0.889[2]
Family history of HCM n (%)	40 (48.8%)	3 (21.4%)	0.521[2]
Cardiovascular Risk Factors, n (%)			
Hypertension	32 (39.0%)	7 (50.0%)	0.440[1]
Dyslipidemia	35 (42.7%)	6 (42.9%)	0.990[1]
Diabetes Mellitus	12 (14.6%)	2 (14.3%)	>0.999[2]
Smoking habits	7 (8.5%)	2 (14.3%)	0.615[2]
Cardiovascular medication at first consult, n (%)			
ACE inhibitors or ARB	31 (38.3%)	5 (35.7%)	0.855[1]
Beta Blocker	49 (60.5%)	11 (78.6%)	0.195[1]
Calcium Channel Blocker	6 (7.4%)	3 (21.4%)	0.125[2]
Loop Diuretics	3 (3.7%)	1 (7.1%)	0.477[2]
Thiazidic Diuretics	16 (19.8%)	3 (21.4%)	>0.999[2]
Vitamin K antagonist	3 (3.7%)	1 (7.1%)	0.477[2]
Anticoagulant	2 (2.5%)	1 (7.1%)	0.384[2]
Aspirin	16 (19.8%)	4 (28.6%)	0.484[2]
Statin	33 (40.7%)	9 (64.3%)	0.101[1]
Oral antidiabetic	5 (6.2%)	1 (7.1%)	>0.999[2]
Eletrocardiogram at first consult			
Resting Heart Rate (bpm), median (P25-P75)	66 (58-75)	68 (60-75)	0.556[1]
PR duration (ms), median (P25-75)	157 (143-174)	222 (208-236)	**<0.001[3]**
QTc duration (ms), median (P25-P75)	427 (411-443)	431 (412-455)	0.449[3]
QRS duration (ms), median (P25-P75)	99 (90-118)	121 (100-141)	**0.022[3]**
Sokolow-Lyon Criteria for Left Ventricle hypertrophy (mm), median (P25-P75)	34 (25-44)	36 (31-44)	0.593[3]
Cornell Criteria for Left Ventricle hypertrophy (mm), median (P25-	25 (18-36)	29 (14-38)	0.839[3]

P75)			
Right Bundle Brunch Block, n(%)	22 (26.8%)	2 (14.3%)	0.506[1]
Left Bundle Brunch Block, n(%)	6 (7.3%)	1 (7.1%)	0.999[1]
Pathologic Q waves, n(%)	32 (39.0%)	4 (11.1%)	0.455[1]
Transthoracic Echocardiography closer to first consult			
Left Atrial diameter (mm), median (P25-P75)	39 (31-43)	37 (24-53)	0.619[3]
Index Left Atrial Volume, median (P25-P75)	44 (32-56)	46 (43-52)	0.585[3]
Diastolic Left Ventricule Diameter (mm), median (P25-P75)	47 (43-50)	47 (41-54)	0.718[3]
Septal thickness (mm), median (P25-P75)	16 (13-19)	16 (13-18)	0.734[3]
Posterior Wall thickness (mm), median (P25-75)	10 (9-12)	11 (10-12)	0.194
Left Ventricle Ejection Fraction (%), median (P25-P75)	65 (60-68)	62 (59-64)	0.094[3]
E/e` ratio, median (P25-P75)	8.3 (7.3-10.6)	11.0 (9.3-22.0)	**0.039[3]**
Cardiac Magnetic Resonance closer to first consult			
Index systolic volume of left ventricle (ml/m^2), median (P25-P75)	24 (20-30)	28 (18-35)	0.781[3]
Index diastolic volume of left ventricle (ml/m^2), median (P25-P75)	73 (60-86)	78 (58-85)	0.525[3]
Maximum Left Ventricular Thickness (mm), median (P25-P75)	19 (16-21)	16 (14-17)	**0.011[3]**
Left Ventricle Ejection Fraction (%), median (P25-P75)	67 (62-70)	62 (47-72)	0.397[3]
Right Ventricle Ejection Fraction (%), median (P25-P75)	69 (63-72)	68 (57-72)	0.788[3]
Presence of late gadolunium enhancement, any localization, n (%)	56 (68.2%)	8 (57.1%)	0.630[2]
Presence of early gadolunium enhancement, any localization, n (%)	1 (1.2%)	1 (7.1%)	0.242[2]
Holter closer to first consult			
Mean Heart rate (bpm), median (P25-P75)	70 (61-75)	63 (61-66)	0.136[3]
Paroxysmal atrial fibrillation	2 (2,4%)	1 (7,1%)	>0.999[2]
Non sustained ventricular tachycardia, n (%)	4 (4,4%)	2 (2,2%)	>0.999[2]

[1]Chi-Square Test; [2]Fisher exact test , [3]Mann Whitney U test; FDAVB, first-degree atrioventricular block; HCM, hypertrophic cardiomyopathy; bpm, beats per minute; ms, miliseconds; ACE, angiotensin converting enzyme; angiotensin receptor blockers.

Table 2. Logistic multivariable regression for first degree atrioventricular block.

	OR	95% CI		p value
Median E/e` ratio	1.588	1.020	2.473	0.041
QRS duration (ms)	1.079	0.964	1.208	0.186
Left Ventricular Maximum Wall Thickness (mm)	0.771	0.439	1.354	0.366

Hosmer-Lesmeshow p-value=0,966; AUC, 0,920 [0,813-1,000]

Table 3. Outcomes during the follow-up in patients with and without first-degree atrioventricular block.

Outcomes, n(%)	Patients without FDAVB (PR <= 200 ms) (n=82)	Patients with FDAVB (PR > 200 ms) (n=14)	p value
Cardiovascular Death	0 (0.0%)	0 (0.0%)	-
De novo Atrial Fibrillation	12 (14.6%)	1 (7.1%)	0.684[2]
New onset Stroke	7 (8.5%)	1 (7.1%)	>0.999[2]
Placement of ICD for secondary prevention	2 (2.4%)	0 (0.0%)	>0.999[2]
Hospitalization related to HCM	7 (8.5%)	1 (7.1%)	>0.999[2]
Myocardial Infarction	4 (4.6%)	0 (0.0%)	-
Patients with at least one of the following events (Stroke/ Atrial Arrhythmia/ Secondary ICD implantation/ Hospitalization related to Cardiovascular cause/ Myocardial Infarction)	24 (29.3%)	3 (21.4%)	0.751[2]

[1]Chi-Square Test; [2]Fisher exact test; ICD, implantable cardio-defibrillator, HCM, hypertrophic cardiomyopathy.