Frontal QRS-T angle is related with hemodynamic significance of coronary artery stenosis in patients with single vessel disease

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ABSTRACT

Objective: Fractional flow reserve (FFR) measurement is used to decide the hemodynamic significance of coronary artery lesion. QRS-T angle (QRSTa) is a novel marker of myocardial repolarization abnormality and is affected by obstructive coronary artery disease. The aim of the present study was to evaluate the association between QRSTa and coronary FFR measurement in patients with isolated left anterior descending (LAD) artery stenosis.

Methods: A total of 197 patients undergoing FFR measurement for isolated LAD artery stenosis were retrospectively enrolled in the present study. According to FFR value, patients were divided into two groups as 139 patients with normal FFR (>0.80, group 1) and 58 patients with low FFR (≤0.80, group 2). A 12-lead surface electrocardiography of all subjects that had been recorded before performing coronary angiography was evaluated to measure QRSTa, as well as baseline demographic and clinical variables.

Results: The mean age of group 2 was significantly higher than that of group 1 (61±11 and 64±11, p=0.044). While there were no differences in heart rate, QRS duration, and corrected QT interval between the two groups, QT interval [377 (359–397) and 379 (367–410), p=0.045] and frontal QRSTa [59 (10–120) and 86 (22–132), p<0.001] were higher in group 2. QT interval [odds ratio (OR)=1.046, 95% confidence interval (CI)=1.010–1.084, p=0.012] and frontal QRSTa (OR=1.025, 95% CI=1.010–1.041, p=0.001) were found to be independent predictors of low FFR value in multivariate logistic regression analysis.

Conclusion: In the present study, FFR measurement was demonstrated to be correlated with wide QRSTa as a noninvasive and easy method. Thus, we suggest that the results of FFR measurement as an invasive modality can be previously predicted with a simple electrocardiographic evaluation, such as QRSTa. *(Anatol J Cardiol 2019; 22: 194-201)*

Keywords: coronary artery disease, fractional flow reserve, QRS-T angle, QT interval, single vessel disease

Introduction

Coronary artery disease (CAD) is still the leading cause of morbidity and mortality worldwide. Coronary angiography is important for the diagnosis and treatment of coronary atherosclerotic diseases. Coronary revascularization provides angina relieving and myocardial ischemia resolving via epicardial flow improvement. However, the angiographic severity of stenosis-guided coronary intervention results in increased revascularization rates in patients without hemodynamically significant coronary artery stenosis. According to recent guidelines, fractional flow reserve (FFR) measurement is strongly recommended to evaluate the hemodynamic significance of coronary lesions when the coronary artery stenosis is between 50% and 90%

(1). It has been demonstrated in several clinical studies that FFR-guided coronary intervention improves cardiovascular outcomes and reduces adverse coronary events (2, 3).

The frontal QRS-T angle (QRSTa) was first described as the absolute value of the difference between ventricular depolarization (QRS axis) and repolarization (T axis) as a novel marker of myocardial depolarization and repolarization heterogeneity (4). QRSTa abnormalities reflect the electrical instability of ventricular myocardium and predict adverse cardiovascular outcomes and total mortality, especially in patients with CAD (5). It was demonstrated that obstructive coronary artery stenosis linked to transient ischemic episodes causes ventricular axis changes (6). However, the functional significance of coronary lesions related to QRSTa changes has not been studied until now. The aim of the present study was to evaluate the association between QRSTa

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and hemodynamic significance of coronary artery stenosis in patients with isolated left anterior descending (LAD) artery stenosis.

Methods

Study population

A total of 197 consecutive patients with stable angina pectoris and/or with positive exercise testing undergoing FFR measurement for isolated proximal or midsegment of LAD artery stenosis from August 2009 to June 2018 were retrospectively enrolled in the present study. Patients with complete and incomplete right or left bundle branch block, acute coronary syndrome, pathological Q wave on a 12-lead electrocardiography (ECG), known cardiomyopathy or moderate to severe valvular heart disease, history of percutaneous or surgical coronary revascularization procedure, history of previous myocardial infarction, ECGs without clearly analyzable QRS and T axes, and obstructive coronary atherosclerosis >50% stenosis with the exception of LAD artery were excluded from the study.

Demographic and clinical variables, prior to FFR measurement, were recorded. Biochemical analyses including complete blood count, serum creatinine, total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglyceride (TG), and serum electrolyte levels were assessed. A 12-lead surface ECG of all subjects that had been recorded before performing coronary angiography was evaluated. The study was approved by the local ethics committee.

Electrocardiography

A 12-lead surface ECG (Cardiofax M Model ECG-1250; Nihon Kohden Corporation, Tokyo, Japan) that had been performed in the supine position, with a 25 mm/s paper speed and a voltage of 10 mm/s, before performing coronary angiography, was evaluated retrospectively. Patients with complete and incomplete right or left bundle branch block or pathological Q wave on a 12-lead ECG were excluded from the study. The frontal QRSTa was calculated as the absolute value of the difference between the frontal plane QRS and T axes. If such a difference was >180°, QRSTa was adjusted to the minimal angle as 360° minus the absolute value of the difference between the frontal plane QRS and T axes (Fig. 1) (4). Control ECG was obtained 3 months later after the procedure for patients undergoing revascularization with an FFR value ≤0.80 to determine QRSTa differences. Additionally, QT and QTc values were measured. The QT interval was measured from the beginning of the QRS complex to the end of the T wave. QTc interval was calculated by using Bazett's formula as QTc interval=QT/√(RR interval) (7). While the frontal QRSTa was measured automatically, QT and QTc interval measurements were performed by two different cardiologists who were blinded to the patient data via using a software after ×400 magnification.
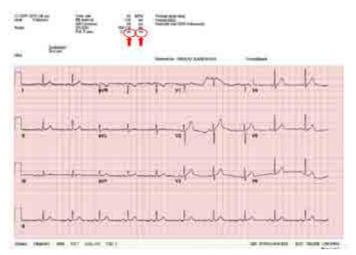

Figure 1. An ECG example demonstrating the measurement of the frontal QRS-T angle. The QRS axis and T axis were calculated automatically (arrowheads). Then, the frontal QRSTa was calculated as the absolute value of the difference between the frontal plane QRS and T axes (frontal QRS-T angle=|QRS axis−T axis|). For the ECG of the patient demonstrating above, frontal QRS-T angle=|46° (QRS axis)−44° (T axis)|=2°

ECG - electrocardiography

The observer agreement for cross-sectional measurements was excellent for both intra-observer variability (r=0.98, p<0.001) and inter-observer variability (r=0.99, p<0.001).

FFR measurement

Coronary angiography was performed through femoral access for all subjects. Left main coronary artery ostium was cannulated with a guiding catheter without side holes after the administration of an intra-arterial heparin bolus of 5000 U. The pressure monitoring guidewire (PrimeWire, Volcano, San Diego, CA, USA) was positioned and calibrated before the LAD artery stenosis. Then, guidewire passed through into the lesion to the distal arterial bed, and baseline distal intracoronary pressure was recorded before adenosine administration. FFR is expressed as the ratio of distal coronary pressure and proximal coronary or aortic pressure measured at the tip of the guiding catheter during maximal hyperemia. An FFR value ≤0.80 was defined as low FFR and functionally significant myocardial ischemia. If such a ratio >0.80, intracoronary adenosine administration was performed to obtain maximal hyperemia by successively increasing the adenosine dose until no further decrement in the FFR value was observed (8). According to the FFR value, patients were divided into two groups as group 1 with normal FFR value (>0.80) and group 2 with low FFR value (≤0.80).

Statistical analysis

Statistical analysis was made using the SPSS software (IBM SPSS Statistics for Windows, version 21.0, released 2012; IBM Corp., Armonk, NY, USA). Pearson chi-square test or Fisher's exact test was performed for categorical variables.

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Kolmogorov–Smirnov test was used to analyze the distribution of variables. Data were expressed as mean±standard deviation for normal distribution, median (25th–75th percentiles) for non-normal distribution, and n (%) for categorical variables. While Mann-Whitney U test was used for comparison of quantitative variables with non-normal distribution, Student's t-test was used for comparison of the means between the two groups with normal distribution. Paired sample t-test was used for related samples with normal distribution. Spearman or Pearson correlation analyses were performed for correlations between ordinal variables or continuous variables. Receiver operating characteristic (ROC) analysis was conducted to determine the optimal QRSTa cut-off value to indicate the hemodynamic significance of coronary artery lesion with respect to both sensitivity and specificity. Multivariate logistic regression analysis was used for predicting the independent predictors of low FFR value. A p-value <0.05 was considered statistically significant.

Results

A total of 197 patients undergoing FFR measurement due to isolated LAD artery stenosis were formed into two groups, with 139 patients as group 1 with normal FFR value (>0.80) and 58 patients as group 2 with low FFR value (≤0.80). There were only seven patients who had a basal FFR value ≤0.80 without adenosine administration and 51 patients who had ≤0.80 after adenosine administration. The baseline demographic and clinical variables of the study population are shown in Table 1. There were no statistically significant differences in age; gender; smoking status; diabetes mellitus; hypertension; hy-

perlipidemia; peripheral arterial disease; atrial fibrillation presence; complete blood count measurements; creatinine, total cholesterol, LDL cholesterol, HDL cholesterol, and TG levels; medication usage; body mass index; left ventricle end-diastolic and end-systolic diameters; interventricular septum (IVS) thickness; and ejection fraction rates between the two groups. However, the mean age of group 2 was significantly higher than that of group 1 (61±11 and 64±11, p=0.044). Adenosine dosage (μg) [250 (120–600) and 225 (150–400), p=0.009], pre-adenosine FFR value [0.94 (0.82–1.0) and 0.89 (0.62–1.0), p<0.001], and post-adenosine FFR value [0.87 (0.81–0.97) and 0.76 (0.64–0.79), p<0.001] were lower in group 2 than in group 1 with statistical significance.

Electrocardiographic measurements of the whole group are shown in Table 2. While there were no differences in heart rate, QRS duration, and QTc interval between the two groups, QT interval [377 (359–397) and 379 (367–410), p=0.045] and frontal QRSTa [59 (10–120) and 86 (22–132), p<0.001] were higher in group 2 with statistical significance (Fig. 2). Based on 58 patients undergoing revascularization with an FFR value ≤0.80, post-procedural QRSTa values were lower than pre-procedural values (80.24±58 and 76.28±58, p=0.014). While the mean QRSTa value was higher in patients with a basal FFR value ≤0.80 without intracoronary adenosine administration, there was no statistically significant difference in QRSTa between patients without and with a basal FFR value ≤0.80 [66 (56–89) and 86 (57–100), p=0.244].

Univariate logistic regression analysis was used to evaluate predictors of hemodynamically significant coronary lesion with pre-procedural or post-procedural FFR value utmost 0.80. Variables, with statistical significance in univariate analysis, were
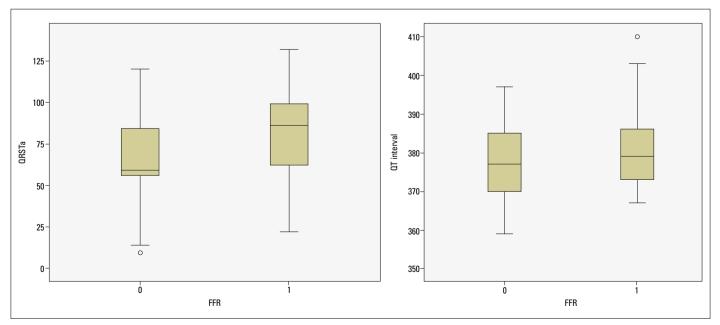

Figure 2. The comparison of QT interval and QRSTa of the normal and low FFR groups
FFR - fractional flow reserve; QRSTa - QRS-T angle

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Table 1. Basal demographic and clinical factors of the normal and low FFR groups

	Normal FFR (>0.80) (n=139)	Low FFR (≤0.80) (n=58)	*P*
Age	61±11	64±11	**0.044**
Gender (female), n (%)	36 (50%)	31 (18%)	0.507
Smoking, n (%)	38 (27.3%)	12 (20.7%)	0.328
Diabetes mellitus, n (%)	41 (29.5%)	17 (29.3%)	0.979
Hypertension, n (%)	74 (53.2%)	30 (51.7%)	0.846
Hyperlipidemia, n (%)	60 (43.2%)	24 (41.4%)	0.817
Peripheral arterial disease, n (%)	6 (4.3%)	1 (1.7%)	0.337
Atrial fibrillation, n (%)	11 (7.9%)	3 (5.2%)	0.366
Hemoglobin (g/dL)	13.8±1.7	13.6±2.0	0.437
Leukocyte (×10³/mm³)	8.0 (6.80-9.80)	7.85 (6.80-9.48)	0.713
Thrombocyte (×10³/mm³)	251±66	260±74	0.387
Creatinine (mg/dL)	0.80 (0.70-0.97)	0.85 (0.70-0.94)	0.837
Total cholesterol (mg/dL)	193±46	188±52	0.560
LDL cholesterol (mg/dL)	121 (90-143)	114 (87-140)	0.322
HDL cholesterol (mg/dL)	43 (38-51)	41 (32-50)	0.168
Triglyceride (mg/dL)	138 (108-208)	145 (98-219)	0.967
Medication usage, n (%)			
Beta-blocker	48 (34.5%)	19 (32.8%)	0.811
ACEI	47 (33.8%)	19 (32.8%)	0.886
ARB	1 (0.7%)	0 (0%)	0.706
Calcium channel blocker	6 (4.3%)	5 (8.6%)	0.192
Statin	15 (10.8%)	7 (12.1%)	0.795
BMI (kg/m²)	23.3 (21.0-26.0)	24.0 (21.5-28.0)	0.761
LVEDD (mm)	49 (45-50)	48 (45-51)	0.791
LVESD (mm)	30 (28-35)	31 (29-34)	0.264
IVS thickness (mm)	9 (8-10)	9 (8-10)	0.238
Ejection fraction %	60 (55-63)	60 (55-63)	0.765
Adenosine dosage (µg)	250 (200-300)	225 (200-300)	**0.009**
Pre-procedural FFR value	0.94 (0.92-0.96)	0.89 (0.85-0.93)	**<0.001**
Post-procedural FFR value	0.87 (0.83-0.90)	0.76 (0.73-0.79)	**<0.001**

ACEI - angiotensin-converting enzyme inhibitor; ARB - angiotensin receptor blocker; BMI - body mass index; FFR - fractional flow reserve; HDL - high-density lipoprotein; IVS - interventricular septum; LDL - low-density lipoprotein; LVEDD - left ventricle end-diastolic diameter; LVESD - left ventricle end-systolic diameter

evaluated in multivariate logistic regression analysis, and adenosine dosage [odds ratio (OR)=0.995, 95% confidence interval (CI)=0.991–0.999, p=0.011], QT interval (OR=1.046, 95% CI=1.010–1.084, p=0.012), and frontal QRSTa (OR=1.025, 95% CI=1.010–1.041, p=0.001) were found to be independent predictors of low FFR value (≤0.80) (Table 3).

While Spearman correlation analysis revealed a negative correlation between QRSTa and post-adenosine FFR value (r=−0.149, p=0.041), there was no correlation between QRSTa and pre-adenosine FFR value (r=−0.048, p=0.505). Additionally,

there was a positive correlation between QRSTa and IVS thickness (r=0.244, p=0.001) (Fig. 3). However, there was no correlation between FFR value and QT interval (r=−0.083, p=0.255) and QTc interval (r=−0.107, p=0.144). There were also no correlations between age and QT interval (r=−0.17, p=0.811), QTc interval (r=0.001, p=0.991), and QRSTa (r=0.119, p=0.096).

ROC analysis was conducted to determine the optimal QRSTa cut-off value to indicate the hemodynamic significance of coronary artery lesion. The highest combined sensitivity and specificity values crossed the curve at 63.5° (sensitivity 74%

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Table 2. Electrocardiographic parameters of patients with normal and low FFR

	Normal FFR (>0.80) (n=139)	Low FFR (≤0.80) (n=58)	P
Heart rate (beat/min)	76 (71-85)	79 (69-90)	0.477
QRS duration (ms)	81 (76-86)	76 (74-85)	0.358
QT interval (ms)	377 (370-385)	379 (373-386)	**0.045**
QTc interval (ms)	430±31	438±44	0.261
Frontal QRS-T angle	59 (56-86)	86 (62-99)	**<0.001**
QRS-T angle >63.5°, n (%)	60 (43.2%)	43 (74.1%)	**<0.001**
QRS-T angle <63.5°, n (%)	79 (56.8%)	15 (25.9%)	
	Before revascularization	After revascularization	P
Frontal QRS-T angle*	80.24±58	76.28±58	**0.014**

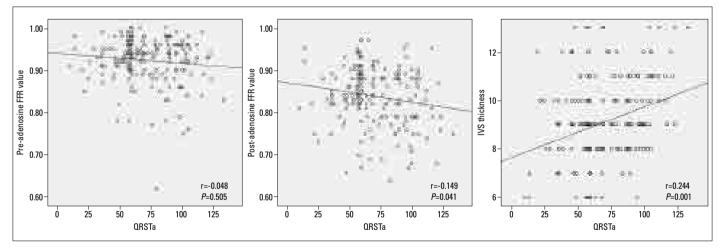*Based on 58 patients undergoing revascularization. FFR - fractional flow reserve

Figure 3. The correlation between QRSTa and both pre-adenosine and post-adenosine FFR values and IVS thickness
FFR - fractional flow reserve; IVS - interventricular thickness; QRSTa - QRS-T angle

and specificity 57%). The area under the curve was 0.665 (95% CI=0.578–0.752) (Fig. 4).

Discussion

In the present study, frontal QRSTa was demonstrated to be significantly wider in the presence of low FFR value in patients with isolated LAD artery stenosis, and that also QT interval was longer in the same group than in patients with normal FFR value. Additionally, there was an inverse association between QRSTa and post-adenosine FFR value that predicts functionally significant coronary lesion, and there was a positive correlation between QRSTa and IVS thickness. Frontal QRSTa and QT interval were also determined as independent predictors of low FFR value.

Obstructive coronary atherosclerosis is still the most important determinant on prognosis worldwide (1). Hemodynamically

significant lesions cause epicardial coronary flow impairment resulting in ischemia-related adverse events. Detecting ischemia is of importance for avoiding ischemia linked to adverse cardiac outcomes and improvement of symptoms due to the mentioned reasons. Proven ischemia has been documented before performing revascularization due to the incoherence between angiographic and functional severity of coronary stenosis in patients with stable CAD. Owing to this, in recent guidelines, invasive hemodynamic evaluation with FFR measurement is recommended to treat patients with ischemic heart disease (1). While FFR-guided coronary intervention leads to relieve anginal symptoms with similar low rates of adverse events and improves cardiovascular outcomes, it also reduces the number of unnecessary revascularization procedures (4, 5, 9). Thus, FFR correlated new indicators are needed to predict ischemia due to the mentioned proven efficacy of FFR on detecting ischemia.

The frontal QRSTa is a novel marker as the absolute value of the difference between frontal QRS axis and T axis on 12-lead sur-

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Table 3. Multivariate logistic regression analysis showing the independent predictors of the functional significance of coronary lesion

	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI (lower–upper)	*P*	Odds ratio	95% CI (lower–upper)	*P*
Age	**1.031**	**1.001-1.062**	**0.046**	1.025	0.992-1.059	0.135
Gender	1.248	0.648-2.404	0.507	-	-	-
Smoking	1.442	0.690-3.013	0.330	-	-	-
Diabetes mellitus	1.009	0.515-1.977	0.979	-	-	-
Hypertension	1.063	0.575-1.962	0.846	-	-	-
Hyperlipidemia	1.076	0.578-2.002	0.817	-	-	-
Peripheral arterial disease	2.571	0.303-21.847	0.387	-	-	-
Atrial fibrillation	1.576	0.423-5.869	0.498	-	-	-
Hemoglobin	0.934	0.786-1.109	0.435	-	-	-
Leukocyte	0.991	0.885-1.111	0.883	-	-	-
Thrombocyte	1.002	0.998-1.006	0.386	-	-	-
Creatinine	1.608	0.429-6.030	0.481	-	-	-
Total cholesterol	0.998	0.992-1.005	0.558	-	-	-
LDL cholesterol	0.997	0.990-1.004	0.407	-	-	-
HDL cholesterol	0.978	0.952-1.006	0.120	-	-	-
Triglyceride	1.000	0.997-1.003	0.872	-	-	-
BMI	1.017	0.935-1.106	0.692	-	-	-
LVEDD	0.993	0.919-1.074	0.870	-	-	-
LVESD	1.032	0.961-1.108	0.385	-	-	-
IVS thickness	1.134	0.952-1.351	0.158	-	-	-
Ejection fraction	0.991	0.929-1.057	0.785	-	-	-
Adenosine dosage	**0.994**	**0.991-0.998**	**0.003**	**0.995**	**0.991-0.999**	**0.011**
Heart rate	1.009	0.984-1.035	0.468	-	-	-
QRS duration	0.987	0.952-1.023	0.479	-	-	-
QT interval	**1.038**	**1.007-1.071**	**0.018**	1.046	1.010-1.084	0.012
QTc interval	1.006	0.997-1.014	0.195	-	-	-
Frontal QRS-T angle	**1.025**	**1.011-1.040**	**<0.001**	1.025	1.010-1.041	0.001

BMI - body mass index; FFR - fractional flow reserve; HDL - high-density lipoprotein; IVS - interventricular septum; LDL - low-density lipoprotein; LVEDD - left ventricle end-diastolic diameter; LVESD - left ventricle end-systolic diameter

face ECG. QRSTa abnormalities reflect the heterogeneity of myocardial repolarization and electrical instability. It has been demonstrated that frontal QRSTa becomes effective on determining the repolarization abnormalities before overt ECG changes appear (4). Normally, the consequence of the balanced regulation of electrical activity and recovery, ventricular depolarization, and repolarization axis are in similar direction (10), and it results in sharp QRS axis. Chronically ischemic myocardium causes delayed conduction in the local Purkinje fibers and partial depolarization and repolarization of the ventricle (11). It results in slow activation of the myocardium. This slow activation is one of the most important reasons of the instability of depolarization and repolarization homogeneity

(12). In conclusion, damaged or inhomogeneous areas of the myocardium due to ischemia result in abnormal ventricular repolarization, and a widening QRSTa appears. In our study, we revealed that hemodynamically significant occlusion into the epicardial coronary artery results in ischemia-related wider QRSTa. Moreover, a significant narrowing in the QRSTa after revascularization was demonstrated. It supports the impact of ischemia on ventricular repolarization calculated by QRSTa. Owing to the mentioned reasons, patients with ischemic myocardium with low FFR value and with wider QRSTa at the same time.

In previous studies, QRS and T axis changes have been found to be related with transient ischemic episodes in patients
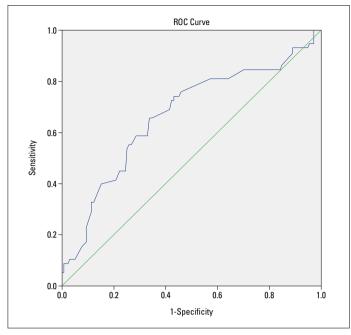
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Figure 4. Receiver operating characteristic curves indicating the discriminative ability of the QRSTa
QRSTa- QRS-T angle

with coronary artery occlusion (6), and also the relationship between multivessel CAD and wide QRSTa was demonstrated by Colluoglu et al. (13). It supports the QRSTa as an important predictor of ischemia. Additionally, QRSTa is associated with adverse cardiac events in several populations. In the previous study by Aro et al. (14), 10,957 middle-aged subjects from the general population were evaluated, and wide QRSTa was found to be associated with 2.26-fold increased sudden arrhythmic death and 1.57-fold increased all-cause mortality. Gotsman et al. (15) evaluated 5038 patients with heart failure during the mean follow-up period of 576 days. QRSTa wideness was a predictor of rehospitalization due to heart failure and also increased mortality rates. Wide QRSTa was associated with increasing 30-day and 2-year mortality in a study with two large cohort groups including 1843 and 550 patients with acute coronary syndrome, respectively (16). In the ARIC study, 13,973 participants were evaluated by Zhang et al. (17). With adjustment for demographic and clinical characteristics, frontal QRSTa was a strong predictor of total mortality with a >50% increased risk and was a strong predictor of incident CAD with a 74% increased risk. de Torbal et al. (18) also revealed that wide QRSTa is associated with a 1.5 times higher risk of 6-year mortality in patients with ischemic chest pain. These results could be explained by clinically significant coronary atherosclerosis-related QRS axis changes. In support to these, there was a strong association between wide QRSTa and hemodynamically significant coronary obstruction. It may be one of the most important reasons of QRSTa linked to adverse cardiac events.

FFR measurement is important to detect the extent and importance of ischemia (1-3). In our study, post-adenosine FFR value

was demonstrated to be negatively correlated with QRSTa. This means that wide QRSTa becomes more apparent in the presence of increased ischemia. However, pre-adenosine FFR measurement did not show the same correlation. It may result from the insufficient number of patients with baseline low FFR value before adenosine administration. On the other hand, it could be the reason of increased adenosine dosage for patients with normal FFR value (>0.80).

In previous studies, it was demonstrated that ventricular repolarization markers can be prolonged in the presence of left ventricle hypertrophy (LVH). Tanriverdi et al. (19) demonstrated that patients with LVH have wider frontal QRSTa than patients without LVH. Left ventricular mass index was also found to be positively correlated with frontal QRSTa. Additionally, frontal QRSTa was the only independent predictor of LVH (19). According to these findings, there was a strong correlation between QRSTa and IVS thickness as an indicator of LVH.

QT interval reflects ventricular repolarization, such as QRSTa, and prolonged values are related with ischemia. In a meta-analysis, QT interval prolongation was found to be related with coronary atherosclerotic disease and adverse cardiovascular outcomes (20). Similar results have been demonstrated in the MESA study from 6273 participants without clinically apparent cardiovascular disease (21). In our study, the clinical importance of QT interval with prolonged value in the presence of hemodynamically significant coronary artery obstruction was supported. While FFR-based ischemia-related QT prolongation was demonstrated in our study, the same result could not be exhibited for QTc interval due to the small sample size of the study.

In light of foregoing data, ischemia linked to repolarization markers, such as QRSTa and QT interval, appears to be correlated with the hemodynamic significance of coronary obstruction and have a broad usage to detect ischemia before performing an invasive procedure. It was also supported in our study by independent risk factors of FFR-related ischemia, such as prolonged QT interval and wide QRSTa. However, large scale studies are needed for future investigations.

Study limitations

The small sample size of the study was the main limitation. The lack of patient follow-up visits, such as adverse cardiovascular outcomes, including reintervention rates and mortality, was the other limitation. In addition, the association between QRSTa and adverse events was not evaluated. Additionally, in some studies, it was demonstrated that spatial QRSTa can be superior than frontal planar QRSTa for cardiac risk protection. The lack of data about spatial QRSTa values is the other limitation.

Conclusion

In our study, we demonstrated that FFR measurement was correlated and can be anticipated with wide QRSTa as a nonin-

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vasive and easy method. Thus, we suggest that the frontal QRS-T angle can be used for selected patients to determine the hemodynamic significance of coronary artery lesion and treatment modality.

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Peer-review: Externally peer-reviewed.

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References

1. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, et al.; ESC Scientific Document Group. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J 2019; 40: 87-165.[CrossRef]

2. De Bruyne B, Pijls NH, Kalesan B, Barbato E, Tonino PA, Piroth Z, et al.; FAME 2 Trial Investigators. Fractional flow reserve-guided PCI vs. medical therapy in stable coronary disease. N Engl J Med 2012; 367: 991-1001. [CrossRef]

3. Tonino PA, De Bruyne B, Pijls NH, Siebert U, Ikeno F, van' t Veer M, et al.; FAME Study Investigators. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Engl J Med 2009; 360: 213-24. [CrossRef]

4. Oehler A, Feldman T, Henrikson CA, Tereshchenko LG. QRS-T angle: a review. Ann Noninvasive Electrocardiol 2014; 19: 534-42. [CrossRef]

5. Giannopoulos G, Dilaveris P, Batchvarov V, Synetos A, Hnatkova K, Gatzoulis K, et al. Prognostic significance of inverse spatial QRS-T angle circadian pattern in myocardialinfarction survivors. J Electrocardiol 2009; 42: 79-84. [CrossRef]

6. Shirota K, Ogino K, Hoshio A, Kasahara T, Kotake H, Endo S, et al. Changes of QRS axis in transient myocardial ischaemia induced by percutaneous transluminal coronary angioplasty. Eur Heart J 1994; 15: 1391-5. [CrossRef]

7. Goldenberg I, Moss AJ, Zareba W. QT interval: how to measure it and what is "normal". J Cardiovasc Electrophysiol 2006; 17: 333-6.

8. Pijls NH, De Bruyne B, Peels K, Van Der Voort PH, Bonnier HJ, Bartunek J Koolen JJ, et al. Measurement of fractional flow reserve to assess the functional severity of coronary artery stenoses. N Engl J Med 1996; 334: 1703-8. [CrossRef]

9. De Bruyne B, Fearon WF, Pijls NH, Barbato E, Tonino P, Piroth Z, et al. Fractional flow reserve guided PCI for stable coronary artery disease. N Engl J Med 2014; 371: 1208-17. [CrossRef]

10. Scherptong RW, Henkens IR, Man SC, Le Cessie S, Vliegen HW, Draisma HH, et al. Normal limits of the spatial QRST angle and ventricular gradient in 12 lead electrocardiograms of young adults: dependence on sex and heart rate. J Electrocardiol 2008; 41: 648-55.

11. Birnbaum Y, Sclarovsky S. The grades of ischemia on the presenting electrocardiogram of patients with ST elevation acute myocardial infarction. J Electrocardiol 2001; 34 Suppl: 17-26. [CrossRef]

12. Gardner PI, Ursell PC, Fenoglio JJ Jr, Wit AL. Electrophysiologic and anatomic basis for fractionated electrograms recorded from healed myocardial infarcts. Circulation 1985; 72: 596–611. [CrossRef]

13. Colluoglu T, Tanriverdi Z, Unal B, Ozcan EE, Dursun H, Kaya D. The role of baseline and post-procedural frontal plane QRS-T angles for cardiac risk assessment in patients with acute STEMI. Ann Noninvasive Electrocardiol 2018; 23: e12558. [CrossRef]

14. Aro AL, Huikuri HV, Tikkanen JT, Junttila MJ, Rissanen HA, Reunanen A, et al. QRS-T angle as a predictor of sudden cardiac death in a middle-aged general population. Europace 2012; 14: 872–6.

15. Gotsman I, Keren A, Hellman Y, Banker J, Lotan C, Zwas DR. Usefulness of electrocardiographic frontal QRS-T angle to predict increased morbidity and mortality in patients with chronic heart failure. Am J Cardiol 2013; 111: 1452-9. [CrossRef]

16. Lown MT, Munyombwe T, Harrison W, West RM, Hall CA, Morrell C, et al.; Evaluation of Methods and Management of Acute Coronary Events (EMMACE) Investigators. Association of frontal QRS-T angle-age risk score on admission electrocardiogram with mortality in patients admitted with an acute coronary syndrome. Am J Cardiol 2012; 109: 307-13. [CrossRef]

17. Zhang ZM, Prineas RJ, Case D, Soliman EZ, Rautaharju PM; ARIC Research Group. Comparison of the prognostic significance of the electrocardiographic QRS/T angles in predicting incident coronary heart disease and total mortality (from the atherosclerosis risk in communities study). Am J Cardiol 2007; 100: 844-9. [CrossRef]

18. de Torbal A, Kors JA, van Herpen G, Meij S, Nelwan S, Simoons ML, et al. The electrical T-axis and the spatial QRS-T angle are independent predictors of long-term mortality in patients admitted with acute ischemic chest pain. Cardiology 2004; 101: 199–207. [CrossRef]

19. Tanriverdi Z, Besli F, Gungoren F, Altiparmak IH, Yesilay AB, Erkus ME, et al. Frontal QRS-T angle as a marker of left ventricular hypertrophy in patients with essential hypertension. DEU Tip Fakultesi Dergisi 2018; 32: 77-87. [CrossRef]

20. Zhang Y, Post WS, Blasco-Colmenares E, Dalal D, Tomaselli GF, Guallar E. Electrocardiographic QT interval and mortality: a meta-analysis. Epidemiology 2011; 22: 660-70. [CrossRef]

21. Beinart R, Zhang Y, Lima JA, Bluemke DA, Soliman EZ, Heckbert SR, et al. The QT interval is associated with incident cardiovascular events: the MESA study. J Am Coll Cardiol 2014; 64: 2111-9. [CrossRef]