The Predictive Value of Admission Fragmented QRS Complex for In-Hospital Cardiovascular Mortality of Patients with Type 1 Acute Aortic Dissection

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Background: Fragmented QRS (fQRS) arises from impaired ventricular depolarization due to heterogeneous electrical activation of ischemic and/or infarcted ventricular myocardium. The short- and long-term prognostic values of fQRS have been reported for myocardial infarction, heart failure, fatal cardiac arrhythmias, and sudden cardiac death. The aim of this study was to investigate the predictive value of admission fQRS complex for in-hospital cardiovascular mortality of patients with type 1 acute aortic dissection (AAD).

Methods: In this retrospective study, 203 consecutive patients with type 1 AAD who had been admitted to either of two large-volume tertiary hospitals between December 2008 and October 2013 were included. The patients were divided into two groups according to the presence or absence of the fQRS complex on admission.

Results: In-hospital cardiovascular mortality ($P < 0.001$), major adverse cardiovascular events ($P < 0.001$), acute renal failure ($P = 0.022$), multiorgan dysfunction ($P < 0.001$), and acute decompensated heart failure ($P < 0.001$) were observed to be significantly more frequent in the fQRS-positive group than in the fQRS-negative group. fQRS (odds ratio [95% confidence interval]: 4.184 [1.927–9.082], $P < 0.001$), operation duration (4.184 [1.927–9.082], $P = 0.001$), and Killip class IV (3.900 [1.699–8.955], $P = 0.001$) were found to be significant independent predictors of in-hospital cardiovascular mortality after adjustment of other risk factors in the multivariate analysis.

Conclusions: fQRS is a simple, inexpensive, and readily available electrocardiographic entity that provides an additional risk stratification level beyond that provided by conventional risk parameters in predicting in-hospital cardiovascular mortality in type 1 AAD.

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Acute aortic dissection (AAD) still remains one of the most common causes of cardiovascular mortality and morbidity in developing countries, despite modern advances in diagnostic techniques and new approaches to treatment. AAD leads to

life-threatening conditions by several complications due to aortic rupture and/or malperfusion of multiple vital organs. Early diagnosis and urgent appropriate management are important to reduce morbidity and mortality rates.^{1,2} Complicated and

untreated aortic dissection carries a mortality of 40% on admission and an additional 1% per hour thereafter. Its annual mortality rate is 90%.^{3,4} Meanwhile, risk models that include preoperative and intraoperative variables have been developed by the International Registry of Acute Aortic Dissection, and several biochemical markers of vascular injury, thrombosis, and inflammation were evaluated as predictive risk factors of AAD in previous studies. However, the independent predictors of in-hospital and long-term prognoses of AAD have not been fully elucidated. Recent studies have reported the relationship between AAD with both tissue levels and generalized inflammation as indicated by C-reactive protein level.⁵⁻⁷

Fragmented QRS (fQRS), which has been defined as the presence of notched R or S waves without accompanying typical bundle branch block or as the existence of an additional wave-like RSR' pattern in the original QRS complex (with a duration < 120 ms),⁸ arises from impaired ventricular depolarization due to heterogeneous electrical activation of ischemic and/or infarcted ventricular myocardium. It has gained much interest as a new, easy-to-assess, and reliable electrocardiographic (ECG) finding in clinical practice. fQRS was also reported to be an ECG sign of nonhomogeneous ventricular conduction delay around myocardial scar tissue.^{9,10} The presence of fQRS was demonstrated as an independent predictor of decreased myocardial perfusion and left ventricular function in patients with ischemic heart disease.¹¹⁻¹³ Furthermore, the prognostic predictive value of fQRS for other cardiovascular diseases has also been reported.¹⁴⁻²⁰

Although the relationship between high neutrophil-to-lymphocyte ratio (NLR) and long-term cardiovascular mortality was demonstrated in type 1 AAD in a previous study,²¹ the existing literature provides no information about the relationship between the presence fQRS on admission ECG and in-hospital cardiovascular mortality in type 1 AAD. The aim of this study was to investigate the predictive value of admission fQRS complex for in-hospital major adverse cardiovascular events (MACEs), including cardiovascular mortality, in patients with type 1 AAD who had undergone emergent surgery.

METHODS

In this retrospective case-control study, 322 consecutive patients with type 1 AAD who

were admitted to either of two large-volume tertiary training and research hospitals to undergo emergent surgery between December 2008 and October 2013 were included. The diagnosis of type 1 AAD was established in all the patients based on typical clinical symptoms, and findings from chest radiography, transthoracic echocardiography, and contrast-enhanced computed tomography (CT). Aortic dissection was classified according to DeBakey's classification,²² and any dissections that involve the ascending aorta regardless of the entry site were defined as type 1 aortic dissection. AAD was considered if the time from the onset of the symptoms to admission was within 14 days. The exclusion criteria of this study were history of cardiogenic shock or cardiac tamponade, traumatic aortic dissection, iatrogenic aortic dissection, severe valvular diseases, congenital heart disease, severe organ dysfunction such as liver or kidney failure, malignancy, presence of bundle branch blocks, Wolff-Parkinson-White syndrome, Brugada syndrome, and suspected subclinical myocardial involvement such as positive history of chronic inflammatory disease status or acute infective conditions and paced rhythm. A total of 322 patients were screened, of whom 119 were excluded from further analysis after the initial evaluation. Finally, after applying the exclusion criteria, 203 patients were included in the study (Fig. 1). The study patients were divided into two groups according to the presence or absence of fQRS on admission ECG. The fQRS-positive group (n = 62) was defined as patients with fQRS detected on ECG, and the fQRS-negative group (n = 141) was defined as patients with no fQRS detected on ECG.

All emergent surgical procedures were performed in two high-volume tertiary care centers by expert cardiac surgeons who were independent from the study. The demographic information, cardiovascular risk factors and comorbidities, physical examination data, thoracic CT and transthoracic echocardiographic results, and perioperative characteristics of the patients on admission were recorded during a systematic review of the hospital records. Missing variables were obtained by telephone interviews with the patient and/or relatives.

Written informed consent was obtained from all the participants, and the study was approved by the local ethics committee and institutional review board. The study was consistent with the Declaration of Helsinki.

Figure 1. Selection of the study participants.

Data Analysis

A 12-lead ECG was recorded for each patient immediately after hospital admission. All the ECGs (Nihon Kohden-Cardiofax S, CA; ECG-1250K, filter range: 0.5–150 Hz, AC filter: 60 Hz, speed: 25 mm/s, and amplitude: 10 mm/mV; Nihon Kohden, Tokyo, Japan) were analyzed without using any magnification by two independent clinicians who were blinded to the study design and clinical and surgical data. fQRS was defined as the presence of various RSR' patterns, including an additional R wave (R') or notching of the R or S wave, or the presence of more than one

R' (fragmentation) without typical bundle branch block in two contiguous leads corresponding to a major lead set for major coronary artery territory. A notch on an R or S wave was defined as a definite but transient reversal of direction of the main deflection.²³ The interobserver concordance rate for fQRS detection was 97%. In case of disagreement, the final diagnosis was achieved by a consensus. The intraobserver concordance rate was 98%. QRS duration was determined by measuring the longest QRS in any lead through both manual readings and digital records obtained by the ECG machine. Left ventricular systolic function was quantitatively assessed using the

Figure 2. Comparison of in-hospital cardiovascular mortality between the fQRS-positive and fQRS-negative groups.

modified biplane Simpson's method to calculate the left ventricular ejection fraction (LVEF).²⁴ On admission, venous blood samples were obtained from all the study patients before undergoing the surgical procedure.

Definitions

Smoking was defined as the current regular use of cigarettes. Hypertension was diagnosed if the systolic arterial pressure exceeded 140 mmHg and/or the diastolic arterial pressure exceeded 90 mmHg, or if the patient used antihypertensive drugs. Diabetes mellitus was defined as a previous history of the disease, diet modification, insulin or oral antidiabetic drugs, or fasting venous blood glucose level ≥ 126 mg/dL on two occasions in previously untreated patients. Renal failure was defined as a glomerular filtration rate < 60 mL/(min $\cdot 1.73$ m²), which was estimated by the simplified Modification of Diet in Renal Disease Study equation.²⁵ Hyperlipidemia was defined as a fasting total serum cholesterol level > 200 mg/dL, a low-density lipoprotein cholesterol level > 130 mg/dL, or serum triglyceride levels > 180 mg/dL, or if the patient used lipid-lowering drugs because of a history of hypercholesterolemia.²⁶

Surgical Technique

The standard surgical management of type 1 aortic dissection was performed in all the patients. Cardiopulmonary bypass was initiated via right axillary arterial cannulation, and after median sternotomy, a two-stage venous cannula was inserted through the right atrium. After establishment of moderate hypothermic (28–32 °C) circulatory arrest, the heart was arrested with antegrade

and retrograde cold crystalloid cardioplegia. As a standard surgical procedure, the intimal torn aortic section was resected and the resected aorta was replaced with a presealed woven polyethylene terephthalate fiber graft (Dacron, Boston Scientific, Inc., Natick, MA, USA) in each patient. Seventy-five patients (36.9%) had only supracoronary aortic replacement, and 65 (32%) had supracoronary aortic and hemiarch replacements. The Bentall procedure was applied in 34 patients (16.7%), and combined supracoronary aortic replacement and coronary artery bypass grafting (CABG) was performed in 29 patients (14.2%).

Study End Points and Follow-Up

The in-hospital primary and secondary clinical outcomes of the patients were obtained from hospital records. While the primary outcome of this study was cardiovascular mortality, its secondary outcomes were acute renal failure, acute stroke, multiorgan dysfunction syndrome, and acute decompensated heart failure. All-cause mortality was defined as death due to sepsis, acute renal failure, acute respiratory failure, or cardiovascular dysfunction. Cardiovascular mortality was defined as unexplained sudden cardiac death, death due to acute ST-segment elevation myocardial infarction (STEMI), cardiogenic shock, acute decompensated heart failure, or acute hemodynamically significant arrhythmia.

Statistical Analysis

Quantitative variables were expressed as mean $\pm$ standard deviation values, and qualitative variables were expressed as percentages (%). Parametric values were compared between the two groups using the two-tailed Student's t-test. Categorical variables were also compared by the likelihood ratio chi-square (χ^2) or Fisher's exact test. Correlations between fQRS and the other parameters were assessed using the Spearman rank correlations test. Univariate and backward stepwise multivariate Cox regression analyses, which included variables with $P < 0.1$, were performed to identify independent predictors of cardiovascular mortality. Statistical significance was indicated when the two-sided $P < 0.05$. All the statistical analyses were conducted using the SPSS version 16.0 statistical software (SPSS Inc., Chicago, IL, USA).

Table 1. Baseline Demographic, Clinical, and Laboratory Characteristics of the fQRS-Positive and fQRS-Negative Groups

	fQRS-Negative (n = 141)	fQRS-Positive (n = 62)	P ^a
Age (years)	53.9 ± 11.8	54.8 ± 11.5	0.588
Sex, male (n[%])	103 (73)	46 (74)	0.505
BMI (kg/m ²)	27.5 ± 3.8	27.2 ± 4.0	0.492
HT (n [%])	96 (68)	41 (66)	0.453
DM (n [%])	33 (23)	20 (32)	0.126
Dyslipidemia (n[%])	23 (16)	14 (22)	0.192
Family history of CAD (n [%])	11 (8)	3 (5)	0.331
Current smoking (n [%])	52 (37)	15 (24)	0.052
History of MI or CABG (n [%])	7 (5)	14 (22)	<0.001
History of stroke (n [%])	3 (2)	0 (0)	0.333
Heart rate (beats/min)	91.0 ± 18.2	91.6 ± 19.4	0.787
SBP (mmHg)	130.4 ± 32.3	120.0 ± 34.3	0.035
DBP (mmHg)	70.9 ± 18.3	64.9 ± 19.3	0.035
Time from symptom onset to hospitalization (hours)	14.0 ± 20.3	16.1 ± 21.4	0.510
Killip class IV (n [%])	20 (14)	18 (29)	0.012
Operation duration (minutes)	172.9 ± 72.1	182.9 ± 83.3	0.385
Cross clamp duration (minutes)	78.1 ± 42.7	80.6 ± 44.3	0.713
Intensive care unit stay (days)	4.4 ± 2.5	4.5 ± 1.5	0.738
Aortic valve replacement (n [%])	29 (20)	9 (15)	0.207
Glucose (mg/dL)	136.6 ± 42.5	148.5 ± 60.4	0.109
Creatinine (mg/dL)	1.42 ± 0.53	1.48 ± 0.62	0.481
ALT (U/L)	54.4 ± 152.6	83.1 ± 168.8	0.234
AST (U/L)	63.6 ± 135.8	108.6 ± 233.2	0.086
LDH (U/L)	488.6 ± 273.9	632.2 ± 433.2	0.005
Troponin I (ng/mL)	1.41 ± 2.4	0.97 ± 1.5	0.189
Hemoglobin (g/dL)	12.7 ± 1.8	12.4 ± 1.7	0.349
Platelet count (×10 ³ /mm ³)	214.5 ± 78.9	202.6 ± 87.5	0.342

The variables are expressed as means ± standard deviation for normally distributed data, as median values for nonnormally distributed data, and as percentages (%) for categorical variables. Bold values indicate statistical significance.

^aStudent's *t*, Mann-Whitney U, and chi-square tests.

Abbreviations as in text. ALT = alanine amino transaminase; AST = aspartate aminotransferase; BMI = body mass index; CABG = coronary artery bypass grafting; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; DBP = diastolic blood pressure; DM = diabetes mellitus; HT = hypertension; MI = myocardial infarction; LDH = lactate dehydrogenase; SBP = systolic blood pressure.

RESULTS

In this study, 203 patients (mean age, 55.5 ± 12.8 years; 149 men and 54 women) were enrolled. The patients were classified into either a fQRS-positive group (n = 62) or a fQRS-negative group (n = 141) according to the presence of fQRS on admission ECG. Three patients (4.8%) had new onset fQRS complex in our study group. The baseline demographic, clinical, and laboratory characteristics of the patients in both groups are presented in Table 1. The fQRS-positive group tended to have a higher lactate dehydrogenase level (P = 0.005), higher incidence rate of Killip class IV (P = 0.012), and higher incidence rate of prior MI or CABG surgery (P < 0.001) compared with the fQRS-negative group. However, systolic

and diastolic blood pressures were found to be significantly lower in the fQRS-positive group than in the fQRS-negative group (both P = 0.035). No differences were observed between the two groups with respect to other demographic, clinical, and laboratory characteristics (all P > 0.05). Moreover, no significant difference was found between the two groups in terms of the standard medical therapy (i.e., the use of a β -blocker, an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, or a vasodilator) administered in the coronary care unit on the first day of admission (all P > 0.05).

No significant difference was observed between the two groups in terms of incidence of surgical procedural characteristics such as operation duration, cross-clamp duration, cardiopulmonary

Table 2. Comparison of Computed Tomographic and Echocardiographic Characteristics between the fQRS-Positive and fQRS-Negative Groups

	fQRS-Negative (n = 141)	fQRS-Positive (n = 62)	P
LVEF (%)	56.8 ± 5.9	52.9 ± 7.7	<0.001
Moderate-to-severe aortic valve regurgitation (n [%])	28 (20)	12 (19)	0.549
Ascending aorta diameter (mm)	53.3 ± 8.8	56.8 ± 10.6	0.015
Lower extremity or subclavian artery involvement (n [%])	23 (16)	16 (26)	0.084
Coronary artery involvement (n [%])	18 (13)	18 (29)	0.006
Renal artery involvement (n [%])	6 (4)	6 (10)	0.120
Mesenteric artery involvement (n [%])	1 (0)	2 (1)	0.222

Variables are expressed as means ± standard deviation for normally distributed data, as median values for nonnormally distributed data, and as percentages (%) for categorical variables. Bold values indicate statistical significance. Abbreviation as in text. LVEF = left ventricular ejection fraction.

Table 3. Comparison of In-Hospital Adverse Clinical Events between the fQRS-Positive and fQRS-Negative Groups

	fQRS-Negative (n = 141)	fQRS-Positive (n = 62)	P
MACEs (n [%])	63 (45)	47 (75)	<0.001
All-cause mortality (n [%])	28 (20)	32 (51)	<0.001
CV mortality (n [%])	21 (15)	30 (48)	<0.001
Acute renal failure (n [%])	17 (12)	15 (24)	0.026
MODS (n [%])	12 (9)	19 (30)	<0.001
Coronary artery involvement (n [%])	18 (13)	18 (29)	0.006
Stroke (n [%])	7 (5)	6 (9)	0.169
Acute heart failure (n [%])	16 (11)	26 (42)	<0.001

Bold values indicate statistical significance. Abbreviations as in text. MACEs = major adverse cardiovascular events (the sum of in-hospital adverse clinical events); MODS = multiorgan dysfunction syndrome.

bypass duration, stay duration in the intensive care unit, ventilation duration, amount of major or minor bleeding, and types of vascular surgery (all $P > 0.05$). Furthermore, when the extent of the dissection, including the peripheral, coronary, renal, and mesenteric arterial systems, was assessed between the study groups, only coronary vessel involvement was found to be significantly different. The fQRS-positive group had more frequent acute coronary events than the fQRS-negative group ($P = 0.006$; Table 2).

When the two groups were investigated in terms of echocardiographic characteristics, the ascending aortic diameter on admission was found to be significantly increased in the fQRS-positive group as compared with the fQRS-negative group ($P = 0.015$). Moreover, the LVEF was significantly lower in the fQRS-positive group than in the fQRS-negative group ($P < 0.001$; Table 2).

The results of the between-group comparison of in-hospital adverse cardiovascular events are presented in Table 3. The evaluation results of the clinical end points in relation to the presence

of fQRS on admission ECG indicated that 28 (45.9%) and 23 patients (16.1%) died in the fQRS-positive and fQRS-negative groups, respectively. The distribution of all-cause mortality in both groups was as follows: 32 patients (51%) in the fQRS (+) group and 28 patients (20%) in the fQRS (−) group ($P < 0.001$). Moreover, the distribution of the causes of cardiovascular death was as follows: unexplained sudden cardiac death ($n = 5$), death due to acute STEMI ($n = 8$), cardiogenic shock ($n = 10$), acute decompensated heart failure ($n = 12$), and acute hemodynamically significant arrhythmia ($n = 16$). In-hospital cardiovascular mortality ($P < 0.001$) (Fig. 2), MACEs ($P < 0.001$), acute renal failure ($P = 0.022$), multiorgan dysfunction ($P < 0.001$), and acute decompensated heart failure ($P < 0.001$) were observed to be significantly more frequent in the fQRS-positive group than in the fQRS-negative group. However, no difference was found between the two groups with respect to the incidence of acute stroke ($P = 0.344$).

When correlation between fQRS and some important parameters that affect AAD prognosis

Table 4. Results of the Spearman Correlations Analysis between fQRS and the Other Parameters

	r	P
Age	0.041	0.560
Killip class IV	0.175	0.012
LVEF	−0.258	<0.001
Ascending aortic diameter	0.157	0.025
Systolic blood pressure	−0.146	0.038
Coronary artery involvement	0.196	0.005
Operation duration	0.065	0.359
Prior MI	0.266	<0.001

Bold values indicate statistical significance. Abbreviations as in text. LVEF = left ventricular ejection fraction; MI, myocardial infarction.

was assessed, we found that fQRS was significantly positively correlated with ascending aortic diameter ($P < 0.025$), prior MI ($P < 0.001$), Killip class IV ($P = 0.012$), and coronary involvement ($P = 0.005$). Furthermore, a significant inverse relationship was found between fQRS, and LVEF ($P < 0.001$) and systolic blood pressure ($P < 0.038$). However, fQRS was not correlated with the other parameters (Table 4).

The independent predictors of in-hospital cardiovascular mortality, including age, fQRS, LVEF, prior MI, operation duration, Killip class, coronary artery involvement, systolic blood pressure, and ascending aortic diameter, were included in a Cox proportional hazard model and analyzed in a stepwise fashion. In the multivariate analysis, fQRS [odds ratio [95% confidence interval]: 4.184 [1.927–9.082], $P < 0.001$], operation duration (4.184 [1.927–9.082], $P = 0.001$), Killip class IV (3.900 [1.699–8.955], $P = 0.001$) were found as significant independent predictors of in-hospital cardiovascular mortality after adjusting for other risk factors that had been found as significant predictors in the univariate analysis (Table 5).

DISCUSSION

The main findings of this study were as follows: (1) the incidences of in-hospital cardiovascular mortality, MACEs, acute renal failure, multiorgan dysfunction, and acute decompensated heart failure were found to be significantly higher in the fQRS-positive group than in the fQRS-negative group; (2) fQRS was found to be significantly positively correlated with ascending aortic diameter, prior MI, Killip class IV, and coronary involvement but negatively correlated with LVEF and systolic

blood pressure; (3) fQRS, prior MI, Killip class IV, and operation duration were found to be significant independent predictors of in-hospital cardiovascular mortality after adjusting for other risk factors in the multivariate analysis. To the best of our knowledge, this is the first time the predictive value of admission fQRS complex for in-hospital cardiovascular mortality in patients with type 1 AAD was investigated.

Aortic dissection is characterized by the splitting of the aortic wall caused by a tear in the intima layer that allows blood to enter the media layer through an intimomedial entrance tear, subsequently dividing the layer into true and false lumens. The pathogenesis of aortic dissection is a complex process that is based on the interplay between degenerative, proteolytic, and inflammatory processes. Aortic dissections may propagate either proximally or distally from the entry tear and may involve vessel branches, leading to malperfusion syndrome.^{27–30} Several risk factors have been associated with the development and progression of aortic dissection, including hypertension, male sex, genetic factors, connective tissue diseases, aging, smoking, previous repair of aortic aneurysm or dissection, trauma, vasculitis, and aneurysm of the ascending aorta. Moreover, it may lead to life-threatening complications, including acute aortic rupture, acute myocardial ischemia or infarction, acute severe aortic regurgitation, cardiac tamponade, hypotension and cardiogenic shock, end organ ischemia, and cardiac death.^{27–31}

Mortality and complications due to type 1 AAD are associated with the following two factors: (1) preoperative conditions (being prior MI and low EF, the two well-recognized factors for worse outcomes in the short- and long-term evolutions, and the natural course of the dissection that could potentially kill the patient undergoing operation); and (2) intraoperative factors that are related to the characteristics and location of the dissection, among others. In our study, no difference was found between the fQRS-positive and fQRS-negative groups in terms of risk factors of AAD, such as age, male sex prevalence, hypertension, smoking habit, and connective tissue disorder. However, the rate of history of prior MI or CABG was higher in the fQRS-positive group than in the fQRS-negative group. Furthermore, fQRS was found to be significantly positively related with ascending aortic diameter, prior MI, Killip class IV, and coronary involvement. As expected, the incidence of LVEF was lower in the fQRS group

Table 5. Results of the Univariate and Multivariate Logistic Regression Analyses of the Predictors of In-Hospital Cardiovascular Mortality in Type 1 Acute Aortic Dissection

	Univariate				Multivariate		
	β	P	OR	95% CI	P	OR	95% CI
Age	0.044	0.004	1.045	1.014–1.077			
Coronary involvement	1.104	0.004	3.017	1.417–6.424			
fQRS	1.678	<0.001	5.357	2.713–10.579	<0.001	4.184	1.927–9.082
Killip class IV	1.569	<0.001	4.803	2.275–10.138	0.001	3.900	1.699–8.955
LVEF	–0.085	0.001	0.919	0.876–0.964			
Operation duration	0.008	<0.001	1.009	1.004–1.013	0.001	4.184	1.927–9.082
Prior MI	1.818	0.040	16.158	2.380–15.930	0.006	4.549	1.538–13.456
AA diameter	0.418	0.012	1.519	1.098–2.101			
SBP	–0.015	0.003	0.985	0.975–0.995			

Bold values indicate statistical significance. Abbreviations as in text. AA = ascending aorta; CI = confidence interval; LVEF = left ventricular ejection fraction; MI = myocardial infarction; OR = odds ratio; SBP = systolic blood pressure.

and was negatively associated with the presence of fQRS in the patients with type 1 AAD.

fQRS is a simple, inexpensive, and readily available ECG entity that can be easily identified by clinicians. It may occur due to nonhomogeneous activation of ischemic or infarcted ventricles during ischemic or inflammatory heart disease. Furthermore, scar tissue formation, which occurs from cardiac remodeling after ischemic heart disease or cardiomyopathy, predisposes patients to arrhythmias and heart failure that can result in cardiovascular mortality. The presence of fQRS was demonstrated to be an independent predictor of decreased myocardial perfusion and left ventricular function in patients with ischemic heart disease.^{11–13} Moreover, fQRS, which may be widened or narrowed, has been reported to be related with high mortality and morbidity, including hemodynamically significant arrhythmic events in coronary artery disease, coronary slow flow,¹⁴ acute coronary syndromes,^{17,18,32} ischemic and nonischemic cardiomyopathies,^{16,19} hypertrophic obstructive cardiomyopathy,¹⁵ and decompensated systolic heart failure.²⁰ In this study, the predictive value of admission fQRS complex for in-hospital adverse cardiovascular events in patients with a type 1 AAD was investigated. The incidences of in-hospital cardiovascular mortality, MACEs, acute renal failure, multiorgan dysfunction, and acute decompensated heart failure were found to be significantly higher in the fQRS-positive group. Furthermore, fQRS was found to be a significant independent predictor of in-hospital cardiovascular mortality after adjustment of other risk factors in the multivariate analysis.

Although the main underlying pathophysiological mechanisms between fQRS and AAD were not elucidated in previous studies, cardiac arrhythmias, and conduction disturbances, including fQRS, may due to acute myocardial inflammation or previous myocardial ischemia or infarction that leads to cardiac remodeling, which in turn results in ischemic cardiomyopathy. Supporting this theory, the incidence rate of coronary artery disease, prior MI, or CABG was found to be higher in the fQRS-positive group as compared to nonfragmented group in this study, which may significantly affect the results. Moreover, coronary artery involvement was demonstrated to be higher in the fQRS-positive group than in the fQRS-negative group. In concordance with previous studies, the presence of fQRS on admission ECG was reported to be inversely related with LVEF in type 1 AAD. Moreover, in-hospital acute decompensated heart failure was found to be higher in the fQRS-positive group than in the fQRS-negative group.

STUDY LIMITATIONS

This study has some limitations. First, it had a nonrandomized retrospective design with small study groups. Second, inflammatory prognostic markers such as leukocyte count, C-reactive protein level, and pro-brain natriuretic peptide level were not measured in this study. Third, because of the lack of long-term follow-up data on adverse cardiovascular events, the medium- and long-term prognostic values of fQRS were not assessed.

CONCLUSION

We demonstrated a significant predictive value of admission fQRS complex for in-hospital MACEs, including the cardiovascular mortality of type 1 AAD patients who had undergone emergent surgery. fQRS, which originates from abnormal ventricular depolarization due to nonhomogeneous electrical activation of ischemic and/or injured ventricular myocardium, is a simple, inexpensive, and readily available ECG entity that provides an additional risk stratification level beyond that provided by conventional risk parameters in predicting in-hospital cardiovascular mortality of patients with type 1 AAD. Further studies with larger patient groups are needed to clarify the pathophysiological mechanisms of fQRS and in-hospital MACEs, and the short- and long-term prognoses in this setting.

REFERENCES

- Mészáros I, Mórocz J, Szlávi J, et al. Epidemiology and clinicopathology of aortic dissection. *Chest* 2000;117:1271–1278.
- Erbel R, Alfonso F, Boileau C, et al. Task force on aortic dissection, european society of cardiology. Diagnosis and management of aortic dissection. *Eur Heart J* 2001;22:1642–1681.
- Klompas M. Does this patient have an acute thoracic aortic dissection? *JAMA* 2002;287:2262–2272.
- Strayer RJ, Shearer PL, Hermann LK. Screening, evaluation, and early management of acute aortic dissection in the ED. *Curr Cardiol Rev* 2012;8:152–157.
- Rampoldi V, Trimarchi S, Eagle KA, et al. International Registry of Acute Aortic Dissection (IRAD) investigators. Simple risk models to predict surgical mortality in acute type A aortic dissection: The International Registry of Acute Aortic Dissection score. *Ann Thorac Surg* 2007;83:55–61.
- del Porto F, Proietta M, Tritapepe L, et al. Inflammation and immune response in acute aortic dissection. *Ann Med* 2010;42:622–629.
- Luo F, Zhou XL, Li JJ, et al. Inflammatory response is associated with aortic dissection. *Ageing Res Rev* 2009;8:31–35.
- Das MK, Khan B, Jacob S, et al. Significance of a fragmented QRS complex versus a Q wave in patients with coronary artery disease. *Circulation* 2006;113:2495–2501.
- Guo R, Li Y, Xu Y, et al. Significance of fragmented QRS complexes for identifying culprit lesions in patients with non-ST-elevation myocardial infarction: A single-center, retrospective analysis of 183 cases. *BMC Cardiovasc Disord* 2012;12:44.
- Pietrasik G, Zareba W. QRS fragmentation: Diagnostic and prognostic significance. *Cardiol J* 2012;19:114–121.
- Michael MA, El Masry H, Khan BR, et al. Electrocardiographic signs of remote myocardial infarction. *Prog Cardiovasc Dis* 2007;50:198–208.
- Mahenthiran J, Khan BR, Sawada SG, et al. Fragmented QRS complexes not typical of a bundle branch block: A marker of greater myocardial perfusion tomography abnormalities in coronary artery disease. *J Nucl Cardiol* 2007;14:347–353.
- Flowers NC, Horan LG, Thomas JR, et al. The anatomic basis for high-frequency components in the electrocardiogram. *Circulation* 1969;39:531–539.
- Yilmaz H, Gungor B, Kemaloglu T, et al. The presence of fragmented QRS on 12-lead ECG in patients with coronary slow flow. *Kardiol Pol* 2014;72:14–19.
- Femenía F, Arce M, Van Grieken J, et al. Fragmented QRS in Hypertrophic Obstructive Cardiomyopathy (FHOCM) Study Investigators. Fragmented QRS as a predictor of arrhythmic events in patients with hypertrophic obstructive cardiomyopathy. *J Interv Card Electrophysiol* 2013;38:159–165.
- Yusuf J, Agrawal DK, Mukhopadhyay S, et al. Fragmented narrow QRS complex: Predictor of left ventricular dyssynchrony in non-ischemic dilated cardiomyopathy. *Indian Heart J* 2013;65:172–179.
- Stavileci B, Cimci M, Ikitimur B, Barman HA, Ozcan S, Ataoglu E, Enar R. Significance and usefulness of narrow fragmented QRS complex on 12-lead electrocardiogram in acute ST-segment elevation myocardial infarction for prediction of early mortality and morbidity. *Ann Noninvasive Electrocardiol* 2014;19:338–44.
- Erdem FH, Tavil Y, Yazici H, et al. Association of fragmented QRS complex with myocardial reperfusion in acute ST-elevated myocardial infarction. *Ann Noninvasive Electrocardiol* 2013;18:69–74.
- Das MK, Saha C, El Masry H, et al. Fragmented QRS on a 12-lead ECG: A predictor of mortality and cardiac events in patients with coronary artery disease. *Heart Rhythm* 2007;4:1385–1392.
- Ozcan S, Cakmak HA, Ikitimur B, et al. The prognostic significance of narrow fragmented QRS on admission electrocardiogram in patients hospitalized for decompensated systolic heart failure. *Clin Cardiol* 2013;36:560–564.
- Lafci G, Cicek OF, Uzun HA, et al. Relationship of admission neutrophil-to-lymphocyte ratio with in-hospital mortality in patients with acute type-I aortic dissection. *Turk J Med Sci* 2014;44:186–192.
- DeBaakey ME, Henly WS, Cooley DA, et al. Surgical management of dissecting aneurysms of the aorta. *J Thorac Cardiovasc Surg* 1965;49:130–149.
- Take Y, Morita H. Fragmented QRS: What is the meaning? *Indian Pacing Electrophysiol J* 2012;12:213–225.
- Lang RM, Bierig M, Devereux RB, et al. Chamber Quantification Writing Group; American Society of Echocardiography's Guidelines and Standards Committee; European Association of Echocardiography. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005;18:1440–1463.
- Stevens LA, Coresh J, Greene T, et al. Assessing kidney function—measured and estimated glomerular filtration rate. *N Engl J Med* 2006;354:2473–2483.
- European Association for Cardiovascular Prevention & Rehabilitation. Reiner Z, Catapano AL, De Backer G, et al. ESC Committee for Practice Guidelines (CPG) 2008–2010 and 2010–2012 Committees. ESC/EAS Guidelines for the management of dyslipidaemias: the Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). *Eur Heart J* 2011;32:1769–1818.
- Baumann F, Makaloski V, Diehm N. Aortic aneurysms and aortic dissection: Epidemiology, pathophysiology and diagnostics. *Internist (Berl)* 2013;54:535–542.

28. Czermak BV, Waldenberger P, Fraedrich G, et al. Treatment of Stanford type B aortic dissection with stent-grafts: preliminary results. *Radiology* 2000;217:544-550.
29. Golledge J, Eagle KA. Acute aortic dissection. *Lancet* 2008;372:55-66.
30. Tsai TT, Nienaber CA, Eagle KA. Acute aortic syndromes. *Circulation* 2005;112:3802-3813.
31. Thrumurthy SG, Karthikesalingam A, Patterson BO, et al. The diagnosis and management of aortic dissection. *BMJ* 2011;344:d8290.
32. Bekler A, Gazi E, Tenekecioglu E, et al. Assessment of the relationship between red cell distribution width and fragmented QRS in patients with non-ST elevated acute coronary syndrome. *Med Sci Monit* 2014;20:413-419.