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Ventricular arrhythmias and new acute coronary syndrome in patients with infarction and prolonged QT dispersion

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Acronyms
ECG: electrocardiogram
ACS: acute coronary syndrome
AMI: acute myocardial infarction
VT: ventricular tachycardia
VE: ventricular extrasystole

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ABSTRACT

Introduction and objective: Myocardial ischemia increases QT dispersion in the electrocardiogram because, in these circumstances, the action potential duration decreases in the ischemic insult area by creating a dispersion of repolarization. The rapid succession of local metabolic and ionic alterations creates favorable situations in the genesis of ventricular arrhythmias during ischemia. The objective was to determine the association of the prolonged QTc dispersion, in the acute coronary syndrome, with ventricular arrhythmias and the recurrence of acute coronary disease.

Method: A total of 194 patients with acute myocardial infarction were studied. The QT interval duration was measured in a 12-lead electrocardiogram and it was corrected for heart rate in each of these leads. The dispersion of the interval was also assessed. It was taken into account the electrocardiographic evolution of these patients in relation to the occurrence of ventricular arrhythmias and a new acute coronary syndrome in a 30-day follow-up.

Results: Among the patients who had a prolonged QT dispersion, there was a prevalence of the deceased due to ventricular fibrillation (7 cases) for 7.5%, and only 2 patients (2.2%) who suffered from this arrhythmia were discharged alive. A new acute coronary syndrome was found in 17 patients with prolonged QT dispersion, versus 8 patients with normal QT dispersion.

Conclusions: Ventricular extrasystoles was the most common arrhythmia in patients with normal QT dispersion, and ventricular fibrillation was the most common in patients with prolonged QT dispersion. Most patients who had a new acute coronary syndrome had a prolonged QTc.

Key words: QT interval, Acute Coronary Syndrome, Acute Myocardial Infarction

Arritmias ventriculares y nuevo síndrome coronario agudo en pacientes con infarto y dispersión del intervalo QT prolongado

RESUMEN

Introducción y objetivo: La isquemia miocárdica aumenta la dispersión del intervalo QT del electrocardiograma, ya que en estas circunstancias la duración del potencial de acción disminuye en la zona del insulto isquémico, al crear una dispersión de la repolarización. La rápida sucesión de alteraciones iónicas y metabólicas locales crea situaciones favorecedoras en la génesis de arritmias ventriculares durante la isquemia. El objetivo fue determinar la asociación de la dispersión del intervalo QT corregido prolongado, en el síndrome coronario agudo, con las arritmias ventriculares y la ocurrencia de un nuevo episodio agudo de enfermedad coronaria.

Método: Se estudiaron 194 pacientes con infarto miocárdico agudo, a los cuales se les midió la duración del intervalo QT en un electrocardiograma de 12 derivaciones y se corrigió por la frecuencia cardíaca en cada una de esas derivaciones; asimismo se calculó la dispersión de dicho intervalo. Se tomó en cuenta la evolución electrocardiográfica de estos pacientes relacionada con la aparición de arritmias ventriculares y de un nuevo síndrome coronario agudo a los 30 días de seguimiento.

Resultados: Entre los pacientes que presentaron una dispersión prolongada del intervalo QT, prevalecieron los fallecidos con fibrilación ventricular (7 casos) para un 7,5 % y sólo 2 enfermos (2,2 %), que presentaron esta arritmia, egresaron vivos. Se observó un nuevo síndrome coronario agudo en 17 pacientes con dispersión del QT prolongado, contra 8 con dispersión del QT normal.

Conclusiones: Las extrasístoles ventriculares constituyeron la arritmia más observada en los pacientes con dispersión del intervalo QT normal y la fibrilación ventricular, la más observada en los pacientes con dispersión del intervalo QT prolongado. La mayor cantidad de pacientes que presentaron un nuevo síndrome coronario agudo tenían un intervalo QT corregido prolongado.

Palabras clave: Intervalo QT, Síndrome Coronario Agudo, Infarto Agudo de Miocardio

INTRODUCTION

Myocardial ischemia increases QT interval dispersion in the electrocardiogram (ECG), as in these circumstances the action potential duration decreases in the area of the ischemic process and a shortening of this interval in the ECG affected leads is produced. In acute coronary syndrome (ACS), the dispersion of repolarization is determined by the influence of sympathetic discharge as well as hemodynamic and electrophysiological changes that occur in cardiac tissue secondary to ischemia[1].

The reduction of oxygen and metabolic substrates that occur during ischemia and myocardial necrosis, trigger a rapid succession of local metabolic and ionic abnormalities that unevenly modify the cell electrophysiological properties of the different tissue subtypes and create favorable conditions in the genesis of ventricular arrhythmias.

The reentrant arrhythmias in acute myocardial infarction (AMI) are dependent, therefore, on these regional differences, disturbances in impulse conduction, duration of refractory periods and action potentials in addition to the already known differences between intact and ischemic myocardium, and its necrotic areas. The QT interval dispersion is higher in patients with AMI that in those with angina. Increase of dispersion values is associated with an increased likelihood of lethal arrhythmias and death risk, with figures above 80 ms related to it. Successful thrombolysis is often associated with smaller QT interval dispersion. This reduction in time dispersion of ventricular repolarization can be a beneficial mechanism with relation to the risk of malignant arrhythmias generated by the use of thrombolytic therapy, which is added to the already well demonstrated decreased rates of mortality and frequency of reinfarction in these patients[2].

Successful reperfusion shows a more stable subs-

trate than when occlusion persists, so that QT interval dispersion, its effects on the electrical stability and patient prognosis after myocardial infarction, depend on the recanalization of the infarct-related artery, its site, extent of the occlusion and infarct size. Therefore, better reperfused patients have lower incidence of arrhythmias[3].

Different investigations reflect the prognostic significance of ventricular repolarization dispersion, first demonstrated in ACS with ST segment elevation and later in those without ST elevation, which portends the onset of malignant ventricular arrhythmias and sudden death, and the risk of recurrence of a new ACS, both in short and long terms. Among electrocardiographic independent predictors of sudden death, besides QT interval dispersion, the following are also noted: presence of nonsustained ventricular tachycardia (NSVT), sustained ventricular tachycardia (SVT) and inducible ventricular tachycardia by electrophysiological study, T wave alternans and heart rate variability. The presence of ventricular extrasystole (VE) is questionable; its value depends on the frequency of occurrence, the state of coupling, morphology and association with impaired ventricular function and other ECG risk markers[4-7].

This study was performed to determine the association of the prolonged QTc dispersion in ACS with ventricular arrhythmias, and its association with a new acute event of coronary disease.

METHOD

A descriptive and retrospective study, related to the behavior of QT dispersion in 237 patients admitted to the Intensive Care Unit (ICU) of Celestino Hernández Robau Hospital with the diagnosis of ACS, was conducted during the period January 2010 to June 2011.

The (unintentional) sample was made up of 194 cases, after having reviewed the inclusion and exclusion criteria.

Inclusion criteria

- Patients admitted to the ICU with a diagnosis of ACS.

Exclusion criteria

- Patients admitted to the ICU with another diagnosis and during their stay in the unit they had an ACS.
- K serum concentration ≤ 3.5 mEq / L.
- Treatment with antiarrhythmic drugs that modify QT interval.
- Rhythm or conduction disorders, such as Wolff-Parkinson-White, complete atrioventricular blocks, the pacemaker rhythm, atrial fibrillation, atrial flutter and frequent ventricular or atrial extrasystoles previous to ACS.
- Previous channelopathies.
- Typical ECG changes: less than 7 useful leads for measurement, poor trace definition.
- Mortality for non-cardiovascular cause.

Obtaining ECG and QT interval measurement

Each patient underwent a 12-lead ECG at 25 mm / s and standard gain, measured with a Cardiocid equipment (ICID, Cuba). To complete the research, the QT reading of the first ECG after onset of symptoms of acute coronary syndrome was conducted.

The QT interval was measured manually from the beginning of the QRS complex to the end of the T wave, defined as the point of return of the T wave to the isoelectric line, or the nadir between the T wave and U-wave, when it was present. The Bazzet formula[8] was used to obtain the QTc value according to the heart rate. In practice, the dispersion of this interval can be defined as the difference between the maximum QTc and minimum QTc, as determined in a standard 12-lead ECG, although there are various methods for measuring them. Up to 50 ms was considered normal value[9] and ≥ 50 ms as prolonged QT dispersion.

The electrocardiographic evolution of patients related with the occurrence of ventricular arrhythmias was taken into account: VE, NSVT, SVT and ventricular fibrillation (VF).

The patient's condition at discharge and the occurrence of a new ACS during the first 30 days after discharge that required rehospitalization were also taken into account.

RESULTS

Table 1 shows the distribution of patients with normal QT interval dispersion, according to the types of ventricular arrhythmias and their status at discharge. In patients with no pathological dispersion of repolarization, an equal number of cases presented VF and NSVT with 6 patients for a 5.9%, in addition, in these illnesses, there was the same amount of deaths (2 patients), representing a 33.3% for arrhythmia. For cases with SVT (4, representing 4%), there was one

Table 1. Normal QT interval dispersion, according to the patient's status at discharge and types of ventricular arrhythmias.

Ventricular Arrhythmias	Status at discharge				Total	
	Diseased		Alive			
	Nº	%	Nº	%	Nº	%
VF	2	33,3	4	66,7	6	5,9
SVT	1	25,0	3	75,0	4	4,0
NSVT	2	33,3	4	66,7	6	5,9
VE	0	0,0	9	100	9	8,9
None	3	3,9	73	96,1	76	75,2
Total	8	7,9	93	92,1	101	100

p = 0.005; X^2 = 14,645

Table 2. Dispersión del iQT prolongado, según el estado del paciente al egreso y los tipos de arritmias ventriculares.

Arritmias Ventriculares	Status at discharge				Total	
	Diseased		Alive			
	Nº	%	Nº	%	Nº	%
VF	7	77,7	2	22,3	9	9,7
SVT	2	25,0	6	75,0	8	8,6
NSVT	1	12,5	8	87,5	9	9,7
VE	1	9,0	10	91,0	11	11,8
None	4	7,0	52	93,0	56	60,2
Total	15	16,1	78	83,9	93	100

p = 0.000; X^2 = 29,664

death (which accounts for the fourth part). All the cases with VE (9) were discharged alive. Generally there were a total of 8 deaths for 7.9% and 93 patients were discharged alive, representing 92.1%.

In Table 2, where patients with prolonged QT dispersion are distributed, it was found that although patients discharged alive prevailed (78 of 93), for a 83.9%, the behavior was not similar when analyzed according to the type of arrhythmia. Deceased patients with FV prevailed, 7 cases, accounting for 77.7% of deaths in patients with this arrhythmia, and only 2 (the remaining 22.3%), were discharged alive. There were 8 patients with SVT (8.6%), of which 2 cases (25.0%) died. Of the 9 patients with NSVT (9.7% of total), only 1 died (9.0% of total NSVT) just like it occurred in 1 of the 11 cases (9.0%) with VE.

During evolution, from discharge to the first 30 days of hospital discharge, a statistically significant association between the QT interval dispersion variables and the presence of a new ACS (p = 0.015) was shown. 14.6% of patients had a new ACS (25 cases), of which 17 (9.9%) showed prolonged repolarization dispersion. Other 61 (35.7%) suffered from the same disorder, making a total of 78 (45.6%), while in those with normal dispersion, only 8 patients (4.7%) had a new acute ischemic event, of a total of 93 (54.4%) with this type of QT interval dispersion (Table 3).

DISCUSSION

In a recently published article[10], 6355 patients who suffered a non-ST- elevation ACS were studied. Those with persistent ischemia and ventricular tachycardia (VT) had a high risk of sudden cardiac death (7.8% vs. 0.9%, p <0.001) and myocardial infarction (15.4% vs. 6.2%, p <0.001) compared to those without these complications. Within the study, those who suffered from NSVT were identified (n = 1978, 31.2%), in the absence of ischemia, the presence of this arrhythmia was not associated with an increased risk of sudden death (3.0% vs. 2.3%, p = 0.206)[10].

VF was the most lethal arrhythmia in the study of Machin et al.[11] (16% of all cases with prolonged dispersion), followed by VT, observed in 5% of the sample.

The prognostic significance of ventricular ectopia remains controversial to this day. Numerous researchers have emphasized that the most effective predictors are: frequency of occurrence of more than 10 per hour, the ultrashort coupling interval, multiform and bigeminal complexes, and runs of three or more beats, mainly when more than one of these characteristics are present and associated with other predictors of

Table 3. QTc dispersion, according to the appearance of a new acute coronary syndrome.

QTc dispersion	New acute coronary syndrome				Total	
	Yes		No			
	Nº	%	Nº	%	Nº	%
Normal	8	4,7	85	49,7	93	54,4
Prolonged	17	9,9	61	35,7	78	45,6
Total	25	14,6	146	85,4	171	100

p = 0.015; X^2 = 5,915; OR: 3,97; IC 95 % (1,75-9,01)

sudden death[5,12].

Jiménez-Candil[13], in a research published in Journal of Electrocardiology, gave an average time of 118 min for ECG completion from the first symptom, which had the highest value of dispersion in 69% of cases, in the remaining patients it was recorded in another measurement on the following 48 hours. In these patients, the risk of malignant ventricular arrhythmias was strongly associated with mortality (area under the ROC curve: 0.77, p <0.001). Also, Ashikaga *et al*.[14] studied 7 patients who had ventricular arrhythmias as a complication of coronary angioplasty, 6 of them had polymorphic VT, and 1 monomorphic VT. In 5 cases, the polymorphic VT quickly degenerated into VF. Arrhythmias appeared during coronary occlusion in 4 patients and in 3 of them during reperfusion. The QT interval dispersion before the procedure was recorded in 40 ± 9 ms and after angioplasty in 86 ± 19 ms (p <0.001).

Interestingly, arrhythmias were associated with mortality, both in patients with normal and prolonged dispersion. The first edge of this observation is that patients with prolonged QT interval dispersion contributed with the most lethal cargo, with almost a 2 to 1 proportion, the second point of view is that the dispersion of repolarization is not the only responsible for the genesis and the maintenance of malignant arrhythmias in acute ischemic context, and the third aspect is based on the fact that ventricular arrhythmias, regardless of their electrophysiological substrate, constitute an adverse factor in the prognosis of ACS[5,15], and this might explain the association of arrhythmias with mortality in patients without dispersion of repolarization. The role of Purkinje cells in the origin of the ventricular arrhythmia due to its automatic nature or triggered activity (focal mechanism) is well demonstrated, and they are responsible for idioventricular rhythm or for most monomorphic VT[16-21].

In Perkdemir's[22] work, the relationship between the QT interval dispersion (greater than 40 ms) with the occurrence of a new ACS and mortality was demonstrated, despite presenting a normal baseline ECG. Among the results obtained by Machin *et al*.[11] reinfarction was shown to prevail in 26% of patients studied and in 86% of these, it occurred with prolonged QT interval dispersion, with a highly significant association (p = 0.009).

Jiménez-Candil[13] explained that the dispersion of repolarization or only QT interval prolongation was associated with the occurrence of a new nonfatal ACS within three months following admission (OR: 3.5; 95% CI: 1.6 - 7.5, p = 0.001). In this research, the author added that unlike what is reported after transmural myocardial infarction, the negative prognostic impact of prolonged QT interval in NSTEACS did not result in an increased risk of sudden death, presumably due to ventricular arrhythmias, but in an increase in the incidence of new acute coronary syndromes. The same author in another study published in the International Journal of Cardiology[23] obtained a significant high incidence of deaths or angina within the first 28 days after discharge in patients with prolonged QT interval and positive stress test (p = 0.023).

This research only recognized the existing association between the development of complications and adverse events, but did not assess variables that might predict whether these associations were in relation to the degree of reperfusion or patency achieved by the affected coronary vasculature and responsible for the ACS. Therefore, this must be the starting point for

future research.

CONCLUSIONS

Ventricular extrasystoles and VF were the most observed arrhythmias in patients with normal QT interval dispersion and with prolonged QT interval dispersion, respectively. Most patients who had a new acute coronary syndrome had a prolonged QTc dispersion.

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