RELATIONSHIP BETWEEN VENTRICULAR REPOLARIZATION PARAMETERS AND THE INDUCIBILITY OF VENTRICULAR ARRHYTHMIAS DURING ELECTROPHYSIOLOGICAL STUDY IN PATIENTS WITH CORONARY ARTERY DISEASE

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ABSTRACT

INTRODUCTION: Malignant ventricular arrhythmias (MVA) are often the main cause of sudden cardiac death (SCD), especially in patients with pre-existing coronary artery disease (CAD). The identification of factors associated with SCD in this clinical setting is important and might help physicians in identifying this high risk group of patients. We evaluated the association between 12-lead ECG ventricular repolarization parameters and the induction of MVA on the electrophysiological study (EPS).

METHODS AND RESULTS: 177 patients [mean age 65±10.1yo, 83.6% male, mean LV ejection fraction (LVEF) 37.5±13.6%] were analyzed. For each 10ms increment in the QT interval, an increase of 7% in MVA inducibility was observed. The QT cut-off point of 452 ms had and accuracy of 0.611 for predicting MVA (p=0.011). Male gender (OR=4.18, p=0.012), LVEF < 35% (OR=2.32, p=0.013), amiodarone use (OR=2.01, p=0.038) and prolonged QT (OR=1.07, p=0.023) were independent factors associated with MVA. QT > 452ms in patients with ventricular dysfunction was associated with significant increased risk of MVA (OR=5.44, p=0.0004). In patients with LVEF ≥ 35%, QT dispersion (QTd) was significantly higher in those with inducible MVA. QTd > 20ms had an accuracy of 0.638 in predicting MVA, with 81.3% negative predictive value (95% CI 63-92.1%).

CONCLUSION: QT interval was an independent factor associated with MVA in patients with CAD. The combination of ventricular dysfunction and prolonged QT interval was associated with a 5-fold increase of MVA induction. Male gender, amiodarone use and decreased LVEF were also associated with increased risk of inducibility of MVA on the EPS.

INTRODUCTION

Malignant ventricular arrhythmias (MVA), such as ventricular tachycardia (VT) and ventricular fibrillation (VF), are common causes of sudden cardiac death (SCD)(1–3).

Up to 80% of SCD cases occur in patients with pre-existing coronary artery disease (CAD)(4,5).The current strategy for the prevention of SCD includes, in addition to managing the treatment of underlying disease such as CAD and heart failure, the use of antiarrhythmic agents and implantable cardioverter defibrillator (ICD). The identification of factors associated with SCD in this clinical setting is important and might help physicians in identifying this high risk group of patients. Currently, the most commonly used parameter for this purpose is the left ventricular ejection fraction (LVEF), which has limited sensitivity(4,5).

In recent decades, some parameters of ventricular repolarization have proven to be useful tools in stratifying the risk of death in several clinical conditions. The most used in clinical practice are the QT interval along with its corrected index (QTc) and its dispersion (QTd); and the interval between the peak and the end of the T wave (T p-e), in conjunction with its dispersion (T p-e d) and its relationship with QT (T p-e / QT). These 12-lead electrocardiogram (ECG) markers were associated with increased risk of MVA and mortality in a variety of settings, including channelopathies, acute myocardial infarction (AMI), cardiomyopathies, systemic hypertension and Chagas disease(1,2,6).

The aim of this study was to evaluate the association between ventricular repolarization parameters measured on a 12-lead ECG and inducibility of MVA during programmed electrical stimulation in patients with CAD undergoing electrophysiological study (EPS).

METHODS

This was a cross-sectional study that included patients with CAD who underwent EPS in a tertiary hospital.

Inclusion and exclusion criteria

Inclusion criteria were diagnosis of CAD, defined by either 1. history of acute coronary syndrome (ACS) or 2. symptoms of angina *pectoris* and/or dyspnea on exertion associated with ≥ 50% obstruction of the vascular lumen of epicardial coronary arteries on cineangiocoronariography or myocardial ischemia on non-invasive exam (treadmill test, myocardial perfusion scintigraphy and/or stress echocardiogram).

Other cardiomyopathies, channelopathies and non-interpretable 12-lead ECG within the six months preceding the EPS were considered exclusion criteria.

ECG measurements

Cardio Calipers© software (version 3.3) was used for ECG measurements. The QT interval was measured in lead II using the tangent method, described and validated by Postema *et al*(7); QTc was calculated using Bazett's formula, by measuring the QT interval of the second complete beat registered in lead II and the RR between this and the previous beat of the respective lead; QT dispersion was obtained by the difference between the longest and shortest QT interval among all the available beats in long lead II.

T p-e was measured in V5 using the tangent method. The T p-e dispersion was calculated by subtracting the longest and shortest T p-e intervals in V5; for T p-e/QT calculation, both T p-e and QT were measured on the first beat of V6, which better reflects the transmural left ventricular axis(8).

Electrophysiological study

The selected patients were submitted to EPS according to the following protocol: programmed ventricular stimulation with two basic cycles and up to three extra-stimuli at the apex and right ventricular outflow tract. Rapid ventricular stimulation (up to 250 ms or until 2:1 ventricular capture) was also performed in the same sites.

Sustained ventricular tachycardia, ventricular *flutter* and ventricular fibrillation were considered EPS induced MVA, according to definitions proposed by the current guidelines(9).

Statistical analysis

Given that there is no robust evidence in the literature on the incidence of EPS induced MVA in the setting of ischemic heart disease, a rate of 50% was assumed. Considering a 95% confidence level, a total of 151 patients would be necessary.

Variables were presented by means, standard deviation, medians, minimum and maximum values; categorical variables were presented by frequencies and percentages. MVA inducibility was compared with ventricular repolarization parameters considering the model of analysis of variance (ANOVA) with one factor or Kruskal-Wallis non-parametric test.

For univariable analysis of factors associated with MVA induction, Fisher's exact test or Chi-square test was used for categorical variables. For those with a quantitative character, Student's "t" test for independent samples or Mann-

Whitney's non-parametric test were used. The normal condition of the quantitative variables was assessed using Kolmogorov-Smirnov's test.

As for the multivariable analysis, a logistic regression model was adjusted including variables that showed statistical significance in the univariable analysis. Wald's test was used to make decisions about the significance of the variables and the estimated association measure was OR with 95% CI. For model validation, Hosmer-Lemeshow's test was applied and the value of the area under the ROC curve was estimated. Values of $p < 0.05$ indicated statistical significance. The data were analyzed with Stata/SE v.14.1. StataCorp LP, USA software.

RESULTS

One hundred and eighty two consecutive patients met the inclusion criteria. Five of them were excluded - three due to non-interpretable ECG, one due to concomitant Chagas' disease and one due to associated hypertrophic cardiomyopathy (Figure 1).

Mean age was 65 ± 10.1 years and 83.6% of patients were male. Mean LVEF was 37.5 ± 13.6% (< 35% in 53.1% of cases). The majority of patients (76.8%) had history of ACS and previous aborted SCD occurred in 16.9%. Angina was not reported by the majority (85.3%) of patients and only 3.4% (n = 6) had significant limitation (grades 3 and 4) according to the Canadian Cardiovascular Society (CCS) classification; the majority of patients were on either I or II New York Heart Association (NYHA) functional class. Among the comorbidities, the prevalence of systemic arterial hypertension (89.8%), dyslipidemia (66.7%) and diabetes mellitus (41.2%) stood out.

In most cases, medical treatment was in accordance with the recommendations of current guidelines for CAD and heart failure: 92.1% of individuals were on statins, 89.8% on acetylsalicylic acid, 88.1% on beta-blockers, and 82.5% on blockers of the renin-angiotensin-aldosterone system. EPS was indicated for ventricular stability assessment and for evaluation of syncope in 67.8% and 32.2% of cases, respectively (Table 1).

In the univariable analysis of demographic and clinical characteristics, male gender ($p = 0.03$), lower LVEF ($p = 0.01$) (especially < 35%; $p = 0.033$), and the use of amiodarone ($p = 0.032$) were associated with higher rates of MVA on EPS. None of the evaluated comorbidities were related to the proposed outcome.

Regarding the electrocardiographic parameters of ventricular repolarization, QT interval was significantly longer in the group with MVA induction ($p = 0.015$) (Table 2).

In the multivariable analysis, male gender (OR = 4.37, 95% CI 1.1 - 12.6), LVEF < 35% (OR = 2.25, 95% CI 1.17 - 4.35) and QT interval (OR = 1.07, 95% CI 1.01 - 1.12) remained independent risk predictors of MVA induction. For each

10ms increase in the QT interval, there was a 7% increase in MVA inducibility. The use of amiodarone, in turn, did not demonstrate a statistically significant relationship with the occurrence of MVA (Table 3).

QT cutoff point of 452 ms was associated with a 42.7% sensitivity (95% CI 31.5 - 54.6%), 79.4% specificity (95% CI 70 - 86.5%), 60.4% positive predictive value (PPV) (95% CI 46 - 73.2%) and 65.3% negative predictive value (NPV) (95% CI 56.2 - 73.5%) for MVA inducibility (Figure 2).

Another model of logistic regression was performed, based on the cutoff point of the QT indicated by the operational curve. All the variables included were associated with the proposed outcome, including the use of amiodarone (Table 4).

On the other hand, past history of ACS was not found to be a risk predictor of MVA induction**.** In this subgroup of patients, in the univariable analysis, QT interval remained associated with arrhythmic induction on EPS (p = 0.013). The other electrocardiographic parameters showed no association with the proposed outcome. In individuals without previous coronary events, there was no association between the electrocardiographic variables and MVA.

In the subgroup of patients with previous ACS, QT interval > 432 ms was associated with 55% sensitivity (95% CI 41.7 - 67.7%), 68% specificity (95% CI 56.3 - 78.3%), 57.9% PPV (95% CI 44.1 - 70.6%) and 65.8% NPV (95% CI 54.2 - 75.9%) for MVA induction (Figure 3).

Regarding to individuals with LVEF < 35%, none of ventricular repolarization parameters were related to arrhythmic inducibility on univariable analysis.

When the LVEF and QT interval variables were evaluated together, prolonged QT (> 452 ms) and significant ventricular dysfunction increased the risk of MVA in 5-fold (OR of 5.44, 95% CI 2.13 - 12.89, p = 0.0004) (Table 5).

In the subgroup of patients with LVEF ≥ 35%, QT dispersion was significantly higher in those with inducible MVA; such association was not verified in the other studied variables. QT interval dispersion > 20 ms had an accuracy of 0.638, 78.6% sensitivity (95% CI 59 - 91.7%), 47.3% specificity (95% CI 33.7 - 61.2%), 43.1% PPV (95% CI 29.6 - 57.7%) and 81.3% NPV (95% CI 63 - 92.1%) in predicting MVA (Figure 4).

DISCUSSION

Cardiovascular diseases are responsible for 17 million deaths annually worldwide, 25% of which result from SCD, which makes it an important public health problem(10). The average population risk is 1-2 cases/100.000 inhabitants per year, however the global incidence of SCD is difficult to characterize, since the data available in the literature vary

depending on the prevalence of CAD in several countries(11–13). It is estimated that in the US between 300 and 350 thousand cases of SCD occur annually, accounting for 50% of all deaths from cardiovascular etiology(9).

Despite all the advances in diagnostic strategies for risk stratification, depressed LVEF remains the best predictor of SCD(14,15). However, in adults over 35 years of age, about 2/3 of SCD present as the first clinical event in individuals without previously identified heart disease as well as in patients with heart disease without significant associated risk factors(12). Therefore, the identification of factors associated with MVA is important and might help physicians in identifying this high risk group of patients(1).

The role of EPS in the risk stratification of SCD is relevant in the setting of ischemic heart disease, especially in those with left ventricular dysfunction and non-sustained VT in 24-hour Holter monitoring. In these cases, MVA induction has a high PPV(14).

In a study of 100 consecutive patients, Wilber *et al* demonstrated an incidence of SCD of 54% in two years in those with induced arrhythmias compared to 6% in the group with non-induced MVA, making the finding of invasive assessment an independent predictor of the outcome, with a relative risk of 3.5 (95% CI 2.1 - 4.9; $p < 0.001$)(16). Similarly, the MUSTT study, which involved 2202 patients with CAD and LVEF < 40%, showed that patients with inducible MVA have higher all-cause mortality rates (58 versus 46%, $p = 0.004$)(17).

In the present study, longer QT interval was associated with higher risk of MVA induction on EPS in patients with CAD. Each 10ms increase in the QT augmented in 7% the risk of MVA. These findings are in agreement with the data published by Dekker *et al*(18), in which patients with prolonged QT had higher rates of death from cardiovascular causes, even after adjusting for age, gender, ethnicity, and other risk factors. Male gender was also associated with increased risk of MVA and this finding is consistent with the data from the cohort conducted by Schouten *et al*(19), who was a pioneer in demonstrating the predictive value of increased mortality from cardiovascular disease (RR = 1.8), especially CAD (RR = 2.1) in men.

QT interval greater than 452ms had moderate power to estimate MVA induction (AUC = 0.611; $p = 0.011$), with an OR = 2.7 (95% CI = 1.37 - 5.36; $p = 0.004$), similar to that seen in a multicenter study carried out in Denmark that included 3455 patients, in which QT intervals lasting 430ms or more were associated with increased cardiovascular mortality [RR = 3.15 (95% CI 1.10 - 9.83)](20).

The use of amiodarone (OR = 2.01; 95% CI = 1.04 - 3.89; $p = 0.038$) as well as LVEF ≤ 35% (OR = 2.32; 95% CI = 1.20 - 4.48; $p = 0.013$) were also related to MVA in the multivariable analysis. While the latter is the most well

established predictor of SCD in the context of CAD(5), the former may reflect the previous presence of ventricular arrhythmias in those under drug treatment and, consequently, the greater severity of these patients.

The prolongation of QT interval in ACS is associated with the development of MVA, increased rates of SCD, and reduced survival in resuscitated patients from out-of-hospital VF. The magnitude of the increase in the QT is related not only to the severity and extent of CAD, but also to the depression of myocardial function, reflecting metabolic and electrolytic changes in ischemic tissue, hypoxemia and imbalance in the activity of the autonomic nervous system(6,21).In the present study, in patients with previous ACS, QT interval was significantly longer in individuals with MVA. Similar finding was reported in the study conducted by Schwartz and Wolf, in which longer QT interval was observed in those with AMI when compared to healthy persons(22). An analysis of the literature that encompassed 12 studies and a total of 6953 patients strongly reinforced this association by showing a relationship between the QT interval and SCD (RR 1.7; 95% CI 1.3 - 2.2) and death from cardiovascular causes (RR 3.1; 95% CI 2.2 - 23.2) in patients with a history of AMI(6). The cutoff point of 432 ms showed moderate predictive capacity in discriminating MVA induction on EPS in individuals with history of ACS. This finding is in agreement with a case-control study of 110 patients followed for 7-years, in which QT interval > 440 ms in patients with previous AMI was associated with increased risk of SCD (RR = 2.16 , p = 0.005)(22).

Reduced LVEF is the most consistent risk factor for general and sudden mortality in patients with CAD. Values ≤ 40% are usually used for identifying patients at high risk(5,23–26). In the context of acute coronary events, LVEF is primarily a marker of mortality from pump failure and the dynamic nature of myocardial remodeling provides a substrate on which ICD implantation offers less benefit(5). On the other hand, in the late post-AMI phase, ventricular dysfunction is strong independent risk predictor of MVA and SCD and there is robust evidence supporting the indication of ICD for primary prevention of SCD (17,27–29) with reduction in total mortality of around 25%(30,31).

In the present study, patients with QT intervals > 452 ms and LVEF < 35% (p = 0.0003) presented higher incidence of inducible MVA on EPS. In the multivariable analysis, the combination of both parameters was an independent risk predictor for the outcome, with an OR = 5.44 (p = 0.004; 95% CI 2.13 - 13.89). Brendorp *et al*, in a multicenter trial, showed that in individuals with ventricular dysfunction and QT intervals > 479 ms had higher all-cause and cardiovascular mortality(32). Similarly, in the study of Padmanabhan *et al*, which included 2265 patients with systolic dysfunction, patients with QT > 450 ms had a mortality rate of 75% in 5 years, compared to 52% in the group with QT < 450 ms (p < 0.0001)(33).

Finally, among individuals with LVEF ≥ 35%, those with inducible MVA had longer QTd compared to those without MVA on EPS (30 ms versus 28 ms; p = 0.041). These values are lower than previously reported by Bogun *et al*. (126 ± 35 ms and 67 ± 25 ms, in groups with and without arrhythmia induction, respectively)(34). In the present study, QTd below 20 ms had 78.6% sensitivity and 81.3% NPV to predict MVA induction, which denotes discriminatory capacity of patients at lower risk, a finding that is in line with that evidenced in the prospective study mentioned above.

This study has some limitations such as the cross-sectional and observational nature, the inclusion of a single center, and the use of induction of arrhythmias in EPS as a surrogate outcome to mortality. As a future perspective and clinical applicability, we highlight the fact of adding the QT interval as an electrocardiographic variable to predict the risk of MVA in patients with CAD, a non-invasive and easily obtained marker that adds strength of association, especially in those with LVEF < 35% and with previous ACS; additionally, in patients with LVEF ≥ 35%, we highlight the high QTd NPV, which makes it possible to discern a subgroup of individuals at lower risk.

CONCLUSION

The QT interval was associated with increased risk of MVA inducibility in patients with CAD and also in those with previous ACS. The combination of ventricular dysfunction and prolonged QT interval was associated with a 5-fold increase in MVA induction. Male gender, amiodarone use and decreased LVEF were also associated with MVA inducibility on EPS.

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Figure 1 – Study flowchart

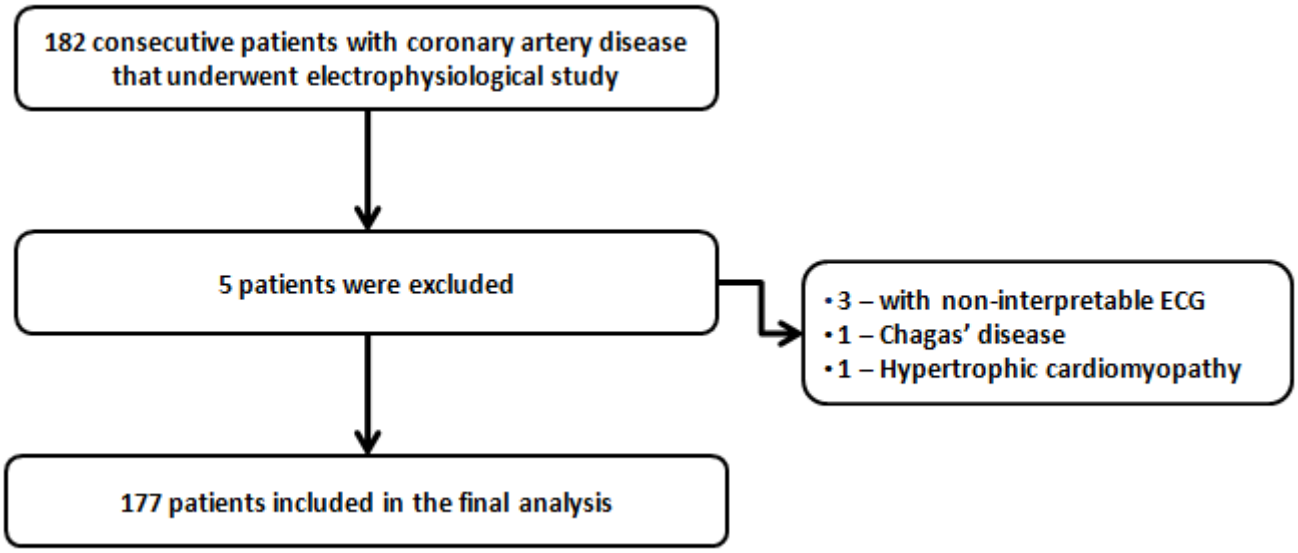

Table 1 – Baseline clinical and demographic characteristics

Variable	Classification	Result
Age (years)		65 ± 10,1 (35 - 94)
Gender	Male	148 (83,6)
	Female	29 (16,4)
Ejection fraction (%)		37,5 ± 13,6 (18 - 75)
Ejection fraction (%)	≥ 35	83 (46,9)
	< 35	94 (53,1)
Previous ACS	No	41 (23,2)
	Unstable angina	4 (2,3)
	NSTEMI	45 (25,4)
	STEMI	87 (49,2)
Angina	No	151 (85,3)
	CCS 1	5 (2,8)
	CCS 2	15 (8,5)
	CCS 3	5 (2,8)
	CCS 4	1 (0,6)
Intolerance on exertion	No	63 (35,6)
	NYHA I	19 (10,7)
	NYHA II	64 (36,2)
	NYHA III	28 (15,8)
	NYHA IV	3 (1,7)
Aborted SCD	No	147 (83,1)
	Yes	30 (16,9)
Comorbidities		**n (%)**
Hypertension		159 (89,8)
Dyslipidemia		118 (66,7)
Diabetes *mellitus*		73 (41,2)
Syncope		56 (31,6)
Chronic kidney disease		34 (19,2)
Stroke or TIA		20 (11,3)
Peripheral artery disease		20 (11,3)
ICD carrier		4 (2,3)
Pacemaker carrier		3 (1,7)
Medications in use		**n (%)**
Statins		163 (92,1)
Aspirin		159 (89,8)
Beta-blockers		156 (88,1)
ACEi / ARB's		146 (82,5)
Furosemide		87 (49,2)
Amiodarone		73 (41,2)
Spironolactone		60 (33,9)
Nitrates		47 (26,6)

Calcium channel blockers	32 (18,1)
P2Y12 receptor inhibitors	29 (16,4)
Oral anticoagulants	26 (14,7)
Hidralazine	9 (5,1)
Ivabradine	3 (1,7)
Trimetazidine	3 (1,7)
EPS indication	**n (%)**
Ventricular stability assessment	120 (67,8)
Previous documented ventricular arrhythmias	66 (37,3)
Aborted SCD	30 (17,0)
Sustained VT	17 (9,6)
Non-sustained VT	19 (10,7)
Absence of previous ventricular arrhythmias	54 (30,5)
Syncope	57 (32,2)

Subtitle:
ACS – Acute coronary syndrome
NSTEMI – Non-ST elevation acute myocardial infarction
STEMI – ST elevation acute myocardial infarction
CCS – *Canadian Cardiovascular Society*
NYHA – *New York Heart Association*
SCD – Sudden cardiac death
TIA – Transient Ischemic Attack
ICD – Implantable cardiac defibrillator
ACEi – Angiotensin converting enzyme inhibitor
ARB – Angiotensin receptor blocker
EPS – Electrophysiological study
SCD – Sudden cardiac death
VT – Ventricular tachycardia

Table 2 – Univariable analysis of clinical, demographical and electrocardiographic characteristics and their association with MVA induction on EPS

Variable	Classification	n	Arrhythmia		p
			No	Yes	
Age (years)			65,5 ± 10,2	64,3 ± 10,1	0,406*
Gender	Male	148	78 (52,7)	70 (47,3)	0,003*
	Female	29	24 (82,8)	5 (17,2)	
Ejection fraction (%)			39,7 ± 14,7	34,5 ± 11,4	0,010*
Ejection fraction (%)	≥ 35	83	55 (66,3)	28 (33,7)	0,033*
	< 35	94	47 (50,0)	47 (50,0)	
Previous ACS	No	41	26 (63,4)	15 (36,6)	
	Unstable angina	4	4 (100)	0 (0)	
	NSTEMI	45	27 (60)	18 (40)	
	STEMI	87	45 (51,7)	42 (48,3)	0,183*
Angina	No	151	87 (57,6)	64 (42,4)	
	Yes	26	15 (57,7)	11 (42,3)	1*
Intolerance on exertion	No	63	42 (66,7)	21 (33,3)	
	NYHA I	19	11 (57,9)	8 (42,1)	
	NYHA II	64	34 (53,1)	30 (46,9)	
	NYHA III	28	14 (50)	14 (50,0)	
	NYHA IV	3	1 (33,3)	2 (66,7)	0,402*
Aborted SCD	No	147	87 (59,2)	60 (40,8)	
	Yes	30	15 (50)	15 (50)	0,419*
Amiodarone use	No	104	67 (64,4)	37 (35,6)	0,032*
	Yes	73	35 (47,9)	38 (52,1)	
Hypertension	No	18	9 (50,0)	9 (50,0)	
	Yes	159	93 (58,5)	66 (41,5)	0,616*
Dyslipidemia	No	59	32 (54,2)	27 (45,8)	
	Yes	118	70 (59,3)	48 (40,7)	0,524*
Diabetes *mellitus*	No	104	61 (58,7)	43 (41,4)	
	Yes	73	41 (56,2)	32 (43,8)	0,759*
Syncope	No	121	67 (55,4)	54 (44,6)	
	Yes	56	35 (62,5)	21 (37,5)	0,416*
Chronic kidney disease	No	143	84 (58,7)	59 (41,3)	
	Yes	34	18 (52,9)	16 (47,1)	0,567*
Stroke or TIA	No	157	93 (59,2)	64 (40,8)	
	Yes	20	9 (45,0)	11 (55,0)	0,239*
Peripheral arterial disease	No	157	89 (56,7)	68 (43,3)	
	Yes	20	13 (65,0)	7 (35,0)	0,632*
ICD Carrier	No	173	101 (58,4)	72 (41,6)	
	Yes	4	1 (25,0)	3 (75,0)	0,313*
Pacemaker carrier	No	174	101 (58,1)	73 (42,0)	
	Yes	3	1 (33,3)	2 (66,7)	0,575*
QT interval			418 ± 54 (292 - 544)	442 ± 68 (268 - 632)	0,015†
Corrected QT interval			448 ± 55 (323 - 659)	455 ± 57 (322 - 602)	0,449†

QT dispersion	28 (4 – 80)	28 (0 – 136)	0,756[†]
T peak-end	84,5 ± 30,9 (32 - 236)	88,1 ± 38,2 (36 - 236)	0,499[†]
T peak-end dispersion	12 (0 – 40)	12 (0 – 60)	0,583[†]
T peak-end / QT	0,20 ± 0,06 (0,09 - 0,44)	0,20 ± 0,08 (0,08 - 0,46)	0,975[†]

*Student's t test for independent samples (quantitative variables); Chi-square test or Fisher's exact test (categorical variables); p < 0,05

[†]Student's t test for independent samples or Mann-Whitney's non-parametric test; p < 0.05

Subtitle:
MVA – Malignant ventricular arrhythmias
EPS – Electrophysiological study
n – number
p – p value
ACS – Acute coronary syndrome
NSTEMI – Non-ST elevation acute myocardial infarction
STEMI – ST elevation acute myocardial infarction
CCS – *Canadian Cardiovascular Society*
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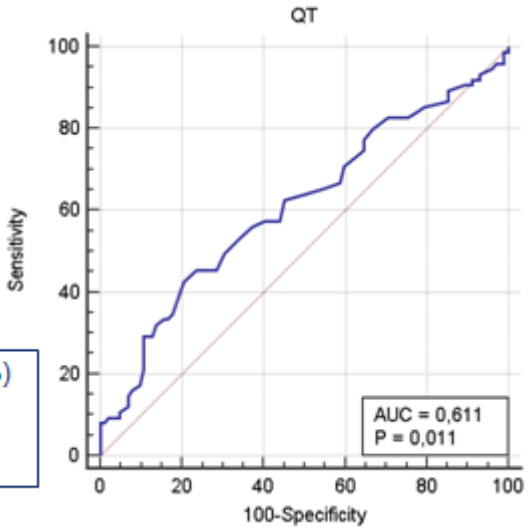
SCD – Sudden cardiac death
TIA – Transient Ischemic Attack
ICD – Implantable cardiac defibrillator

Figure 2 – Determination of an induced MVA associated measured QT interval cutoff point

QT	Arrhythmia	
	No	Yes
≤ 452 ms	81	43
> 452 ms	21	32
Total	102	75

- **Sensibility:** 42,7% (95% CI: 31,5% - 54,6%)
- **Specificity:** 79,4% (95% CI: 70% - 86,5%)
- **PPV*:** 60,4% (95% CI: 46% - 73,2%)
- **NPV*:** 65,3% (95% CI: 56,2% - 73,5%)



*For the calculation of the predictive values, the prevalence considered was that seen in the study sample (42.4%)

Subtitle:
MVA – Ventricular malignant arrhythmias
ms – milliseconds
PPV – Positive predictive value
NPV – Negative predictive value
95% CI – 95% confidence interval
AUC – Area under the curve
p – p value

Table 3 – Multivariable analysis of parameters associated with MVA induction on EPS

Variable	Classification	p*	OR*	95% CI
Gender	Female			
	Male	0.006	4.37	1.51 – 12.6
Amiodarone use	No			
	Yes	0.052	1.91	0.99 – 3.70
Ejection fraction (%)	≥ 35			
	< 35	0.015	2.25	1.17 – 4.35
QT†		0.023	1.07	1.01 – 1.12

*Logistic regression model and Wald's test; $p < 0.05$

†QT/10 (each 10 ms increase on QT implies in a 7% enhancement of arrhythmia inducibility)

Subtitle:

MVA – Ventricular malignant arrhythmias

EPS – Electrophysiological study

p – p value

OR – O*dds ratio*

95% CI – 95% confidence interval

Table 4 – Multivariable analysis of parameters associated with MVA induction on EPS using the cutoff indicated by the ROC curve

Variable	Classification	p*	OR*	95% CI
Gender	Female			
	Male	0.012	4.18	1.45 – 12.05
Amiodarone use	No			
	Yes	0.038	2.01	1.04 – 3.89
Ejection fraction (%)	≥ 35			
	< 35	0.013	2.32	1.20 – 4.48
QT† (ms)	≤ 452			
	> 452	0.004	2.70	1.37 – 5.36

*Logistic regression model and Wald's test; $p < 0.05$

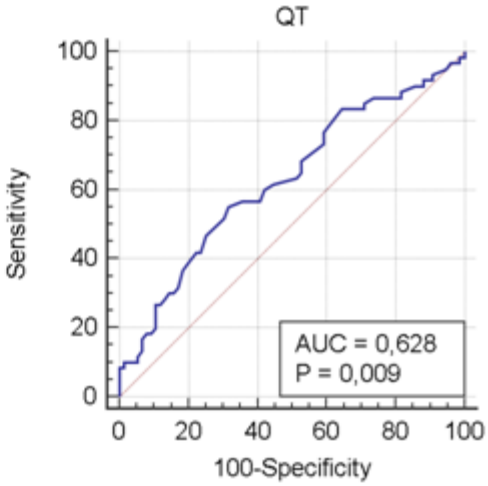
†Cutoff point indicated by the ROC curve

Subtitle:
MVA – Ventricular malignant arrhythmias
EPS – Electrophysiological study
ROC – Receiver operating characteristic
p – p value
OR – O*dds ratio*
95% CI – 95% confidence interval
ms – milliseconds

Figure 3 – Determination of an induced MVA associated measured QT interval cutoff point in patients with previous ACS

QT	Arrhythmia	
	No	Yes
≤ 432 ms	52	27
> 432 ms	24	33
Total	76	60

- **Sensibility:** 55% (95% CI: 41,7% a 67,7%)
- **Specificity:** 68% (95% CI: 56,3% a 78,3%)
- **PPV*:** 57,9% (95% CI: 44,1% a 70,6%)
- **NPV*:** 65,8% (95% CI: 54,2% a 75,9%)



*For the calculation of the predictive values, the prevalence considered was that seen in the study sample (42.4%)

Subtitle:
MVA – Ventricular malignant arrhythmias
ms – milliseconds
PPV – Positive predictive value
NPV – Negative predictive value
95% CI – 95% confidence interval
AUC – Area under the curve
p – p value

Table 5 – Multivariable analysis of ventricular repolarization parameters in addition to LVEF association with MVA induction

Variable	p*	OR*	95% CI
LVEF < 35% e QT > 452 ms	0.0004	5.44	2.13 – 12.89
LVEF ≥ 35% e QT > 452 ms	0.064	2.59	0.95 – 7.08
LVEF < 35% e QT ≤ 452 ms	0.12	1.82	0.86 – 3.86
LVEF ≥ 35% e QT ≤ 452** ms(reference)	-	-	-

*Logistic regression model and Wald's test; $p < 0.05$

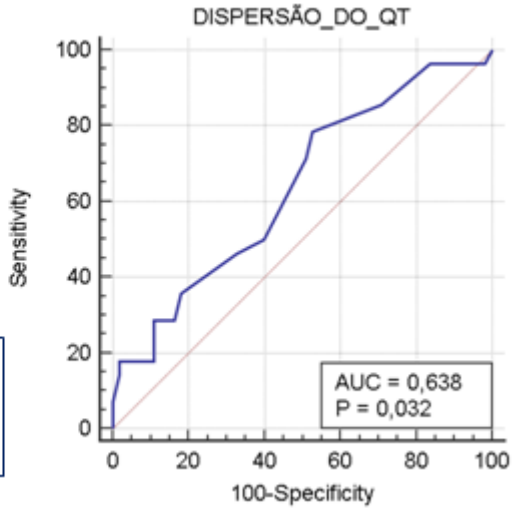
†Cutoff point indicated by the ROC curve

Subtitle:
MVA – Ventricular malignant arrhythmias
LVEF – Left ventricular ejection fraction
p – p value
OR – O*dds ratio*
95% CI – 95% confidence interval
ms – milliseconds
ROC – Receiver operating characteristic

Figure 4 – Determination of an induced MVA QT dispersion cutoff point in patients with LVEF ≥ 35%

QTd	Arrhythmia	
	No	Yes
≤ 20 ms	26	6
> 20 ms	29	22
Total	55	28

- **Sensibility:** 78,6% (95% CI: 59% - 91,7%)
- **Specificity:** 47,3% (95% CI: 33,7% - 61,2%)
- **PPV*:** 43,1% (95% CI: 29,6% - 57,7%)
- **NPV*:** 81,3% (95% CI: 63% - 92,1%)



*For the calculation of the predictive values, the prevalence considered was that seen in the study sample (42.4%)

Subtitle:
MVA – Ventricular malignant arrhythmias
LVEF – Left ventricular ejection fraction
ms – milliseconds
PPV – Positive predictive value
NPV – Negative predictive value
95% CI – 95% confidence interval
AUC – Area under the curve
p – p value