

# QRS duration: a novel marker of microvascular reperfusion as assessed by myocardial blush grade in ST elevation myocardial infarction patients undergoing a primary percutaneous intervention

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**Objectives** Prolonged QRS duration is a predictor of poor prognosis in patients with coronary artery disease. The association between the duration of QRS and myocardial reperfusion is not very well understood. Our aim was to assess the relationship between the measurements of QRS duration and myocardial blush grade (MBG) in patients with ST elevation myocardial infarction (STEMI) who were treated with a primary percutaneous intervention.

**Patients and methods** A total of 213 patients (mean age:  $57.5 \pm 11$  years) with STEMI were included. ECG recordings were obtained for the evaluation of the QRS duration before and after primary percutaneous coronary intervention. Angiographic assessment in the infarct-related artery was performed using the MBG. Patients were categorized into two groups of those with impaired microvascular reperfusion (MBG: 0–1) and those with normal microvascular reperfusion (MBG: 2–3).

**Results** Overall, 105 and 108 patients had an MBG of 0–1 or 2–3, respectively. There is no significant difference between patient's characteristics. Despite the absence of a difference between two groups in terms of the QRS duration at presentation ( $P: 0.57$ ), patients with impaired

microvascular reperfusion were found to have longer QRS duration at immediately postprocedure ( $P: 0.003$ ) and postprocedure 60 min time-points ( $P < 0.001$ ). Correlation analyses showed a positive correlation between pain-to-balloon time and QRS duration at postprocedure 60 min time-points ( $r: 0.137$  and  $P: 0.04$ ).

**Conclusion** Our results suggest that longer QRS duration after angioplasty seemed to indicate the presence of impaired microvascular reperfusion in patients with STEMI. *Coron Artery Dis* 26:583–586 Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

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## Introduction

ST elevation myocardial infarction (STEMI) generally results from intraluminal thrombus formation and occlusion of a ruptured or an unstable plaque [1]. The main goal of therapy in STEMI is to restore microvascular flow and sustain the myocardial perfusion [2].

A variety of markers including ECG and coronary angiography have been utilized to assess myocardial reperfusion [3,4]. The prolongation of QRS duration, evaluated by a standard 12-lead ECG, is a marker of ventricular dysfunction and has been associated with a poor prognosis in STEMI [2]. In previous studies examining QRS duration at admission, prolonged QRS was associated with an increased risk of impaired ventricular systolic function and adverse events [5–7].

Although successful recanalization of the epicardial vessels is an essential target of therapeutic interventions, microvascular reperfusion in fact represents a stronger predictor of the cardiac outcomes. Parameters that are believed to correlate with microvascular perfusion include ST segment resolution and myocardial blush grade (MBG) [8]. MBG, a widely used angiographic parameter, provides a means to evaluate the washout of myocardial blush during angiography. Studies have clearly established a remarkably consistent relationship between microvascular reperfusion, left ventricle dilatation, heart failure, and mortality [9,10].

In the present study, we assessed the relationship between assessments of QRS duration and MBG in the patients with STEMI treated with primary percutaneous coronary intervention (PCI).

## Patients and methods

This study enrolled 213 consecutive patients with a diagnosis of STEMI within 12 h of symptom onset.

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Patients were categorized into normal ventricular reperfusion (MBG: 2–3) and impaired ventricular reperfusion (MBG: 0–1) groups on the basis of postangioplasty MBG. The diagnosis of STEMI was made on the basis of the presence of at least two of the following: chest pain lasting longer than 30 min, increase in the creatinine kinase myocardial band, and new ST elevation of at least 0.1 mV in two or more contiguous leads. All patients were administered 300 mg aspirin and 600 mg clopidogrel loading dose before the procedure. Blood samples were obtained on admission, and patients with normal creatinine levels were included in the present study. Exclusion criteria were previous myocardial infarction, bundle branch block, cardiogenic shock, and chronic kidney disease. The study protocol was approved by the local Ethics Committee and informed written consent was obtained from all patients.

### ECG

A 12-lead ECG with a paper speed of 50 mm/s was recorded at admission as well as at the immediate post-procedure period and 60 min following primary PCI in each patient. The duration of QRS was calculated manually by two cardiologists blinded to the clinical status of the patients, and was measured from the beginning of the earliest to the end of the last QRS deflection. Measurements of three continuous beats by an independent observer were averaged for each ECG, and all measurements were obtained from the infarct-related artery leads. The average QRS duration of two observers was utilized for analysis. The interobserver and intraobserver variability was very low (<3% and <2%, respectively). Patients with complete bundle branch block, or second-degree or third-degree atrioventricular block were excluded.

### Echocardiography

Echocardiographic evaluation was performed by two cardiologists blinded to the current study within the first 24 h after primary PCI according to the proposed criteria of the American Society of Echocardiography using a Hewlett Packard SONOS 4500 and 2.5–3.5 MHz transducer (Hewlett Packard, Dublin, Ohio, USA). The left ventricular ejection fraction (EF) was measured according to the modified Simpson's method.

### Coronary angiography

At the start of the procedure, intravenous heparin 10 000 U and intracoronary nitroglycerin (if the patient was not hypotensive) were administered. The use of glycoprotein IIb/IIIa inhibitor (tirofiban) was left to the discretion of the operator. All patients underwent initial balloon angioplasty, followed by coronary artery stenting, if necessary. The purpose of the primary PCI procedure was to obtain a residual stenosis of less than 20% in the infarct-related artery (IRA) by visual evaluation. All coronary angiograms were recorded using a Philips

AlluraXper FD device (Philips Medical Systems Nederland B.V., Veldhoven, the Netherlands), and the contrast injector used was set at a contrast infusion rate of 4 ml/s for the left coronary artery (8 ml bolus) and 3 ml/s for the right coronary artery (6 ml bolus). The MBG was used to assess the washout of myocardial blush during angiography. Grade 0 was defined as the failure of the contrast to enter the microvasculature. In grade 1 cases, contrast enters slowly, but fails to exit the microvasculature. Grade 2 defines delayed entry and exit from the microvasculature. Finally, grade 3 indicates normal entry and exit from the microvasculature [11]. Myocardial blush grading was performed visually with a cine-film at a 25 frame/s rate in the catheterization laboratory. The length of the coronary angiographic run had to be adequate, and our final coronary angiographic run was long enough to visualize the venous phase of the contrast passage. These coronary angiographic runs were performed in identical views with respect to the IRA. From multiple orthogonal views, the single view was chosen to minimize superimposition of noninfarcted territories in the assessment of the MBG. The laterolateral view for the left anterior descending artery, right anterior oblique view for right coronary artery and laterolateral or right anterior oblique views for circumflex coronary artery were used in most patients. Two experienced cardiologists blinded to the clinical history and laboratory results of the patients performed MBG grading. All cardiologists provided the required conditions such as administering an adequate amount of contrast medium and allowing adequate duration of angiographic runs to assess the myocardial blush score. Reproducibility of the MBG was evaluated by two observers viewing 30 samples of the coronary angiograms. Intraobserver and interobserver agreement was 95 and 90%, respectively. The other angiographic variables assessed were multivessel coronary artery, IRA, and thrombolysis in myocardial infarction (TIMI) flow before primary PCI. TIMI flow grades were assessed as described previously [12].

### Statistical analyses

SPSS 18.0 (SPSS Inc., Chicago, Illinois, USA) was used for statistical analyses. The normality of the distribution of continuous variables was evaluated using the Kolmogorov–Smirnov test. For continuous variables, the Student *t*-test was used to test differences between groups. For correlation analysis, Spearman's correlation analysis was used. Two-tailed *P* values less than 0.05 were considered statistically significant. Continuous variables were expressed as mean ± SD and categorical variables were expressed as percentages.

### Results

Two study groups were defined on the basis of impaired microvascular reperfusion (MBG: 0–1) and normal microvascular reperfusion (MBG: 2–3). Of the overall participants, 105 and 108 patients had an MBG of 0–1

**Table 1 Demographic parameters of the study groups**

	MBG		<i>P</i>
	MBG: 0–1 ( <i>n</i> = 105)	MBG: 2–3 ( <i>n</i> = 108)	
Age	57 ± 11	58.3 ± 12	0.27
Sex (female/male)	13/92	24/84	0.06
DM	9	18	0.05
HT	24	27	0.71
Smoking	50	42	0.20
Family history	17	9	0.08
Pain-to-balloon time (h)	5.2 ± 1.6	3.3 ± 1.2	<0.001
EF (%)	42.7 ± 9	48.2 ± 8	<0.001
Glucose (mg/dl)	171 ± 82	155 ± 75	0.14
LDL (mg/dl)	123 ± 32	118 ± 33	0.27
Peak CKMB (IU/l)	199.2 ± 18	170.3 ± 16	<0.001
Infarct-related artery [ <i>n</i> (%)]			
LAD	61 (58.1)	46 (42.6)	0.005
RCA	18 (17.1)	13 (12)	
CX	26 (24.8)	49 (45.4)	
Multivessel disease [ <i>n</i> (%)]			
1 vessel	48 (45.7)	54 (50)	0.80
2 vessel	38 (36.2)	33 (30.6)	
3 vessel	19 (18.1)	21 (19.4)	
Baseline TIMI flow [ <i>n</i> (%)]			
TIMI 0–1	102 (97.1)	71 (65.7)	<0.001
TIMI 2–3	3 (2.9)	37 (34.3)	
MI subgroup [ <i>n</i> (%)]			
Anterior wall	62 (59)	47 (43.5)	0.02
Nonanterior wall	43 (41)	61 (56.5)	
Stent use [ <i>n</i> (%)]	97 (92.4)	103 (95.4)	0.52
Glycoprotein IIb/IIIa antagonist [ <i>n</i> (%)]	30 (28.6)	42 (38.8)	0.06

CX, circumflex; CKMB, creatinine kinase myocardial band; DM, diabetes mellitus; EF, ejection fraction; HT, hypertension; LAD, left anterior descending artery; MBG, myocardial blush grade; MI, myocardial infarction; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction.

and 2–3, respectively. Demographic parameters in both groups are shown in Table 1. As shown in the table, the two groups were similar in terms of age, sex, history of family, smoking, and hypertension ( $P > 0.05$ ). A significant difference in EF was found between the two groups as well as in the pain-to-balloon time, which was longer in those with impaired microvascular reperfusion. In addition, patients with impaired ventricular reperfusion had significantly longer pain-to-balloon time ( $P < 0.001$ ).

QRS duration and MBG in the study groups are shown in Table 2. Although the two groups were comparable in terms of QRS duration at presentation ( $P: 0.57$ ), patients with impaired microvascular reperfusion were found to

**Table 2 Relation between the QRS duration and the MBG in the study groups**

	MBG		<i>P</i>
	MBG: 0–1 ( <i>n</i> = 105)	MBG: 2–3 ( <i>n</i> = 108)	
QRS duration on admission (ms)	73 ± 18	72 ± 14	0.57
QRS duration at postprocedure (ms)	81 ± 11	74 ± 20	0.003
QRS duration in postprocedure 60 min (ms)	88 ± 10	78 ± 16	<0.001

MBG, myocardial blush grade.

have longer QRS duration at immediate postprocedure ( $P: 0.003$ ) and postprocedure 60 min time-points ( $P < 0.001$ ). In other words, patients in the impaired ventricular reperfusion group had significantly longer QRS duration at postangioplasty compared with the patients in the normal reperfusion group. In addition, correlation analyses showed a positive correlation between the pain-to-balloon time and QRS duration at postprocedure 60 min ( $r: 0.137$  and  $P: 0.04$ ).

## Discussion

In the present study, prolonged QRS duration after the angioplasty in patients with STEMI was associated with impaired microvascular reperfusion as evidenced by angiographic results.

Acute myocardial infarction represents a major cause of heart failure, arrhythmia, and mortality in patients with coronary artery disease and impaired microvascular reperfusion is an important prognostic determinant in patients undergoing a primary PCI after STEMI. The success of primary PCI in STEMI is evaluated by a number of different methods including TIMI flow classification, MBG classification, and ST segment resolution. Of these, MBG is a marker of microvascular reperfusion and, compared with TIMI flow, represents a better predictor of clinical outcomes [13,14].

The standard 12-lead ECG should be used for risk stratification in STEMI patients.

In addition, QRS duration has been considered an important prognostic marker, and the significance of QRS duration is well known in patients with heart failure or myocardial infarction [15,16]. In recent studies, prolongation of QRS duration has also shown correlations with interventricular conduction delay because of myocardial ischemia [17,18]. Similarly, in the HERO-2 study, the QRS duration at baseline and 60 min after fibrinolytic therapy was associated with increased 30-day mortality after myocardial infarction, and only patients with normal QRS duration ( $< 125$  ms) were included in the study. [19]. A similar relationship was shown in the GUSTO-1 population with QRS prolongation within the normal range (100 vs. 80 ms) postanterior myocardial infarction carrying the strong association for 30-day mortality [5]. Another study found that patients with QRS prolongation had increased ventricular volumes, decreased left ventricular EF, and higher incidence of sudden cardiac death [20]. Kosuge *et al.* [21] observed a relationship between high admission QRS score and impaired myocardial reperfusion. Again, in a previous study by Ilkay *et al.* [22], QRS duration emerged as a strong marker of myocardial reperfusion. Maden *et al.* [23] detected an association between QRS duration on admission and no-reflow. Tao and Fan [24] found an association between the prolongation of QRS duration and prognosis. In the present study, we observed a relationship between the normal

QRS duration (<100 ms) and impaired myocardial reperfusion because the upper limit of normal QRS duration is generally considered less than 100 ms, and this criterion has also been used in a previous study [25].

Certain limitations of this study need to be addressed. First, the sample size was relatively small. Second, the present study lacked a long-term follow up of cardiac complications. In addition, the method used for the measurement of QRS duration was manual, and therefore not standardized.

## Conclusion

In our study, longer QRS duration after angioplasty seemed to indicate the presence of impaired microvascular reperfusion in patients with STEMI. The QRS duration may be recommended as a novel marker of impaired microvascular reperfusion in patients with STEMI. Further studies are needed to better elucidate the association between the duration of QRS and reperfusion parameters in STEMI.

## Acknowledgements

### Conflicts of interest

There are no conflicts of interest.

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