The relation between coronary artery disease severity and fragmented QRS complex in patients with left bundle branch block

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Abstract *Background:* The diagnosis of coronary artery disease (CAD) in patients with LBBB represents a clinical challenge. The presence of fragmented QRS (fQRS) complex on surface ECG may be related to myocardial ischemia, scarring or fibrosis.
Objectives: To investigate the relation between fQRS and the presence and severity of CAD in patients with LBBB.
Patients and methods: 56 patients with symptoms suggesting CAD and complete LBBB were submitted to full history taking and clinical examination, complete 12-leads electrocardiography (ECG) to confirm the diagnosis of LBBB and to diagnose the fragmented wide QRS (f-wQRS) complex, echocardiography, and coronary angiography; lesions with ⩾70% narrowing in major epicardial artery or ⩾50% narrowing in the left main coronary artery were considered significant; and Gensini score was calculated. Patients were classified into two groups according to the presence or absence of f-wQRS.
Results: There were significantly more patients with obstructive CAD among patients with f-wQRS ($p = 0.000053$). Gensini score was significantly higher in patients with than in patients without fwQRS ($p < 0.00001$). f-wQRS was the only significant independent predictor of obstructive CAD. Sensitivity of f-wQRS in predicting obstructive CAD was 80.1%, specificity was 73.3%, positive predictive value was 72.4%, negative predictive value was 81.5%, and overall accuracy was 76.8%, $p = 0.0022$.
Conclusion: Seeking for f-wQRS in patients with LBBB and suspected CAD is a simple, easy, available, method that may be helpful in noninvasive prediction of obstructive CAD.
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1. Introduction

The likelihood of having obstructive coronary artery disease (CAD) is higher in patients with left bundle branch block (LBBB).[1] In comparison with normal subjects, patients with

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LBBB showed a significantly higher mortality in the Framingham heart study.[2] Also, the presence of LBBB was found to be associated with increased risk of progressive heart failure, acute myocardial infarction, and complete atrioventricular block.[3] Patients with CAD tend to have a worse prognosis when associated with LBBB.[4]

The diagnosis of CAD in patients with LBBB represents a clinical challenge. The non-invasive evaluation of CAD in these patients has several limitations. The available modalities include exercise ECG, stress echocardiography and myocardial perfusion imaging, which all become less accurate in the presence of LBBB.[5]

The presence of fragmented QRS (fQRS) complex on surface ECG was found to be related to myocardial ischemia, scarring or fibrosis. This QRS fragmentation may be due to changes in Purkinje fibers.[6]

In previous studies, the presence of fQRS was found to be useful in detection of myocardial scar,[7] and in prediction of myocardial infarction and reperfusion parameters.[8] However, these studies were designed for fQRS in patients with narrow QRS.

The aim of the current study was to investigate the relation between fQRS and the presence and severity of CAD in patients with LBBB.

2. Patients and methods

This study had been carried out in the Cardiology Department, Zagazig University Hospitals. The study included 56 patients (28 males and 28 females, their mean age was 61.1 ± 9.5 years) with symptoms suggesting CAD and LBBB on
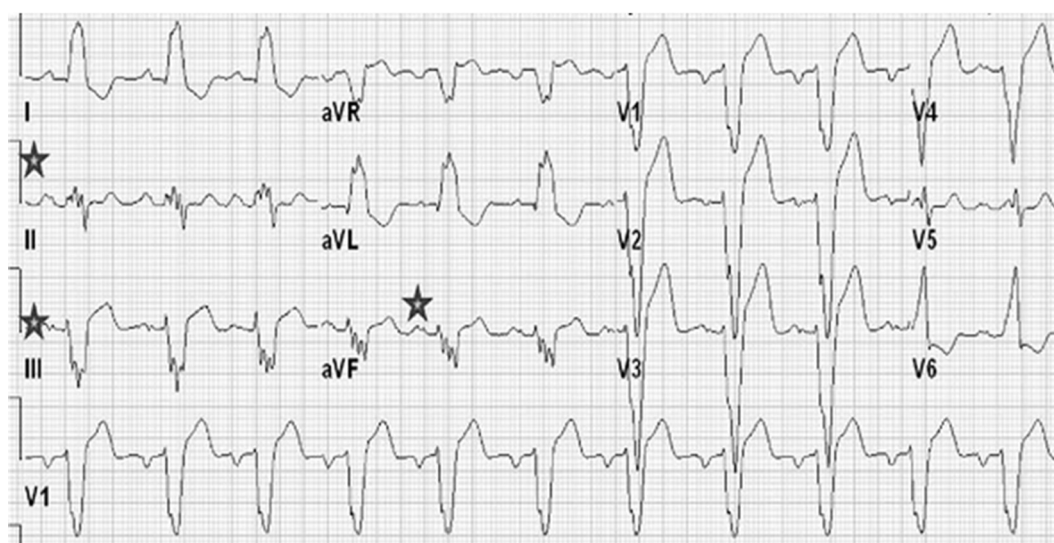

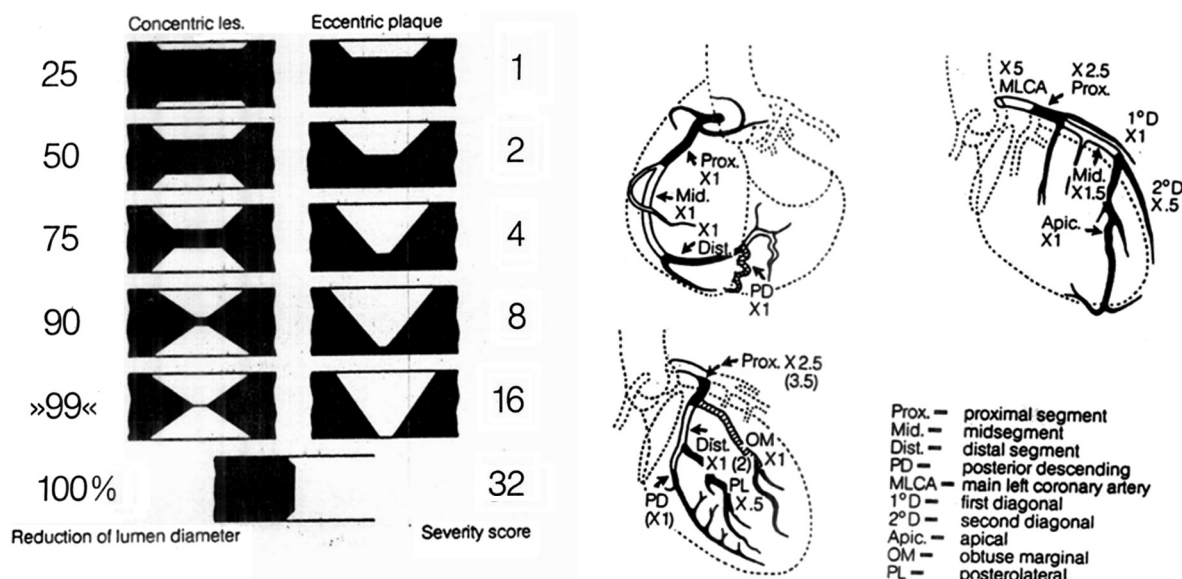
Figure 1 Fragmented wide QRS (12).

Figure 2 Method of calculating Gensini score (15).

Table 1 Comparison between the two groups.

		f-wQRS ($n = 26$)	No f-wQRS ($n = 30$)	p
Age (y)		62.5 ± 7.4	59.6 ± 8.3	0.173
Sex	Male	15 (57.7%)	13 (43.3%)	0.284
	Female	11 (42.3%)	17 (56.7%)	
Diabetes		10 (38.5%)	9 (30%)	0.505
Hypertension		11 (42.3%)	12 (40%)	0.861
Dyslipidemia		12 (46.2%)	11 (36.7%)	0.472
Smoking		8 (30.1%)	7 (23.3%)	0.531
LVEDD (mm)		51.3 ± 5.22	50.2 ± 6.43	0.483
LVESD (mm)		34.1 ± 3.86	32.3 ± 4.33	0.106
FS (%)		33.5 ± 4.85	35.7 ± 5.12	0.105
EF (%)		63.1 ± 6.19	65.5 ± 6.53	0.164
Obstructive CAD		21 (80.8%)	8 (26.7%)	0.000053
Gensini score		36.8 ± 12.1	6.1 ± 2.3	<0.00001

Table 2 Regression analysis.

| Variables	Score	Degree of freedom	p
f-wQRS	8.426	1	0.0043
Age	0.868	1	0.251
Heart rate	0.354	1	0.332
Systolic blood pressure	0.162	1	0.687

their surface ECG. Left bundle branch block was diagnosed by the presence of QRS duration ⩾ 120 ms in addition to a QS or rS complex in lead V_1 in the absence of pre-excitation.[9] Coronary angiography was indicated in all patients according to the 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the diagnosis and management of patients with stable ischemic heart disease.[10]

Patients were excluded from the study if they had one or more of the following:

– Moderate or severe valvular heart disease.
– Previous coronary revascularization.

After giving an informed written consent, all patients underwent the following:

(1) Full history taking and thorough clinical examination.
(2) Complete 12-leads electrocardiography: 12-lead ECG (0.5–150 Hz, AC filter 60 Hz, 25 mm/s, 10 mm/mV) was done to every patient to confirm the diagnosis of
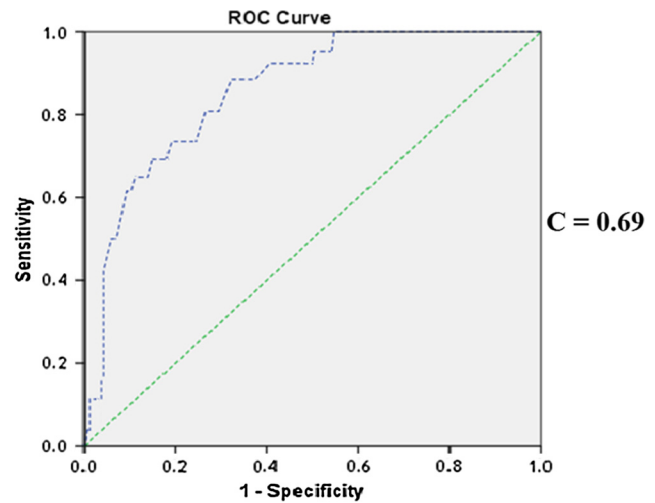
Figure 3 ROC curve for f-wQRS with obstructive CAD.

LBB and to detect QRS fragmentation (Fig. 1). The fragmented wide-QRS (fwQRS) complex was diagnosed by the presence of >1 R′ (fragmentation) or notching in the nadir of the S wave in at least 2 contiguous leads, corresponding to a major coronary territory.[11,12]

According to the presence or absence of f-wQRS, patients were classified into two groups:

Table 3 Validity of f-wQRS in predicting significant CAD.

	Obstructive CAD	No obstructive CAD	Total
f-wQRS	21	5	26
No f-wQRS	8	22	30
Total	29	27	56

Sensitivity	Specificity	PPP	NPV	Overall accuracy	Kappa	p
80.1%	73.3%	72.4%	81.5%	76.8%	0.518	0.0022

PPV = positive predictive value, NPV = negative predictive value.
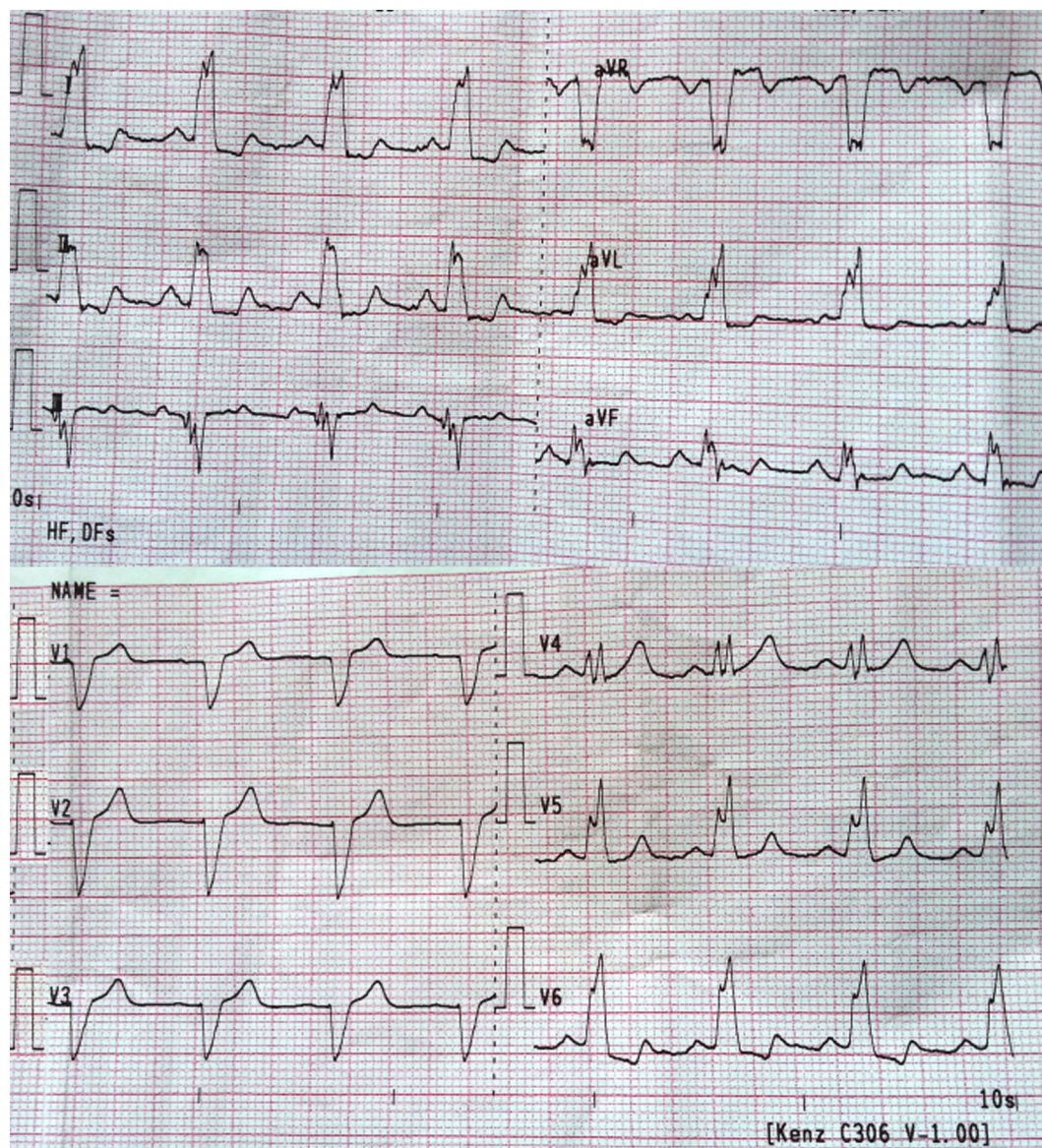
Figure 4 ECG of one of our patients showing LBBB with fQRS in leads L II, L III, aVF, L I, and aVL.

Group I: Patients with f-wQRS (26 patients, 15 males and 11 females, their mean age was 62.5 ± 7.4 years).

Group II: Patients without f-wQRS (30 patients, 13 males and 17 female, their mean age was 59.6 ± 8.3 years).

(3) Echocardiography: Echocardiographic and Doppler studies were performed for all patients using GE VIVID E9 machines with 2.5 MHz transducers. The echocardiograms were obtained at rest with the subjects in the left lateral position. Two-dimensional guided M-mode measurements of left ventricular end-diastolic dimension (LVEDD), left ventricular end-systolic dimension (LVESD), fraction of shortening (FS) and ejection fraction (EF) were taken.[13]

(4) Coronary angiography: Coronary angiography was done to all patients. The coronary artery narrowing was visually estimated by an expert angiographer and expressed as percentage of luminal diameter stenosis. Lesions with ⩾70% narrowing in one or more of the major epicardial arteries and/or ⩾50% narrowing in the left main coronary artery were considered significant angiographic stenosis.[14]

The angiographic severity was estimated by calculating Gensini score.[15] In this score, we give 1 for 25% stenosis, 2 for 50%, 4 for 75%, 8 for 90%, 16 for 99% and 32 for total occlusion. The score is then multiplied by a factor according to the site of the lesion (Fig. 2).

All data were analyzed using the SPSS 19 package program. Differences between patients' group and control group were analyzed using χ^2 test and Student's t-test. Correlations between different variables were investigated by Pearson correlation analysis. According to the presence of f-wQRS and significant angiographic stenosis, patients were divided into true positive (TP), true negative (TN), false positive (FP), and false negative (FN). Sensitivity, specificity and accuracy were calculated as follows: Sensitivity = TP/(TP + FN),
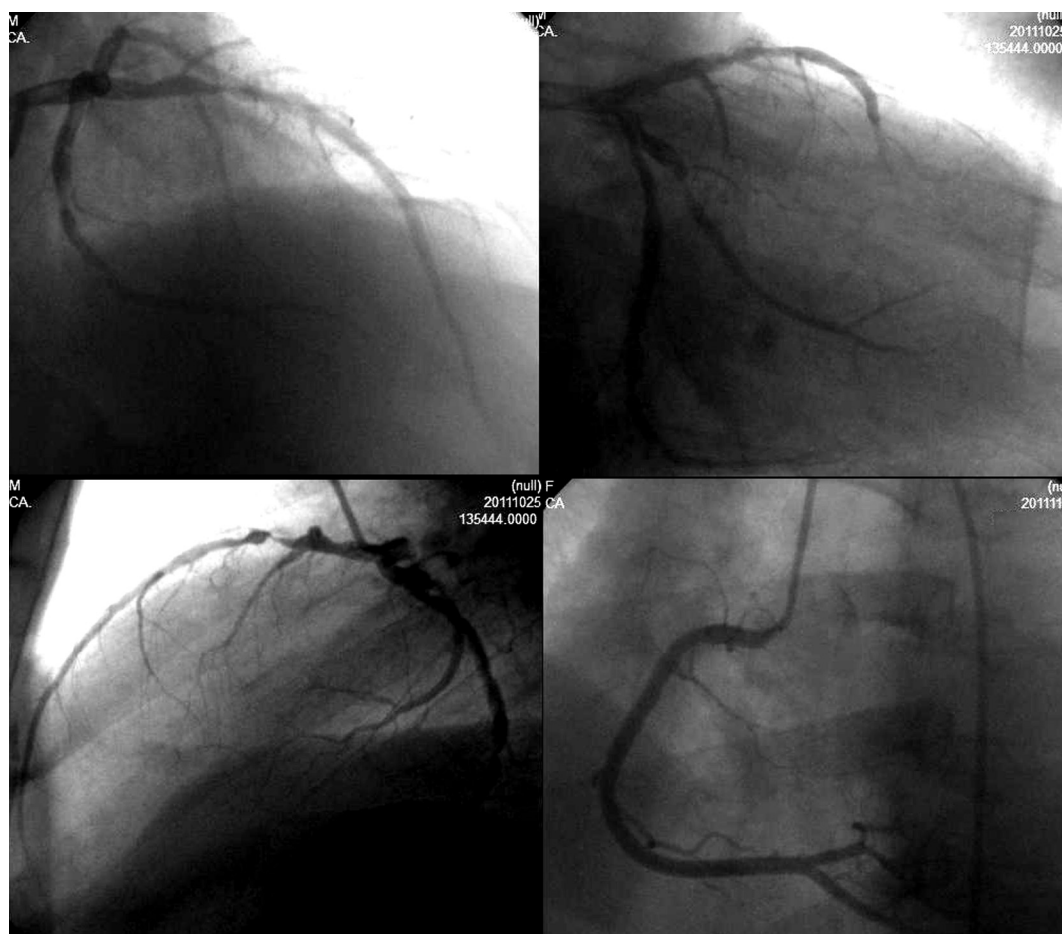
Figure 5 Coronary angiography of the same patient showing proximal lesion 99% of LAD, distal 2 successive lesions each 75% of LCX, and proximal lesion 99% of OM1.

Specificity = TN/(TN + FP), and Accuracy = (TN + TP)/(TN + TP + FN + FP). A p value < 0.05 was regarded as being statistically significant.

The study protocol had been approved by the Institutional Review Board of the Faculty of Medicine, Zagazig University.

3. Results

As shown in Table 1, there was no significant difference between the study groups concerning population characteristics, CAD risk factors, or echocardiographic parameters.

Regarding angiographic data, there were significantly more patients with obstructive CAD among patients with fwQRS than among patients without fwQRS ($p = 0.000053$). Gensini score was significantly higher in patients with fwQRS than in patients without fwQRS ($p < 0.00001$).

Regression analysis of the relation of different parameters to the presence of obstructive CAD is shown in Table 2. The only significant independent predictor for the presence of obstructive CAD was fwQRS ($p = 0.0043$). Other parameters were not significant predictors for the presence of obstructive CAD such as age ($p = 0.251$), heart rate ($p = 0.332$), and systolic blood pressure ($p = 0.687$).

The validity of fwQRS in prediction of obstructive CAD is shown in Table 3. Sensitivity was 80.1%, specificity was 73.3%, positive predictive value was 72.4%, negative predictive value was 81.5%, overall accuracy was 76.8%, Kappa was 0.518, and $p = 0.0022$. The receiver operating characteristic (ROC) curve analysis is shown in Fig. 3, with area under ROC-curve of 0.69. Figs. 4–7 show examples of fragmented and non fragmented QRS in the ECGs of two of our cases and the corresponding coronary angiography of each case.

4. Discussion

One of the common conduction defects is LBBB. Its incidence increases with age from 0.4% in the sixth decade to 5.7% in the ninth decade.[16]

The probability of developing CAD is higher in patients with LBBB;[4] however, identifying CAD in these patients been the subject of many studies and remains a clinical challenge.

In this study, we evaluated the relation between f-wQRS and the presence and severity of CAD in patients with LBBB, and we have found that the presence of f-wQRS was a good predictor of obstructive CAD and was associated with more severe CAD as estimated by Gensini score. Our results showed that the sensitivity of f-wQRS in detecting obstructive CAD was 80.1%, specificity was 73.3%, positive predictive value

was 72.4%, negative predictive value was 81.5%, and overall accuracy was 76.8%. Gensini score was significantly higher in patients with f-wQRS denoting more extensive CAD.

Fragmented QRS is a deviation in the QRS morphology. Although the exact cause of fQRS is not entirely known, it was found to predict cardiac events in different populations.[6]
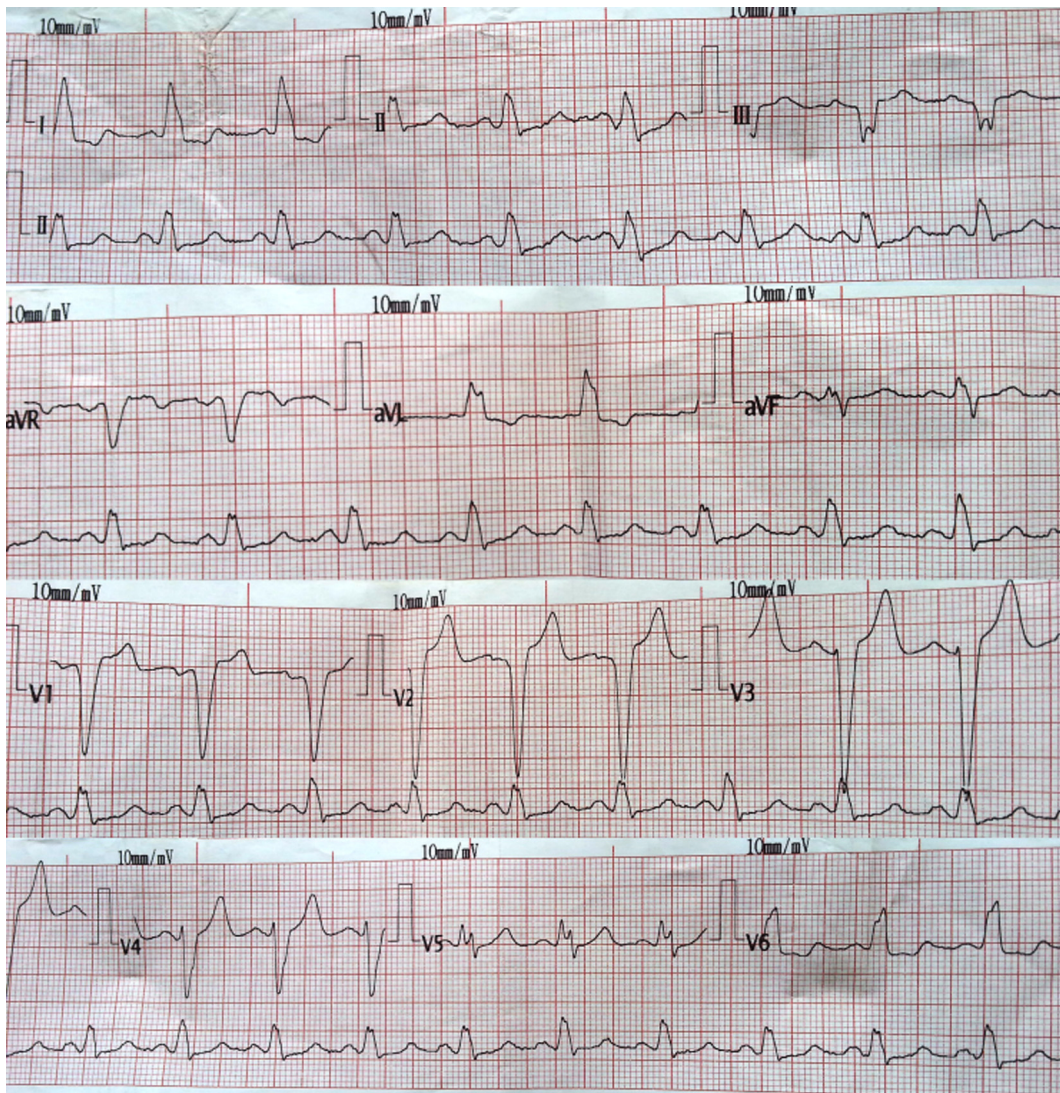
Figure 6 ECG of one of another patient showing LBBB without fQRS.

Figure 7 Coronary angiography of the same patient showing normal coronary angiography.

From the pathophysiologic point of view, fQRS is generally due to regional myocardial fibrosis or scarring.[17] Available data suggest that ischemia might cause fQRS and this may be due to lack of homogeneous myocardial electrical activation.[8]

Fragmented narrow QRS complexes (< 120 ms) on a 12-lead ECG were found to signify an old MI scar,[18] and were found to be associated with a poor prognosis.[19]

The sensitivity of fQRS for diagnosing myocardial scarring was found to be 72.7% for anterior scarring, 62.9% for posterolateral scarring, and 82.7% for inferior scarring. This was even higher than the sensitivity of pathological Q waves 22.2%, 17.1%, and 50% for anterior, posterolateral, and inferior scarring, respectively.[11]

In the year 2008, Das and his colleagues[12] have tested the validity of different models of f-wQRS in detecting myocardial scar compared to gated SPECT analysis, echocardiography, and left ventriculography. They found that the sensitivity of fragmented bundle branch block in general in predicting myocardial scar was 88.6%, specificity was 94.4%, positive predictive value was 95.9%, and negative predictive value was 85%, while the sensitivity of fragmented left bundle branch block in predicting myocardial scar was 88.6%, specificity was 90.2%, positive predictive value was 95.1%, and negative predictive value was 78.7%.

The figures found by Das et al.[12] were higher than ours. These differences may be explained by the higher number of patients they used (310 patients with bundle branch block including 129 patients with LBBB). Other explanation is the multiple parameters they used to detect myocardial scarring (gated SPECT analysis, echocardiography, and left ventriculography) while we tested the validity of f-wQRS only to detect angiographically significant CAD.

5. Conclusion

– The presence of f-wQRS in patients with LBBB is a good predictor of obstructive CAD and is associated with more severe CAD.
– Seeking for f-wQRS in patients with LBBB and suspected CAD is a simple, easy, available method that may be helpful in the noninvasive prediction of obstructive CAD in this group of patients.

Study limitations

- Relatively small number of patients.
- The study was done in a single center.

Disclosures

The authors declare that there is no conflict of interest.

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