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LEADING ARTICLE

Can QRS Duration Predict Microvascular Reperfusion after Primary Percutaneous Coronary Intervention?

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Background. *In patients with ST-segment elevation myocardial infarction (STEMI), primary percutaneous coronary intervention (PCI) was associated with early and sustained restoration of blood flow compared to fibrinolytic therapy. Impaired myocardial blush grade (MBG), may be present in many after successful PCI. Prolonged QRS was found to be associated with an increased morbidity and mortality after STEMI.*

Objectives*. To find out if prolonged QRS in STEMI patients can predict low MBG after primary PCI.*

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Patients and Methods. *Sixty STEMI patients were included in our study. History taking, clinical examination, ECG with measuring of QRS duration, primary PCI, and echocardiography were done to them. QRS duration was measured before and after PCI and the change was calculated.*

Results. *Patients with low MBG (0-1) had significantly higher QRS duration before and after PCI and significantly lower change after PCI (p <0.00001 for each).Independent predictors for MBG were in order of significance: QRS duration before PCI (p <0.00001), QRS duration after PCI (p <0.00001), Troponin level (p <0.00001), symptom to balloon time (p =0.0063), and CK-MB level (p=0.015). QRS duration 89 ms could predict low MBG with sensitivity 82.6%, specificity86.5%, positive predictive value 79.2%, and negative predictive value 88.9%.*

Conclusion. *In STEMI patients undergoing primary PCI, prolonged QRS duration was associated with a low MBG, a sign of impaired microvascular reperfusion. QRS duration before and after PCI were found to be independent predictors for low MBG (0-1).*

Keywords: *primary PCI; Microvascular Reperfusion; Myocardial Blush Grade; STEMI; QRS duration.*

Conflicts of interest: None declared.

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Introduction

Despite the major advances in its management, ST-segment elevation myocardial infarction (STEMI) is still a leading cause of death and morbidity all over the globe [1, 2].The main goal of therapy in STEMI is to open the occluded artery, restore transluminal coronary flow, restore microvascular flow and sustain the myocardial perfusion [3].Primary percutaneous coronary intervention (PCI) was found to be superior to fibrinolytic therapy in treating STEMI patients. Primary PCI was associated with early and sustained restoration of thrombolysis in myocardial infarction (TIMI) flow 3 compared to fibrinolytic therapy [4]. However, even after successful opening of infarct related artery with primary PCI and restoration of TIMI flow 3, an impaired myocardial reperfusion as shown by poor myocardial blush grade (MBG), may be present in many patients which is associated with poor short and long term outcome [5]. So, it might be useful to search for predictors for poor myocardial perfusion in STEMI patients undergoing primary PCI.

The prolongation of QRS duration, evaluated by a standard 12-lead ECG, is a marker of left ventricular dysfunction and has been associated with a poor prognosis in STEMI patients [6] and was also found to be associated with an increased risk of impaired ventricular systolic function and adverse events [7, 8]. However, the relation between QRS duration and microvascular reperfusion as manifested by impaired MBG after primary PCI in STEMI patients has not been yet studied. Therefore, the aim of our work was to find outif the presence of prolonged QRS in the surface ECG of STEMI patients can predict a poor microvascular reperfusion and a low MBG after primary PCI.

Patients and Methods

This observational study was performed in the Cardiology Department, Zagazig and Benha Universities in co operation with National Heart Institute during the period from January 2016 till May 2017. Sixty STEMI patients undergoing primary PCI were included in our study. The inclusion criteria were: confirmed first acute STEMI, which was defined by the presence of typical chest pain that lasts for at least 20 minutes in addition to ST-segment elevation ⩾ 0.1 mV in at least two contiguous leads [9].All patients were presented within 12 hours of beginning of symptoms. Primary PCI was done to all patients, primary PCI with considered successful when there is less than 20% residual stenosis and TIMI flow 3 of the infarct-related artery defined as normal flow, which fills the distal coronary bed completely [10].

Patients with left bundle branch block, with prior coronary revascularization, prior STEMI, or when primary PCI was not performed, were excluded from our. Our study included 60STEMI patients. Our Institutional Review Board had approved the study protocol.

After we obtained a written informed consent, an in addition to routine history and clinical examination, we did the following to every patient:

Complete standard 12-lead electrocardiography (ECG) was done on arrival to every patient. In the present study, all measurements were obtained from infarct-related artery leads. Admission ECG was uti-

lized for diagnosis of STEMI and for measurement of QRS duration. The QRS duration was measured manually with the help of a caliper and a magnifying lens (to diminish the effect of the ST deviation on the measurement). Measurements were done by two expert cardiologists who were unaware of other clinical and angiographic data. The average value of the measurements obtained by the two investigators was taken into account for statistical analysis in each patient. ECG was repeated 60 minutes after PCI and change in QRS duration was calculated by subtracting post-angioplasty QRS duration from pre-angioplasty QRS duration.

Primary PCI was done to all patients within 12 hours of onset of symptoms by at least two expert interventionists. At least one of the operators met the criteria of individual operator level of the 2007 Clinical Competence Statement on Cardiac Interventional Procedures and its revision [11].Direct stenting, balloon dilatation and stenting, balloon dilatation alone, and/or thrombus aspiration were done as indicated. Glycoprotein (GP) IIb/IIIa inhibitor (eptifibatide) was given as appropriate, according to operator opinion.

TIMI flow was assessed by operators. Only patients with TIMI 3 flow were considered as successful PCI and included in our study [10].

Myocardial blush grade (MBG) was assessed offline by two expert angiographers who were unaware of each other's results and of the patients' other data. MBG was assessed visually following the dye density score: MBG 0 = contrast density or no myocardial blush, MBG 1 = minimal contrast density or myocardial blush, MBG 2 = moderate contrast density or myocardial blush but did not reach that obtained during angiography of a noninfarct-related coronary artery, MBG 3 = normal contrast density or myocardial blush whichequals that obtained during angiography of a noninfarct-related coronary artery [12].

Echocardiographic studies were performed for all patients using the GE VIVID E9 machine with 2.5-MHz transducer within 24 hours of admission. The studies were performed by two operators unaware of each other's measures and of the patients' clinical and angiographic data. Views were taken while the patients were in the left lateral position.Left ventricular end-diastolic volume (LVEDV) and end-systolic volume (LVESV) was measured from the apical two-chamber and apical four-chamber views. Ejection fraction (EF) was calculated using the Simpson's method [13]. Wall motion score (WMS) was measured from the apical-4 and apical-2 chamber views using the sixteen segments model and giving a score to each segment according to its motion as following, normal = 1, hypokinetic = 2, akinetic = 3, dyskinetic = 4, and aneurysm = 5, and then WMS was calculated as the sum of scores of the 16 segments. Wall motion score index (WMSI) was calculated by dividing WMSI by 16 [13].

Statistical analysis. All data were analyzed using the SPSS for Windows package program (Version 20.0, Armonk, NY, USA: IBM Corp.). Differences between patients' group and control group were analyzed using x2 test and student's t-test. Correlations between different variables were investigated by Pearson correlation analysis. The logistic regression analysis was evaluated by the Hosmer–Lemeshow goodness-of-fit test.The receiver operating characteristic (ROC) curve was made to analyze for cutoff points of different parameters and their relation to MBG. A p value < 0.05 was regarded as being statistically significant.

Results

Our study included 60 STEMI patients, 49 males and 11 females. Their ages ranged from 34 to 83 years, with a mean age of 55.8±10.62 years. Patients were divided into two groups according to MBG:

Group 1: Included patients with MBG 0 or 1. This group included 23 patients, 19 males and 4 females; their mean age was 55.4±10.46 years.

Group 2: Included patients with MBG 2 or 3. This group included 37 patients, 30 males and 7 females; their mean age was 56.1±10.85 years.

There was no significant difference between the two study groups regarding other clinical, echocardiographic, angiographic, or PCI data. Patients with MBG 0-1 had significantly higher Troponin I level (p <0.00001), higher CK-MB level (p = 0.002), significantly higher QRS duration at first ECG (p <0.00001), significantly higher QRS duration after PCI (p <0.00001), significantly lower change in QRS duration (p <0.00001). Coronary angiography and PCI data showed that patients with MBG 0-1 had significantly lower incidence of left anterior descending artery (LAD) as a culprit for STEMI (p = 0.02) and significantly higher incidence of right coronary artery (RCA) as a culprit for STEMI (p = 0.009) (Table 1).

The independent predictors for myocardial blush grade in the order of significance were QRS duration before PCI (p <0.00001), QRS duration after PCI (p<0.00001), Troponin I level (p <0.00001), symptom to balloon time (p = 0.0063), and CK-MB level (p = 0.015) (Table 2).

Table 1. **Comparison between the two groups.**

	Group I MBG 0-1 (n = 23)	Group II MBG 2-3 (n = 37)	P value
Age (years)	55.4±10.46	56.1±10.85	0.137
Sex Male Female	19 (82.6 %) 4 (17.4%)	30 (81.1 %) 7 (18.9 %)	0.882
Hypertension	14 (60.9 %)	24 (64.9 %)	0.755
Diabetes	5 (21.7 %)	12 (32.4 %)	0.371
Smoking	17 (73.9 %)	28 (75.7 %)	0.878
Dyslipidaemia	7 (30.4 %)	13 (35.1 %)	0.707
Anterior STEMI	12 (52.2 %)	27 (73 %)	0.101
Troponin I level (ng/ml)	1.52±0.45	0.86±0.55	< 0.00001
CK-MB (IU/L)	82.4±29.77	59.1±23.02	0.002
QRS duration: - First (ms)	89.35±9.05	77.08±9.30	< 0.00001
- Second (ms)	85.52±8.51	71.14±8.35	< 0.00001
- Change (%)	3.83±2.72	7.71±3.59	< 0.00001
LVEDV (ml)	103.7±21.8	98.2±19.4	0.326
LVESV (ml)	43.8±13.6	39.7±15.2	0.283
EF (%)	59.4±9.11	60.7±10.21	0.61
Stenting	22 (95.6 %)	35 (94.6 %)	0.855
Baseline stenosis (%)	96.2±3.6	95.5±4.3	0.499
Stent diameter (mm)	2.89±0.626	3.11±0.714	0.215
Stent length (mm)	14.9±5.81	16.2±6.27	0.417
Culprit vessel: - LAD	13 (56.5 %)	31 (83.8 %)	0.02
LCX	2 (8.7 %)	2 (5.4 %)	0.619
RCA	8 (34.8 %)	3 (8.1 %)	0.009
OM	0 (0 %)	1 (2.7 %)	0.427

Data are expressed as mean±SD or number (%).STEMI: ST-segment elevation myocardial infarction. LVEDV= left ventricular end diastolic volume, LVESV= left ventricular end systolic volume, EF = ejection fraction. LAD = left anterior descending artery. LCX = left circumflex artery. RCA = right coronary artery. OM = obtuse marginal artery. TIMI = thrombolysis in myocardial infarction.

Table 2. **Logistic regression analysis for independent predictors of myocardial blush grade.**

Predictor	Odd ratio	95 % CI	P value
QRS duration before PCI	11.89	9.52-14.26	<0.00001
QRS duration after PCI	10.79	8.75 - 12.83	<0.00001
Troponin I level	9.16	7.54 - 10.79	<0.00001
Symptom to balloon time	6.11	4.87-7.35	0.0063
CK-MB level	4.49	3.21-5.78	0.015

CI = confidence interval. PCI = percutaneous coronary intervention. CK = creatine kinase.

The cut-off values for predictors of myocardial blush grade were shown in (Table 3). Regarding QRS duration before PCI, the cut-off point was 89 ms, the area under the curve (AUC) was 0.852, sensitivity was 82.6%, specificity was 86.5 %, positive predictive value (PPV) was 79.2 %, and negative predictive value (NPV) was 88.9 %. Regarding symptom to balloon time, the cut-off point was 4 hours, AUC was 0.798, sensitivity was 67.6%, specificity was 82.6%, PPV was 86.2%, and NPV was 61.3%.Regarding Troponin I level, the cut-off point was 1.2 ng/ml, AUC was 0.716, sensitivity was77.8%, specificity was 73.9 %, PPV was 82.4 %, and NPV was 68.1%.Regarding CK-MB level, the cut-off point was 44 ng/ml, AUC was 0.699, sensitivity was37.8 %, specificity was 95.6%, PPV was 93.3%, and NPV was 48.9%. The receiver operating characteristic (ROC) curves for different parameters are shown in (figure 1).

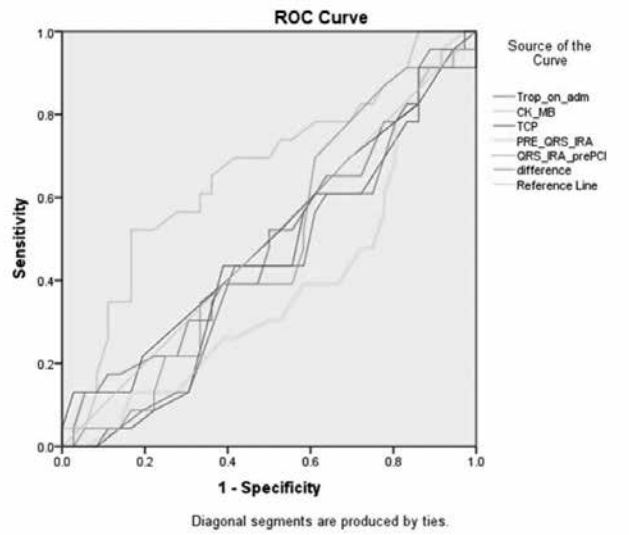

Figure 1. The receiver operating characteristic (ROC) curves for different parameters.

Discussion

In the present work, we tried to explore the relation between the QRS duration and the degree of microvascular reperfusion as assessed by MBG after successful primary PCI in STEMI patients. Our results showed a strong relation between them. Patients with low MBG (0-1) had significantly wider QRS either before or after

Table 3. **Cut-off values for predictors of myocardial blush grade.**

Predictor	Cut-off point	AUC	Sensitivity	Specificity	PPV	NPV
QRS duration before PCI	89 ms	0.852	82.6 %	86.5 %	79.2 %	88.9 %
Symptom to balloon	4 hours	0.798	67.6 %	82.6 %	86.2 %	61.3 %
Troponin	1.2 ng/ml	0.716	77.8 %	73.9 %	82.4 %	68.1 %
CK-MB	44 ng/ml	0.699	37.8 %	95.6 %	93.3 %	48.9 %

AUC = area under the curve. PCI = percutaneous coronary intervention. CK = creatine kinase.

PCI and the change of QRS duration was significantly lower in them. Among independent predictors for low MBG, QRS duration was the most significant. QRS duration before PCI was a good predictor for MBG with good sensitivity, specificity, positive, and negative predictive values.

Acute myocardial infarction is a noteworthy reason for mortality and major morbidities such as heart failure and fatal arrhythmias [2]. Impaired microvascular reperfusion is a critical prognostic determinant in patients experiencing primary PCI [4]. In spite of the fact that primary PCI is capable of restoring blood flow in the infarct-related artery in the vast majority of STEMI patients, however left ventricular dilatation, systolic dysfunction, and heart failure still occur in a significant proportion of patients after successfully performed primary PCI [14]. Many investigators had studied the relation between microvascular reperfusion, MBG, and their effect on LV dilatation and outcome after primary PCI. Henriques and his colleagues have found that MBGwas able to predict mortality in patients after primary angioplasty even in the presence of with TIMI 3 flow. They also found that infarct size was larger and left ventricular EF was lower in patients low MBG (0-1) [15].

In patients with cardiogenic shock, a high MBG (2-3) was found to be a strong indicator of survival after rescue PCI [16]. Myocardial blush grade, symptom to door time, and symptom to balloon time were found to be the only independent and significant predictors for left ventricular dilatation and remodeling in STEMI patients after successful primary PCI [17]. In their study, Şahan and Karamanlıoglu [18] have found a strong association between low MBG and ventricular arrhythmias in STEMI patients after primary PCI. This association was especially manifest in patients with who experienced ventricular fibrillation during their hospital stay. The simple resting 12-lead ECG is an exceedingly important tool not only in diagnosing STEMI patients but also on risk stratifying them. The initial ECG was able to predict 30 days all-cause mortality after STEMI in the GUSTO-I population. The sum of ST-segment deviation, QRS duration, and evidence of prior myocardial infarction were independent predictors of mortality in this study [19]. The presence of fragmented QRS complex at the 48th hour of STEMI was found to be a strong predictor of mortality and major adverse cardiovascular events in patients experiencing primary PCI [20].

In the Hirulog and Early Reperfusion or Occlusion-2 trial study, the initial QRS duration and its changes after 60 minutes was strongly related to 30-days mortality in STEMI patients receiving thrombolytic therapy [21]. Also the VALIANT trial investigators have found that when the QRS duration was prolonged it was associated with larger LVEDV, LVESV, and reduced EF even when it was still within the normal range. Prolonged QRS was also associated with an increased risk for development of heart failure cardiovascular mortality after STEMI [22]. In concordance with our study, Maden and his colleagues have found that the initial QRS duration on admission was related to the development of no-reflow in acute STEMI patients treated with primary PCI [23].

The association between QRS duration, extent of myocardial ischemia, and prognosis is quite complex. From the pathological point of view, myocardial necrosis and scarring with possible injury to Purkinje fibers may result in impaired myocardial conduction [24] which results in prolongation of QRS duration. So, prolonged QRS duration after STEMI may be a sign of prolonged ischemia which in turn may explain its association with the impaired microvascular reperfusion which is presented in our study by low MBG.

Conclusion

In STEMI patients undergoing primary PCI, prolonged QRS duration was associated with a low MBG, a sign of impaired microvascular reperfusion.

QRS duration before and after PCI and the change in QRS duration were found to be independent predictors for low MBG (0-1). Further studies with larger scales of patients may be needed to uncover the association between QRS duration, myocardial reperfusion, and prognosis in STEMI patients undergoing primary PCI.

Study limitations

Actually our study had several limitations. First, we measured the QRS duration manually, that means there was no standardization. Second,we did not follow-up our patients to find the effect of prolonged QRS and impaired MBG on cardiac events. Third, we included a relatively small number of patients.

Conflict of interest: None declared.

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