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# Fragmented QRS (fQRS) Complex Predicts Adverse Cardiac Events of ST-Segment Elevation Myocardial Infarction Patients Undergoing Percutaneous Coronary Intervention and Thrombolysis

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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**Background:** ST-segment elevation myocardial infarction (STEMI) is an acute and life-threatening disease. Adverse cardiac events (ACEs) are defined as cardiovascular death or worsening congestive heart failure in STEMI patients. The present study investigated the predictive role of fragmented QRS complex (fQRS) in risks of ACEs in STEMI.

**Material/Methods:** This study was a retrospective analysis involving patients who underwent percutaneous coronary intervention (PCI) or thrombolysis. STEMI patients were divided into the fQRS group (259 cases) and the non-fQRS group (161 cases). Basic information and clinical parameters were evaluated. ACEs, including hemodynamic instability, electrical instability (ventricular tachycardia event, ventricular fibrillation or atrioventricular heart-block) and death, were observed. The 12-lead ECG was used to obtain fQRS recordings. Thrombolytic recanalization was evaluated to confirm clinical outcomes of PCI and thrombolysis therapy.

**Results:** Hemodynamic instability rates, electrical instability rates, and death in the fQRS group were significantly higher compared to the non-fQRS group (*P*=0.002, 0.000, and 0.010, respectively). PCI triggered significantly fewer ACEs compared to thrombolytic therapy in the fQRS group (*P*=0.000, 0.000, and 0.019, respectively). The fQRS group had higher thrombolysis failure rates and three-vessel lesion of coronary artery rates compared to the non-fQRS group (*P*=0.009 and 0.029, respectively). There were no differences between fQRS and non-fQRS groups in death rates of STEMI patients undergoing PCI and thrombolytic therapy. GRACE scores more than 140, EF less than 35%, and fQRS illustrated predictive potential for ACEs of STEMI patients.

**Conclusions:** fQRS is an independent predictor for the adverse cardiac events of STEMI patients undergoing PCI or thrombolysis.

**MeSH Keywords:** **Lown-Ganong-Levine Syndrome • Myocardial Infarction • Percutaneous Coronary Intervention**

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2469 7 — 32





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## Background

The ST-segment elevation myocardial infarction (STEMI) is a critical and acute disease that threatens the life of patients [1,2]. The STEMI patients always have a higher incidence rate of in-hospital mortality and in-hospital adverse cardiovascular events [3]. Adverse cardiac events were defined as cardiovascular death or unplanned admission to hospital for management of worsening congestive heart failure in STEMI patients [3]. In clinical practice, the commonly used method for STEMI is primary percutaneous coronary intervention (PCI), which decreases the risk and occurrence of the recurrent myocardial infarction (MI) [4]. According to the Global Registry of Acute Coronary Events, over a half of STEMI patients worldwide receive early reperfusion treatment, and about 55% of STEMI patients in Europe received it in 2000 [5,6]. In China, early reperfusion treatment of STEMI patients is less commonly used than in the developed countries [7–9].

Usually, the STEMI patients are younger and have several risk factors, such as hypertension, diabetes, and dyslipidemia [10]. A recent study [11] reported that the risk factors are mainly associated with the inflammation and pathogenesis of acute coronary syndrome (ACS). Meanwhile, myocardial infarction reoccurs in about 2% to 6% of STEMI patients after successful PCI, and always induces poor clinical outcomes [12]. Therefore, it is critical to discover risk factors and predictive biomarkers helpful to treat STEMI patients.

The fragmented QRS complex (fQRS) is frequently observed on routine surface electrocardiograms (ECG), and is characterized by wide or narrow QRS complex, such as bundle branch block, paced rhythm, or ventricular premature beats [13]. The fQRS on the surface ECG has been proven to be correlated with the enhanced adverse cardiac events in clinical, especially for coronary diseases [14]. Therefore, this study aimed to investigate the predictive role of fQRS in the occurrence risks of adverse cardiac events during treatment.

## Material and Methods

### Patients and trial grouping

The present study was a retrospective analysis of patients who underwent PCI or thrombolysis therapy between January 2016 and December 2016 at the Cardiology Department, Tianjin Center Hospital, Tianjin, China. According to the European Society of Cardiology/American College of Cardiology consensus document [15], we included patients who illustrated at least 2 of the following criteria: 1) electrocardiographic changes, 2) characteristic severe chest pain lasting over 30 min, and 3) elevation of the cardiac biomarkers in serum. We also excluded patients who had previous myocardial infarction history or patients who had bundle-branch heart-block, because both these diseases may affect the ECG recordings of STEMI patients. Finally, we included 420 consecutive STEMI patients who underwent PCI or thrombolysis. According to the existence of fQRS of ST-segment elevation lead, the patients were divided into the fQRS group (259 cases) and the non-fQRS group (161 cases).

This study was approved by the Ethics Committee of the Cardiology Department, Tianjin Center Hospital, Tianjin, China. Written informed consents were obtained from all of the patients included in this study.

### Data collection

The following basic data were collected: demographics, sex, age, diabetes history, hypertension history, coronary disease history, heart failure history, history of myocardial protection in coronary artery bypass surgery (CABG), therapy of PCI, and smoking history. The clinical materials prior to hospitalization, including heart rate, blood pressure, ECG, interval between onset and the visit time, site of acute myocardial infarction, were also collected. Post-admission clinical data, including findings of ECG and coronary angiography, serum creatinine, myocardial enzyme, drugs applied within 24 h of hospitalization, and the Global Registry of Acute Coronary Events (GRACE) scores, were examined. We also evaluated adverse cardiac events, including hemodynamic instability (occurrence of heart failure, shock or non-drug caused systolic pressure lower than 90 mmHg), electrical instability (occurrence of ventricular tachycardia event, ventricular fibrillation or atrioventricular heart-block), and death.

### Definition of fQRS

In this study, the 12-lead ECG was used to obtain the recordings of STEMI patients. The parameters were designed as the following: filter ranges from 0.5 Hz to 150 Hz, and AC filter designs as 60 Hz, 25 mm/s, and 10 mm/mV. The ECG recordings were observed and recorded by 2 independent clinicians who were blinded to all of the information of the present study.

The definition of fQRS was made according to previous studies [16,17]. Briefly, fQRS is defined as the occurrence of typical RSR' patterns (with the QRS duration less than 120 ms) with or without the Q wave, which includes a notching of R wave or S wave or an additional R wave, or the presence of more than 1 R prime without the typical bundle branch block. The triphasic or multiple-phasic fQRS waves appeared in 2 or more leads corresponding to coronary artery blood supply regions were excluded due to the different leads. Complete or incomplete bundle branch block or intraventricular block were also excluded.



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**Table 1.** Basic and clinical data for patient in fQRS and non-fQRS group.

| Parameters | fQRS group (259 cases) | Non-fQRS group (161 cases) | $\chi^2$/t values | *P* values |
|---|---|---|---|---|
| Male (cases, %) | 145 (56) | 97 (60) | 0.739 | 0.39 |
| Age (mean ±SD) | 62.1±18.6 | 61.5±19.4 | 1.262 | 0.208 |
| Hypertension (cases, %) | 139 (54) | 91 (57) | 0.326 | 0.568 |
| Diabetes mellitus (cases, %) | 147 (57) | 99 (61) | 0.917 | 0.338 |
| Coronary disease (cases, %) | 61 (24) | 43 (27) | 0.531 | 0.466 |
| CABG/PCI (cases, %) | 41 (16) | 25 (16) | 0.007 | 0.934 |
| Smoking (cases, %) | 185 (71) | 119 (74) | 0.307 | 0.580 |
| Anterior wall myocardial infarction (cases, %) | 153 (59) | 97 (60) | 0.057 | 0.811 |
| Inferior wall myocardial infarction (cases, %) | 89 (34) | 53 (33) | 0.092 | 0.761 |
| Right ventricular myocardial infarction (cases, %) | 40 (15) | 30 (19) | 0.727 | 0.394 |
| EF (%) | 38±11 | 50±12 | 2.500 | 0.024 |
| EF <35% (cases, %) | 118 (46) | 51 (32) | 7.957 | 0.005 |
| Onset to treatment time <8 h (cases, %) | 213 (82) | 140 (87) | 1.648 | 0.199 |
| Onset to treatment time <12 h (cases, %) | 235 (91) | 150 (93) | 0.770 | 0.380 |
| Aspirin (cases, %) | 259 (100) | 159 (99) | 3.233 | 0.072 |
| Clopidogrel (cases, %) | 253 (98) | 159 (99) | 0.613 | 0.434 |
| β-blockers (cases, %) | 153 (59) | 97 (60) | 0.057 | 0.811 |
| ACEI (cases, %) | 229 (88) | 149 (93) | 1.881 | 0.170 |
| Thrombolytic therapy (cases, %) | 91 (35) | 70 (43) | 2.924 | 0.087 |
| Emergency PCI treatment (cases, %) | 168 (64) | 91 (57) | 2.924 | 0.087 |

CABG – coronary artery bypass surgery; EF – ejection fraction; ACEI – antiotensin-converting enzyme inhibitor.

### Thrombolytic recanalization criteria

Thrombolytic recanalization was defined as the following criteria: 1) The ST-segment elevation of ECG down-backed more than 50% within 2 h. 2) The chest pain was disappeared within 2 h. 3) The reperfusion arrhythmia was appeared within 2 h. 4) The peak of serum creatine kinase MB (CK-MB) was appeared ahead of time (within 14 h).

### Statistical analysis

Quantitative data are reported as mean ±SD or median, and the categorical variables are reported as the number of positive cases or positive rates. Data were analyzed using SPSS 21.0 software (SPSS Inc, Chicago, IL, USA). Quantitative data were analyzed using the *t* test. Categorical data were analyzed by using the $\chi^2$-square test. The hazard ratio (HR) and 95% confidence intervals (CI) were employed to evaluate the risk factors of adverse cardiac events in STEMI patients and were analyzed using multiple-factor logistic regression analysis. A *P* value less than 0.05 was considered as statistically significant.

## Results

### Basic and clinical data

We enrolled 420 consecutive STEMI patients in this study, including 259 cases in the fQRS group and 161 cases in the non-fQRS groups. The basic and clinical characteristics in the fQRS and non-fQRS group were compared (Table 1). The results showed that there were no significant differences in the basic and clinical data between the 2 groups.





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**Table 2.** Comparison for adverse cardiac events between fQRS and non-fQRS group.

| Adverse events | fQRS group (259 cases) | Non-fQRS group (161 cases) | $\chi^2$ values | *P* values |
|---|---|---|---|---|
| Hemodynamic instability (cases, %) | 105 (41) | 41 (25) | 9.949 | 0.002 |
| Electrical instability (cases, %) | 97 (37) | 23 (14) | 26.108 | 0.000 |
| Death (cases, %) | 35 (14) | 9 (6) | 6.646 | 0.010 |

fQRS – fragmented QRS complex.

**Table 3.** Comparison for PCI and thrombolytic therapy caused adverse cardiac events in fQRS patients.

| Adverse events | Thrombolytic therapy (91 cases) | Emergency PCI treatment (168 cases) | $\chi^2$ values | *P* values |
|---|---|---|---|---|
| Hemodynamic instability (cases, %) | 65 (71) | 39 (23) | 57.100 | 0.000 |
| Electrical instability (cases, %) | 59 (65) | 37 (23) | 46.378 | 0.000 |
| Death (cases, %) | 9 (10) | 5 (3) | 5.518 | 0.019 |

PCI – percutaneous coronary intervention, fQRS – fragmented QRS complex.

**Table 4.** Comparison for PCI and thrombolytic therapy caused adverse cardiac events in non-fQRS patients.

| Adverse events | Thrombolytic therapy (70 cases) | Emergency PCI treatment (91 cases) | $\chi^2$ values | *P* values |
|---|---|---|---|---|
| Hemodynamic instability (cases, %) | 20 (29) | 12 (13) | 5.880 | 0.015 |
| Electrical instability (cases, %) | 12 (17) | 8 (9) | 2.537 | 0.111 |
| Death (cases, %) | 5 (7) | 2 (2) | 2.326 | 0.127 |

PCI – percutaneous coronary intervention, non-fQRS – non fragmented QRS complex.

### Higher adverse cardiac events and death rates appear in fQRS group

There were significantly higher hemodynamic instability rates in the fQRS group (41%) compared to the non-fQRS group (25%) (Table 2, *P*=0.002). The electrical instability rates in the fQRS group (37%) were also significantly higher compared to the non-fQRS group (14%) (Table 2, *P*=0.000). Moreover, the death rates of STEMI patients in the fQRS group (14%) were also significantly higher compared to the non-fQRS group (6%) (Table 2, *P*=0.010).

### PCI triggers few adverse cardiac events compared to thrombolytic therapy in fQRS group

In this study, both PCI and thrombolytic therapy were applied to observe the adverse cardiac events in STEMI patients. The results showed that both the hemodynamic instability rates and electrical instability rates were significantly lower in the PCI group compared to the thrombolytic therapy group (Table 3, both *P*=0.000) in fQRS group. Death rates were also significantly lower in the PCI group compared to the thrombolytic therapy group (Table 3, *P*=0.019). For the STEMI patients in the non-fQRS group, the hemodynamic instability rate in the PCI group was significantly lower compared to the thrombolytic therapy group (Table 4, *P*=0.015). However, there were no significant differences in electrical instability rates and death rates between the PCI and thrombolytic therapy groups (Table 4, *P*=0.111 and 0.127, respectively).

### The fQRS group had higher thrombolysis failure rates and three-vessel lesion of coronary artery rates

There were 91 patients receiving thrombolytic therapy in the fQRS group and 70 patients receiving thrombolytic therapy in the non-fQRS group. The results indicated that the thrombolysis





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**Table 5.** Thrombolysis failure rates and three-vessel lesion of coronary artery rates in fQRS and non-fQRS patients.

| Therapeutic outcomes | fQRS group | Non-fQRS group | $\chi^2$ values | *P* values |
|---|---|---|---|---|
| Thrombolysis failure rates (cases/cases, %) | 43/91 (47) | 19/70 (27) | 6.757 | 0.009 |
| Three-vessel lesion of coronary artery rates (cases/cases, %) | 77/168 (46) | 29/91 (32) | 4.762 | 0.029 |

fQRS – fragmented QRS complex, non-fQRS – non fragmented QRS complex.

**Table 6.** Therapeutic method analysis for 21 dead patients in fQRS and non-fQRS patients.

| Therapeutic method | fQRS group (14/259 cases) | Non-fQRS group (7/161 cases) | $\chi^2$ values | *P* values |
|---|---|---|---|---|
| Thrombolytic therapy (cases/cases,%) | 9/91 (10) | 5/70 (7) | 0.376 | 0.540 |
| Emergency PCI treatment (cases/cases,%) | 5/168 (3) | 2/91 (2) | 0.136 | 0.712 |

PCI – percutaneous coronary intervention, fQRS – fragmented QRS complex; non-fQRS – non fragmented QRS complex.

**Table 7.** Multiple-factor logistic regression analysis for investigating the independent predictor for adverse cardiac events of STEMI patients.

| Predictive factors | OR (95% CI) | *P* values |
|---|---|---|
| GRACE score >140 | 3.003 (1.504–6.032) | 0.001 |
| EF <35% | 2.547 (1.334–4.353) | 0.002 |
| fQRS | 1.112 (1.029–1.178) | 0.005 |

STEMI – ST-segment elevation myocardial infarction; fQRS – fragmented QRS complex; EF – ejection fraction; OR – odd ratio; CI – confidential interval; GRACE – Global Registry of Acute Coronary Events.

failure rates were significantly higher in the fQRS group (47%) compared to the non-fQRS group (27%) (Table 5, *P*=0.009). There were 168 patients receiving PCI therapy in the fQRS group and 91 patients receiving PCI therapy. The results indicated that the three-vessel lesion of coronary artery rates in the fQRS group (46%) were higher significantly compared to the non-fQRS group (32%) (Table 5, *P*=0.029).

### No differences between fQRS and non-fQRS groups in death rates of STEMI patients undergoing PCI and thrombolytic therapy

To compare and observe the effects of fQRS occurrence on the outcomes of PCI and thrombolytic therapy, the death rates were analyzed in the fQRS and non-fQRS groups. The results showed that there were no significant differences in the death rates of STEMI patients undergoing PCI (*P*=0.540) and thrombolytic therapy (*P*=0.712) between the fQRS and non-fQRS group (Table 6).

### fQRS acts as an independent predictor for adverse cardiac events of STEMI patients

The logistic analysis results showed that GRACE scores more than 140 (HR: 3.003 (1.504–6.032), Table 7) and ejection fraction (EF) less than 35% (HR: 2.547 (1.334–4.353), Table 7) were predictors for adverse cardiac events. Importantly, the fQRS (HR: 1.112 (1.029–1.178), Table 7) also had significant potential for predicting adverse cardiac events in the STEMI patients during hospitalization.

## Discussion

fQRS was recently discovered in the ECG of acute myocardial infarction patients and has become an important research topic in the ECG field. The previous studies pointed out the following mechanisms [18,19]: 1) infarction block, 2) block surrounding infarction region, 3) multi-focal infarction, 4) local myocardial scars, 5) changes of cell impedance. According to the conclusions of previous reports [20,21], the prevalence of fQRS in acute coronary syndrome patients ranges from 34.9% to 60.1%. The difference in fQRS prevalence may be associated with the different evaluative time of fQRS waves, the inclusion criteria, and the difference in the leads used in different studies. In the present study, we found that the prevalence of fQRS in STEMI patients was about 60%, which is consistent with previous studies [21,22].

In this study, there were no significant differences in sex, age, disease history, smoking history, location of myocardial infarction, onset to treatment time, and therapeutic methods between patients in the fQRS group and non-fQRS group. However, the EF values were significantly lower in the fQRS group compared to the non-fQRS group, which suggests that





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infarct size is larger and the coronary artery disease is more serious in patients in the fQRS group compared to the non-fQRS group. The present study also discovered that the three-vessel lesion of coronary artery rates in the fQRS group were significantly higher compared to the non-fQRS group, which also proves the finding of EF changes.

The hemodynamic instability rates and electrical instability rates in the fQRS group were significantly higher than in the non-fQRS group. We speculate that hemodynamic instability and electrical instability changes in the fQRS group may be associated with the increased severity of coronary artery disease, enlarged myocardial ischemic necrosis region size, and the decreased EF values of STEMI patients. Tanriverdi et al. [23] also reported that the fragmented QRS was associated with the severity of myocardial infarction in STEMI patients.

In this study, we treated STEMI patients in the fQRS group and fQRS group by using PCI and thrombolytic therapy, respectively. The results indicated that both hemodynamic instability rates and electrical instability rates were significantly lower in the PCI group compared to the thrombolytic therapy group in both the fQRS and non-fQRS groups. Meanwhile, the death rates were also significantly lower in the PCI group compared to the thrombolytic therapy group. For STEMI patients in the non-fQRS group, the hemodynamic instability rates in the PCI group were significantly lower compared to the thrombolytic therapy group. The above results may be correlated with the increased severity of coronary artery disease, enlarged myocardial ischemic necrosis region size, and the lower efficacy of thrombolysis for opening diseased vessels, which are consistent with previous studies [24]. Moreover, we also found that thrombolysis failure rates were significantly higher in the fQRS group (47%) compared to the non-fQRS group (27%), and the three-vessel lesion of coronary artery rates in the fQRS group (46%) were significantly higher compared to the non-fQRS group (32%). These results also suggest that fQRS may act as a risk factor for STEMI patients undergoing the clinical therapy, which is consistent with the report of Cakmak et al. [25] showing the potential predictive role of fQRS in myocardial infarction.

There were no differences between the fQRS and non-fQRS group in death rates of STEMI patients undergoing PCI and thrombolytic therapy. However, death rates were relative higher in the fQRS group. This result suggests that fQRS-specific or -associated higher death rates may also be related to the severity of coronary artery disease and enlarged myocardial ischemic necrosis region size. Furthermore, the occurrence time of fQRS was later than the occurrence of super-acute-period ST-segment and injury ST-segment. The fQRS mainly occurs from a few hours or more than 10 hours after the ischemia myocardial, or even occurs a few days after the acute ischemia myocardial [20,21,26]. A few patients exhibited potential for delayed hospitalization, which may be a reason for the poor treatment effects.

fQRS is an ECG manifestation of myocardial ischemia in acute myocardial infarction patients with myocardial scars [27]. The degrees of myocardial ischemia and myocardial scars were correlated with the poor prognosis of patients [28]. However, previous studies [29–31] reported that the occurrence of myocardial coronary perfusion abnormality in fQRS patients is significantly enhanced, and the predictive value for the cardiac death is significantly higher compared to non-fQRS patients. A previous study [32] reported that the fQRS complex acts as a prognostic marker for microvascular reperfusion and LV dysfunction. However, the present study investigated the function of fQRS in the adverse cardiac events in STEMI patients for the first time. Our study suggests that there were significantly more adverse cardiac events in fQRS patients compared to non-fQRS patients. Multiple-factor logistic regression analysis suggests that GRACE scores more than 140, EF less than 35%, and existence of fQRS are independent predictors of adverse cardiac events in STEMI patients during their hospitalization. The findings of this study show that doctors need to perform PCI therapy as soon as possible according to the fQRS recordings, to improve the clinical prognosis.

Although this study produced some interesting findings, there are also a few limitations. Firstly, the sample of patients was relative small. Secondly, this study is only a single-center study. Thirdly, the changes of fQRS in ECG waves were not observed. Fourthly, the effects of constant fQRS and disappeared fQRS on adverse cardiac events during hospitalization have not been fully clarified. Fifthly, long-term follow-up was not performed and research on factors affecting the long-term prognosis of fQRS patients is needed.

## Conclusions

The occurrence of fQRS in ECGs of STEMI patients suggests severe coronary artery disease and serious myocardial ischemia injury. fQRS is an independent predictor for the adverse cardiac events of STEMI patients during hospitalization, and could predict high-risk STEMI. Our results suggest that the STEMI patients with fQRS must receive PCI therapy as soon as possible to decrease death rates, enhance survival, and improve prognosis.

**Conflict of interests**

None.





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