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# Prognostic significance of QRS fragmentation and correlation with infarct size in patients with anterior ST-segment elevation myocardial infarction treated with percutaneous coronary intervention: Insights from the INFUSE-AMI trial

Björn Redfors [a], Ioanna Kosmidou [a,c,*], Aaron Crowley [a], Akiko Maehara [a,b], Ori Ben-Yehuda [a,b], Arslan Arif [a], José M. Dizon [a,b], Gary S. Mintz [a], Gregg W. Stone [a,b]

[a] Clinical Trials Center, Cardiovascular Research Foundation, New York, NY, United States
[b] NewYork-Presbyterian Hospital/Columbia University Medical Center, New York, NY, United States
[c] Arrhythmia & Pacemaker Center, Department of Cardiology, St. Francis Hospital, Roslyn, NY, United States

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ABSTRACT

*Background:* QRS fragmentation (fQRS) is believed to reflect myocardial scar formation in patients with coronary disease. Whether early formation of fQRS in patients with ST-segment elevation myocardial infarction (STEMI) treated with percutaneous coronary intervention (PCI) is correlated with infarct size and prognosis is unknown. We assessed the prognostic value of fQRS at 60 min post-PCI and its correlation with infarct size in patients with anterior STEMI managed with primary PCI.

*Methods:* The INFUSE-AMI trial enrolled 452 patients with anterior STEMI undergoing primary PCI. Electrocardiograms (ECGs) were performed at baseline and 60 min post-PCI. Infarct size was evaluated using cardiac magnetic resonance imaging at 30 days post-PCI. Target vessel failure (TVF) was defined as the composite of cardiac death, target vessel myocardial infarction, or ischemia-driven target vessel revascularization. Study groups were defined as patients with versus without fQRS at 60 min post-PCI.

*Results:* Out of 421 patients with ECG data 60 min post-PCI, 68 patients (16.2%) had fQRS. Patients with versus without fQRS had similar baseline characteristics and infarct size (16.9% ± 8.7% vs. 16.1% ± 10.5%, p = 0.62), but patients with fQRS had higher adjusted risk of 1-year TVF (adjusted HR 2.27, 95% CI 1.06–4.89, p = 0.036) and a trend toward a higher risk of the composite cardiac death or target vessel myocardial infarction (9.0% vs. 4.1%, p = 0.08) at 1 year.

*Conclusion:* fQRS in patients with STEMI is associated with TVF but does not correlate with infarct size.



## 1. Introduction

Mechanical reperfusion therapies for ST-segment elevation myocardial infarction (STEMI) have led to significant improvements in short- and long-term cardiac outcomes, but risk stratification of patients with STEMI following percutaneous coronary intervention (PCI) remains challenging. Infarct size and post-STEMI myocardial function are important predictors of future cardiovascular events, but imaging modalities that allow a complete assessment of these variables are costly and not always readily available [1–3]. QRS fragmentation (fQRS) on a 12-lead electrocardiogram (ECG) has been identified as a marker of myocardial depolarization abnormalities and has been linked to poor long-term prognosis in patients with non-ischemic as well as ischemic heart disease [4]; however, there is a paucity of data on the prognostic value of fQRS after STEMI and the association between the presence of fQRS and the extent of myocardial damage [5]. Therefore, we sought to assess the association between fQRS, infarct size and clinical outcomes after STEMI.

## 2. Methods

### 2.1. Study design

The design of the Intracoronary Abciximab and Aspiration Thrombectomy in Patients With Large Anterior Myocardial Infarction (INFUSE-AMI) trial has been previously described [6,7]. INFUSE-AMI was an open-label, 2 × 2 factorial, randomized, multicenter, single-blind evaluation of bolus intracoronary abciximab and manual aspiration thrombectomy in patients undergoing primary PCI for anterior STEMI. PCI was performed using standard techniques, with bivalirudin

* Corresponding author at: Cardiovascular Research Foundation, 1700 Broadway, 9th Floor, New York, NY 10019, United States.
*E-mail address:* ikosmidou@crf.org (I. Kosmidou).

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as the procedural anticoagulant and with bare metal or drug-eluting stent implantation at operator discretion. After PCI, all patients were treated with aspirin indefinitely and with clopidogrel or prasugrel for at least 1 year. Cardiac magnetic resonance imaging was scheduled in all patients at 30 days. Clinical follow-up was scheduled at 30 days and at 1 year. All components of the primary endpoint as well as stent thrombosis were adjudicated by an independent clinical events committee.

### 2.2. Infarct size assessment

CMR was performed using a commercially available 1.5 Tesla scanner (Siemens [Malvern, PA, USA]; Philips [Andover, MA, USA]; or GE Healthcare [Port Washington, NY, USA]) as previously described [7]. Infarct size was evaluated by manual tracing of delayed enhancement CMR images [7]. All CMR images were evaluated by an independent core laboratory (Cardiovascular Research Foundation, New York, NY, USA).

### 2.3. Electrocardiographic analysis

ECGs were collected at baseline, 60 min post-PCI, and 1 month post-PCI. All ECGs were reviewed by an independent core laboratory (Cardiovascular Research Foundation). For the purpose of this analysis, all available ECGs were analyzed for the presence of fQRS (Fig. 1), defined as follows [5,8]: (i) Narrow QRS (<120 ms duration): RSR′ pattern with or without a Q wave, such as an additional R wave (R′), notching of the downstroke or upstroke of the S wave or presence of >1 R′ in two contiguous leads corresponding to a major coronary artery territory or (ii) wide QRS (>120 ms duration): RSR′ pattern with or without a Q wave, such as an >2 R′, >2 notches of the R wave or >2 notches in the upstroke or downstroke of the S wave in two contiguous leads corresponding to a major coronary artery territory. Premature ventricular depolarizations and paced QRS were not included in this analysis. The presence versus absence of fQRS was assessed independently by a second physician and the inter-observer agreement was calculated as the kappa statistic [9]. In cases of disagreement between the two observers, the ECG was re-evaluated and a joint decision was made.

### 2.4. Study groups and definitions

We defined the primary analysis groups as patients with versus without fQRS at 60 min post-PCI. For the purpose of assessing the overall risk of adverse ischemic events we defined the primary endpoint target vessel failure (TVF) as the composite of cardiac death, target vessel myocardial infarction or ischemia-driven target vessel revascularization at 1 year.

### 2.5. Statistical analysis

Categorical variables were compared by $\chi^2$ or the Fisher exact test. Continuous variables are presented as mean ± standard deviation and compared using the Student *t*-test. Kaplan-Meier time-to-event estimates for clinical outcomes were compared with the log-rank test. Multivariable linear regression was used to assess the adjusted association between fQRS and infarct size. The following variables were included in the regression model: fQRS, age, sex, diabetes, and current smoking. Multivariable Cox proportional hazard models were used to assess the adjusted association between fQRS and adverse outcomes. The pre-specified primary model included the following covariates: fQRS, age, sex, and diabetes. A secondary model was fitted that included the same covariates with the addition of an indicator variable for the presence of Q-waves on the ECG. In the latter model the estimates for fQRS and Q-wave were compared using a test for linear contrast. All statistical tests were 2-sided. A p value <0.05 was considered significant for all analyses. All statistical analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC, USA).

## 3. Results

### 3.1. Patient characteristics

Among the 452 patients enrolled in INFUSE-AMI, ECG data 60 min post-procedure was available for 421 (93.1%), 68 of whom (16.2%) had fQRS. Inter-observer agreement in fQRS assessment, as assessed by the kappa statistic, was 0.84 (95% confidence interval [CI] 0.77 to 0.91) [9]. Baseline characteristics were similar for patients with versus without fQRS at 60 min post-procedure except that patients with fQRS were more likely to be male and more likely to have a history of cigarette smoking (Table 1). There were no significant differences between

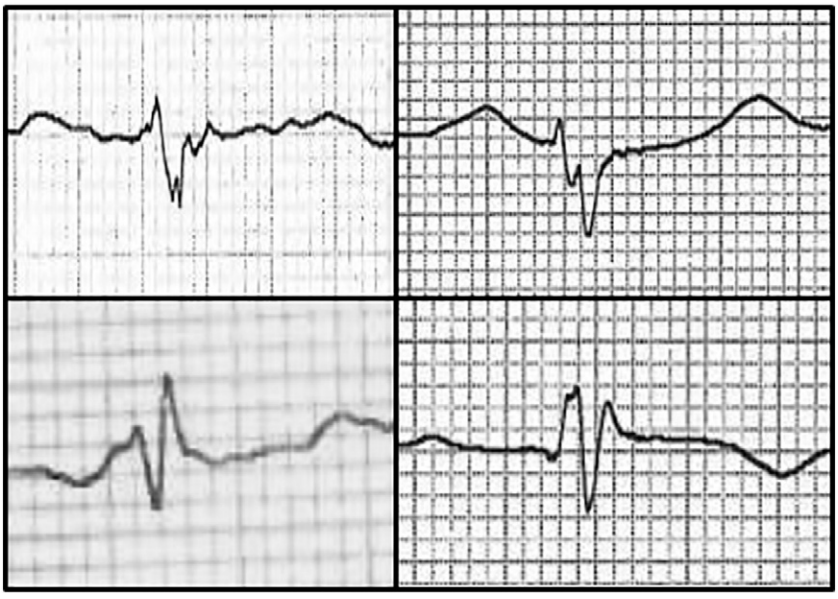

**Fig. 1.** Examples of QRS fragmentation among patients in INFUSE-AMI. Examples of fragmented QRS complexes, demonstrating notching of the QRS (upper panels) and typical RSR' patterns (lower panels).