Ventricular Arrhythmias and Left Ventricular Hypertrophy in Hypertrophic Cardiomyopathy

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Abstract

Background: In hypertrophic cardiomyopathy (HCM), the degree of left ventricular hypertrophy (LVH) could influence the development of ventricular arrhythmias.

Objective: In HCM, analyze the association between the occurrence of ventricular arrhythmias on Holter electrocardiogram (Holter ECG) and the degree of LVH determined by maximum wall thickness (MWT) and mass index (MI) on echocardiography.

Methods: Fifty-four consecutive patients with HCM underwent 24-hour Holter ECG and echocardiography for assessment of degree of LVH through MWT and MI. Two levels were established for the occurrence of ventricular arrhythmias: I - isolated or paired extrasystoles and II – non- sustained ventricular tachycardia (NSVT).

Results: In 13 patients (24%) with NSVT (level II), there was a higher frequency of left ventricular (LV) MWT ≥ 21 mm (n = 10, 77%, 25 ± 4 mm) and LVMI≥144g/m² (n = 10, 77%, 200 ± 30 g/m²), in comparison with those presenting with only extrasystoles (level I) (n = 41, 76%), in which these measures were identified in, respectively, 37 % (n = 15, 23 ± 1 mm), p = 0.023, and 39% (n = 16, 192 ± 53 g / m²) of the cases p = 0.026. The cut-off values mentioned were determined by the ROC curve with a 95% confidence interval. NSVT was more common in patients with LVMWT ≥ 21 mm and LVMI ≥ 144 g/m² (8 of 13, 62%) than in those with one (4 of 13, 31%) or none (1 of 13; 8%) echocardiographic variables above cut-off values (p = 0.04).

Conclusion: In HCM, the occurrence of ventricular arrhythmias on Holter-ECG was associated with the degree of LVH assessed by echocardiography through MWT and MI (Arq Bras Cardiol. 2013; 100(5):452-459).

Keywords: Arrhythmias, Cardiac; Hypertrophy, Left Ventricular; Cardiomyopathy, Hypertrophic.

Introduction

Hypertrophic cardiomyopathy (HCM) is a complex genetic disease, the diagnosis of which is based on the identification of left ventricular hypertrophy (LVH) demonstrated in the absence of chamber dilatation and any other condition that can cause an abnormality of a similar degree[1]. In young people under 25 years of age and athletes, it is the main cause of sudden death, produced by ventricular fibrillation that may or may not be preceded by ventricular tachycardia[2-4]. A characteristic histopathological pattern represented by hypertrophy and cellular disarray, coupled with fibrosis, predisposes victims to the onset of ventricular arrhythmias, which express the abnormal electrophysiological conduction and the electric instability of the myocardium[5-7].

Recording of non-sustained ventricular tachycardia on Holter electrocardiogram-(Holter ECG) and massive LVH with a maximum wall thickness $\geq$ 30 mm are considered predictors of sudden death in this disease[4,8-11]. Studies based on necropsy or in explanted HCM hearts identify a direct relation between the degree of fibrosis and the left ventricular maximum wall thickness[12,13]. Areas of fibrosis, detected in the form of late enhancement by magnetic resonance imaging with gadolinium, relate to the risk of ventricular arrhythmias and, probably, to sudden death[14-19]. However, it has not yet been clearly shown if the increase in the left ventricular wall thickness favors the occurrence of ventricular arrhythmias[14,20-22]. The objective of this study is to analyze the association between the degree of LVH, determined by echocardiogram, and the occurrence of ventricular arrhythmias on 24-hour Holter ECG in a non-referred outpatient HCM cohort.

Methods

Patient selection

Fifty-four consecutive patients were selected from an non-referred cohort registered at the HCM Outpatient Clinic of the Cardiology Service of the Hospital de Clinicas de Porto Alegre, UFRGS, between March 2007 and December 2011.

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The HCM diagnosis was established based on the clinical condition and on the echocardiographic identification of asymmetrical LVH with maximum wall thickness ≥ 15 mm in any segment and septum/posterior wall ratio of > 1.3 in the absence of dilatation of the chamber and another cause. Exclusion criteria included the following: LV concentric hypertrophy, other forms of cardiomyopathy, coronary artery disease, and/or valvular and congenital heart disease. Patients underwent a preliminary clinical and electrocardiographic evaluation, followed by resting echocardiography and 24-hour Holter ECG performed close in time. The echocardiogram was recorded by a single examiner. The results of the Holter ECG were evaluated blindly, without prior knowledge of the diagnosis. The use or not of cardioactive medication was considered in the analysis. This study was approved by the local Research Ethics Committee. All patients signed an informed consent form.

Echocardiography

M-mode and two-dimensional transthoracic echocardiography with pulsed and continuous color Doppler was performed at rest to evaluate the structure and function of the heart chambers, including spectral flow analysis according to current recommendations[23]. The evaluations were performed with Vivid 7 General Electric equipment (GE Healthcare, Milwaukee, WI, USA). The images obtained included parasternal long and short axis views and apical two, three, four and five chamber views with multifrequency transducers of 2.5 to 3.5 MHz, performed in a standardized manner with the patient in the left lateral supine position. The following measures were considered: left atrial diameter, left ventricular end diastolic diameter, left ventricular end systolic diameter, end diastolic thickness of the interventricular septum, end diastolic thickness of the posterior wall of the left ventricular, left ventricular mass indexed with body surface area and ejection fraction. The maximum wall thickness was regarded as the one corresponding to the left ventricular segment, which exhibited the greatest degree of thickening. The degree of LVH was evaluated by the maximum wall thickness and mass index. The maximum gradient in the left ventricular outflow tract was measured at rest and during the Valsalva maneuver in the apical five chamber view, with continuous Doppler directed parallel to the outflow tract of this chamber according to Bernoulli's modified equation. The presence of obstruction was defined as the mechanical impedance to the left ventricular outflow tract, resulting from contact or approximation of the mitral valve with the interventricular septum in mesosystole. The recordings of a maximum systolic gradient ≥ 30 mmHg at rest was considered compatible with obstructive forms. Latent obstruction was defined by a gradient <30 mm Hg at rest and ≥ 30 mmHg with Valsalva maneuver. Non-obstructive forms corresponded to a gradient at rest and with Valsalva < 30 mmHg.

Holter electrocardiogram

The 24 hourHolter ECG was obtained with three modified leads, D2, V1 and V5. Recordings were analyzed using the GE Mars 8000 and the recorder was the GE Seer Light (GE Medical Systems, Milwaukee, WI, USA). Paired ventricular extrasystoles were characterized as two consecutive extrasystoles, and non-sustained ventricular tachycardia was characterized by the presence of three or more consecutive extrasystoles with a rate of ≥ 100 beats / minute. In patients with more than one Holter ECG, close in time to the echocardiography, the one with the greatest frequency of ventricular arrhythmia was selected. Two levels were established for ventricular arrhythmias: level I - isolated or paired extrasystoles and level II – non-sustained ventricular tachycardia.

Statistical Analysis

Quantitative data were described by mean and standard deviation, or by median (Md) and interquartile intervals (25th and 75th percentiles). The category variables were expressed by absolute and relative frequency. The differences between two groups, based on the comparison of continuous variables with symmetric and asymmetric distribution, were analyzed, respectively, using the Student *t* test for independent samples and the Mann-Whitney test. Category variables were compared using the chi-square test for heterogeneity and chi-square for linear trend. From the ROC curve with a 95% confidence interval (CI), cutoff values for echocardiographic measurements regarding the left ventricular maximum wall thickness and left ventricular mass index were determined, in order to discriminate between patients with higher and lower frequency of ventricular arrhythmias. The data were processed using SPSS software, version 18.0 (SPSS Inc., Chicago, Illinois, USA). The level of statistical significance adopted was $p < 0.05$.

Results

Characteristics of the patients

Mean age was 54 ± 13 years, with 48 (89%) ≥ 40 years; 33 (61%) were female. There was a predominance of cases with mild or moderate impairment of functional capacity (New York Heart Association Functional Class - NYHAFC I/II, n = 40, 74%) compared with those with severe limitation (NYHAFC III/IV, n = 14, 26%). All patients were taking prescribed medication: 41 (76%) used beta-blockers, 17 (31%) used calcium channel blockers such as verapamil or diltiazem, and 5 (9%) used amiodarone (Table 1).

Holter electrocardiogram

Ventricular arrhythmias on Holter ECG were identified in all cases. Isolated ventricular extrasystoles were seen in 46 (85%) patients, ranging from 1 to 1461, with an average of 130 ± 277. Twenty (37%) had paired ventricular extrasystoles numbering 1 to 15, and 13 (24%) experienced non-sustained ventricular tachycardia, with 1 to 7 runs, ranging from 3 to 24 beats. Patients with non sustained ventricular tachycardia presented, relative to those without this arrhythmia (n = 41, 76%), a higher number of isolated ventricular extrasystoles (Md 131, p25 = 6.25 and p75 = 316 *versus* Md 9, p25 and p75 = 1 and p75 = 91, p = 0.27) and paired extrasystoles (Md 2, p25 = 0, p75 = 5 *versus* Md 0 p25 = 0, p75 = 1,

Table 1 - Demographic and clinical characteristics of 54 consecutive patients with hypertrophic cardiomyopathy and ventricular arrhythmias in 24-hour Holter electrocardiogram

	All patients (n = 54)	Level I (n = 41)	Level II (n = 13)	p
Age (years)	54 ± 13	54 ± 14	53 ± 14	0,902
≥ 40 years	48 (89%)	37 (90%)	11 (85%)	0,623
female gender	33 (61%)	27 (66%)	6 (46%)	0,328
NYHA FC				
I /II	40 (74%)	28 (68%)	12 (92%)	0,146
III/IV	14 (26%)	13 (32%)	1 (8%)	0,146
Medications				
Beta blockers.	41 (76%)	30 (73%)	11 (85%)	0,485
Calcium channel blockers	17 (31%)	13 (32%)	4 (31%)	1,00
Amiodarone	5 (9%)	5 (12%)	0 (0%)	0,321

P values refer to the comparison of patients with Level I and II of ventricular arrhythmias; Level I - isolated or paired extrasystoles; Level II-non-sustained ventricular tachycardia, FC - functional class; NYHA - New York Heart Association.

p = 0.013). Demographic and clinical data did not differ between patients with level I and II ventricular arrhythmias (Table 1).

Echocardiography

The mean left ventricular maximum wall thickness observed was 20 ± 4 mm, with a variation of 15 to 34 mm. There was a predominance of mild or moderate LVH: 26 (48%) had measurements between 15 and 19 mm, 21 (39%) measured between 20 and 24 mm, six (11%) measured between 25 and 29 mm and only one (2%) measured ≥ 30 mm. The LV mass index showed a variation from 97 to 248 g/m², with a mean of 158 ± 18 g / m². Obstructive forms occurred in 21 (39%) patients, latent obstructive forms in 6 (11%) and non-obstructive forms in 27 (50%) (Table 2).

Ventricular Arrhythmias and left ventricular hypertrophy

The left ventricular maximum wall thickness was significantly higher in patients with non-sustained ventricular tachycardia (level II) compared with those who only experienced extrasystoles (level I) (23 ± 5 mm *versus* 19 ± 4 mm, p = 0.001). The left ventricular mass index was significantly higher in level II patients (182 ± 45 g /m² *versus* 151 ± 48 g/m²; p = 0.049). The other echocardiographic variables did not differ among the groups (Table 2).

Through the ROC curve with a 95% CI, it was demonstrated that left ventricular maximum wall thickness of ≥ 21 mm and a left ventricular mass index of ≥ 144 g/m² represented cutoff values capable of identifying patients with patients with non-sustained ventricular tachycardia on ECG-Holter. In the 13 patients (24%) with non-sustained ventricular tachycardia, there was a higher frequency of left ventricular maximum wall thickness ≥ 21 mm (n = 10, 77%, 25 ± 4 mm) and an left ventricular mass index ≥ 144 g / m² (n = 10, 77%; 200 ± 30 g/m²), in relation to those with extrasystole arrhythmia only (n = 41, 77%), where these measures were identified, respectively, in 37% (n = 15, 23 ± 1 mm), p = 0.023 and 39% (n = 16,192 ± 53 g/m²) of the cases, p = 0.026 (Figure 1).

The recording of non-sustained ventricular tachycardia was more common in patients with a left ventricular maximum wall thickness ≥ 21 mm and an LV mass index ≥ 144 g/m² (8 of 13, 62%) than in those with one (4 of 13; 31%) or no (1 of 13; 8%) echocardiographic variable above the cutoff values (p = 0.04). The recording of non-sustained ventricular tachycardia on Holter ECG increased directly and progressively with the number of echocardiographic descriptors of LVH considered for analysis (chi-square for linear trend, p = 0.04) (Figure 2). The ROC curve showed that left ventricular maximum wall thickness ≥ 21 mm had a sensitivity of 77% and a specificity of 64%, with positive and negative predictive values of 40% and 90%, respectively, for detection of non-sustained ventricular tachycardia on Holter ECG (area under the ROC curve 0.767; 95%CI 0.614 – 0.920). Left ventricular mass index ≥ 144 g/m² showed a sensitivity of 77% and a specificity of 61%, with a positive predictive value of 39% and a negative predictive value of 89% (area under the ROC curve 0.713; 95%CI 0.534 – 0.892) (Figure 3).

Discussion

This study demonstrated that the more severe the LVH, the more it favors arrhythmogenesis in HCM. The occurrence of non-sustained ventricular tachycardia was associated with greater impairment of the LV, when assessed by maximal wall thickness and mass index. The recording of non-sustained ventricular tachycardia was more frequent in patients in which both ecocardiography descriptors of LVH were higher. The asymmetrical character of the hypertrophy and its heterogeneous distribution, make the assessment of LV mass by echocardiography less reliable in HCM[24]. Even though LV mass index is frequently high, it shows a weak correlation with the left ventricular maximum wall thickness when evaluated by means of magnetic resonance imaging[25].

Table 2 - Echocardiographic measurements of 54 consecutive patients with hypertrophic cardiomyopathy and ventricular arrhythmias in 24-hour Holter electrocardiogram

	All patients (n = 54)	Level I (n = 41)	Level II (n = 13)	p
Left atrial diameter (mm)	45 ± 7	45 ± 8	44 ± 4	0,573
LV diastolic diameter (mm)	43 ± 6	43 ± 6	44 ± 5	0,381
LV systolic diameter (mm)	26 ± 6	26 ± 6	27 ± 4	0,576
Ejection fraction (%)	72 ± 6	73 ± 7	71 ± 4	0,145
LV maximum wall thickness (mm)	20 ± 4	19 ± 4	23 ± 5	0,001
LV mass index (g/m²)	158 ± 48	151 ± 48	182 ± 45	0,049
Obstructive forms	21 (39%)	18 (44%)	3 (23%)	0,21
Gradient at rest (mm Hg)*	59 (37;79)	54 (32;81)	64 (38;-)	0,802
Latent obstructive forms	6 (11%)	2 (5%)	4 (31%)	0,025
Gradient at rest (mm Hg)*	23 (8;25)	13 (0;-)	23 (13;25)	0,623
Non-obstructive forms	27 (50%)	21 (51%)	6 (46%)	1,00
Gradient at rest (mm Hg)*	0 (0;10)	0 (0;21)	0 (0;9)	0,451

*P values refer to the comparison of patients with Level I and II of Ventricular Arrhythmias; Level I: isolated or paired extrasystoles; Level II-non-sustained ventricular tachycardia, LV: left ventricular; * analysis by Mann-Whitney test.*

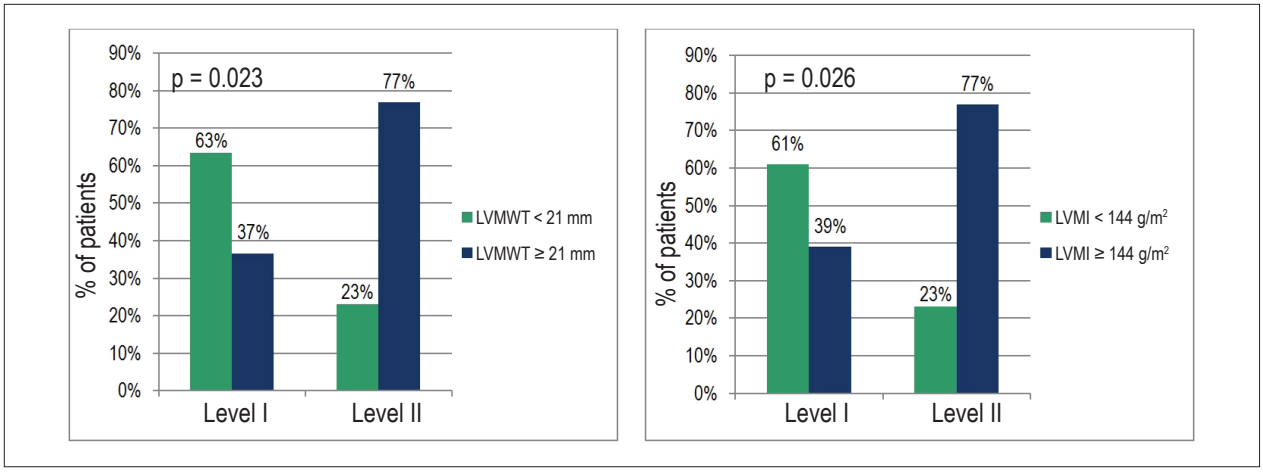

Figure 1 - *Association of the degree of left ventricular hypertrophy assessed on echocardiography by maximum wall thickness and mass index, with ventricular arrhythmias on 24-hour Holter ECG in 54 consecutive patients with hypertrophic cardiomyopathy; Level I: isolated or paired extrasystoles; Level II: non-sustained ventricular tachycardia; LVMWT: left ventricular maximum wall thickness; LVMI: Left ventricular mass index.*

However, in this analysis, it is noted that the recording of non-sustained ventricular tachycardia, in addition to its association with a higher mass index, was more frequent in the cases where the maximum wall thickness was high.

Ventricular arrhythmias are the characteristic manifestation of HCM, a disease that is considered unpredictable due to its arrhythmogenic potential, with annual rates of sudden death estimated at 1%[26]. Studies based on 24- to 48-hour Holter ECG analysis in community-based populations[20] and in referral centers [27-29] identified ventricular extrasystoles in 80% to95% of the cases, with numbers of extrasystoles varying from 1 to 5,000. Paired ventricular extrasystolic beats were found in 30% to 40% of the recordings, and non-sustained ventricular tachycardia was found in 20% to 30%, in brief runs with a frequency ranging from 3 to 36 beats. In this study, paired ventricular extrasystoles were observed in 37% of the patients and non-sustained ventricular tachycardia in 24%, with runs of 3-24 beats. Compared with previous studies, we observed a similar prevalence of ventricular arrhythmias, despite the lowest degree of sample selection and the prevalence of patients aged ≥ 40 years with mild or moderate degree of LVH.

The recording of non-sustained ventricular tachycardia on Holter ECG would seem to increase the susceptibility to sudden death, but has a low positive predictive

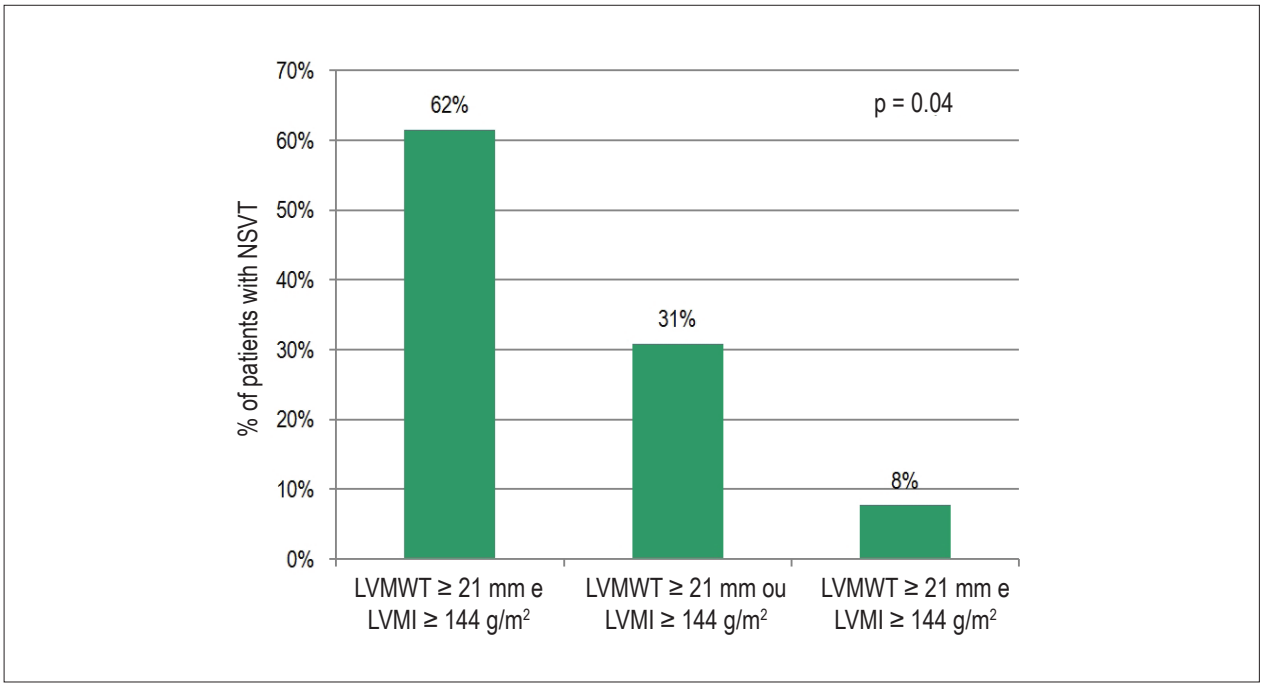

Figure 2 - *The prevalence of non-sustained ventricular tachycardia increased directly and progressively with the number of echocardiographic descriptors of left ventricular hypertrophy considered for analysis (chi-square for linear trend, p = 0.04); LVMWT: left ventricular maximum wall thickness; LVMI: Left ventricular mass index.*

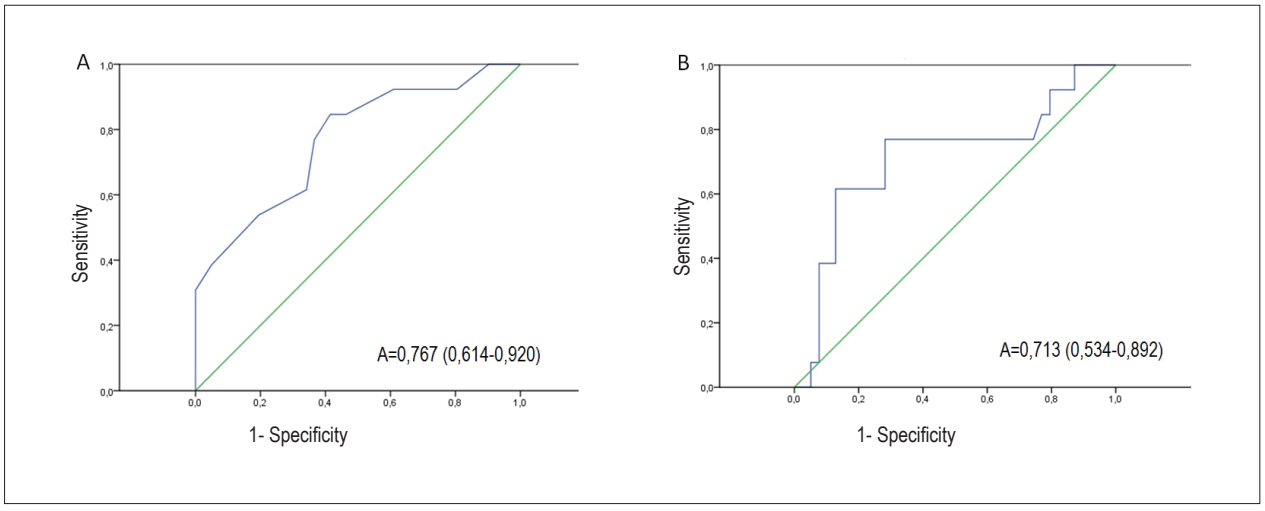

Figure 3 - *ROC curves to evaluate the ability of left ventricle maximum wall thickness ≥ 21 mm (A) and mass index ≥ 144 g/m² (B) to discriminate patients with hypertrophic cardiomyopathy and non-sustained ventricular tachycardia on Holter-electrocardiogram.*

value[27-30]. Ventricular arrhythmias in HCM originate from reentry and arise from an electrophysiological substrate characterized by slow conducting pathways and delayed ventricular activation[4,7]. In electrograms, the recording of small amplitude and late inscription potentials, called fractionations, would reflect abnormal ventricular activation and would predispose to sudden death[7]. Most of the ventricular tachycardia episodes observed here were monomorphic, preceded by extrasystoles, and would possibly be abolished by antitachycardia pacing[31].

Support for the hypothesis that the degree of LVH would influence arrhythmogenesis in HCM is considerable[10,11], although it has not been properly confirmed. Early investigation showed a relation between the extent of LVH and occurrence of ventricular tachycardia on Holter ECG[32]. Subsequent studies that assessed the relationship between the left ventricular maximum wall thickness and the occurrence of non-sustained ventricular tachycardia showed conflicting results[14,20,21], even when carried out in the same institution, with some presumable degree of sample superposition[14,20].

In one of these analyses, it was shown that the recording of non-sustained ventricular tachycardia was proportionally to the degree of LVH, affecting 50% of those with a maximum wall thickness ≥ 30 mm[20]. Divergent conclusions could be attributed to the degree of sample selection, to the methodology used and to the heterogeneous character of the disease. Unlike our study, none of the mentioned studies included isolated or paired extrasystolic beats. However, the prevalence of multifocal or paired ventricular extrasystoles and of non-sustained ventricular tachycardia was previously described in patients with extensive septal or free anterolateral wall LVH, in comparison with cases with involvement restricted to the septum[22]. In models with human mutations of HCM, an association between the degree of hypertrophy and induced ventricular arrhythmias was seen[33]. In the presence of mutation of the α-tropmyosin gene, ventricular arrhythmias were induced in one-third of the cases; a correlation was also observed with the left ventricular maximum wall thickness and the number of risk factors for sudden death[34].

Patients with a left ventricular maximum wall thickness ≥ 30 mm, particularly the young and elderly, are at increased risk of cardiovascular mortality and sudden death[10,11,35]. LVH, when increasing parietal stress and oxygen consumption, would lead to myocardial ischemia, an important stimulus for the development of arrhythmias[1]. The role of myocardial hypertrophy in arrhythmogenesis in HCM was questioned considering the description of sudden death in troponin T gene mutations carriers with normal or slightly increased LV wall thickness[6]. Ventricular fibrillation is also reported in patients with mutations of the cardiac β-myosin heavy chain with absent or late LVH[36].

The anomalous architecture of the myocardium, represented by cellular disarray and fibrosis, interferes with the conduction of the stimulus, producing unidirectional block and favoring a reentry mechanism.[4,7,11]. Reparative fibrosis probably develops, induced by silent myocardial ischemia and cellular death as a consequence of myocyte hypertrophy and small vessell disease[12,15]. Prefibrotic conditions indicative of the increase in collagen synthesis would precede LVH development in HCM[37]. The deposition of collagen in the form of reparative fibrosis is identified at an early age and tends to worsen with age[5]. in HCM carriers who are victims of sudden death, with disease caused by other genes than the troponin T gene the presence of extensive areas of fibrosis shows the potential relationship between the histopathological substrate and the development of fatal ventricular arrhythmias[6]. More recently, the analysis of endomyocardial biopsies in HCM showed that the increase in the collagen volume fraction was associated with higher mortality[38].

The increase in myocardial mass and left ventricular wall thickness in HCM is determined not only by myocyte hypertrophy, but is also largely due to the expansion of the extracellular matrix resulting from reparative fibrosis[12,15]. Studies with magnetic resonance imaging using gadolinium showed correlation of fibrosis detected by late enhancement with the thickness of the interventricular septum, determined both by this method and by echocardiogram[16,39], the same not occurring in relation to the global left ventricular mass[39]. Late enhancement identifies the presence of intramyocardial fibrosis of a reparative nature in 40% to 80% of HCM cases, occupying from 0.4% to 65% of the ventricular myocardium[16-18]. In a multivariate analysis[18] and in a recent meta-analysis[19], the fibrosis detected by magnetic resonance proved to be an independent predictor of mortality. However, for this to be considered a marker of prognosis and sudden death, additional confirmation is required[1]. The association of fibrosis identified by magnetic resonance imaging[14-17] or computed tomography with multiple detectors[40] and fatal or non-fatal ventricular arrhythmias suggests the existence of a physiopathological link between arrhythmogenesis and fibrosis in HCM. This fact justifies the association observed between the higher frequency of ventricular arrhythmias and left ventricular wall thickening, of which fibrosis is one of the determining factors. However, it is unclear whether the increase in left ventricular wall thickness is dependent on fibrosis, reflecting the consequences of a process of chronic myocardial ischemia influenced by cellular hypertrophy and small vessel disease, or whether it results from activation or genetic factors not yet understood or discovered.

The association demonstrated here between the occurrence of ventricular arrhythmias and the degree of LVH could contribute to individualization of factors that predispose to arrhythmogenesis in HCM. The present study showed that the left ventricular maximum wall thickness ≥ 21 mm and the mass index ≥ 144 g/m² are characteristics that may lead to greater myocardial electrical instability in these patients.

Limitations of the study

The possibility that our results reflect, to some degree, the very characteristics of the sample cannot be ruled out. The predominant inclusion of individuals in an older age group with the lowest degree of selection, although probably with lower risk, could limit our conclusions to populations with this profile. However, it must also be noted that the study population may also be representative of the disease, as well as those treated at referral centers.

Conclusions

In this study based on a non-referred outpatient HCM cohort, of a predominant age group above 40 years, there was an association between the occurrence of ventricular arrhythmias found on Holter ECG and the degree of LVH evaluated by echocardiography and determined by maximum wall thickness and mass index. A higher prevalence of non-sustained ventricular tachycardia was evidenced when both echocardiographic descriptors of LVH were higher.

Author contributions

Conception and design of the research: Mattos BP, Torres MAR, Scolari FL; Acquisition of data: Mattos BP, Freitas VC; Analysis and interpretation of the data: Mattos BP, Torres MAR, Freitas VC, Scolari FL, Loreto MS; Statistical analysis: Mattos BP, Scolari FL, Loreto MS; Writing of the manuscript: Mattos BP, Scolari FL; Critical revision of the manuscript for intellectual content: Mattos BP, Torres MAR.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Study Association

This study is not associated with any post-graduation program.

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References

1. Gersh BJ, Maron BJ, Bonow RO, Dearani JA, Fifer MA, Link MS, et al; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines; American Association for Thoracic Surgery; American Society of Echocardiography; American Society of Nuclear Cardiology; Heart Failure Society of America; Heart Rhythm Society; Society for Cardiovascular Angiography and Interventions; Society of Thoracic Surgeons. 2011 ACCF/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2011;124(24):e783-831.
2. Mattos BP, Torres MA, Freitas VC. Avaliação diagnóstica da cardiomiopatia hipertrófica em fase clínica e pré-clínica. Arq Bras Cardiol. 2008;91(1):51-62.
3. Elliot PM, Poloniecki J, Dickie S, Sharma S, Monserrat L, Varnava A, et al. Sudden death in hypertrophic cardiomyopathy: identification of high-risk patients. J Am Coll Cardiol. 2000;36(7):2212-8.
4. Maron BJ. Contemporary insights and strategies for risk stratification and prevention of sudden death in hypertrophic cardiomyopathy. Circulation. 2010;121(3):445-56. Erratum in: Circulation. 2010 Jul 6;122(1):e7.
5. Shirani J, Pick R, Roberts WC, Maron BJ. Morphology and significance of the left ventricular collagen network in young patients with hypertrophic cardiomyopathy and sudden cardiac death. J Am Coll Cardiol. 2000;35(1):36-44.
6. Varnava AM, Elliot PM, Baboonian C, Davison F, Davies MJ, McKenna WJ. Hypertrophic cardiomyopathy: histopathological features of sudden death in cardiac troponin T disease. Circulation. 2001;104(12):1380-4.
7. Saumarez RC, Pytkowski M, Sterlinski M, Bourke JP, Clague JR, Cobbe SM, et al. Paced ventricular electrogram fractionation predicts sudden death in hypertrophic cardiomyopathy. Eur Heart J. 2008:29(13):1653-61.
8. Mattos BP. Estratificação de risco para morte súbita na cardiomiopatia hipertrófica: bases genéticas e clínicas. Arq Bras Cardiol. 2006;87(3):391-9.
9. Medeiros Pde T, Martinelli Filho M, Arteaga E, Costa R, Siqueira S, Mady C, et al. Cardiomiopatia hipertrófica: importância dos eventos arrítmicos em pacientes com risco de morte súbita. Arq Bras Cardiol. 2006:87(5):649-57.
10. Spirito P, Bellone P, Harris KM, Bernabo P, Bruzzi P, Maron BJ. Magnitude of left ventricular hypertrophy and risk of sudden death in hypertrophic cardiomyopathy. N Engl J Med. 2000;342(24):1778-85.
11. Elliot PM, Gimeno Blanes JR, Mahon NG, Poloniecki JD, McKenna WJ. Relation between severity of left ventricular hypertrophy and prognosis in patients with hypertrophic cardiomyopathy. Lancet. 2001;357(9254):420-4.
12. Basso CD, Thiene G, Corrado D, Buja G, Melacini P, Nava A. Hypertrophic cardiomyopathy and sudden death in the young: pathologic evidence of myocardial ischemia. Hum Pathol. 2000;31(8):988-98.
13. Varnava AM, Elliott PM, Sharma S, McKenna WJ, Davies MJ. Hypertrophic cardiomyopathy: the interrelation of disarray, fibrosis, and small vessel disease. Heart. 2000;84(5):476-82.
14. Adabag AS, Maron BJ, Appelbaum E, Harrigan CJ, Buros JL, Gibson CM, et al. Occurrence and frequency of arrhythmias in hypertrophic cardiomyopathy in relation to delayed enhancement on cardiovascular magnetic resonance. J Am Coll Cardiol. 2008;51(14):1369-74.
15. Kwon DH, Setser RM, Popovic ZB, Thamilarasan M, Sola S, Schoenhagen P, et al. Association of myocardial fibrosis, electrocardiography and ventricular tachyarrhythmia in hypertrophic cardiomyopathy: a delayed contrast enhanced MRI study. Int J Cardiovasc Imaging. 2008;24(6):617-25.
16. Rubinshtein R, Glockner JF, Ommen SR, Araoz PA, Ackerman MJ, Sorajja P, et al. Characteristics and clinical significance of late gadolinium enhancement by contrast-enhanced magnetic resonance imaging in patients with hypertrophic cardiomyopathy. Circ Heart Fail. 2010;3(1):51-8.
17. O'Hanlon R, Grasso A, Roughton M, Moon JC, Clark S, Wage R, et al. Prognostic significance of myocardial fibrosis in hypertrophic cardiomyopathy. J Am Coll Cardiol. 2010;56(11):867-74.
18. Bruder O, Wagner A, Jensen CJ, Schneider S, Ong P, Kispert EM, et al. Myocardial scar visualized by cardiovascular magnetic resonance imaging predicts major adverse events in patients with hypertrophic cardiomyopathy. J Am Coll Cardiol. 2010;56(11):875-87.
19. Green JJ, Berger JS, Kramer CM, Salermo M. Prognostic value of late gadolinium enhancement in clinical outcomes for hypertrophic cardiomyopathy. JACC Cardiovasc Imaging. 2012;5(4):370-7.
20. Adabag AS, Casey SA, Kuskowski MA, Zenovich AG, Maron BJ. Spectrum and prognostic significance of arrhythmias on ambulatory Holter electrocardiogram in hypertrophic cardiomyopathy. J Am Coll Cardiol. 2005;45(5):697-704.
21. Olivotto I, Gistri R, Petrone P, Pedemonte E, Vargiu D, Cecchi F. Maximum left ventricular thickness and risk of sudden death in patients with hypertrophic cardiomyopathy. J Am Coll Cardiol. 2003;41(2):315-21.
22. Cheng X, Kusachi S, Urabe N, Nogami K, Takemoto M, Morishita N, et al. Association between high grade ventricular arrhythmia and extent of left ventricular hypertrophy in hypertrophic cardiomyopathy. Acta Med Okayama. 1991;45(3):155-9.
23. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al; Chamber Quantification Writing Group; American Society of Echocardiography's Guidelines and Standards Committee; European Association of Echocardiography. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr. 2005;18(12):1440-63.
24. Klues HG, Schiffers A, Maron BJ. Phenotypic spectrum of left ventricular hypertrophic in hypertrophic cardiomyopathy: morphologic observations and significance as assessed by two-dimensional echocardiography in 600 patients. J Am Coll Cardiol. 1995;26(7):1699-708.

25. Olivotto I, Maron MS, Autore C, Lesser JR, Rega L, Casolo G, et al. Assessment and significance of left ventricular mass by cardiovascular magnetic resonance in hypertrophic cardiomyopathy. J Am Coll Cardiol. 2008;52(7):559-66.

26. Sen-Chowdhry S, McKenna WJ. Sudden death from genetic and acquired cardiomyopathies. Circulation. 2012;125(12):1563-76.

27. Maron BJ, Savage DD, Wolfson JK, Epstein SE. Prognostic significance of 24 hour ambulatory electrocardiographic monitoring in patients with hypertrophic cardiomyopathy: a prospective study. Am J Cardiol. 1981;48(2):252-7.

28. McKenna WJ, England D, Doi YL, Oakley C, Goodwin JF. Arrhythmia in hypertrophic cardiomyopathy. I: Influence and prognosis. Br Heart J. 1981;46(2):168-72

29. Monserrat L, Elliott PM, Gimeno JR, Sharma S, Penas-Lado M, McKenna WJ. Non-sustained ventricular tachycardia in hypertrophic cardiomyopathy: an independent marker of sudden death risk in young patients. J Am Coll Cardiol. 2003;42(5):873-9.

30. Elliott PM, Gimeno JR, Tomé MT, Shah J, Ward D, Thaman R, et al. Left ventricular outflow tract obstruction and sudden death risk in patients with hypertrophic cardiomyopathy. Eur Heart J. 2006;27(16):1933-41.

31. O'Mahony C, Lambiase PD, Rahman SM, Cardona M, Calcagnino M, Quarta G, et al. The relation of ventricular arrhythmia electrophysiological characteristics to cardiac phenotype and circadian patterns in hypertrophic cardiomyopathy. Europace. 2012;14(5):724-33.

32. Spirito P, Watson RM, Maron BJ. Relation between extent of left ventricular hypertrophy and occurrence of ventricular tachycardia in hypertrophic cardiomyopathy. Am J Cardiol. 1987;60(14):1137-42.

33. Wang L, Seidman JG, Seidman CE. Narrative review: harnessing molecular genetics for the diagnosis and management of hypertrophic cardiomyopathy. Ann Intern Med. 2010;152(8):513-20.

34. Hedman A, Hartikainen, Vanninen E, Laitinen T, Jääskeläinen P, Laakso M, et al. Inducibility of life-threatening ventricular arrhythmias is related to maximum left ventricular thickness and clinical markers of sudden cardiac death in patients with hypertrophic cardiomyopathy attributable to the Asp175Asn mutation in the α-tropomyosin gene. J Moll Cell Cardiol. 2004;36(1):91-9. Erratum in J Moll Cell Cardiol. 2004;36(4):607-8.

35. Sorajja P, Nishimura RA, Ommen SR, Ackerman MJ, Tajik AJ, Gersh BJ. Use of echocardiography in patients with hypertrophic cardiomyopathy: clinical implications of massive hypertrophy. J Am Soc Echocardiogr. 2006;19(6):788-95.

36. Cristiaans I, Lekanne dit Deprez RH, van Langen IM, Wilde AA. Ventricular fibrillation in MYH7-related hypertrophic cardiomyopathy before onset of ventricular hypertrophy. Heart Rhythm. 2009;6(9):1366-9.

37. Ho CY, López B, Coelho-Filho OR, Lakdawala NK, Cirino AL, Jarolim P, et al. Myocardial fibrosis as an early manifestation of hypertrophic cardiomyopathy. N Engl J Med. 2010;363(6):552-63.

38. Arteaga E, de Araújo AQ, Bernstein M, Ramires FJ, Ianni BM, Fernandes F, et al. Valor prognóstico da fração de volume de colágeno na cardiomiopatia hipertrófica. Arq Bras Cardiol. 2009;92(3):210-4, 216-20.

39. Prinz C, Hering D, Bitter T, Horstkotte D, Faber L. Left atrial size and left ventricular hypertrophy correlate with myocardial fibrosis in patients with hypertrophic cardiomyopathy. Acta Cardiol. 2011;66(2):153-7.

40. Shiozaki AA, Senra T, Arteaga E, Pita CG, Martinelli Filho M, Ávila LF, et al. Fibrose miocárdica em pacientes com cardiomiopatia hipertrófica com alto risco para morte súbita cardíaca. Arq Bras Cardiol. 2010;94(4):535-40.