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QRS distortion in pre-reperfusion electrocardiogram is a bedside predictor of large myocardium at risk and infarct size (a METOCARD-CNIC trial substudy)

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ABSTRACT

Background: QRS distortion is an electrocardiographic (ECG) sign of severe ongoing ischemia in the setting of ST-segment elevation acute myocardial infarction (STEMI). We sought to evaluate the association between the degree of QRS distortion and myocardium at risk and final infarct size, measured by cardiac magnetic resonance (CMR).

Methods: A total of 174 patients with a first anterior STEMI reperfused by primary angioplasty were prospectively recruited. Pre-reperfusion ECG was used to divide the study population into three groups according to the absence of QRS distortion (D0) or its presence in a single lead (D1) or in 2 or more contiguous leads (D2+). Myocardium at risk and infarct size were determined by CMR one week after STEMI. Multiple regression analysis was used to study the association of QRS distortion with myocardium at risk and infarct size, with adjustment for relevant clinical and ECG variables.

Results: 101 patients (58%) were in group D0, 30 (17%) in group D1, and 43 (25%) in group D2+. Compared with group D0, presence of QRS distortion (groups D2+ and D1) was associated with a significantly adjusted larger extent of myocardium at risk (group D2+: absolute increase 10.4%, 95% CI 6.1–14.8%, $p < 0.001$; group D1: absolute increase 3.3%, 95% CI 1.3–7.9%, $p = 0.157$) and larger infarct size (group D2+: absolute increase 10.1%, 95% CI 5.5–14.7%, $p < 0.001$; group D1: absolute increase 4.9%, 95% CI 0.08–9.8%, $p = 0.046$).

Conclusions: Distortion in the terminal portion of the QRS complex on pre-reperfusion ECG in two or more leads is independently associated with larger myocardium at risk and infarct size in the setting of primary angioplasty-reperfused anterior STEMI. QRS distortion in only one lead is independently associated with larger infarct size in this setting. Our findings suggest that QRS distortion analysis could be included in risk-stratification of patients presenting with anterior STEMI.

1. Introduction

The electrocardiogram (ECG) is the first diagnostic test used in the triage of patients with suspected acute myocardial infarction (MI) [1,2]. ECG must be obtained and interpreted as quickly as possible after clinical presentation, in order to establish a prompt and appropriate diagnosis and treatment [3]. The presence of ST segment elevation in two

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or more contiguous leads in an appropriate clinical context (e.g. typical symptoms of myocardial ischemia) allow the clinician to anticipate the affected artery and select an appropriate emergency reperfusion strategy [1,2]. ECG can also provide valuable prognostic information. In patients presenting with ST-segment elevation myocardial infarction (STEMI), distortion in the terminal portion of the QRS complex in admission ECG is associated with poor prognosis when present in two or more contiguous leads. This electrocardiographic pattern was first described by Birnbaum et al. in the era of thrombolytic therapy [4–7] and was recently validated by our group for infarcts reperfused with thrombolytics or by primary angioplasty [8–11]. However, the precise association between terminal QRS distortion at admission and myocardium at risk and infarct size after reperfusion therapy are unknown. Additionally, the significance of terminal QRS distortion in only one lead has not been studied. Here we present the pre-specified ECG substudy of the METOCARD-CNIC randomized clinical trial, which recruited anterior STEMI patients undergoing primary angioplasty (percutaneous coronary intervention, PCI) within 6 h of symptom onset [12]. We prospectively evaluated the association between the presence of terminal QRS distortion (in one lead and in two or more leads) and cardiac magnetic resonance (CMR) measures of myocardium at risk, infarct size and left ventricular ejection fraction (LVEF).

2. Methods

2.1. General considerations

The METOCARD-CNIC trial prospectively recruited patients with first anterior STEMI presenting early (anticipated reperfusion within 6 h from symptom onset) and undergoing primary angioplasty [12–14]. A pre-specified subanalysis of this trial included study of the association between the presence of QRS distortion in admission ECG and CMR measures 5–7 days after reperfusion. Inclusion/exclusion criteria can be found elsewhere [12]. The present study analyzed data from the 220 patients undergoing CMR one week after infarction. All patients gave informed consent and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki, reflected in a priori approval by the corresponding institutional human research committee.

2.2. ECG analysis

The following information was collected from pre-reperfusion (pre-PCI) ECG: heart rate (beats per minute), PR interval (milliseconds), QRS duration (milliseconds), ST segment elevation (mm), conduction abnormalities (right bundle branch block pattern [left bundle branch block was a trial exclusion criterion]), and the pattern and degree of QRS distortion. Electrocardiograms were scanned and sent to a central core lab at the *Centro Nacional de Investigaciones Cardiovasculares Carlos III-CNIC* (National Centre for Cardiovascular Research, Madrid-Spain) for blinded analysis after recruitment was closed. The ST segment deviation was measured with digital calipers to the nearest 0.01 mV 20 ms after the end of the QRS complex, using the TP-segment as the isoelectric baseline. ECG was recorded from anterior leads (V1 to V6, I, and aVL) and inferior leads (II, III, and aVF). QRS distortion was analyzed by two independent expert observers, using the 2004-revised Birnbaum QRS distortion criteria. According to these criteria, QRS distortion is defined as any of the following conditions: (A) J point amplitude ≥ 50% of the R wave amplitude measured from the TP–PR baseline; or (B) absence of an S wave below the TP–PR isoelectric line in leads that usually have a terminal S configuration (leads V1 to V3) [4–7]. Classical criteria required the presence of these conditions in two or more consecutive leads. In our study, we also included evaluation of ECGs fulfilling these criteria but in only one lead as a pre-defined analysis. When right bundle branch block was present, QRS distortion was considered to be present only if criterion A was met.

2.3. CMR protocol

A detailed description of the CMR protocol and methods for imaging analysis has been reported elsewhere [13]. Briefly, cardiac function, cardiac edema (for defining myocardium at risk) and myocardial necrosis (for defining infarct size) were evaluated on day 5–7 CMR. Scans were obtained with a 3.0-Tesla magnet (Achieva Tx, Philips Medical Systems), with vector cardiographic gating and a dedicated cardiac 32-channel phased-array surface coil. All sequences were acquired during expiration breath-hold. After standard localizer scan, a balanced turbo field echo steady-state free precession (SSFP) sequence was run with the sensitivity-encoding fast parallel imaging technique, covering the whole LV for functional cine imaging. Edema imaging was performed by matching the slice position of the cine images using a T2-weighted triple inversion-recovery turbo spin echo (T2W-STIR) sequence. Delayed enhancement images to assess necrotic myocardium were acquired with a T1-weighted 2D segmented inversion-recovery turbo field echo (2D-IRTFE) sequence performed 10–15 min after intravenous administration of 0.20 mmol of gadopentate dimeglumine contrast agent (Magnevist, Schering AG, Berlin, Germany) per kg body weight. The delayed enhancement images were thus acquired in short axis slices that matched function and T2W imaging.

2.4. CMR data analysis

Blinded analyses were conducted by the CMR core laboratory at the CNIC. Data were quantified with dedicated software (QMass MR 7.5; Medis, Leiden, the Netherlands). Parameters measured were LV volumes, LV ejection fraction (LVEF), area of edema, and the extent of necrosis. Left ventricular function was determined from SSFP-cine imaging scans. Endocardial and epicardial borders from short-axis images were automatically traced with manual adjustment to calculate left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), and LVEF. For imaging analysis of edema (myocardium at risk), myocardial signal intensity was measured after manually tracing the endocardial and epicardial contours of T2W-STIR short-axis images. Abnormal areas were defined using the full-width at half-maximum, with manual correction if needed. Areas corresponding to slow-flow artifacts were carefully excluded from edematous area. Hypointense areas within the edematous zone, corresponding to hemorrhagic infarction, were included within the edematous region. Myocardial necrosis was defined according the extent of delayed gadolinium enhancement after manually tracing the endocardial and epicardial contours on 2D-IRTFE short axis images. Hypointense black areas within the necrotic zone, corresponding to microvascular obstruction, were included within the necrotic area. Area of edema and infarct size were expressed as percentage of the left ventricular mass. Myocardial salvage index was calculated as the proportion of salvaged myocardium at risk as follows: (area of edema–infarct size)/area of edema.

2.5. Statistical analysis

For quantitative variables showing a normal distribution, data are expressed as mean ± SD and compared by parametric methods (one-way ANOVA). Non-normal data are reported as medians and interquartile range (IQR), and compared by nonparametric methods (Kruskal–Wallis test). For categorical variables, data are presented as frequencies and percentages, and compared using exact methods (Fisher's test). A priori contrasts were performed after ANOVA or Kruskal–Wallis test to study differences between group D0 and D1, and between groups D0 and D2+.

Multivariate linear regression analysis was performed to study the association between QRS distortion and myocardium at risk or infarct size. The models included the following relevant clinical and ECG prognostic variables on admission : age (years), sex (male/female), body mass index (kg/m^2, hypertension (no/yes), dyslipemia (no/yes), smoking status, diabetes (no/yes), duration of ischemia (time from symptom onset to balloon (min)), sum of anterior ST segment elevation (mm), intravenous metoprolol administration (no/yes), and Killip class ≥ II at admission (no/yes). QRS distortion was included in the analysis as a three-category variable: no distortion (D0), distortion in only 1 lead (D1), and distortion in 2 or more leads (D2+). All statistical tests were 2-sided, and values of $p < 0.05$ were considered statistically significant. All statistical analyses were performed

Table 1
Demographic characteristics and ECG data on admission.

	D0 (n = 101)	D1 (n = 30)	D2+ (n = 43)	P value
Age (years)	59.7 ± 11.8	55.8 ± 12.2	57.3 ± 3.4	0.207
Male sex, n (%)	88 (87.1)	23 (76.7)	41 (95.3)	0.068
Body mass index (kg/m^2)	28.1 ± 3.8	26.9 ± 2.9	27.1	0.132
Hypertension, n (%)	46 (45.5)	15 (50.0)	17 (39.5)	0.670
Dyslipidemia, n (%)	51 (50.5)	8 (26.7)	18 (41.8)	0.064
Diabetes, n (%)	22 (21.8)	4 (13.3)	7 (16.3)	0.511
Smoking, n (%)				0.321
Active	49 (48.5)	20 (66.7)	23 (53.5)	
Quitting <10 years	17 (16.8)	4 (13.3)	3 (7.0)	
Quitting >10 years	12 (11.9)	3 (10.0)	4 (9.3)	
Never smoker	23 (22.8)	3 (10.0)	13 (30.2)	
Killip I at admission, n (%)	95 (93.1)	27 (90.0)	38 (88.4)	0.394
Heart rate (bpm)	79 ± 8	79 ± 16	83 ± 21	0.418
PR segment (ms)	174 ± 64	169 ± 17	164 ± 35	0.569
QRS duration (ms)	94.0 (17.8)	95.9 (20.2)	98.5 (15.8)	0.370
Anterior ST segment elevation (mm)	10.7 ± 5.4	14.1 ± 6.3	20.4 ± 14.9 *	<**0.001**
Total ST segment elevation (mm)	11.0 ± 5.6	14.4 ± 6.5	21.5 ± 16.8 *	<**0.001**
Pain-balloon time (minutes)	198.1 ± 69.4	198.2 ± 68.3	185.1 ± 60.6	0.545
i.v. Metoprolol, n (%)	55 (54.5)	14 (46.7)	14 (32.6)	0.052

ECGs were obtained at admission: D0, patients with no QRS distortion in any lead; D1, patients with QRS distortion in only 1 lead; D2+, patients with QRS distortion in two or more leads. Depending on the distribution of variables, one-way ANOVA or Kruskal–Wallis tests were performed to study differences among the three groups, yielding the p-values indicated in the table. A priori contrasts were performed after ANOVA or Kruskal–Wallis test to study between-group differences for D0 vs. D1 and D0 vs. D2+; *$p < 0.01$ compared with D0.