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Original Article

Normal left ventricular ejection fraction in acute coronary syndrome and associated between fragmented QRS complex and the doppler tissue-obtained criteria

Akram Shariati [1], ***Hossein Aghayi Yamchi*** [1], ***Mohammadreza Dehghani*** [2,*]

[1] Department of Cardiology, School of Medicine, Urmia University of Medical Sciences, Urmia, Iran
[2] Department of Cardiology, Seyyed ol Shohada heart center, Urmia University of Medical Sciences, Urmia, Iran

*** Corresponding Author:**
Address: 17 Shahrivar Street, Seyyed ol Shohada Heart Center, Urmia, Iran. **Postal code:** 5718749441; **Tel:** +98 44325909; **Email:** mr.dehghani@umsu.ac.ir

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Abstract

Objectives: Coronary heart disease (CHD) is the leading significant cause of mortality worldwide. Previous studies have shown that the presence of fragmented QRS (fQRS) in the electrocardiogram (ECG) can be associated with scars in myocardial tissue. This topic seems specific and focused on a particular aspect of cardiology research. It may be of interest to researchers and clinicians in the field of cardiology. This study aimed to investigate the effects of fQRS on diastolic parameters using Tissue Doppler Imaging (TDI) in patients with acute coronary syndrome (ACS) and normal systolic function.

Methods: In this periodic-analytical study, 100 patients (50 with fQRS in superficial ECG and 50 without fQRS) were evaluated by the diagnosis of ACS and ejection fraction (EF) value of over 50 in Seyed al-Shohada Hospital during 2020-2021. The diastolic parameters between these two groups were compared using the Tissue Doppler method.

Results: A total of 100 patients were studied, of which in the first group, 26 (52%) were male and 24 (48%) were female. Also, in the non-fQRS group, 25 (50%) were male, and 25 (50%) were female. The mean age scores for fQRS and non-fQRS groups were 5.10±6.58 and 4.10±3.57 years, respectively. TDI was not significantly different in both groups, yet the mean Tissue Tei Index was less in the non-fQRS group (0.6±0.15 vs. 0.55±0.11, p=0 >005).

Conclusions: The results revealed no significant relationship between Tissue Doppler Indicators in the groups with and without fQRS.

Keywords: Acute coronary syndrome, Left Ventricular Dysfunctions, fQRS Wave, Tissue Doppler, Tei Index

Introduction

Acute coronary syndrome (ACS), diagnosed based on clinical symptoms, electrocardiogram (ECG) abnormalities, and cardiac enzyme levels, is a deadly acute occurrence of myocardial ischemia (MI). High mortality rates are linked to ACS. Therefore, stratifying ACS patients according to risk is important to ensure adequate care and improve outcomes. High-risk ACS patients require more aggressive and intensive treatment to achieve favorable outcomes. As a symptom of acute complete or subtotal coronary blockage, ACS is classified into unstable angina (UA), non-ST elevation myocardial infarction (NSTEMI), and

ST-elevation myocardial infarction (STEMI). It is generally accepted that ST-segment elevation and depression establish the diagnosis of ACS. Fragmented QRS (fQRS) complex is another ECG finding revealed by ECG analysis in patients with ACS, previously associated with the severity and breadth of coronary artery lesions. The fQRS is now recognized as a unique and useful indicator of myocardial fibrosis or myocardial scarring. Therefore, it has become important to investigate the potential application of fQRS in cardiac diseases, especially ACS. In a study by Sharma et al., fQRS was detected in lateral leads in 91.4% of ACS patients with causative lesions with a high specificity of 96.7% (1).

Flowers et al. (2) were the first researchers to investigate the morphological and slurring alterations in the QRS complex since the 1960s. They recorded the occurrence of fragmented QRS (fQRS) complexes, indicated by the presence of an extra R wave (R′) or notch within the nadir of the S wave (3). Additionally, the presence of more than one R′ (fragmentation) in two consecutive ECG leads corresponding to a substantial coronary artery region was designated as fQRS. Furthermore, they defined fragmentation in wide complex QRS, i.e, 120 ms [bundle branch block (BBB) and paced rhythms]. They described it as different RSR′ patterns in 2 contiguous leads corresponding to a significant coronary artery territory in fragmented BBB, with or without a Q wave, with > 2 R waves (R′) or > 2 notches within the R wave, or > 2 notches within the down-stroke or up-stroke of the S wave. The presence of more than two R′ waves or more than two notches within the S waves in two adjacent leads in a fragmented paced QRS was another definition (5). Various studies have shown that fQRS is a predictor of cardiac events in patients with ACS (6) and heart failure which are associated with high morbidity and mortality (7).

Sometimes, despite having a normal ejection fraction (EF) in the examination, with echocardiography cardiovascular disorders (CVD) can be manifested subclinically. In addition to routine cardiac examination, echocardiography can help physicians to determine cases of cardiac dysfunction subclinically. Therefore, they can take appropriate therapeutic and diagnostic measures. Supplementation should be done for this category of patients.

This study determined the TDI indices in hospitalized patients with ACS with normal left ventricular EF and the relationship between fQRS complexes and TDI findings compared to patients without fQRS and used the TDI indices to determine subclinical myocardial dysfunction.

A. Research population

The study's statistical population was all patients referred to Seyed al-Shohada Hospital from 2020 to 2021 with symptoms of ischemic heart disease. The sample size was 50 participants, as obtained using the following formula and based on the average isovolumetric relaxation time (IVRT) in the study by Sezer et al (8).The group with fQRS and without fQRS were7.4±88.12 and 12.4±803.4, respectively. With a confidence interval of 95% (Z_ (1-β=1.64), and a test power of 90% at least 50 people in each group were selected. Sampling was performed sequentially.

$$n = \frac{\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}\right)^2 (\delta_1^2 + \delta_2^2)}{(\mu_1 - \mu_2)^2}$$

B. Electrocardiogram and Coronary Angiography

Having signed up for the health examination, all participants provided written informed consent. The patients' 12-lead ECG were recorded while they were at rest, under typical circumstances, and by the most recent recommendations (0.5 to 150 Hz, 25 mm/s, 10 mm/mv). Then, 50 patients with changes in their ECG indicative of fQRS were contrasted with 50 patients who were without fQRS indications.

Inclusion Criteria

Patients diagnosed with ACS, whose EF were higher than 50%, were included in the study.

Exclusion criteria

Patients with EF less than 50%, previous history of percutaneous coronary intervention (PCI), MI, acute coronary artery bypass grafting (CABG), patients with recurrent premature ventricular contractions (PVCs) or premature atrial contractions (PACs), patients with left bundle branch block (LBBB) and Right bundle branch block (RBBB), patients with restrictive physiology with preserved systolic function in data analysis, any type of congenital disorder, patients with conduction disorder Atrio-ventricular, chronic obstructive pulmonary disease

(COPD), pulmonary arterial hypertension (PAH), and patients who did not meet the conditions for entering the study were excluded.
Patients had their hearts scanned using an echocardiography instrument called the Vivid S6. The most recent echocardiography recommendations were followed for each examination. The TDI was determined in two ways for the evaluation of echocardiography: Tei Index from the following formula.

$$LV\ MPI\ (Tei\ index) = IVCT+IVRT/LVET$$

Isovolumic contraction time+ Isovolumic relaxation time /left ventricular ejection time (IVRT/LVET)

Patients underwent TDI examination. For both groups,the parameters were determined, including the mitral valve (MV) inlet flow, E number, a number, E/e ratio, TAPSE and MAPSE numbers, and left atrium (LA) volume index.The TDI examination of abnormal instances were recorded. The term "impaired cases" refers to subclinical impairment. Patients with an EF of less than 50%, previous PCI or CABG history, acute myocardial infarction (AMI), recurrent PACs, LBBB or RBBB, and restrictive physiology with maintained systolic function are all contraindications. Only patients with ASC were included in the analysis of the data; all other congenital disorders, patients with atrioventricular conduction abnormality, PAH, COPD, and patients who did not match the entry requirements for the research were excluded. Identifying the acute syndrome based on common clinical signs suggested hospitalization and invasive and non-invasive testing. Information on patients' age and gender, diabetes, hypertension, smoking, other risk factors, and presence or absence of comorbidities was recorded and examined. Checklists were developed for both groups and used to capture demographic, echocardiography, and cardiac tape data.

C. Statistical analysis

The software SPPS was used for all statistical analyses. Qualitative factors were expressed as percentages (%) while quantitative variables were expressed as the mean value, standard deviation, or median (minimum-maximum). Kolmogorov-Smirnov test evaluation was performed on each measurement. The Mann-Whitney U-test or student t-test was used to compare parametric values between the two groups. Statistical significance was defined as a p value= 0.05.

Results

The results showed that the average age of patients with fQRS, and without fQRS were 58.6 ± 10.5 and 57.3 ± 10.4, respectively. The age range of all subjects studied was from 20 to 78 years. Table 1 shows the demographic characteristics of the participants.

Table1. Demographic characteristics of the participants

Variable		fQRS		Non-fQRS	
		Frequency	%	Frequency	%
Sex	Male	26	% 52	25	% 50
	Female	24	% 48	25	% 50
High Blood Pressure	Yes	24	% 48	28	% 56
	No	26	% 52	22	% 44
Diabetes	Yes	18	% 36	16	%32
	No	32	% 64	34	%68
Smoking	Yes	9	% 18	14	% 28
	No	41	% 82	36	% 72

In the From among the 50 patients with fQRS, 30 patients (60%) exclusively had ECG abnormalities in the form of fQRS in the inferior leads, with the lower leads having the highest frequency. In this category, nine patients (18%) had the highest frequency related to the inferior and lateral leads simultaneously. The other leads are shown in Table 2.The findings revealed that 48% (24) of patients without abnormal fQRS and 56% (28) of patients with abnormal fQRS and Tissue TITI (higher than 0.55) are abnormal (larger than 0.55). The independent t-test revealed no discernible difference in the patient's cardiac band between the Tei Index in those with and without fQRS (p> 0.05) Table 2.

Table2. Comparison of Tissue Tei Index in patients with fQRS and without fQRS with acute coronary syndrome diagnosis

Tissue Tei Index	Mean Score	Total Score	Test	Value	Sig
fQRS	0.60	0.15	Independent T Test	1.741	0.085
Non-fQRS	0.55	0.11			

The results showed that 96 % (48) of patients with fQRS, Doppler Tei Index (greater than 0.4), and 94 % (47) of patients without fQRS are abnormal (larger than 0.4). Man-Whitney test showed that there is no significant difference between the Doppler Tei Index in patients with fQRS and without fQRS in terms of their ECG ($0.05 < p$) Table 3.

Table3. Comparison of Tei Index Doppler in patients with and without fQRS with acute coronary syndrome diagnosis

Doppler Tei Index	Mean Score	Total Score	Test	Value	Sig
fQRS	52.65	2632.50	Mann-Whitney U	1142.5	0.458

Comparison of Tei Index Doppler in patients admitted to fQRS with and without fQRS in patients' cardiac diagnosis with ACS Table 4.

Table4. Comparison of laboratory and paraclinical parameters in fQRS and fQRS patients in patients with acute coronary syndrome diagnosis

Variables		Mean Score	Total Score	Test	Value	Sig
SBP	fQRS	47.52	50.2623	Mann-Whitney U	1151.5	0.490
	Non-fQRS	53.48	50.2426			
DBP	fQRS	41.43	50.2170	Mann-Whitney U	895.5	0.013
	Non- fQRS	59.57	50.2879			
Cholestrol	fQRS	6.151	1.41	Independent T- test	1.315	0.315
	Non- fQRS	4.140	2.44			
TG	fQRS	32.55	00.6627	Mann-Whitney U	1009	0.097
	Non- fQRS	68.45	00.2284			
HDL	fQRS	8.40	2.10	Independent T- test	0.528	0.598
	Non- fQRS	8.39	3.9			
LDL	fQRS	35.53	50.2667	Mann-Whitney U	5.1107	326.0
	Non- fQRS	47.65	2382.50			
EDT	fQRS	207.68	68.61	Independent T- test	0.836	0.360
	Non- fQRS	194.68	86.00			
LA vol Index	fQRS	46.82	12.12	Independent T- test	0.917	0.362
MAPSE	fQRS	44.72	10.74			
	Non- fQRS	46.31	2315.50	Mann-Whitney U	1040.5	0.145
TAPSE	fQRS	54.69	2734.50			
	Non- fQRS	21.14	3.30	Independent T -test	0.099	0.921
E/e'average	fQRS	21.07	3.76			

SBP: Systolic blood pressure
DBP: Diastolic blood pressure
TG: Triglyceride
HDL: High-density lipoprotein
LDL: Low-density lipoprotein
EDT: Emergency department thoracotomy
LAvol Index: Left atrial end-diastolic volume index
MAPSE: Mitral Annular Plane Systolic Excursion
TAPSE: Tricuspid annular plane systolic excursion

Table 4 compares the laboratory and paraclinical data of patients with the diagnosis of ACS with fQRS and without fQRS using patients' cardiac strips. ACS patients' ESEPTAL distribution index revealed that 42% (21) of patients were aberrant and 58% (29) of fQRS patients had an ESEPTAL over seven. In addition, 56% (28) of the patients (less than 7) in the group without fQRS were

abnormal. ECG results from patients with and without fQRS did not substantially differ in terms of E septal, according to an independent t-test (p = 0.273). Additionally, results from the E-Lateral index distribution investigation of patients undergoing echocardiography diagnosed with ACS revealed that 54% (27) of fQRS patients above 10, and 46% (23) (less than 10) were abnormal. In the group without fQRS, 60% (30) of the patients are abnormal (less than 10) patients and 40% of the patients were over 10. The E-lateral index in patients admitted to Seyed al-Shohada Hospital with and without fQRS was not statistically different from ACS, according to an independent t-test (p=0.544).

Discussion

In this study, we investigated a new criterion called the myocardial functional index or Tei Index to reveal that it can be used as a prognostic factor or predictor of subclinical disorders. We examined Tei Index as a tool to optimize and improve the management of patients with ACS. The results showed no correlation between the age and gender of patients in the two groups with and without fQRS. According to a study by Haukilahti et al., different populations have variable rates of QRS fragmentation (9). Although the underlying heart illness affects both sexes equally, women appear to have a much lower prevalence of fQRS than men in each patient population. The findings revealed no differences in smoking, systolic, or diastolic blood pressure (DBP) between the groups. However, Sezer et al. (2013) demonstrated that the development of left ventricular diastolic dysfunction (LVD), both locally and globally, is correlated with the existence of fQRS in the surface ECG. The tissue level is where this degradation is more noticeable. Another study (2019) demonstrated that fQRS may help predict high-risk hypertensives and may signal myocardial fibrosis, uncontrolled blood pressure, and impaired cardiac structure in hypertensive patients even in the absence of other structural heart illnesses (10). This difference can be justified by working methods and sample sizes. Given that left ventricular hypertrophy and cardiac fibrosis are related to hypertension (11), we believe that BP medication would be an effective treatment for the study's hypertensive participants.

Various CVD such as coronary artery disease (CAD), HF, cardiomyopathies, and genetic arrhythmogenic syndromes including Brugada syndrome, are predicted by fQRS to cause arrhythmic events (12-15). However, its prognostic value for arrhythmias in patients with hypertension is not extensively described. In the examination of the laboratory and paraclinical parameters of the studied patients, it was found that the average levels and the average rank of the factors of the fat profile were not significantly different between the two studied groups. However, another study by Yagi et al. (2021) demonstrated that age, sex, hypertension, hemoglobin A1c, total cholesterol, and diabetes mellitus were all significantly different between the fQRS(+) and fQRS(-) groups. This difference can be justified by different working methods and sample sizes. Doppler analysis of the tissue Tei Index revealed no discernible difference between the two groups in this area. The mean rank of the group with fQRS was greater than the group without fQRS in the Doppler technique investigation of the Tei Index, but this difference was not statistically significant. The outcomes also revealed that there was no discernible difference between the two groups' E septal and lateral structures. A study of cardiovascular diseases in healthy children showed that the Tei index decreased from birth to age three and did not change significantly thereafter. The only instances in which this index significantly changed in the participants under study were those involving children with cardiomyopathy, where the Tei Index increased (16, 17).

Although the average left atrial end-systolic volume index (LAESV) in the fQRS group was larger than the group without fQRS, there was no statistically significant difference between the two groups. There was no discernible correlation between the two groups when the MAPSE and TAPSE indices were evaluated for these two variables. There was no statistically significant difference between the average E deceleration time index in the groups with and without fQRS, which was 207 in the former and 194 in the latter. The E/e' average index higher than 14 indicates an increase in end-diastolic pressure. It is one of the other indicators used in the assessment of diastolic dysfunction. It was 7.9 and 1.8 in the two groups, respectively, and there was no statistically significant difference between the two groups.

The Tei Index has been established in numerous studies to be a trustworthy metric for assessing the left ventricle's systolic and diastolic function. For example, Sezer et al. just applied one technique in the investigation (8), and examined the connection

between fQRS and diastolic parameters in CAD patients without significant lesions. The study revealed that Tei Index in the fQRS group was higher than in the group without fQRS, and this relationship in the Tissue Tei Index was at the threshold of significance. Worse cardiac function was correlated with darnbode and higher index. The Tei Index was in accordance with the fQRS group above the group without fQRS. The lowest performance was accompanied by higher index. However, the Tei Index was examined in the present study using Tissue and Doppler methodologies, and the results were compared with recent studies. In the current study, Doppler was compared to more recent Tei-specific investigations. The Tei Index was in accordance with the fQRS group above the group without fQRS. The lowest performance was accompanied by higher index. Numerous studies have demonstrated that the Tei Index is a reliable metric for assessing the left ventricle's diastolic and systolic function during an echocardiogram. One of the advantages of this study was the comparison of indicators like MAPSE and TAPSE in two groups, which was not investigated in previous research.

Conclusion

There were no discernible differences between the two groups of patients-those with and without fQRS-as measured by diastolic performance parameters. However, measures like the Tissue Tei Index, which can be utilized as a parameter in systolic and systolic performance evaluation, were greater in the group with fQRS. Future research can investigate the benefits of using indices such as Tei index in cardiovascular patients.

Conflicts of Interest

Not applicable

Acknowledgments

The current study was a cross-sectional study approved by the ethics committee of Urmia University of Medical Sciences with the ethics code (IR.UMSU.REC.1400.070). We thank all the patients who participated in this study.

References

1.Sharma SG, Jayakumar TG, Rupesh G, et al. Significance of fragmented QRS complex in acute coronary syndrome and its correlation with coronary angiography to identify the culprit lesion.*I J S S*. 2016;4(4):246-252.

2.Flowers N C, Horan L G, Thomas J R, et al.The anatomic basis for high-frequency components in the electrocardiogram.*Circulation*.1969;39(4):531-9.

3.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(21):2495-501.

4.Das MK, Suradi H, Maskoun W, et al. Fragmented wide QRS on a 12-lead ECG: a sign of myocardial scar and poor prognosis. *Circ Arrhythm Electrophysiol*.2008;1(4):258-68.

5.Das MK, Michael MA, Suradi H, et al. Usefulness of fragmented QRS on a 12-lead electrocardiogram in acute coronary syndrome for predicting mortality. *Am J Cardiol*.2009;104(12):1631-7.

6.Akbarzadeh F, Pourafkari L, Ghaffari S, et al. Predictive value of the fragmented QRS complex in 6-month mortality and morbidity following acute coronary syndrome. *Int J Gen Med*.2013;6:399-404.

7.Basaran Y, Tigen K, Karaahmet T, et al. Fragmented QRS complexes are associated with cardiac fibrosis and significant intraventricular systolic dyssynchrony in nonischemic dilated cardiomyopathy patients with a narrow QRS interval. *Echocardiography*.2011;28(1):62-8.

8.Sezer F, Meriç M, Gedikli Ö, et al.The Relationship between Fragmented QRS and Diastolic Parameters in Coronary Artery Disease Patients with Noncritical Lesions. *JACC*. 2013;18(62):C177.

9.Haukilahti MAE, Holmström L, Vähätalo J, et al. Gender differences in prevalence and prognostic value of fragmented QRS complex. *J Electrocardiol*.2020;61:1-9.

10.Eyuboglu M. Fragmented QRS as a marker of myocardial fibrosis in hypertension: a systematic review. *Curr Hypertens Rep*. 2019;21(10):73.

11.Díez J. Mechanisms of cardiac fibrosis in hypertension. *J Clin Hypertens (Greenwich)*. 2007; 9(7):546-50.

12..Masoumi S, Separham A, Parizad R, et al. Dual Left Anterior Descending Artery: Clinical Overview and Interventional Management. *J Tehran Heart Cent*. 2023;18(2):146–50.

13.Jain R, Singh R, Yamini S, et al. Fragmented ECG as a risk marker in cardiovascular diseases. *Curr Cardiol Rev*. 2014;10(3):277-86.

14.Rattanawong P, Riangwiwat T, Prasitlumkum N, et al. Baseline fragmented QRS increases the risk of major arrhythmic events in Brugada syndrome: Systematic review and meta-analysis. *Ann Noninvasive Electrocardiol*.2018;23(2):e12507.

15.Femenía F, Arce M, Van Grieken J, et al. Fragmented QRS as a predictor of arrhythmic events in patients

with hypertrophic obstructive cardiomyopathy. *J Interv Card Electrophysiol*.2013;38(3):159-65.
16. Haas ZA, Qian C, Dabski MA, et al. The use of contrast may improve aortic valve assessment during transesophageal echocardiography. *J Cardiothorac Vasc Anesth [Internet]*.2023;37(6):904–10.
17. Ishii M, Eto G, Tei C, et al. Quantitation of the global right ventricular function in children with normal heart and congenital heart disease: a right ventricular myocardial performance index. *Pediatr Cardiol*.2000;21(5):416-21.