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Impact of fragmented QRS on in-hospital mortality in emergency coronary artery bypass grafting for STEMI: A retrospective analysis

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ABSTRACT

Objective: Fragmented QRS complex (fQRS) is associated with increased morbidity and mortality, sudden cardiac death, and recurrent cardiovascular events. The role of coronary artery bypass grafting (CABG) in the primary treatment of acute myocardial infarction remains controversial. In this study, we aimed to assess the predictive value of fQRS in-hospital mortality among acute segment elevation myocardial infarction (STEMI) patients undergoing emergency CABG for primary revascularization.

Patients and Methods: Between 2010 and 2020, we retrospectively included 99 consecutive STEMI patients who were not eligible for primary percutaneous intervention and required emergency CABG. The study population was divided into two groups: survivors and non-survivors. We compared the two groups regarding demographic, clinical, and operative characteristics.

Results: fQRS was identified as an independent predictor of in-hospital mortality (p = 0.037). Additionally, left ventricular ejection fraction (LVEF) was an independent predictor of in-hospital mortality (p = 0.028). Glomerular filtration rate (GFR), glucose levels, and Killip class \geq III were significantly associated with in-hospital mortality (p = 0.002), (p = 0.001) and (p < 0.001).

Conclusion: fQRS emerged as an independent predictor of in-hospital mortality among patients undergoing emergency CABG for primary revascularization in cases of STEMI.

Keywords: Fragmented QRS, ST-elevation myocardial infarction, Coronary artery bypass grafting, Mortality

1. INTRODUCTION

Segment elevation myocardial infarction (STEMI) is an acute and potentially fatal condition typically managed through primary percutaneous coronary intervention (pPCI) or thrombolytic therapy [1]. The guidelines for determining when coronary artery bypass grafting (CABG) surgery should be considered in STEMI patients remain somewhat ambiguous. Generally, CABG is regarded as a secondary option in current guidelines, to be pursued when PCI is not technically feasible, fails, or in cases of cardiogenic shock with acute myocardial infarction (AMI) accompanied by mechanical complications. Nevertheless, there is a limited body of research investigating the outcomes of emergent CABG treatment in STEMI patients [2,3].

Fragmented QRS (fQRS) is a depolarization abnormality that reflects delayed ventricular conduction around myocardial scar tissue and has been linked to various cardiac conditions [4-7]. In STEMI patients, fQRS has been demonstrated to be associated with in-hospital mortality, reperfusion failures, and it may serve as an independent predictor for major adverse cardiac events (MACEs) [8,9]. Furthermore, significant correlations have been identified between fQRS and in-hospital MACEs, as well as prognostic factors like hospitalization duration and long-term MACEs in patients undergoing CABG [10]. However, there is a paucity of data concerning the prognostic value of fQRS in patients undergoing emergent CABG.

In this study, we aimed to assess the predictive potential of fQRS in determining in-hospital mortality in STEMI patients undergoing emergent CABG. This study represents the first investigation into the relationship between fQRS and in-hospital mortality in STEMI patients undergoing emergent CABG for primary revascularization.

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2. PATIENTS and METHODS

Study population

A total of 125 patients, who were admitted to the catheter laboratory with a diagnosis of STEMI from the emergency department between 2010 and 2020, and for whom pPCI was either unsuitable or unsuccessful, underwent CABG within 6 hours of their emergency admission and were included in our study. This retrospective screening involved the following exclusion criteria: patients undergoing elective CABG after balloon dilation or stent implantation to the culprit lesion (n=7), patients deemed inoperable due to diffuse vascular disease (n=2), patients necessitating simultaneous valve intervention (n=3), acute STEMI patients with mechanical complications (n=1), individuals with chronic kidney and liver failure (n=3), presence of left or right bundle branch block (BBB) (n=4), patients with a pacemaker rhythm (n=1), patients who were receiving type I and III antiarrhythmic drugs (n=1), patients whose electrocardiogram (ECG) was unsuitable for evaluation (n=3), and patients receiving treatment for a previous cerebrovascular disease (n=1). Following the application of these exclusion criteria, a total of 99 patients were included in the study. Demographic data, laboratory findings, and outcomes were obtained from hospital records, file reviews, and telephone interviews. Our study was conducted per the principles of the Declaration of Helsinki and received approval from Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Ethics Committee with decision number 2023.04-46. Due to the nature of the study, informed consent was not obtained from the patients.

Patient characteristics and definitions

A complete blood count, serum creatinine, total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), and serum electrolyte levels were assessed. Blood samples were collected during the patients' hospitalization in the emergency room. The Killip class was evaluated upon admission and defined as follows: Killip class 1, AMI without heart failure; Killip class 2, AMI with mild heart failure; Killip class 3, AMI with pulmonary edema; and Killip class 4, AMI with cardiogenic shock [11]. Cardiogenic shock was defined as patients exhibiting pulmonary edema or a cardiac index <2.2 l/min/m2 in the absence of vasopressor or inotrope therapy, or systolic arterial pressure <90 mm Hg or mean arterial pressure (MAP) <65 mm Hg without the administration of a vasopressor agent or the need for vasopressor therapy to correct hypotension. It was also defined as pulmonary artery occlusion pressure >15 mm Hg or echocardiographic evidence of high pressure, or at least evidence of tissue hypoperfusion (e.g., skin mottling, oliguria, elevated lactate level, altered consciousness) [11]. Regarding smoking habits, individuals were categorized as "current smokers" or "non-smokers." Hypertension (HT) was defined as systolic arterial pressure >140 mmHg and/or diastolic arterial pressure >90 mmHg or if the patient was currently using antihypertensive medication [12]. Diabetes mellitus (DM) was defined as having

at least two fasting plasma glucose levels $\geq 126 \text{ mg/dL}$ or postprandial plasma glucose levels $\geq 200 \text{ mg/dL}$, or the use of anti-diabetic medication. Hyperlipidemia (HL) was defined as having serum total cholesterol $\geq 200 \text{ mg/dL}$, serum triglycerides $\geq 150 \text{ mg/dL}$, low-density lipoprotein cholesterol $\geq 130 \text{ mg/}$ dL, a previous diagnosis of hyperlipidemia, or the use of lipidlowering medication. Chronic renal failure was characterized as an estimated glomerular filtration rate of $\leq 60 \text{ mL/min}$. Chronic liver disease was defined as conditions requiring hospitalization due to cirrhosis or liver-related events.

Furthermore, all patients underwent echocardiographic imaging immediately before CABG. The echocardiographic examinations were conducted using an echocardiography device (GE Vingmed Ultrasound AS, Horten, Norway) equipped with a 3.2 MHz adult probe, and measurements were performed in accordance with the guidelines of the American Society of Echocardiography [13].

Segment elevation myocardial infarction was diagnosed based on the following criteria: ST-segment elevation ≥ 2.5 mm in men under 40 years of age, ≥ 2 mm in men aged 40 or older, or ≥ 1.5 mm in women in leads V2–V3, and/or ≥ 1 mm in the other leads, all measured at the J point in two contiguous leads [10]. Reperfusion failure during coronary intervention was characterized by the following criteria: less than 50% STsegment regression within 90 minutes of the initial elevation and a thrombolysis in myocardial infarction (TIMI) flow grade of 0 observed in the infarct-related artery following pPCI or thrombolytic therapy [14]. In-hospital mortality was defined as any cause of death occurring from the time of admission to CABG in patients diagnosed with STEMI.

Fragmented QRS

Upon admission to the emergency department, 12-lead electrocardiograms (ECG) of all patients were recorded with the following settings: a filter range of 0.16–100 Hz, a paper speed of 25 mm/s, and an amplitude of 10 mm/mV. FQRS was defined as follows: the presence of an additional R wave (R') or notching in the nadir of the S wave, or the presence of more than one R' (fragmentation) in two contiguous leads, corresponding to a major coronary artery territory [15]. This definition excluded cases with a typical BBB pattern and incomplete right BBB (Figure 1). The interpretation of all ECG findings was conducted independently by two experienced cardiologists who were blinded to the clinical outcomes. The intra – and inter-observer differences for fQRS were both less than 5%.

Statistical Analysis

The data analysis was conducted utilizing the Statistical Package for the Social Sciences version 26.0 (SPSS Inc., Chicago, Illinois, USA). To assess the distribution of variables, both visual methods (histograms, probability curves) and analytical methods (Kolmogorov–Smirnov or Shapiro–Wilk tests) were employed. Numerical variables that exhibited a normal distribution were presented as mean ± standard deviation, while those not conforming to a normal distribution were expressed as median (interquartile range). Categorical variables were reported as percentages (%). To compare numerical variables between the two groups, Student's t-test and Mann–Whitney U test were employed, depending on the distribution. Categorical variables were compared using the Chi-square or Fisher's exact test. Event-free survival curves were constructed utilizing the Kaplan–Meier method and were subjected to comparison using the log-rank test. For calculating hazard ratios (HRs) and their corresponding 95% confidence intervals (95% CI) concerning clinical endpoints, both univariate and multivariate Cox proportional hazards models were applied. In this study, a P-value less than 0.05 was considered statistically significant.

3. RESULTS

This study included a total of 99 patients who presented with acute STEMI and underwent CABG. Among these patients, 59.6% were male, and the mean age was 56 ± 11.2 years. During their hospital admission, 11 (11.1%) patients succumbed to their conditions. Specifically, eight patients died due to low cardiac output syndrome (LCOS), two patients experienced malignant arrhythmias (ventricular fibrillation and tachycardia-resistant LCOS), and two patients passed away as a result of sepsis with accompanying LCOS.

The patients were categorized into two groups: hospital survivors and non-survivors. The baseline demographics, clinical characteristics, and laboratory findings of these study groups are summarized in Table I. While the two groups exhibited similarities in demographics, clinical features, and laboratory characteristics, certain clinical traits such as Killip class > III (p < 0.001), cardiogenic shock (p < 0.001), and preoperative cardiopulmonary resuscitation (p < 0.001) were more prevalent in the non-survivor group. Furthermore, the non-survivor group displayed a higher Thoracic Surgery Society (STS) score (p < 0.001). White Blood Cells (WBC) count (p < 0.001), glucose levels (p = 0.001), and troponin levels (p = 0.032) were elevated in the non-survivor group, whereas glomerular filtration rate (GFR; p = 0.001) and left ventricular ejection fraction (LVEF) were higher in the survivor group. Additionally, the rate of fQRS (p < 0.001) (Figure 1), QRS duration (p = 0.001), and heart rate (p < 0.001) were greater in the non-survivor group compared to the survivor group.

Table II presents the distribution of responsible lesions, as well as intraoperative and postoperative characteristics of the study groups. The non-survivor group exhibited longer ICU length of stay (p < 0.001) and ventilation time (p < 0.001), whereas aortic cross-clamp (ACC) duration (p = 0.049) was prolonged and the use of internal mammary artery (IMA) (p = 0.031) was more common in the survivor group.

Table III provides the results of univariate and multivariate regression analyses aimed at identifying predictors of in-hospital mortality. In the univariate regression analysis, LVEF, GFR, glucose levels, Killip class \geq III, and fQRS were significantly associated with in-hospital mortality. In the multivariate regression analysis, both LVEF (p = 0.028) and fQRS (p = 0.037) emerged as independent predictors of in-hospital mortality.



Figure 1. An exemplary electrocardiogram shows the presence of fragmented QRS in derivatives of DII and AVF in inferior myocardial infarction.

Table I. The baseline demographics, clinical and laboratory characteristics of the study groups

N - 00	Survivors	Non-survivors	Р
N = 99	(n = 88)	(n = 11)	value
Age, years	55.6 ± 10.6	60 ± 15.1	0.267
Gender (male), n (%)	52 (59.1)	7 (63.6)	0.772
Hypertension, n (%)	25 (28.4)	4 (36.4)	0.585
PAD, n (%)	13 (14.8)	2 (18.2)	0.766
CVD, n (%)	7 (8)	1 (9.1)	0.896
COPD, n (%)	14 (15.9)	2 (18.2)	0.847
Atrial fibrilation, n (%)	4 (4.5)	1 (9.1)	0.516
Smoking, n (%)	27 (30.7)	3 (27.3)	0.817
WBC, 10 ⁶ /L	12.3 ± 4.3	18.7 ± 11.2	<0.001
Hemoglobin, g/dL	12.5 ± 2.7	11 ± 1.5	0.087
Platelets, 10^3/uL	236.6 ± 85.8	245.7 ± 94.9	0.744
Glucose, mg/dl	169.2 ± 56.8	238.1 ± 103.5	0.001
Total cholesterol, mg/dL	188.1 ± 40.1	184.5 ± 20.1	0.769
LDL-C, mg/dL	126 ± 34	121.2 ± 17.5	0.645
HDL-C, mg/dL	37.8 ± 7.9	40 ± 6.9	0.371
Triglyceride, mg/dL	175.1 ± 93.2	158.7 ± 59.2	0.573
Troponin, ng/mL	0.120 (0.036-0.256)	0.283 (0.127-0.450)	0.032
GFR, mL/min	87.5 ± 22.3	62 ± 34.8	0.001
LV Ejection Fraction, %	45.4 ± 6.8	35 ± 5.9	<0.001
fQRS	21 (23.9)	9 (81.8)	< 0.001
Q wave on ECG	18 (20.5)	5 (45.5)	0.064
QRS duration, ms	87.6 ± 13	101.6 ± 15.2	0.001
Heart rate, beats / min	82.8 ± 14.4	101.9 ±9.3	<0.001
Correct QT duration, ms	439.2 ± 37.6	450.8 ± 44.1	0.344
Previous PCI, n (%)	11 (12.5)	3 (27.3)	0.185
Failed PCI, n (%)	16 (18.2)	5 (45.5)	0.037
Previous stent thrombosis, n (%)	12 (13.6)	1 (9.1)	0.674
CPR before surgery, n (%)	2 (2.3)	3 (27.3)	<0.001
Killip class, n (%)			<0.001
I	80 (90.9)	3 (27.3)	
	2 (2.3) 6 (6.8)	6 (54.5)	
CAD			0.274
1 vessel	8 (9.1)	3 (27.3)	
2 vessels	31 (35.2)	2 (18.2)	
≥4 vessels	29 (33) 20 (22.7)	4 (36.4) 2 (18.2)	
Cardiogenic shock, n (%)	3 (3.4)	4 (36.4)	<0.001
STS score	5.2 (4.2-6.4)	11.2 (9.4-15.3)	<0.001

Data are expressed as percentage, mean±standard deviation, or median (inter – quartile range).

Abbreviations: CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CPR, cardiopulmonary resuscitation; CVD, cerebrovascular disease; ECG: electrocardiograms; GFR: glomerular filtration rate; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; IVEF: left ventricular ejection fraction; PAD, peripheral artery disease; PCI: percutaneous coronary intervention; STS, Society of Thoracic Surgeons; WBC, White Blood Cells.

Table II. The distribution of culprit lesion, intraoperative and postoperative characteristics of study groups

N = 99	Survivors	Non-survivors	Р
	(n = 88)	(n = 11)	value
Culprit lesion			0.779
LMCA	24 (27.3)	4 (36.4)	
LAD	63 (71.6)	7 (63.6)	
LCX	1 (1.1)	0 (0)	
RCA	0 (0)	0 (0)	
Intraoperative characteristics			
ACC time (min)	47.7 ± 18.7	36 ± 15.5	0.049
CPB time (min)	83.8 ± 35.3	93.8 ± 38	0.381
Grafts per patient (n)	2.74 ± 1.01	2.45 ±1.13	0.388
IMA use	54 (61.4)	3 (27.3)	0.031
Complete revascularization (n)	81 (92)	5 (45.5)	<0.001
Postoperative characteristics			
Drainage (ml)	640.5 ± 162.4	689.1 ± 188.1	0.360
Hospital stay (days)	7.5 ± 3.7	9.2 ± 6.7	0.195
IABP support	30 (34.1)	7 (63.6)	0.056
ICU stay (days)	2.52 ± 1.8	9.18 ± 6.71	<0.001
Ventilation time (h)	9 (6.3-12)	24 (14-214)	<0.001

Abbreviations: ACC, aortic cross-clamp; CPB, cardiopulmonary bypass; IABP, intra-arterial balloon pump; ICU, intensive care unit; IMA, internal mammary artery; LAD, left anterior descending artery; LCX, left circumflexartery; LMCA, left main coronary artery; RCA, right coronary artery.

Table III. Univariate and multiple cox regression analyses to determine predictors of in-hospital mortality

	Univariate analysis			Multi		
	Hazard ratio	95%CI (lower-upper)	P value	Hazard ratio	95%CI (lower-upper)	P value
Age	1.031	0.978-1.088	0.257			
HT	1.427	0.418-4.875	0.571			
COPD	1.168	0.252-5.406	0.843			
PAD	1.266	0.274-5.861	0.763			
CVD	1.107	0.142-8.648	0.923			
LVEF	0.781	0.693-0.879	<0.001	0.862	0.755-0.985	0.028
GFR	0.958	0.933-0.984	0.002	0.983	0.957-1.011	0.231
Glucoseª	1.010	1.004-1.016	0.001	1.001	0.994-1.008	0.717
Troponin ^b	1.708	0.592-4.927	0.322			
Smoking	0.857	0.227-3.231	0.820			
Killip class ≥III	11.016	3.332-36.417	<0.001	0.971	0.183-5.161	0.973
ACC timec	0.959	0.919-1.001	0.055			
IABP support	3.267	0.956-11.166	0.059			
fQRS	11.429	2.467-52.957	0.002	6.337	1.122-35.800	0.037

Abbreviations: ACC, aortic cross-clamp; CAD: coronary artery disease; CI, confidence interval; COPD: chronic obstructive pulmonary disease; CVD: cerebrovascular disease; GFR, glomerular filtration rate; HT: hypertension; IABP, intra-arterial balloon pump; LVEF, left ventricular ejection fraction; OR, odds ratio; PAD: peripheral artery disease.

^aFor each 1 mg/dl increase the odds ratio for mortality.

^{*b*}*For each 1 ng/ml increase the odds ratio for mortality.*

^cFor each 1 minute increase the odds ratio for mortality.



Figure 2. Distribution of fQRS in-hospital survivors and non-survivors groups.

4. DISCUSSION

This study sheds light on a significant clinical issue within our clinical practice, and its main findings can be summarized as follows: I) fQRS is strongly associated with in-hospital mortality in patients undergoing CABG for STEMI. II) fQRS and low LVEF were identified as independent predictors of in-hospital mortality.

Primary percutaneous coronary intervention is the standard treatment for STEMI patients, with only a small proportion (5% or less) requiring emergency CABG surgery [16]. Patients with STEMI may have an increased risk of early CABG, which suggests that if patients are hemodynamically stable, delaying surgical revascularization for at least 24 hours might yield better short-term and long-term outcomes [17]. However, patients experiencing ongoing myocardial ischemia may necessitate emergency CABG when PCI is not feasible or has failed. Prior studies on mortality among patients undergoing emergency CABG for STEMI have primarily focused on the duration of the procedure. For example, Voisine et al., reported a mortality rate of 19.2% in patients operated on within 6 hours, although, they did not account for factors necessitating emergency CABG [18]. Axelsson et al., reported an in-hospital mortality rate of 13% in patients who underwent CABG within 24 hours after STEMI [19], while Uygur et al. found a rate of 10.8% in their study [20], and Lemaire et al. reported an 8.2% mortality rate [21]. In our study, which included patients operated on within 6 hours of symptom onset, the in-hospital mortality rate was 11.1%, consistent with the literature.

Risk assessment of patients before surgery is crucial for guiding clinical decisions. Various risk classification scores such as EuroSCORE, STS score, and ACEF score are well-established and widely used in clinical practice [22,23]. In our study, higher Killip class 3 and STS scores were associated with higher inhospital mortality, in line with the literature. Thielmann et al., demonstrated that preoperative cardiac troponin I (cTnI) levels can predict the risk of in-hospital mortality in patients undergoing emergency CABG for STEMI [24]. Although, troponin levels were elevated in the non-survivor group in our study, it was not identified as an independent predictor in the regression analysis. This may be due to the fact that patients in our study underwent CABG early. Moreover, while high glucose levels were not found to be an independent predictor of in-hospital mortality in our study, they appeared to be a risk factor for such mortality. The role of elevated glucose levels as an independent risk factor for operative mortality after CABG remains controversial in the literature [25,26].

None of the aforementioned risk scores take into account simple ECG findings. fQRS is an ECG finding associated with ventricular conduction disorders observed in various cardiac conditions. The frequency of fQRS on ECG can be as high as 35% in STEMI patients undergoing PCI [27]. In our patient group, the fQRS rate was 30.3%, consistent with the literature. Recent studies have indicated that STEMI patients with fQRS have a significantly higher in-hospital mortality rate and can be used as a risk stratification tool for STEMI patients [28]. It has also been linked to low cardiac output syndrome and inhospital mortality in patients undergoing CABG surgery [29]. In our study, fQRS was shown to be an independent predictor of in-hospital mortality in STEMI patients who underwent emergency CABG.

Additionally, in previous studies, left ventricular (LV) dysfunction has been identified as an independent risk factor for postoperative complications and mortality in CABG surgery [30]. In line with the literature, low LVEF was found to be an independent risk factor for in-hospital mortality in our patient group.

The presence of cardiogenic shock or preoperative cardiopulmonary resuscitation (CPR) in patients undergoing CABG is associated with a high rate of periprocedural mortality and morbidity [31]. In our study, cardiogenic shock or preoperative CPR was statistically more significant in relation to mortality, which is consistent with the literature. The use of intra-aortic balloon pump (IABP) reflects the acuity level and the presence of cardiogenic shock, often associated with poor left ventricular output, and has been linked to in-hospital mortality [32]. Although, IABP was more frequently used in the non-survivor group in our study, it was not identified as an independent predictor of mortality. Patients in our study underwent urgent procedures, and complete revascularization was achieved in 86.9% of them. Additionally, patients underwent an average of 2.7 distal anastomoses, and the internal mammary artery (IMA) was used less frequently (57%) compared to elective CABG (90-95%) [33].

To our knowledge, this study is the first to evaluate the utility of a simple ECG finding in predicting in-hospital mortality in acute STEMI patients undergoing primary revascularization with CABG and to demonstrate the prognostic power of fQRS.

Study limitations

This study has several limitations that should be acknowledged. Firstly, it was a single-center retrospective study, which may limit the generalizability of the findings. Secondly, the nonsurvivor group had a relatively small sample size, which could impact the statistical power and generalizability of the results. Thirdly, the study did not employ other quantitative methods such as myocardial perfusion scanning or magnetic resonance imaging to confirm myocardial ischemia or scar formation in the study's patients. Additionally, the study lacked long-term follow-up data to assess future cardiovascular events.

In essence, this study demonstrated the effectiveness and utility of fQRS on ECG as an indirect method for predicting in-hospital mortality in patients undergoing emergency CABG for STEMI.

Conclusion

As a marker of myocardial fibrosis, fQRS has the potential to serve as a valuable non-invasive risk assessment tool for patients undergoing emergency CABG for STEMI. This study has demonstrated a clear relationship between in-hospital mortality and the presence of fQRS in such patients. The evaluation of fQRS can aid in identifying individuals at higher risk of developing in-hospital mortality among this patient population. This information can be valuable for clinicians in making informed decisions and optimizing care for these highrisk patients.

Compliance with Ethical Standards

Ethical approval: Our study was conducted per the principles of the Declaration of Helsinki and received approval from Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Ethics Committee with decision number 2023.04-46.

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Conflict of interest: Both authors have no conflict of interest to declare.

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