CorSalud 2018 Jan-Mar;10(1):13-20

CorSalud

Cuban Society of Cardiology

Original Article

Cardiocentro Ernesto Che Guevara Santa Clara Cuba

QRS duration as a predictor of low ejection fraction in the ST-segment elevation myocardial infarction

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Este artículo también está disponible en español

ARTICLE INFORMATION

Received: February 16, 2017
Accepted: April 18, 2017

Competing interests
The authors declare no competing interests

Acronyms
LVEF: left ventricular ejection fraction
QRSd: QRS duration
STEACS: ST-segment elevation acute coronary syndrome

On-Line English & Spanish versions

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ABSTRACT

Introduction: The QRS duration is a prognostic element and it has been associated with a decrease in the left ventricular ejection fraction in patients with acute coronary syndrome.
Objective: To assess the prognostic implications of the QRS duration in the depression of the left ventricular ejection fraction at discharge.
Method: A cross-sectional study was conducted with 347 patients with ST-segment elevation myocardial infarction, admitted at the Hospital Universitario Camilo Cienfuegos from January 1st, 2013 to December 31st, 2015. The variables studied were: age, sex, classical cardiovascular risk factors, blood pressure, reperfusion strategy, Killip-Kimball class, glomerular filtration rate, QRS duration and left ventricular ejection fraction. The qualitative variables were analyzed with the Chi-square statistical method and the quantitative with the t of Student and linear regression. The ROC curve was constructed for the discrimination capacity and a multivariate analysis was performed to determine the independence of variables.
Results: The QRS duration was negatively correlated with the ejection fraction r= -0.267; p<0.001) and an adequate discrimination ability as a predictor ejection fraction less than 35% (c=0.643).
Conclusions: The QRS duration greater than 90 milliseconds was independently associated with an ejection fraction lower than 35% at discharge.
Key words: QRS duration, Left ventricular ejection fraction, ST-segment elevation myocardial infarction

Duración del QRS como predictor de baja fracción de eyección en el infarto miocárdico con elevación del ST

RESUMEN

Introducción: La duración del QRS es un elemento pronóstico y se ha asociado a una disminución de la fracción de eyección del ventrículo izquierdo en pacientes con síndrome coronario agudo.
Objetivo: Evaluar la implicación pronóstica de la duración del QRS en la reducción de la fracción de eyección del ventrículo izquierdo al egreso.
Método: Se realizó un estudio analítico transversal con 347 pacientes con infarto agudo de miocárdico con elevación del segmento ST, ingresados en el Hospital Universitario Camilo Cienfuegos del 1 de enero de 2013 al 31 de diciembre de 2015.

Las variables estudiadas fueron: edad, sexo, factores de riesgo cardiovascular clásicos, tensión arterial, estrategia de reperfusión, clase de Killip-Kimbal, filtrado glomerular, duración del QRS y la fracción de eyección del ventrículo izquierdo. Las variables cualitativas se analizaron con el método estadístico Chi cuadrado, las cuantitativas con la t de Student y la regresión lineal. Se construyó la curva ROC para la capacidad de discriminación y se realizó un análisis multivariado para determinar la independencia de variables.

Resultados: La duración del QRS tuvo una correlación negativa con la fracción de eyección (r=-0,267; p<0,001) y una adecuada capacidad de discriminación como predictor de una fracción de eyección inferior a 35% (c=0,643).

Conclusiones: La duración del QRS superior a 90 milisegundos se asoció de manera independiente a una fracción de eyección menor de 35% al egreso.

Palabras clave: Duración del QRS, Fracción de eyección del ventrículo izquierdo, Infarto de miocardio con elevación del ST

INTRODUCTION

The electrocardiogram, due to its wide availability, low cost and simplicity, is an essential tool for the diagnosis and prognostic stratification of ST-segment elevation cute coronary syndrome (STEACS). The QRS width is one of the elements obtained in the electrocardiogram and has been a fundamental pillar for the use of cardiac resynchronization therapy[1]. It is also stated that in patients with heart failure, a longer QRS duration (QRSd) worsens prognosis[2,3].

The association between QRS and left ventricular ejection fraction (LVEF) has been widely explored in heart failure[4,5], but not so much in ischemic heart disease. Ischemia induces cell damage which alters the electrical properties of the heart muscle[6]. Fluctuations in concentrations and ionic currents, as well as local changes in the properties of gap junctions may cause conduction delay and dispersion of the refractoriness of the action potential in the ischemic fibers[7], which could prolong the QRSd.

This study aimed at evaluating the prognostic implication of the QRSd in the reduction of LVEF at discharge.

METHOD

A cross-sectional analytical study was conducted, including all the patients admitted with a diagnosis of type I STACS (atherosclerotic) in the Coronary Intensive Care Unit (ICU) at the Hospital Universitario Camilo Cienfuegos of Sancti Spíritus province, Cuba, from January 1st, 2013 to December 31st, 2015.

An unintentional sample was formed with all the cases that met the inclusion and exclusion criteria (n=347).

Inclusion criteria

Patients treated at the ICU with the aforementioned diagnosis.

Exclusion criteria

Patients with:

- Previous diagnosis of dilated cardiomyopathy and previous baseline LVEF less than 35%.
- Branch block or pacing rhythm that may broaden the baseline QRS.
- Atrial fibrillation prior to the diagnosis of STEACS, since it prevents or interferes with the measurement of electrocardiographic parameters.
- Patients who died before performing the predischarge echocardiogram.

Variables

The variables studied were: age, sex, coronary risk factors (high blood pressure and diabetes mellitus with diagnosis prior to coronary event, smoking, hypercholesterolemia, obesity), blood pressure and heart rate at admission, reperfusion strategy, Killip class-Kimbal, glomerular filtration rate, QRS duration and left ventricular ejection fraction.

Serum cholesterol levels greater than 6.71 mmol/L were considered hypercholesterolemia, according to hospital reference values; Obesity was taken into account in those patients with a body mass index greater than 30 kg/m^2, and history of ischemic heart disease when there was a diagnosis prior to the coronary event.

We also studied the Killip-Kimbal class and the use and success of thrombolysis (clinical or electrical signs of reperfusion: pain relief, hemodynamic

improvement, regression of ST segment elevation greater than 50% or appearance of reperfusion arrhythmias)[8]. It is valid to point out the impossibility of using the enzymatic criterion due to lack of available troponins.

Other variables studied were glomerular filtration rate (GFR), estimated by the Cockcroft-Gault formula[9] and LVEF, by the Simpson biplane method, obtained from the echocardiogram performed before discharge.

The QRS was manually measured[10,11] in a standard 12-lead electrocardiogram, where 10 millimeters (mm) equals 1 millivolt, and the paper speed was 25 mm/second. The QRS was measured from the initial deflection of the wave to its termination at point J, and the QRS of longer duration was recorded.

Information processing

The information was obtained from the medical records located in the Archives and Statistics Department of the hospital.

The data were processed with the Statistical Package for the Social Sciences (SPSS) software, version 17.0, installed in a microcomputer with Microsoft Windows 8 operating system, and analyzed as follows: qualitative variables were expressed in absolute and relative frequencies; quantitative data were expressed in their mean and standard deviation.

To check the strength of association between qualitative variables, the non-parametric Chi square test was selected; in situations where more than 20% of the expected frequencies presented values lower than five, Fisher's exact test was used. To compare the means of quantitative variables, the Student's t-statistic was used for independent samples. For the relationship between QRSd and LVEF, linear regression was used and its discrimination capacity was calculated by constructing the Receiver Operator Curve (ROC) and the area under the curve (index «c»). Considering the results of the ROC curve, a cut-off point was determined to dichotomize the continuous variables and include them in the univariate analysis.

LVEF at discharge, a multivariate analysis was performed with a binary logistic regression model where LVEF of less than 35% was the dependent variable (dichotomous). In the multivariate analysis we considered to identify as factors prone to prediction, those aspects contained in the variables for which the Wald statistic showed a probability lower than 5% ($p<0.05$), when we analyzed the exponential of the coefficients of the exponential model of β (Exp β) as an estimator for the ratio of cross products or odds ratio (OR).

The aggregate nature of the information collection contributed to keep the privacy of the subjects involved in the study and the results have only been used for scientific purposes.

RESULTS

A total 347 patients were studied, 211 men (60.8%) and 136 women (39.2%) (**Table 1**). The mean age in patients with LVEF greater than 35% was 75.88 years, higher than in patients with LVEF less than 35% (68,14). The most frequent risk factor in the sample was HBP with 252 patients (76.2%), diabetes mellitus (25.9%), smoking habit (56.5%), hypercholesterolemia (37.8%) and obesity (21.9%) were also found. The reperfusion strategy used was thrombolysis with Cuban recombinant streptokinase, used in 53% of patients, with a success of 11.2%. Ventricular dysfunction was frequent, with a Killip-Kimbal class superior to I in 46.4% of patients. The mean systolic blood pressure was lower in patients with LVEF less than 35% (79.08 ± 35.82 vs. 124.51 ± 35.03 mmHg), as was the glomerular filtration rate (47.85 ± 12. 72 vs. 70.09 ± 30.05 ml/min/m2). The lethality in the sample was 10,9%.

Figure 1 shows, by means of a linear regression analysis, the inverse correlation between the QRSd and the LVEF, with a very significant statistical signif-

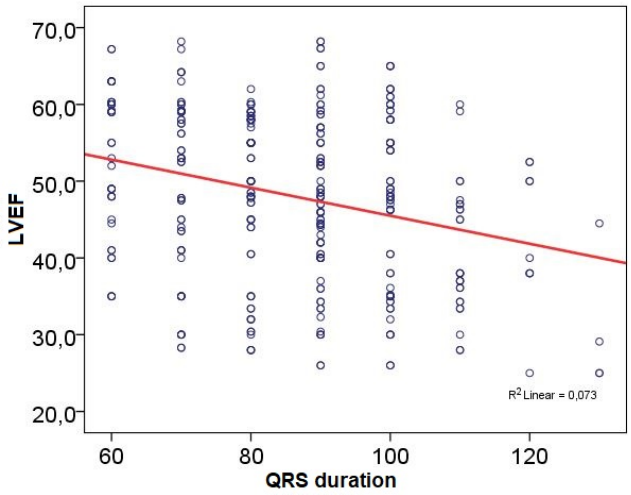


Figure 1: Linear regression between LVEF and QRS duration. LVEF= -0.176 x QRS + 63.097 (r= -0.267, p<0.001).

icance (p <0.001). The area under the ROC curve is the best overall indicator of the accuracy of a diagnostic or prognostic test, and makes it possible to express its performance by a simple number. **Figure 2** shows the ROC curve for the ratio of the QRSd with LVEF less than 35%, with an index under the curve c=0.643 and p=0,001.

The cut-off point found to include the QRSd in the multivariate analysis with better sensitivity and specificity was 90 msec. (**Figure 3**). In the univariate analysis (**Table 2**) were found as risk factors with statistical significance age older than 75 years (p<0.001), diabetes mellitus (p<0.001), unsuccessful reperfusion (p=0.010), Killip class II, III, IV (p<0.001),

Table 1. General characteristics of the population. Hospital "Camilo Cienfuegos" Sancti Spíritus. January 2013-December 2015.

Variables	LVEF > 35% (n=298)	LVEF < 35% (n=49)	Total
Population characteristics			
Age	68.14 ± 11.17	75.88 ± 7.34	69.23 ± 11.04
Male sex	185 (53.31)	26 (7.49)	211 (60.8)
Risk factors			
High blood pressure	224 (64.55)	28 (8.07)	252 (72.6)
Diabetes mellitus	60 (17.29)	30 (8.65)	90 (25.9)
Hypercholesterolemia	114 (32.85)	17 (4.90)	131 (37.8)
Obesity	71 (20.46)	5 (1.44)	76 (21.9)
Smoking habit	176 (50.72)	20 (5.76)	196 (56.5)
Chronic ischemic heart disease	139 (40.06)	17 (4.90)	156 (45)
Reperfusion strategy			
Streptokinase	157 (45.24)	27 (7.78)	184 (53)
Successful reperfusion	38 (10.95)	1 (0.29)	39 (11.2)
ischemic time (minutes)	225.67 ± 143.78	280.0 ± 168.48	233.64 ± 148.41
Killip-Kimbal			
Class I	158 (45.5)	28 (8.07)	186 (53.6)
Class II	48 (13.83)	3 (0.86)	51 (14.7)
Class III	68 (19.60)	15 (4.32)	83 (23.9)
Class IV	24 (6.92)	3 (0.86)	27 (7.8)
Clinical and laboratory variables			
Heart rate	83.30 ± 27.89	86.16 ± 24.31	83.7 ± 27.4
Systolic blood pressure (mmHg)	124.51 ± 35.03	79.08 ± 35.82	118.09 ± 38.5
Glomerular filtration (ml/min/m^2)	70.09 ± 30.05	47.85 ± 12.72	66.94 ± 29.28
Electrocardiographic variables			
QRS duration (mseg.)	84.33 ± 15.87	93.39 ± 17.17	85.6 ± 16.34
State at discharge			
Alive	281 (80.98)	28 (8.07)	309 (89.1)

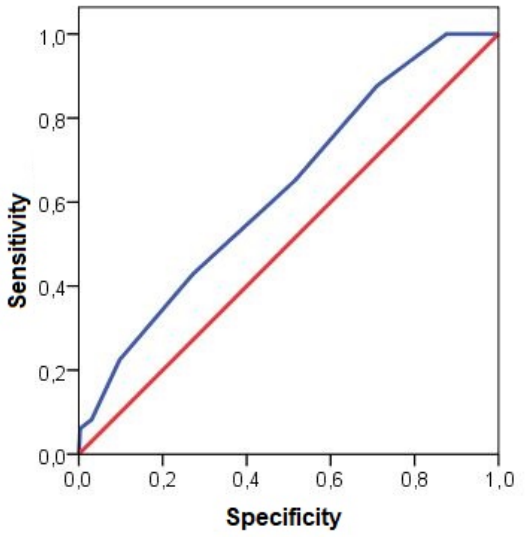
Data express n (%) and mean ± standard deviation.
LVEF, left ventricular ejection fraction.

systolic blood pressure less than 100 mmHg (p< 0.001), glomerular filtration rate less than 60 ml/min/m2 (p<0.001), and QRSd>90 msec. (p=0.004).

In the multivariate analysis (**Table 3**), QRSd > 90 msec. was found to be an independent predictor of LVEF less than 35% (p=0.002), associated with age older than 75 years, diabetes mellitus, Killip-Kimbal class higher than I (II, III, and IV), and stress systolic blood pressure less than 100 mmHg.

DISCUSSION

The QRSd has been associated with alterations in the structure and function of the left ventricle[12]. A greater QRSd after STEACS has been related to involvement of the conduction system due to the extension of the necrotic eschar, which could predispose to ventricular arrhythmias[6,13,14]. LVEF, after STEACS, has become a predictor of sudden independent death with high predictive capacity[15], which



Área bajo la curva	Error estándar	Sig.	IC 95%	
			Inferior	Superior
0,643	0,041	0,001	0,562	0,723

Figure 2: ROC curve of QRSd for the prognostic determination of LVEF less than 35%.

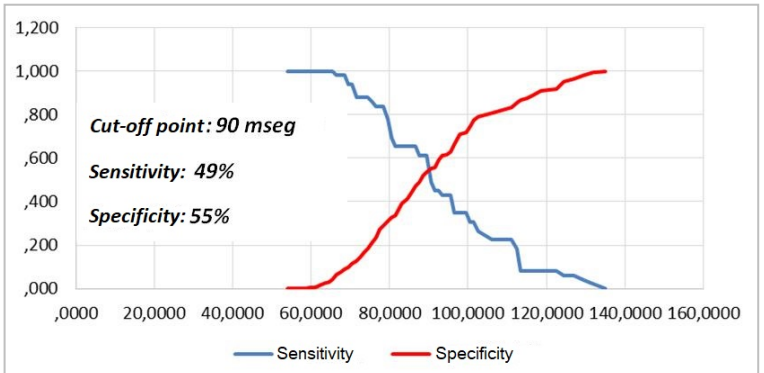


Figure 3: Cut-off point of QRS duration to predict LVEF less than 35%.

Table 2. Predictive variables of LVEF <35% at discharge: Univariate analysis.

Variables	LVEF > 35% (n=298)		LVEF < 35% (n=49)		OR	CI 95%		p
	Nº	%	Nº	%		Inferior	Superior	
Age older than 75 years	76	21.90	32	9.22	5.50	2.89	10.46	<0.001
High blood pressure	224	64.55	28	8.07	0.44	0.24	0.82	0.011
Diabetes mellitus	60	17.29	30	8.65	6.26	3.30	11.89	<0.001
Obesity	71	20.46	5	1.44	0.36	0.14	0.95	0.022
Smoking habit	176	50.72	20	5.76	0.48	0.26	0.88	0.017
Unsuccessful reperfusion	260	74.93	48	13.83	7.02	0.94	52.32	0.010
Killip-Kimbal II, III, IV	116	33.43	45	12.97	17.65	6.18	50.38	<0.001
SBP < 100 mmHg	55	15.85	36	10.37	12.24	6.09	24.60	<0.001
GFR < 60 ml/min/m^2	149	42.94	44	12.68	8.80	3.40	22.81	<0.001
QRS > 90 mseg.	117	33.72	30	8.65	2.44	1.31	4.54	0.004

LVEF, left ventricular ejection fraction; GFR, glomerular filtration rate; CI, confidence interval; SBP, systolic blood pressure.

Table 3. Predictive variables for LVEF <35% at discharge: Multivariate analysis.

Variables	B	Standard error	Wald	Signifi-cance	Exp(B)	CI 95%	
						Inferior	Superior
Age older than 75 years	0.95	0.44	4.59	0.032	2.58	1.08	6.13
Diabetes mellitus	0.87	0.44	4.03	0.045	2.40	1.02	5.62
Killip-Kimbal II, III, IV	2.87	1.04	7.64	0.006	17.64	2.30	135.02
SBP < 100 mmHg	1.92	0.40	22.82	<0.001	6.85	3.11	15.08
GFR < 60 ml/min	-1.34	0.98	1.85	0.174	0.26	0.04	1.80
QRS > 90 mseg.	1.27	0.42	9.20	0.002	3.57	1.57	8.14
Unsuccessful reperfusion	-0.55	1.27	0.19	0.664	0.58	0.05	6.96
Constant	-4.62	1.20	14.93	<0.001	0.01		

LVEF, left ventricular ejection fraction; GFR, glomerular filtration rate; CI, confidence interval; SBP, systolic blood pressure.

is taken into account in our study where the predictive capacity of the QRSd on LVEF at discharge is evaluated.

A recent study by Zou et al.[16] carried out in patients with dilated cardiomyopathy, showed that the normalization of LVEF with drug treatment was related to a decrease in QRSd. Our results show a negative correlation of the QRSd with the LVEF at discharge, as well as an adequate discrimination capacity of the QRSd for a LVEF less than 35%.

In a risk prediction model based on echocardiographic variables, LVEF was an independent predictor in the multivariate analysis (hazard ratio, [HR] 1.45, confidence interval [CI] 95%: 1.02-2.08; p=0.040), and the prognosis was inversely proportional to the LVEF when was less than 40%[17].

Our results coincide with those of Shah et al.[7], who in a study carried out with 536 patients with acute coronary syndrome without ST elevation showed that a QRS>90 msec. turned out to be an independent predictor for three-vessel coronary disease and of serious reduction in LVEF. On the other hand, Winter et al.[18] in a study conducted with 132 patients with coronary artery disease, and a baseline LVEF less than 30%, found no association between QRSd and LVEF. It is worth noting that this study was not performed in patients with acute coronary syndrome and included a baseline LVEF of less than 30%, which differs from our study design (and, therefore, with our results), since patients with known baseline LVEF less than 35% were excluded.

In the multivariate analysis, the QRSD exceeds 90 msec. LVEF less than 35% at discharge was associated as an independent predictor; and when adjusted for age, diabetes mellitus, Killip-Kimbal class and systolic blood pressure (p<0.05) were also associated, besides glomerular filtration rate of less than 60 ml/min/m^2 and unsuccessful reperfusion (p>0.05).

ST elevation, found that the independent variables associated with higher in-hospital mortality were the increase in tropinins (HR=8.1, 95% CI: 1.04-62.8, p=0.045); LVEF less than 40% (HR=12.6, 95% CI: 4.7-34, p<0.001) and age over 65 years (HR=2.1, 95% CI: 1.2-3,4, p=0.03). And in the follow-up of patients after hospital discharge, the QRSd greater than 90 msec. turned out to be an independent predictor for cardiovascular mortality (HR=2.4, 95% CI: 1.2-4.8, p=0.009). On the other hand, Nwakile et al.[20] also found an association of QRSd and mortality due to ventricular arrhythmias. The QRSd>10 msec. was associated with an incidence of 21.8% of ventricular tachycardia and 3.2% of ventricular fibrillation compared with 10.3% and 0.9%, respectively, in patients with QRSd<110 msec.

The QRSd has been used to evaluate mechanical dyssynchrony in the use of cardiac resynchronization therapy[21]. Its usefulness was also demonstrated by Joseph et al.[4] as a predictor of death due to cardiovascular causes, recovered cardiac arrest and hospitalizations due to heart failure. The latter could be related to the results found in our study where there is a negative correlation between the QRSd and LVEF. Another study carried out in patients with STEACS demonstrated an increase in mortality at 30 days, in patients with QRSd>100 msec, a result that was adjusted by LVEF, renal function, hypotension

and tachycardia[22].

CONCLUSIONS

The electrocardiogram continues to be a useful tool for risk stratification of ST-segment elevation acute coronary syndrome. The QRSd greater than 90 msec. was independently associated with an ejection fraction lower than 35% at discharge. QRSd and LVEF presented a negative correlation with statistical significance. The highest QRSd presented an adequate discrimination capacity as a predictor of low LVEF at discharge.

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