CorSalud 2018 Jan-Mar;10(1):4-12

CorSalud

Cuban Society of Cardiology

Original Article

Cardiocentro Ernesto Che Guevara Santa Clara Cuba

QRS duration and its relationship with the postoperative mortality of the coronary artery bypass grafting surgery

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ARTICLE INFORMATION

Received: May 14, 2017
Accepted: September 07, 2017

Competing interests
The authors declare no competing interests

Acronyms
AMI: acute myocardial infarction
CABG: coronary artery bypass grafting
ECG: electrocardiogram
HBP: high blood pressure
LVEF: left ventricular ejection fraction

On-Line English & Spanish versions

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ABSTRACT

Introduction: Due to its availability, the electrocardiogram –and in this, the QRS interval's duration– is a useful tool to predict future adverse events.
Objective: To assess the role of the QRS complex duration as a prognostic factor for cardiovascular mortality in patients treated by a coronary artery bypass grafting surgery.
Method: A prospective cohort research was carried out in the Cardiovascular Surgery Department of the Cardiocentro of the «Hospital Clínico-Quirúrgico Hermanos Ameijeiras», from March 2012 to June 2016. The sample consisted of 340 patients. In the statistical analysis, summary measures were used for quantitative and qualitative variables and the multivariate analysis was performed with dichotomous logistic regression.
Results: The duration of the QRS interval was not significantly associated with mortality (p=0.177). The odds ratio for diabetes mellitus was 3.228; for complications, 4.943; and for perioperative myocardial infarction, 7.016.
Conclusions: The duration of the QRS interval showed a significant association with cardiovascular mortality in the univariate analysis, but its independent effect on cardiac death in patients treated by coronary artery bypass grafting surgery could not be demonstrated when controlling the rest of the variables. The perioperative myocardial infarction, complications and diabetes mellitus were the independent risk factors for cardiovascular death after this type of surgery.
Key words: Coronary artery bypass surgery, Prognostic factors, QRS duration, Mediate mortality, Ischemic heart disease

Duración del QRS y su relación con la mortalidad postoperatoria de la cirugía de revascularización miocárdica

RESUMEN

Introducción: Debido a su disponibilidad, el electrocardiograma –y en éste la duración del intervalo QRS– constituye una herramienta útil para predecir futuros eventos adversos.

Objetivo: Evaluar el papel de la duración del complejo QRS como factor pronóstico para la mortalidad cardiovascular en pacientes tratados mediante cirugía de revascularización miocárdica.
Método: Se realizó una investigación de cohorte prospectiva en el Servicio de Cirugía Cardiovascular del Cardiocentro del Hospital Clínico-Quirúrgico "Hermanos Ameijeiras", desde marzo de 2012 a junio de 2016. La muestra fue de 340 pacientes. En el análisis estadístico se utilizaron medidas de resumen para variables cuanti y cualitativas, y el análisis multivariado se realizó con la regresión logística dicotómica.
Resultados: La duración del intervalo QRS no se asoció de forma significativa con la mortalidad (p=0,177). El índice de probabilidad (odds ratio) para la diabetes mellitus fue de 3,228; para las complicaciones, 4,943; y para el infarto de miocardio perioperatorio, 7,016.
Conclusiones: La duración del intervalo QRS presentó una asociación significativa con la mortalidad cardiovascular en el análisis univariado, pero no se pudo demostrar su efecto independiente sobre la muerte cardíaca en pacientes tratados mediante cirugía de revascularización miocárdica al controlar el resto de las variables. El infarto de miocardio perioperatorio, las complicaciones y la diabetes mellitus, resultaron ser los factores de riesgo independientes para la muerte cardiovascular posterior a la cirugía de revascularización miocárdica.
Palabras clave: Cirugía de revascularización miocárdica, Factores pronósticos, Duración del QRS, Mortalidad mediata, Cardiopatía isquémica

INTRODUCTION

At present, many newer diagnostic and imaging techniques have been developed to assess cardiovascular disease and related complications as well. To this end, electrocardiogram (ECG) remains a very practical technique not only for the diagnosis of heart disease but also for prediction of future adverse events as ECG is relatively available. In each cardiac cycle, ventricular activation is determined by the anatomy and physiology of the heart muscle and the conduction system. An ECG graphically expresses this process through spikes and dips called waves. The QRS complex represents the depolarization (activation) of both ventricles[1].

The QRS complex measures the time from the beginning to the end of ventricular activation. It is measured from the beginning of the Q or R wave to the end of the S wave (or R' if this is the last wave). QRS complex lasts no more than 60 and 100 milliseconds (ms). This corresponds to the complex generated after supraventricular activation which reaches the ventricles and depolarizes them through the entirely intact conduction system (bundle of His and bundle branches)[2]. QRS prolongation may have a number of causes and is associated with adverse events that influence cardiac mortality. Prolongation of the QRS due to intraventricular conduction delay has been shown to have prognostic value in patients with structural heart disease. In the case of acute myocardial infarction (AMI), with ventricular dysfunction, and chronic heart failure, the prognostic value of QRS has been well established[2,3].

Several studies have reported the prognostic value of QRS duration in patients with stable coronary artery disease and preserved left ventricular ejection fraction (LVEF), hypertrophic cardiomyopathy, pacemaker or implantable cardioverter defibrillator (ICD), and even in patients without structural heart disease in the general population[4-6]. A longer QRS complex on electrocardiogram has been associated, in many studies, with an increased risk of sudden death in patients with ischemic cardiomyopathy and with higher overall mortality. Previous studies have demonstrated that QRS duration is an independent predictor of sudden death of cardiovascular causes in the general population, at least in men[7]. Furthermore, it has been observed that patients with QRSd > 110 ms have a greater risk for sudden cardiac death compared with patients with QRSd < 96 ms. A 10 ms increase in QRS duration is an independent predictor of sudden death in patients with LV fractional shortening below the median value[7].

Prolonged QRS duration helps to identify subjects with higher long-term mortality. This finding has potential consequences: firstly, although QRS is an independent predictor of mortality in patients with structural heart disease, QRS prolongation on pre-

operative ECG usually occurs in patients with advanced ischemic cardiomyopathy undergoing coronary artery bypass grafting (CABG) surgery. However, limited data are available about effects on long-term outcome once they have undergone (CABG) surgery. Secondly, prolonged QRS can be easily detected on a previous, rapid ECG examination at admission for preoperative check-up and, thirdly, early measures to prevent complications could benefit patients at higher risk for long-term cardiac death, identified by prolonged QRS duration.

In Cuba, cardiovascular diseases are the second leading cause of death among the working population. They accounted for 22.651 deaths in 2013[8]. Coronary artery bypass grafting (CABG) is one of the standard treatments for ischemic cardiomyopathy, typically aiming at improving coronary flow in regions irrigated by arteries with functionally significant stenoses[9]. Likewise, in Cuba, CABG is the second most commonly performed cardiac surgery so far; exhibiting mortality rates of nearly 8% for an elective surgery[10,11].

Conduction disturbances are common in patients with advanced ischemic cardiomyopathy who require CABG. Hence it is extremely important to estimate the influence of this variable on the mortality of these patients. In this connection, most studies are related to perioperative/postoperative changes in the QRS. Prolonged QRS often occurs during postoperative CABG surgery (between 4 and 50%, depending on the series) which has been associated with higher creatine kinase (MB fraction) elevations, but not to other clinical complications or short/long-term prognosis. A new meta-analysis has corroborated the absence of short/long-term clinical consequences[12]. The QRS prolongation as a prognostic value on the preoperative ECG has been less studied and has been associated with post-operative low cardiac output (in the presence of systolic ventricular dysfunction), cardiac arrest in the immediate postoperative period, and long-term adverse events. Wide preoperative QRS has been shown to be an independent predictor of postoperative, ischemia-related malignant ventricular arrhythmias, and besides, to be associated with ST[13] segment depression[13].

High mortality and re-admission rates in patients with structural heart disease, including those with long-term ischemic cardiomyopathy and prolonged QRS, provide sufficient ground for assessing the usefulness of QRS ECG-trace as a possible prognostic factor for mortality in patients treated with CABG.

A prolonged QRS duration is a specific indicator of delayed ventricular activation. Changes in the normal ventricular activation cause mechanical asynchrony along with hemodynamic disorders and mitral regurgitation. This results in decreased LVEF with an increased risk of heart failure and death. Consequently, prolonged QRS duration may be an easy-to-use marker to assess left ventricular dysfunction. Thus, the association between prolonged QRS and left ventricular impairment may partly explain the association between QRS prolongation and mortality.

Using this variable throughout long-term follow-up in patients who underwent CABG may be an independent predictor of mortality and provide effective prevention for long-term CABG complications, which may help to improve outcome. Therefore, our research aims to assess the significance of QRS complex duration as a prognostic factor for intermediate cardiac mortality in patients treated with CABG.

METHOD

A prospective cohort study was conducted at the "Cardiocentro" in the Hermanos Ameijeiras Clinical-Surgical Hospital, in Havana, Cuba, from March 2012 to June 2016. The population, which coincided with the sample, included 340 patients diagnosed with ischemic cardiomyopathy who needed surgical treatment in the Department of Cardiac Surgery.

The following variables were used: age, sex, high blood pressure, smoking, dyslipidemia, diabetes mellitus, ischemic cardiomyopathy, previous infarction, peripheral artery disease, body mass index, waist-hip ratio, coronary syndrome with and without ST-segment elevation, glomerular filtration, triglycerides, LVEF, duration of the QRS complex, and number of diseased vessels.

Intraoperative variables: type of intervention (whether using support, or cardiopulmonary bypass, or beating-heart), and surgical times.

Postoperative variables: number of arterial and venous anastomoses, extubation time, post-surgical Intensive Care Unit length of stay, perioperative AMI and complications.

All patients were followed up in the postoperative room and during out-patient consultation, starting 30 days after surgery and continuing on for 4

years.

The data of the patients were collected in a predefined manuscript (made up by the authors) and all statistical analyses were performed using Excel and SPSS version 20 program database

We used absolute frequency and percentage to assess qualitative variables. Quantitative variables were expressed as mean ± standard deviation and we utilized median and interquartile range for variables with normal distribution. Logistic regression analyses were performed to detect variables that influenced mortality. Mortality was used as a dependent variable and associated variables or surgically/clinically relevant were used as independent variables, as well as QRS duration.

RESULTS

The research recruited a sample of 340 patients with CABG, 45 of them deceased (13.2%) and 295 alive (86.8%). The age in the deceased group was 65.1±8.8 years. There were no significant differences concerning age or sex (p> 0.05) (**Table 1**).

Regarding their pathological profile, 55.6% of the deceased patients had diabetes, while this antecedent was collected only in 34.2% of those discharged alive, with significant difference (p=0.010) between the two groups studied. The presence of previous myocardial infarction significantly influenced mortality, 11.5% of the patients alive vs. 77.8% of the deceased (p<0.001). The rest of the antecedents had no significant association with intermediate mortality (**Table 2**).

There were no significant differences between the alive and deceased groups in both body mass index and waist-hip ratio (p>0.05) as depicted in **table 3**. Neither significant differences were found (p>0.05) concerning diagnosis at admission (**Table 4**).

The duration of the QRS interval was significantly associated (p=0.021) with higher mortality with a mean 92.0/22.0 ms in the live patients compared to 100.0/24.5 ms in the deceased patients (**Table 5**). Wider QRS is seen in patients with higher mortality after surgery.

Table 1. Patient distribution according to demographic variables and mortality. Hermanos Ameijeiras Hospital. Havana, Cuba, 2016.

Variables	Total (n=340)	Alive (n=295)	Deceased (n=45)	p
Age (years)	63.2 ± 8.8	62.9 ± 8.8	65.1 ± 9.1	0.127[a]
Male	262 (77.1)	228 (77.3)	34 (75.6)	0.946[b]
Female	78 (22.9)	67 (22.7)	11 (24.4)	

Data express n (%) and mean ± standard deviation.
[a]Student t test, [b]Chi square test (χ^2) with correction.

Table 2. Distribution of patients according to antecedents and mortality.

Variables	Total (n=340)	Alive (n=295)	Deceased (n=45)	p
HBP	276 (81.2)	237 (80.3)	39 (86.7)	0.420[a]
Diabetes mellitus	126 (37.1)	101 (34.2)	25 (55.6)	**0.010[a]**
Current smoker	86 (25.3)	72 (24.4)	14 (31.1)	0.500[b]
Previous smoker	166 (48.8)	144 (48.8)	22 (48.9)	
Never smoker	88 (25.9)	79 (26.8)	9 (20.0)	
Previous AMI	69 (54.1)	34 (11.5)	35 (77.8)	**<0.001[a]**
Peripheral artery disease	92 (27.1)	74 (25.1)	18 (40.0)	0.055[a]

Data express n(%).
[a]Chi-square test (χ^2) with correction, [b]Chi-square test (χ^2) without correction.

Table 3. Distribution of patients according to anthropometric variables and mortality.

Variables	Total (n=340)	Alive (n=295)	Deceased (n=45)	p
BMI (kg/m^2)	27.1 ± 3.8	27.1 ± 3.8	27.4 ± 3.7	0.569[a]
Waist/hip index	1.0/0.1	1.0/0.1	1.0/0.1	0.356[b]

Data express mean ± standard deviation and median/interquartile range.
[a]Student t test, [b]Mann-Whitney U test.

The variables in the intraoperative period (**Table 6**) were not significant for mortality. As shown in **table 7**, perioperative AMI (44.4% vs. 9.5%, p<0.001) and postoperative complications (91.1% vs. 54.9%, p<0.001) were more frequent in deceased, compared to patients alive, with statistically significant differences. The extubation time and the Intensive Care Unit stay were close to statistical significance with values p=0.062 and p=0.086, respectively.

QRS duration was not significantly associated

Table 4. Distribution of patients according to diagnosis at admission for surgery and mortality.

Variables	Total (n=340)	Alive (n=295)	Deceased (n=45)	p*
STE-ACS	173 (50.9)	153 (51.9)	20 (44.4)	0.190
NSTE-ACS	14 (4.1)	10 (3.4)	4 (8.9)	
AEEC	153 (45.0)	132 (44.7)	21 (46.7)	

Data express n(%).
* Chi square test (χ^2) without correction.
NSTE-ACS, non-ST-segment elevation acute coronary syndrome; STE-ACS, ST-segment elevation acute coronary syndrome.

Table 5. Characteristics of patients according to mortality and preoperative variables.

Preoperative variables	Total (n=340)	Alive (n=295)	Deceased (n=45)	p
Glomerular filtration rate (ml/min/m^2)	77.1/52.2	76.4/53.0	79.4/57.8	0.738[a]
Cholesterol (mmol/l)	4.6/1.6	4.6/1.7	4.6/2.0	0.371[a]
Triglycerides (mmol/l)	1.5/1.0	1.5/1.1	1.6/1.0	0.626[a]
LVEF (%)	62.0/15.0	62.0/13.0	60.0/21.5	0.183[a]
QRS width (ms)	92.5/22.0	92.0/22.0	100.0/24.5	**0.021**[b]
QRS < 100ms	218 (64.1)	196 (66.4)	22 (48.9)	**0.034**[b]
QRS ≥ 100ms	122(35.9)	99 (33.6)	23 (51.1)	
Number of vessels	4.0/2.0	4.0/2.0	4.0/2.0	0.092[a]

Data express median/interquartile range and n(%).
[a]Mann-Whitney U test, [b] Chi-square test (χ^2) with correction.
LVEF, left ventricular ejection fraction; ms, milliseconds.

Table 6. Characteristics of patients according to intraoperative variables and mortality.

Intraoperative variables	Total (n=340)	Alive (n=295)	Deceased (n=45)	p*
Surgery with support	14 (4.1)	11 (3.7)	3 (6.6)	0.597
Surgery with CPB	153 (45.0)	132 (44.7)	21 (46.7)	
Beating-heart surgery	173 (50.9)	152 (51.5)	21 (46.7)	
Surgical time (hours)	5.5/1.3	5.5/1.3	5.5/2.3	0.732

Data express n(%) and median/interquartile range.
* Mann-Whitney U test.
CPB, cardiopulmonary bypass.

Table 7. Characteristics of patients according to postoperative variables and mortality.

Postoperative variables	Total (n=340)	Alive (n=295)	Deceased (n=45)	p*
Nº of coronary grafts	1.0/1.0	1.0/1.0	1.0/1.0	0.693[a]
Nº of venous grafts	1.0/2.0	1.0/2.0	2.0/1.0	0.505[a]
Extubation time (hours)	6.3/7.0	6.2/5.0	8.0/14.3	0.062[a]
Stay in ICU (hours)	51.0/24.8	48.0/24.0	72.0/63.5	0.086[a]
Perioperative AMI	48 (14.1)	28 (9.5)	20 (44.4)	**<0.001**[b]
Complications	162 (54.9)	162 (54.9)	41(91.1)	**<0.001**[b]

Data express median/interquartile range and n(%).
[a]Mann-Whitney U test, [b]Chi square test (χ^2) with correction
AMI, acute myocardial infarction; ICU, Intensive Care Unit.

with mortality (p=0.177) when controlling the possible confounding variables that may influence on death (**Tabla 8**). Other variables, such as diabetes mellitus (OR 3.228), complications (OR 4.943) and perioperative AMI (OR 7.016) were very strong independent predictors of mortality in these patients.

DISCUSSION

Most studies have suggested that, the highest late mortality occurred in patients older than 70 years. Mortality was lower in the group of patients studied than that of other researches, but it coincides with the results of Riera *et al.*[14] who found an average age of 65 years. In this study, mortality was higher in women than men, yet the difference was not significant, as CABG is performed in women with more severe and advanced coronary artery disease, older age and comorbidities[15,16].

Diabetes mellitus is a risk factor for post-CABG mortality. Likewise, AMI is associated with a higher mortality due to reduced ejection fraction, as well as a high predisposition to cardiac arrhythmias. These findings are consistent with the literature reviewed[17,18]. The same happens in relation to the anthropometric variables and mortality[19].

As reported in prior studies, QRS prolongation correlates with greater dyssynchrony, which in turn, causes deterioration in left ventricular function[20]. Changes that prolong QRS duration express asynchrony, contributing to the decrease in ventricular function and to an electrical disturbance that increases dispersion of ventricular repolarization and predisposes to ventricular arrhythmias, giving the QRS width a prognostic value to predict mortality[21].

The results of our investigation coincide with those by Arribas Leal *et al.*[22] who, in a series of 203 patients, found that average preoperative QRS duration was 92.6±19.4 ms. Prolonged duration was associated with a greater number of diseased coronary

Table 8. Results of multivariate analysis for QRS as a prognostic factor for mortality.

Variables	OR	CI 95%	p
Age	1.039	0.995-1.085	0.080
Male sex	0.716	0.307- 0.671	0.440
LVEF	0.971	0.943-1.001	0.056
Presence of diabetes mellitus	3.228	1.514-6.883	**0.002**
Type of CABG	1.503	0.720-3.141	0.278
Complications	4.943	1.603-15.243	**0.005**
Perioperative AMI	7.016	3.047-16.155	**p<0.001**
Support		(Dummy variable)	
CPB	0.433	0.097-1.937	0.273
Beating-heart surgery	0.326	0.074-1.445	0.140
QRS > 100 ms	1.666	0.795-3.493	0.177

AMI, acute myocardial infarction; CABG, coronary artery bypass grafting; CI, confidence interval; CPB, cardiopulmonary bypass; LVEF, left ventricular ejection fraction; OR, odds ratio.

vessels[22]. This study shows in a univariate way that the duration of the QRS interval in preoperative ECG is associated with higher mortality after CABG surgery, due to higher prevalence of mechanical ventricular desynchronization, with a decrease in normal ventricular contraction, which favors hemodynamic disorders in the postoperative period and is associated with greater long-term mortality[23].

It was also possible to identify the cut-off point by observing that a QRS duration lower than 100 ms had a significant association with intermediate mortality. This was lower than those reported in the literature reviewed, where it is stated that prolonged QRS from 110 ms is usually a predictor of sudden death. Although the normal value of this interval is up to 100 ms. This may be explained by the fact that these investigations were conducted in patients with heart failure and low LVEF. So, QRS was measured as a predictor of sudden death in a different context. But the patients of our investigation had an average normal LVEF.

A study carried out by Gasparini *et al.*[2] shows how cardiac death rate increases every 10 ms, which increases QRS duration, and becomes much longer in patients in the peak of the QRS duration. That is, small variations in QRS duration, lead to significant increase in cardiac mortality (16% for every 10 ms). Mortality after perioperative AMI ranges between 3.5-25%[24]. This AMI and immediate CABG complications are directly related with mortality[25].

Diabetic patients suffer complications more frequently, so they have a worse prognosis after surgery[26]. The QRS, although the sample consisted of patients with preserved LVEF, was not independently associated with mortality, probably because of the sample size and also because there are other factors that are stronger independent predictors of fatal outcome. It is likely that, widening of the QRS is associated with a greater number of complications or hemodynamic disorders due to perioperative AMI in the CABG. Hence, these variables are co-dependent. However, in this investigation, the longest duration of this interval as such could not be demonstrated to be an independent predictor of mortality in the CABG. Although it could also be related to the finding of a lower cut-off point than that described in literature, due to the characteristics of the patients in this study. However, other studies have reported that longer QRS duration in the preoperative period for CABG has been associated with lower postoperative outcomes in the presence of systolic ventricular dysfunction, cardiac arrest in the immediate postoperative period and long-term adverse events. Those related to higher mortality[27].

The results of this investigation do not detract QRS measurement to provide prognostic information, although the current risk models for mortality, EuroSCORE and Parsonnet, do not include any electrocardiographic variable.

Further study on broader populations is needed to define the prognostic role of this variable after CABG.

CONCLUSIONS

The duration of the QRS interval showed significant association with cardiovascular mortality in the univariate analysis, but its independent effect on cardiac death in patients treated with coronary artery bypass grafting surgery could not be demonstrated when controlling the rest of the variables.

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