Malignant Arrhythmias and Sudden Death in Carriers of Non-Compacted Cardiomyopathy Determining by Non-Invasive Electrical Markers

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Abstract

Non-compacted ventricle cardiomyopathy characterized by spongiform morphology of the left ventricle, with ventricular trabeculations and intertrabecular spaces, secondary to arrest of the embryological compaction process.

Objective: To evaluate the behavior of arrhythmias through non-invasive electrical markers in carriers of non-compacted ventricular cardiomyopathy.

Methodological Design: An observational case-control and descriptive, cross-sectional study was conducted in 52 patients with non-compacted ventricular cardiomyopathy from the cases included between January 2006, December 2016, in a specialized consultation of the Institute of Cardiology, comparing them with the group selected from the same database, according to age, sex, race, of 65 patients with dilated cardiomyopathy of ischemic etiology and a control group (60). We explore: Personal pathological history, cardiovascular risk factors, echocardiography specifying the diagnostic criteria, non-invasive electrical markers: late potentials, prolongation and dispersion of QTc> 460 ms -ΔQT> 65 ms, Tp –Te> 100msec and ΔTp –Te > 30msec, T Wave variability, positivity of Holter arrhythmias, sudden death events.

Results: A mean age (42 ± 13.09), male sex, black and mixed race, alcoholism, smoking, prevailed, echocardiogram established diagnosis, positive late potentials 57 (87.6%) ischemic, upper 38 (73.0%) not compacted, Prolonged QTc 26 (50.0%) and dispersed in 38 (73.0%) not compacted, inferior (85.3%) ischemic dilated (85.3%), Tpeak-Tend prolongation and superior dispersion in ischemic, the T-wave widened in non-compacted and inverted in ischemic, documented arrhythmias in both groups, sudden death 9 (13.8%) ischemic, over 4 (7.69%) not compacted.

Conclusion: Non-invasive electrical markers, although positive in non-compacted ones, were more prevalent in ischemic dilatation, in correspondence with arrhythmias and sudden death events.

Keywords: Non-Compacted Cardiomyopathy; Non-Invasive Electrical Markers; Malignant Arrhythmias; Sudden Death

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Introduction

Non-compacted ventricular cardiomyopathy, which clinically manifests as progressive heart failure or failure (with a worse prognosis) [1], in the form of arrhythmias [2], or by systemic embolisms, [3] it also has asymptomatic forms and other symptoms as a form of presentation, it has generated great controversy from its definition, evolution etiology and therapeutic behavior.

The approach to the management of Non-Compacted Ventricular Cardiomyopathy (MVNC) is not similar to the management of dilated cardiomyopathy, with the meaning of cautious management of anticoagulation, even if the ejection fraction is not severely depressed, of the same This is the case with antiarrhythmics since malignant arrhythmia events are not uncommon [4,5].

The stratification of the vulnerable groups and those at risk of suffering arrhythmia events and secondary to them sudden death, remains perhaps the greatest challenge of Cardiology, however the emergence a few years ago of a group of non-invasive electrical markers, either by the use of the high-resolution electrocardiogram and signal averaging, or measured on the 12-lead ECG, the prolongation of the QTc Interval, its dispersion, the prolongation and dispersion of the Tpeak-Tend, the variability and alternation of the T Wave, between others, those that are more sensitive and specific when evaluated together, rather than in isolation [2,4], opened an opportunity to document such events and even define therapeutic behavior based on their results [6].

Methodological design

A descriptive observational study of cases and controls, cross-sectional, was carried out in 52 patients with non-compacted ventricular cardiomyopathy from the cases included between January 2006, December 2016, in a specialized consultation of the Institute of Cardiology, comparing them with the selected group of the Same database, according to age, sex, race, of 65 patients with dilated cardiomyopathy of ischemic etiology and a control group (60). We explored: Personal pathological history, cardiovascular risk factors, echocardiography specifying diagnostic criteria, non-invasive electrical markers: late potentials, QTc prolongation and dispersion> 460 ms -ΔQT > 65 ms, Tp –Te > 100msec and ΔTp –Te > 30msec, T-wave variability, Holter arrhythmia positivity, sudden death events. Meeting the inclusion criteria, over 18 years, both sexes, diagnosis of Dilated Cardiomyopathy due to non-compacted ventricle, diagnosis of Dilated Cardiomyopathy of ischemic etiology, voluntary nature of the patient to participate in the study, and exclusion: patients with a history of dilated Cardiomyopathy from another etiology, patients with primary valve disease, presence of pacemakers and/or Implantable Automatic Defibrillator, patients who do not tolerate the suspension of all types of medications for at least a period of five half-lives (intolerance for at least five days of discontinuation of drug treatment), refusal of the patient to participate in the study.

The data was processed on a personal computer using the SPSS statistical package version 21.0. Tables and graphs were used and made where the information was summarized. The percentage was used as a summary measure for qualitative and quantitative variables, descriptive statistical techniques such as the arithmetic mean or average, dispersion measures such as standard deviation, inferential statistical techniques were used to determine the association between categorical variables: the test of Pearson's Chi Square, and the t-Student test to verify significant differences between the variables involved. Calculations were made for a 95% confidence interval.

Results

Our study was made up of 177 people, with a mean age of 48.75 ± 9.68 years, the youngest being carriers of cardiomyopathy due to non-compacted ventricle 42.0 ± 13.09, p = 0.1. There was prevalence of the male sex with 90 patients. The main epidemiological variables, arterial hypertension (HT) present in 45 (69.2%) of the patients with ischemic cardiomyopathy p = 0.0001, smoking in turn reported in 19 (36.5%) of those dilated by an uncompacted ventricle and in 30 (46.1%) of the dilated ischemic p = 0.001, alcoholism was documented in 12 (23.0%) of the carriers of MVNC. The mixed races predominated 54 (46.1%) and the black with 43 (36.7%), among the studied patients.

The echocardiogram confirmed the diagnostic criteria of the entities and negativity in the control group.

The total number of patients with the presence of late potentials (PT) is shown in table 1 to 3; being higher in the group of ischemic dilated cardiomyopathy, 57 for 87.6% p = 0.002, compared with the group of patients with non-compacted ventricular cardiomyopathy 38 for 73.0% p = 0.02.

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Variables		Groups			p*<0.005
VINC n=52		MCD Ischemic n=65	Control n=60		
Sex	F	12 (23.0%)	15 (23.0%)	20 (33.3%)	0.03
	M	40 (76.9%)	50 (76.9%)	40 (66.6%)	0.02
Race	White	8 (15.3%)	12 (18.4%)	7 (11.6%)	0.8
	Mixed race	33 (63.4%)	21 (32.3%)	38 (63.3%)	0.4
	Black	11 (21.1%)	32 (49.2%)	15 (25.0%)	0.3
Age		42.0 ± 13.09	57.75 ± 9.84	46.50 ± 8.12	0.1
APP-FRC					
CI		4 (7.69%)	65 (100%)	0 (0%)	0.00001*
HTA		5 (9.61%)	45 (69.2%)	0 (0%)	0.0001*
DM		1 (1.92%)	39 (60.0%)	0 (0%)	0.0002*
Dyslipidemia		6 (11.5%)	42 (64.6%)	0 (0%)	0.0003*
Smoking		19 (36.5%)	30 (46.1%)	5 (8.33%)	0.001
Alcoholism		12 (23.0%)	2 (3.07%)	0 (0%)	0.001*

Table 1: *Sociodemographic and Epidemiological Variables in the Patients Studied.*

Source: Database

F: Female, M: Male, DCM: Dilated Cardiomyopathy, PAD: Personal Pathological History, CRF: Cardiovascular Risk Factors, HT: Arterial Hypertension, IC: Ischemic Heart Disease, DM: Diabetes Mellitus. p: Statistical Significance.*

Group	N	DdVI (mm)	DsVI (mm)	FEVI (%)	Morphology VI (n -%)	
					Expanded	Trabeculated
		Half ±DS	Half ± DS	Half ± DS	Efferoidal	Recesses IT
					Remodeled	
MVINC	52(100%)	62.14 ± 6.26	54.32 ± 16.13	35.65 ± 3.18	52(100%)	52(100%)
MCD Ischemic	65(100%)	65.23 ± 6.35	56.32 ± 18.13	35.20 ± 3.34	65(100%)	0
Control	60(100%)	42.16±11.34	36.37± 4.41	63.55 ± 4.98	0	0
p*<0.005		0.37	0.33	0.34	0.02	0.001

Table 2: *Echocardiographic Variables of the Study Sample.*

Source: Database

DCM: Dilated Cardiomyopathy, p: Statistical Significance, DS: Standard Deviation.*

Group	N	Late Potentials				p*
		SI	%	NO	%	
MVINC	52 (100%)	38	73.0%	22	42.3%	0.02
MCD Ischemic	65 (100%)	57	87.6%	8	12.3%	0.002
Control	60 (100%)	2	3.33%	58	96.6%	0.001
Total	185 (100%)	97	52.4%	88	48.55	0.16

Table 3: *Behavior of the Late Potentials in the Groups Studied.*

Source: Database

DCM: Dilated Cardiomyopathy, p: Statistical Significance.*

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The behavior of the prolongation and dispersion of the QTc-ΔQT interval. Longer prolonged QTc interval in the group of carriers of Ischemic Cardiomyopathy, 54 (83.0%), p = 0.001, over Uncompacted Cardiomyopathy, 26 (50.0%), p = 0.2. QTc dispersion was also documented more prevalent in Dilated Ischemic Cardiomyopathy, 57 (87.6%) with p = 0.002, over 38 (73.0%) non-compacted cardiomyopathy, p = 0.02. They are shown in table 4.

Group	N	Extension of QTc QTc > 460 ms		Extension of QTc ΔQT > 65 ms		p*
		T	%	T	%	
MVINC	52(100%)	26	50.0%	38	73.0%	0.02
MCD Ischemic	65(100%)	54	83.0%	57	87.6%	0.7
Control	60(100%)	0	0%	0	0%	0
Total	185(100%)	80	63.1%	95	75.4%	0.6

Table 4: Behavior of the prolongation and dispersion of the QTc- ΔQT Interval in the studied groups.

Source: Database

QTc Corrected QT Interval, ΔQT: Dispersion of the corrected QT Interval, Ms: millisecond.

The mean Tp-Te interval in the groups with dilated ischemic cardiomyopathy (130ms ± 21.26), exceeded the non-compacted ones (112 ms ± 20.87) and both were greater than the control (97 ms ± 5.36), p = 0.02. The mean of the ΔTp-Te dispersion in ischemic dilated patients (53.30ms ± 18.20), higher than the non-compacted ones (41.50ms ± 12.56), and the control group (30.30ms ± 11.17), p = 0.12, as documented in the table 5.

Group	N	Tp –Te >100mseg	ΔTp –Te >30mseg
		Media ± DS	Media ± DS
MVINC	52(100%)	112 ± 20.87	41.50 ± 12.56
MCD Ischemic	65(100%)	130 ± 21.26	53.30 ±18.20
Control	60(100%)	97 ± 5.36	30.30 ± 11.17
p*<0.005		0.02	0.12

Table 5: Behavior of the prolongation and dispersion of the interval Tp - Te- ΔTp – Te in each group studied.

Source: Database

Tp-Te: Tpeak-Tend interval, ΔTp –Te: Prolongation of Tpeak - Tend, Ms: millisecond.

The Variability of the T Wave, table 6, in ischemic dilated pathological morphology of the T Wave reported alterations in a total of 59 (90.7%), more prevalent was the inverted T Wave documented in 19 (29.2%) p = 0.02 patients, followed by the widened T Wave with 10 (15.3%) patients, while those dilated by the non-compacted ventricle reported alterations in morphology in a total of 36 (60.0%) patients, with a higher prevalence of nicked T Wave in 10 (16.6%) p = 0.2 patients, and a widened T Wave in 8 (13.3%) p = 0.1 patients.

Variables		MVINC		MCD Ischemic		Control		P*<0.005
T		%	T	%	T	%		
Wave Morphology T	Beak	4	6.66%	5	7.69%	0	0	0.1
	Dented	0	16%	8	12.3%	0	0	0.2
	Widened	8	13.3%	0	15.3%	0	0	0.1
	Flattened	2	3.33%	9	13.8%	0	0	0.2
	Reversed	4	6.66%	19	29.2%	0	0	0.02
	Biphasic	4	6.66%	2	3.07%	0	0	0.2
	Three-phase	2	33%	3	4.61%	0	0	0.1
	Variation in its amplitude and vector	2	33%	3	4.61%	0	0	0.1
Total		6	60.0%	9	90.7%	0	0	0.01

Table 6: Behavior of T Wave Variability of the patients studied.

Source: Database.

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Graph 1 and 2 illustrate the results of the 24-hour electrocardiographic record and the different documented arrhythmias. When comparing both results, there was no statistical significance between the two groups. CVP p = 0.2, FA p = 0.3, atrial flutter p = 0.3, CAP p = 0.1, TA p = 0.1, Ventricular tachycardia p = 0.2, ventricular flutter p = 0.2. Furthermore, there was no report of arrhythmias in the control group.
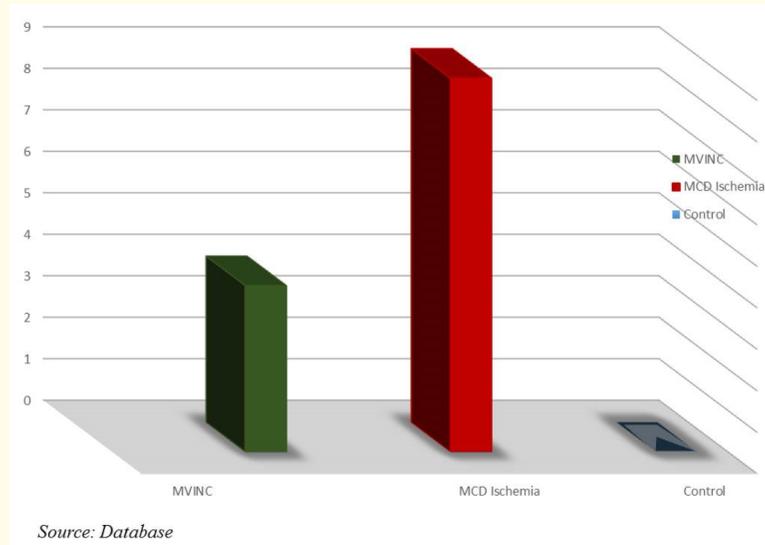

Source: Database
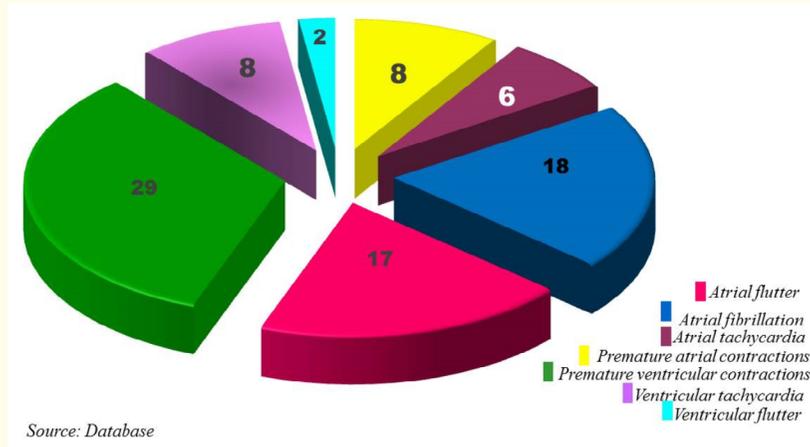
Graph 1: *Documentation of arrhythmias according to Holter, in carriers of dilated ischemic cardiomyopathies.*

Source: Database
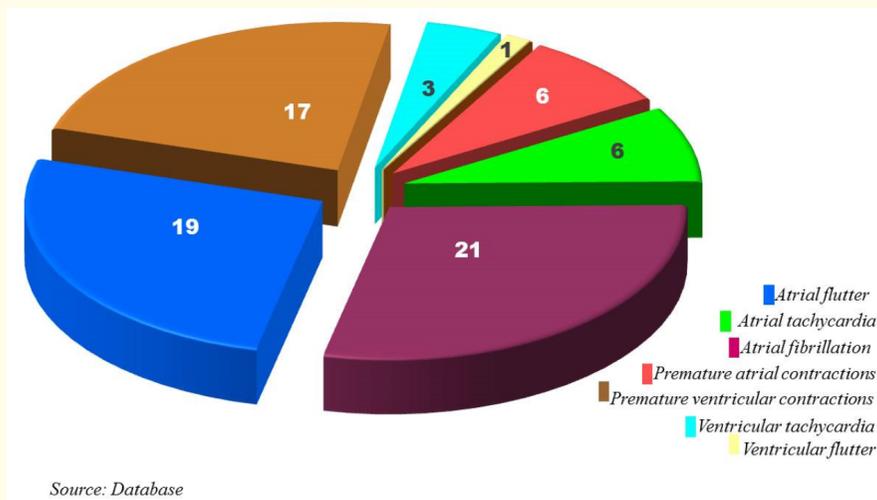
Graph 2: *Documentation of arrhythmias according to Holter, in carriers of cardiomyopathies by non-compacted ventricle.*

Finally, Graph 3 registered 9 (13.8%) sudden death events in the ischemic dilated patients and 4 (7.69%) in those dilated due to an uncompacted ventricle, obviously no report of a sudden death event in the control group, p = 0.2.

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Source: Database

Graph 3: *Documentation of sudden death events in the studied patients.*

Discussion

Several theories on electrophysiological mechanisms have been proposed with cardiac arrhythmias, these can be divided into disorders of impulse formation, disorders of impulse conduction or the combination of both [7]. In addition, other mechanisms are related such as: ischemia, electrophysiological abnormalities, cardiomyocyte abnormalities, fluctuations in blood pressure, sympathetic hyperactivity, and electrolyte imbalances such as hypokalemia and hypomagnesemia resulting from diuretic therapy, which can be arrhythmogenic by increasing automatism or triggered activity and prolong QT interval [7].

How do such arguments about the pathophysiological mechanisms involved in arrhythmias apply to our MVNC carriers? In this sense, Professor Margarita Dorantes addresses the main electrocardiographic alterations and the value of the electrophysiological study in this entity [8]. and points out that, in general, no specific electrocardiographic findings are found, although a systematic analysis of the electrocardiogram is not usually carried out. There is a marked overlap between left bundle branch block in particular, atrial conduction delay, long PR interval, or atrioventricular block, increased QT interval, reduced LV systolic function, and dilated LV and the left atrium. Patients with signs of left ventricular hypertrophy had more frequent systemic embolic events. There was a 35% mortality in 44 months of follow-up (cardiac MS in half of the cases), tachycardia was present in 41% and the electrocardiogram was mentioned to be abnormal in 94% of the patients (with a higher frequency of conduction block in the left or right branches, and abnormal repolarization).

Brescia., *et al.* [9] studied 242 children in the period 1990 - 2009 and reported: mortality 12.8%, electrocardiographic abnormalities 87% (the most frequent, hypertrophy of the LV and repolarization abnormalities), arrhythmias 33.1%, MS 6.2% and ventricular tachycardia 17.4%. Other findings were: T wave inversion, ST segment abnormality, atrial growth, left axis deviation, increased QT interval, preexcitation, atrial tachycardia and other supraventricular arrhythmias, atrial flutter and fibrillation, and accelerated rhythm of the union.

Stöllberger., *et al.* [10] studied 105 patients (1995 - 2011) in whom VINC was associated with neuromuscular diseases. They analyzed the electrocardiographic abnormalities and reported: ST interval and T wave abnormalities, left anterior fascicular block, atrial

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fibrillation, widening of the QRS, abnormal Q waves, intraventricular conduction disorders, LV hypertrophy, low voltage, right and left branches, prolonged PR, increased QT interval, sinus tachycardia and, above all, they required the evolutionary changes of these disorders. However, one wonders how much to attribute to VINC and how much to associated neuromuscular disorders.

An article on the subject Professors Stöllberger and Finsterer, present the results of their work [11], in a series of patients describing ventricular tachycardia, which is present in (n = 135), atrial fibrillation in (n = 96), ventricular atrial block in (n = 55), and QT interval prolongation in (n = 47). In the pediatric population they describe Wolf Parkinson White Syndrome (WPW) as the most frequent arrhythmias, present among their results in (n = 24), followed in order of prevalence by ventricular atrial block (n = 24), ventricular tachycardia in (n = 17) and bradycardia in (n = 15). 11. The pathophysiological mechanism of arrhythmias in MVNC is unknown, especially in patients with associated neurological involvement. Greater clarity in their triggering mechanisms is needed since 18% of patients with MVNC and documented malignant arrhythmic events preserved systolic function [11].

The electrocardiogram in the MVNC is usually abnormal. 87% present with hypertrophy (LV or biventricular) due to voltage criteria, T wave inversion, ST segment abnormalities or overload, left atrial growth, left axial deviation, prolonged QT or pre-excitation.

Arrhythmias are supraventricular and ventricular, there may be bradyarrhythmias, many of them life-threatening. The subtype with early rhythm abnormalities is at risk for MS. CDAI is very effective in preventing sudden arrhythmic death (MS), including those with severe LV dysfunction, a previous history of supraventricular tachycardia or fibrillation, recurrent syncope of unknown origin, or a family history of cardiac MS. Ventricular tachyarrhythmias (including those with ventricular fibrillation that cause cardiac arrest) are reported in 38 - 47% of adults with MVNC and in 13 - 18% of those who die suddenly [12].

Adults may be at high risk for ventricular tachyarrhythmias and episodes of cardiac MS, 47 - 74% of symptomatic patients die within 6 years from presentation. More recent research speaks of a more benign natural history, with a lower risk of ventricular arrhythmias. In a study of 241 adult patients with isolated MVNC, there was 6.2% of cardiovascular death with associated measures (transplant, CDAI) and 8.6% of cardiovascular events (death, stroke, CDAI shock, transplant) [12].

Ventricular arrhythmias in MVNC have been related to: microentry in the trabeculated myocardium, epicardial coronary hypoperfusion and deficit in the development of the conduction system. It has been suggested that ventricular extrasystoles in this disease originate primarily from the conduction system and related myocardium, and not from echocardiographic areas affected by noncompaction. Van Malderen., *et al.* [13] studied 101 patients with MVNC to determine the origin of the extrasystoles, compared the segments affected by non-compaction with said origin and found that 95% of them were not born in the MVNC areas, and 10% it had a true myocardial origin. The rest originated from other structures (outflow tract, fascicles, and mitral and tricuspid rings). Identifying the basic electrophysiological mechanism of arrhythmogenesis is of interest when selecting therapy in these patients (antiarrhythmic drugs, EEPC, ablation) [13].

Arrhythmogenesis in NCVM can be explained by dispersion of repolarization, myocardial ischemia and genetic causes, in a population of great heterogeneity and with the possible existence of subtypes (normal, dilated, hypertrophic or a mixture of them), whose spectrum moves from a high mortality with progressive myocardial dysfunction, up to low risk of SD if cardiac dimensions and function are normal.

In the opinion of this expert, they continue to be contradictory, and referred mostly to the population without demonstrable structural pathology, in which entities such as the one explored by us with their known peculiarities is even more difficult, not having these studies that allow us to make disquisitions in this sense, which further complicates the issue.

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Conclusions

Although the carriers of dilated cardiomyopathy secondary to ischemic heart disease showed greater positivity of non-invasive electrical markers, the documentation of arrhythmias and sudden death events from their use, in patients with non-compacted cardiomyopathy, allowed the implementation of secondary prevention, through pharmacological and non-pharmacological therapeutics.

Limitations

Low case series.

Declaration of Interests

No declaration of interests.

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