Fragmented QRS as an early predictor of left ventricular systolic dysfunction in healthy individuals: A nested case-control study in the era of speckle tracking echocardiography

CURRENT STATUS: UNDER REVIEW

Mohammad Hossein Nikoo
Shiraz University of Medical Sciences

Zahra Jamali
Shiraz University of Medical Sciences

Iman Razeghian-Jahromi
Shiraz University of Medical Sciences

ORCiD: 0000-0001-8137-786X

Mehrab Sayadi
Shiraz University of Medical Sciences

Firoozeh Abtahi  abtahifa@sums.ac.ir
Corresponding Author

DOI: 10.21203/rs.2.20205/v1

SUBJECT AREAS
Cardiac & Cardiovascular Systems

KEYWORDS
fragmented QRS, global longitudinal strain, left ventricular dysfunction, healthy subjects
Abstract

Background: The burden of cardiovascular diseases have been become a concerning health challenge throughout the world. Stopping this condition needs applying early, yet inexpensive diagnostic methods. The aim of this study is to evaluate the capacity of fragmented QRS (fQRS) on 12-lead EKG for detecting left ventricular dysfunction in healthy individuals.

Methods: Out of 500 healthy participants without detected cardiovascular disorders from Shiraz Heart Study cohort, 20 subjects diagnosed with fQRS (case) and 20 peers without fQRS (control) were participated. Global longitudinal strain was measured by speckle tracking echocardiography for two groups. Comparison was made between case and control groups by using chi-square or independent sample t-test or ANOVA. P value of less than 5% considered statistical significance.

Results: There was no difference between the case and the control groups in terms of age, gender, ejection fraction, left ventricular volume and dimensions. Out of 40 subjects, 14 had reduced GLS (≤20%) with 10 of them had fQRS. GLS in the case group was significantly lower than in the control group.

Conclusions: Apparent healthy subjects with fQRS diagnosed with left ventricular systolic dysfunction with respect to GLS despite normal ejection fraction. It seems that EKG, as one of the simplest way toward assessing heart function, could be a prominent informative clue to detect high-risk individuals among healthy population in advance.

Background

Left ventricular (LV) systolic function is an important clinical finding in the era of cardiology. It is applied in prevention, diagnosis, treatment, or make a prognosis for a wide variety of cardiovascular diseases. Speckle tracking echocardiography (STE)
measures LV systolic function quantitatively through detecting subtle myocardial deformations. In this technique, the most sensitive and reproducible parameter capable of early detection of malfunctions is global longitudinal strain (GLS) \(^1\). The functionality of GLS is more pronounced in the case of left ventricular ejection fraction (LVEF) being normal \(^2\).

Less than two decades ago, fragmentation of QRS complex (fQRS) was coined on 12-lead EKG \(^3\). Abnormal deflections in QRS morphology is simply known as fQRS which originates from conduction delay and disrupted ventricular depolarization due to myocardial scarring \(^4\), \(^5\). fQRS is found in several cardiovascular and non-cardiovascular disorders including structural heart diseases \(^6\)-\(^8\). fQRS has shown its superiority in different studies. For example, although pathologic Q-wave is known as the marker of myocardial infarction (MI) on a 12-lead EKG, but its capacity in detecting myocardial scars confines to only about one third of documented MI \(^9\), \(^10\). It was shown that fQRS is more sensitive than Q-wave for identifying myocardial scars \(^11\). Also, association of fQRS with regional and global LV dysfunction was reported in patients with coronary artery disease (CAD). Despite normal ejection fraction, adverse cardiac events were predicted in these patients \(^12\).

About 6-10% of apparent healthy individuals show fQRS \(^13\). It was reported that in general population free of clinical cardiac diseases, fQRS is a common finding \(^14\). Given that in the majority of studies fQRS was studied in diseased populations, the aim of this study was to seek the capacity of fQRS to be an early predictor of LV systolic dysfunction in apparent healthy people.

**Methods**

This nested case-control study was done in the setting of a prospective cohort, Shiraz
Heart Study, which is conducted on general population of Shiraz city aiming to analyze cardiovascular risk factors. The present study is in accordance to the declaration of Helsinki and has approved by the Ethical Committee of Shiraz University of Medical Sciences. All the study subjects signed an informed written consent.

Among those without overt known cardiovascular diseases, 500 subjects were randomly selected. Exclusion criteria were history of CAD, history of major risk factors for CAD (hypertension, diabetes mellitus, and hyperlipidemia), angina pectoris, acute coronary syndrome, cardiomyopathies, receiving any cardiovascular-related medications, implantation of pacemaker, heart valve disease, atrial fibrillation and flutter, rheumatism, renal disease, malignancy, pulmonary hypertension, and chronic obstructive pulmonary disease. Also, they had negative past medical history, normal lipid profile, normal blood pressure, normal anthropometric indices as well as non-smokers and non-diabetics. In case of mismatching, an appropriate person was randomly selected and substituted.

A resting 12-lead EKG has obtained previously from the participants as the cohort scheduled procedure (filter settings: 0.5–150 Hz, 25 mm/s, 10 mm/mV). The EKGs of 500 subjects were thoroughly evaluated by two independent cardiologists seeking for QRS fragmentation. Notching in the R or S wave in the absence of a branch block, or an RSR' pattern additional to the original QRS wave (< 120 ms) were defined as fQRS. After unanimous reports, existence of fQRS was confirmed in twenty subjects (case group). In a similar way, twenty subjects without fQRS were assigned as control group. Fragmentation was classified based on its location to anterior (correspond to V1 to V5 leads), inferior (correspond to DII, DIII and aVF leads), or lateral (correspond to DI, aVL and V5, V6 leads). Subjects in the two groups were asked to attend in the clinic. EKGs were repeated in order to find any possible new changes or arrhythmias by an expert who was blinded to
grouping. Then, STE was performed with a commercially available ultrasound scanner (Vivid E9, General Electric Medical Systems, Horten, Norway) with a 2.5-MHz transducer by a single blinded echoman cardiologist. Echocardiograms were obtained in three-, two- and four-chamber apical views at a rate of 50 to 70 frames/s with the patient holding their breath during at least three cardiac cycles. Endocardial borders were automatically marked and tracking was applied to each image. In satisfactory tracking, the entire cardiac wall (endocardium through myoepicardial border) was covered. The LV was divided into four segments in 3-chamber view, and six segments in 2- and 4-chamber view, totally 16 segments were assessed. If the segments were marked by the software automatically, the obtained data were recorded. Otherwise, they were corrected manually. Image analysis was done by AFI system. Peak systolic longitudinal strains (LS) of different segments were calculated and then, average LS for each view was produced. GLS was the arithmetic mean of LSs in three apical views. GLS of >20% was assumed to be normal 17. Dimensions and volumes of the left ventricle were measured according to the guidelines of the American Society of Echocardiography. Also, LVEF was calculated by Simpson rule 18. Preserved EF was considered as EF ≥50% 19.

The statistical analysis was done in SPSS for Windows (release 14.0, SPSS Inc., Chicago, Illinois). Categorical variables are expressed as number (percentages) and continuous variables as mean±standard deviation (SD). Comparison between variables were done using chi square, independent samples t test or ANOVA when appropriate. P value of less than 0.05 was considered statistically significant.

results

The age range of the participants was 40 to 60 years old with a mean of 50.35±6.54 and
dominance of male (75%). The mean LVEF was 59.30±2.89% and the mean GLS was 20.68±1.83 which both were within the normal range \(^{17,19}\). Participants were grouped into those with (case) and without (control) fQRS (20 subjects in each group). According to the table 1, there were no significant differences in age, gender, EF, left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), and LV size between case and control groups. GLS in 14 subjects were below the normal range (≤20%). Out of 14, 10 had fQRS. Of note, EF as well as other variables were not significantly different between those with reduced GLS and peers with normal GLS. Of the case group, 50% demonstrated fQRS at inferior leads with the remaining equally distributed in anterior and lateral leads. The position of fragmentation did not significantly associate to abnormal changes in GLS or EF (Table 2).

Given the measurement of LS in different segments, the case group showed lower LS than the control group in five segments including base-, mid-, and apex- of septal, base of anteroseptal and base of inferior. Also, there was significant reduction of LS in apical 4-chamber view while LS in apical three- and two-chamber views did not differ significantly between case and control groups. In total, GLS was significantly lower in the case than the control group (Table 3).

Discussion

This nested case-control study was designed in order to investigate the possible correlation between existence of fQRS and left ventricular dysfunction in apparent healthy people. It is noteworthy that Shiraz Heart Study is the first cardiovascular-oriented cohort in one of Iran’s metropolitan city \(^{15}\). Although the correlation between fQRS and cardiac disorders has been demonstrated in several diseased status \(^{6,20}\), but the importance of this QRS alteration has been ignored in general population. The main finding of the
present study is that in apparent healthy subjects with normal EF, those with fQRS had lower GLS than those without fQRS.

Scarring of the myocardium following by zigzag pattern of electrical conduction produces fQRS spikes\textsuperscript{21}. fQRS is known as an indicator of previous myocardial injury and warns possible future adverse cardiac events\textsuperscript{21}. It was reported that fQRS possibly is the only evidence of silent MI in high risk individuals\textsuperscript{3}. Moreover, fQRS was known as a sign of premature ventricular contractions in individuals without obvious structural heart diseases\textsuperscript{22}. It was shown to be superior than Q wave for detecting myocardial scar in terms of sensitivity and negative predictive value, but not of specificity\textsuperscript{23}. However, in a more recent study, higher sensitivity and specificity of fQRS than Q wave was declared\textsuperscript{24}. Also, in case of disappearance of MI-related Q wave due to revascularization therapies, fQRS would be a validated replacement\textsuperscript{20}.

Existence of fQRS in different EKG leads simply translates into tissue scarring in different segments of the heart and is associated to the higher incidence of cardiac death and hospitalization\textsuperscript{21}. Severity and complexity of CAD was reported to be in relation with the number of EKG leads with fQRS\textsuperscript{25}. Accordingly, fQRS could be a guiding tool to identify regions of interest for ablation, those of prone for ventricular arrhythmias\textsuperscript{20}. The potential of fQRS in predicting arrhythmic events, need for revascularization, MI, cardiac death, and all-cause mortality was shown in subjects with different cardiac disorders\textsuperscript{23,26,27}. Also, the prognostic significance of fQRS was seen in stable CAD and acute MI. However, there are contrary reports which consider the role of fQRS with doubt in myocardial scar detection, predicting arrhythmic events, and mortality\textsuperscript{28-33}. Some of these studies expressed that fQRS was not a good predictor of arrhythmic events\textsuperscript{4,34}. 
EF, which is a popular means through assessment of LV function, is only able to reflect moderate to severe impairment in the ventricles. Also, this parameter suffers several limitations. Of note, EF mostly contributes to the myocardial changes in radial axis while longitudinal deformations are being neglected. Strain is the more developed and accurate measurement than volumetric parameter of EF. It demonstrates fine myocardial deformations in longitudinal, circumferential, and radial axis and also, changes in torsion.

Among strains, GLS is of eminent importance due to its sensitivity and robustness. The association of mortality with GLS was stronger than LVEF. GLS, which is obtained by STE, measures myocardial deformations via tracing of speckles’ displacement. Reduction in absolute GLS value is an indicator of a myocardial disease in most cases and portends future adverse events.

In an investigation on patients with systemic sclerosis, fQRS was present while LVEF and LV dimensions were normal. Importantly, GLS was significantly lower in these patients than control group. In a comparison within apparent healthy individuals, GLS was significantly lower in those with fQRS than those without fQRS despite normal similar EF. Further evaluation showed impairment in ventricular diastolic function as well as greater thickness in epicardial adipose tissue in subjects with vs. without fQRS. Although GLS reduction is a sign of LV malfunction, but GLS is also affected by other factors such as age, gender, and ethnicity. Also, changes in physiological parameters like heart rate affects GLS in healthy individuals. Hypertension, obesity, dyslipidemia, diabetes and medications were also considered as factors that modifies GLS value. As all these factors are known as cardiovascular risk factors, but of interest is that smoking do not change GLS. Vendor-specific disparities and timing of measurements should also be considered in
GLS evaluation \(^{36}\).

fQRS in individuals with normal EF may be due to the existence of myocardial fibrosis of subclinical scale which in turn boasts fQRS sensitivity \(^{22,24}\). EKG as the mainstay is a convenient, cost-effective, and informative instrument. It seems that EKG-born fQRS could play a critical role in identifying individuals among general population who are prone to LV systolic dysfunction and consequent heart failure. A simple EKG has the potential to draw cardiologists' attention for further assessment of the heart function with more sophisticated tools and parameters such as STE and GLS to find minor, but life-threatening events.

**Conclusion**

According to the upcoming importance of notch in QRS in diverse diseases, we tried to investigate its importance in healthy participants of Shiraz Heart Study cohort program. Although we only pick up subtle changes in a sensitive echocardiography tool, the notched QRS should not consider a normal finding in any electrocardiography.

**Abbreviations**

LV: left ventricular, STE: speckle tracking echocardiography, GLS: global longitudinal strain; LVEF: left ventricular ejection fraction, fQRS: fragmentation of QRS complex, CAD: coronary artery disease, LS: longitudinal strains, LVEDV: left ventricular end-diastolic volume, LVESV: left ventricular end-systolic volume

**Declarations**

Ethics approval and consent to participate: The present study is in accordance to the declaration of Helsinki and has approved by the Ethical Committee of Shiraz University of Medical Sciences. All the study subjects signed an informed written consent.
Consent for publication: Not applicable

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

Funding: This work was financially supported by Vice Chancellor of Research of Shiraz University of Medical Sciences. The funding body had no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Authors' contributions: MHN contributed substantially to the concept and design of the study. ZJ and FA acquired the data. MHN, IRJ, MS, and FA had roles in data analysis and interpretation. IRJ drafted the manuscript. All authors read and approved the final manuscript.

Acknowledgements: Not applicable

References

1. Bansal M, Kasliwal RR. How do I do it? Speckle-tracking echocardiography. Indian heart journal. 2013;65(1):117-123.

2. Marwick TH. Methods used for the assessment of LV systolic function: common currency or tower of Babel? Heart. 2013;99(15):1078-1086.

3. Das MK, Khan B, Jacob S, Kumar A, Mahenthiran J. Significance of a fragmented QRS complex versus a Q wave in patients with coronary artery disease. Circulation. 2006;113(21):2495-2501.

4. Hayashi T, Fukamizu S, Hojo R, et al. Fragmented QRS predicts cardiovascular death of patients with structural heart disease and inducible ventricular tachyarrhythmia. Circulation Journal. 2013:CJ-13-0335.

5. Bayramoğlu A, Taşolar H, Bektaş O, Kaya A, Günaydın ZY. Association between fragmented QRS complexes and left ventricular dysfunction in healthy smokers.
6. Das MK, Zipes DP. Fragmented QRS: a predictor of mortality and sudden cardiac death. *Heart Rhythm*. 2009;6(3):S8-S14.

7. Balta S, Demirkol S, Kucuk U, Arslan Z, Unlu M, Demir M. Fragmented QRS in patients with acute myocardial infarction. *Heart & Lung: The Journal of Acute and Critical Care*. 2013;42(6):448.

8. Chatterjee S, Changawala N. Fragmented QRS complex: a novel marker of cardiovascular disease. *Clinical cardiology*. 2010;33(2):68-71.

9. Abdulla J, Brendorp B, Torp-Pedersen C, Køber on behalf of the TRACE study group L. Does the electrocardiographic presence of Q waves influence the survival of patients with acute myocardial infarction? *European heart journal*. 2001;22(12):1008-1014.

10. Voon W-C, Chen Y-W, Hsu C-C, Lai W-T, Sheu S-H. Q-wave regression after acute myocardial infarction assessed by Tl-201 myocardial perfusion SPECT. *Journal of nuclear cardiology*. 2004;11(2):165.

11. Sadeghi R, Dabbagh V-R, Tayyebi M, Zakavi SR, Ayati N. Diagnostic value of fragmented QRS complex in myocardial scar detection: systematic review and meta-analysis of the literature. *Kardiologia Polska (Polish Heart Journal)*. 2016;74(4):331-337.

12. Yan G-H, Wang M, Yiu K-H, et al. Subclinical left ventricular dysfunction revealed by circumferential 2D strain imaging in patients with coronary artery disease and fragmented QRS complex. *Heart Rhythm*. 2012;9(6):928-935.

13. DB BÁ. From the boundaries of normality to the acknowledgement of a new nosological entity. *Revista portuguesa de cardiologia: orgao oficial da Sociedade Portuguesa de Cardiologia*= Portuguese journal of cardiology: an official journal of the Portuguese Society of Cardiology. 2018;37(6):477.
14. Tangcharoen T, Wiwatworapan W, Praserkulchai W, Apiyasawat S, Yamwong S, Sritara P. Fragmented QRS on 12-lead EKG is an independent predictor for myocardial scar: a cardiovascular magnetic resonance imaging study. *Journal of Cardiovascular Magnetic Resonance.* 2013;15(S1):P192.

15. Zibaeenezhad MJ, Ghaem H, Parsa N, et al. Analysing cardiovascular risk factors and related outcomes in a middle-aged to older adults population in Iran: a cohort protocol of the Shiraz Heart Study (SHS). *BMJ open.* 2019;9(4):e026317.

16. Bayramoğlu A, Taşolar H, Bektaş O, et al. Association between metabolic syndrome and fragmented QRS complexes: Speckle tracking echocardiography study. *Journal of electrocardiology.* 2017;50(6):889-893.

17. Yingchoncharoen T, Agarwal S, Popović ZB, Marwick TH. Normal ranges of left ventricular strain: a meta-analysis. *Journal of the American Society of Echocardiography.* 2013;26(2):185-191.

18. Cheitlin MD, Armstrong WF, Aurigemma GP, et al. ACC/AHA/ASE 2003 guideline update for the clinical application of echocardiography: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASE Committee to Update the 1997 Guidelines for the Clinical Application of Echocardiography). *Journal of the American College of Cardiology.* 2003;42(5):954-970.

19. Ponikowski P, Voors A, Anker S, et al. Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail.* 2016;18(8):891-975.

20. Fares H, Heist K, Lavie CJ, et al. Fragmented QRS Complexes—a novel but underutilized electrocardiographic marker of Heart Disease. *Critical pathways in cardiology.* 2013;12(4):181-183.

21. Take Y, Morita H. Fragmented QRS: What is the meaning? *Indian pacing and
22. Temiz A, Gazi E, Altun B, et al. Fragmented QRS is associated with frequency of premature ventricular contractions in patients without overt cardiac disease. *Anatolian journal of cardiology*. 2015;15(6):456.

23. 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(11):1385-1392.

24. MacAlpin RN. The fragmented QRS: does it really indicate a ventricular abnormality? *Journal of Cardiovascular Medicine*. 2010;11(11):801-809.

25. Bekler A, Barutçu A, Tenekecioglu E, et al. The relationship between fragmented QRS complexes and SYNTAX and Gensini scores in patients with acute coronary syndrome. *Kardiologia Polska (Polish Heart Journal)*. 2015;73(4):246-254.

26. Maskoun W, Suradi H, Mahenthiran J, Bhakta D, Das M. Fragmented QRS complexes on a 12-lead ECG predict arrhythmic events in patients with ischemic cardiomyopathy who receive an ICD for primary prophylaxis. *Heart Rhythm*. 2007;4(Suppl.):S211-S212.

27. Pietrasik G, Goldenberg I, Zdzienicka J, Moss AJ, Zareba W. Prognostic significance of fragmented QRS complex for predicting the risk of recurrent cardiac events in patients with Q-wave myocardial infarction. *The American journal of cardiology*. 2007;100(4):583-586.

28. Brenyo A, Pietrasik G, McNitt S, Zareba W. QRS fragmentation: Lack of association with cardiac events in patients with a normal QRS duration in MADIT II. *Heart Rhythm*. 2010.

29. Cheema A, Khalid A, Wimmer A, et al. Fragmented QRS and mortality risk in patients with left ventricular dysfunction. *Circulation: Arrhythmia and Electrophysiology*. 
30. Forleo GB, Della Rocca DG, Papavasileiou LP, et al. Predictive value of fragmented QRS in primary prevention implantable cardioverter defibrillator recipients with left ventricular dysfunction. *Journal of cardiovascular medicine.* 2011;12(11):779-784.

31. Pietrasik GM, Polonsky S, Moss AJ, Zareba W. PRESENCE OF FRAGMENTED WIDE-QRS COMPLEX AND THE RISK OF DEATH AND SUDDEN CARDIAC DEATH AMONG MADIT-II PATIENTS WITH LEFT BUNDLE BRANCH BLOCK. *Journal of the American College of Cardiology.* 2010;55(10 Supplement):A13. E126.

32. Carey MG, Luisi Jr AJ, Baldwa S, et al. The Selvester QRS Score is more accurate than Q waves and fragmented QRS complexes using the Mason-Likar configuration in estimating infarct volume in patients with ischemic cardiomyopathy. *Journal of electrocardiology.* 2010;43(4):318-325.

33. Wang DD, Buerkel DM, Corbett JR, Gurm HS. Fragmented QRS complex has poor sensitivity in detecting myocardial scar. *Annals of Noninvasive Electrocardiology.* 2010;15(4):308-314.

34. Ahn M-S, Kim J-B, Yoo B-S, et al. Fragmented QRS complexes are not hallmarks of myocardial injury as detected by cardiac magnetic resonance imaging in patients with acute myocardial infarction. *International journal of cardiology.* 2013;168(3):2008-2013.

35. Nesbitt GC, Mankad S, Oh JK. Strain imaging in echocardiography: methods and clinical applications. *The international journal of cardiovascular imaging.* 2009;25(1):9-22.

36. Collier P, Phelan D, Klein A. A test in context: myocardial strain measured by speckle-tracking echocardiography. *Journal of the American College of Cardiology.* 2017;69(8):1043-1056.
37. Negishi K, Negishi T, Kurosawa K, et al. Practical guidance in echocardiographic assessment of global longitudinal strain. *JACC: Cardiovascular Imaging*. 2015;8(4):489-492.

38. Kalam K, Otahal P, Marwick TH. Prognostic implications of global LV dysfunction: a systematic review and meta-analysis of global longitudinal strain and ejection fraction. *Heart*. 2014;100(21):1673-1680.

39. Sengeløv M, Jørgensen PG, Jensen JS, et al. Global longitudinal strain is a superior predictor of all-cause mortality in heart failure with reduced ejection fraction. *JACC: Cardiovascular Imaging*. 2015;8(12):1351-1359.

40. Tigen K, Sunbul M, Ozen G, et al. Regional myocardial dysfunction assessed by two-dimensional speckle tracking echocardiography in systemic sclerosis patients with fragmented QRS complexes. *Journal of electrocardiology*. 2014;47(5):677-683.

41. Yaman M, Arslan U, Bayramoglu A, Bektas O, Gunaydin ZY, Kaya A. The presence of fragmented QRS is associated with increased epicardial adipose tissue and subclinical myocardial dysfunction in healthy individuals. *Revista portuguesa de cardiologia*. 2018;37(6):469-475.

42. Kocabay G, Muraru D, Peluso D, et al. Normal left ventricular mechanics by two-dimensional speckle-tracking echocardiography. Reference values in healthy adults. *Revista Española de Cardiología (English Edition)*. 2014;67(8):651-658.

43. Marwick TH, Leano RL, Brown J, et al. Myocardial strain measurement with 2-dimensional speckle-tracking echocardiography: definition of normal range. *JACC: Cardiovascular Imaging*. 2009;2(1):80-84.

44. Takigiku K, Takeuchi M, Izumi C, et al. Normal range of left ventricular 2-dimensional strain. *Circulation Journal*. 2012;76(11):2623-2632.

45. Zghal F, Bougteb H, Réant P, Lafitte S, Roudaut R. Assessing global and regional left
ventricular myocardial function in elderly patients using the bidimensional strain method. *Echocardiography*. 2011;28(9):978-982.

46. Cifra B, Mertens L, Mirkhani M, et al. Systolic and diastolic myocardial response to exercise in a healthy pediatric cohort. *Journal of the American Society of Echocardiography*. 2016;29(7):648-654.

### Tables

**Table 1.** Baseline characteristics of the participants based on fQRS and GLS status

|                  | fQRS     | P value | GLS                  | p value |
|------------------|----------|---------|----------------------|---------|
|                  | - (n=20) |         | + (n=20)             |         |
| Age (yrs.)       | 49.55±6.51 | 0.446   | 49.65±7.25           | 0.366   |
| Gender (male, %) | 16 (80)  | 0.465   | 18 (69.2)            | 0.251   |
| LVEDV (ml)       | 83.15±24.85 | 0.599   | 82.80±23.79          | 0.557   |
| LVESV (ml)       | 35.20±9.87  | 0.423   | 34.38±9.88           | 0.739   |
| D-LVSIZE (cm)    | 4.69±0.48  | 0.792   | 4.65±0.58            | 0.780   |
| S-LVSIZE (cm)    | 3.08±0.41  | 0.612   | 3.06±0.46            | 0.744   |
| EF (%)           | 59.20±2.53 | 0.830   | 59.23±2.80           | 0.840   |

Data were presented as mean±sd. Normal GLS: >20%. Reduced GLS: ≤20%. LVEDV: left ventricular end-diastolic volume. LVESV: left ventricular end-systolic volume. D-LVSIZE: left ventricular size in diastole. S-LVSIZE: left ventricular size in systole. EF: ejection fraction.

**Table 2.** EF and GLS of the case group based on fQRS position

| Fragmentation | Anterior (25%)     | Lateral (25%) | Inferior (50%) | P value^a |
|---------------|--------------------|---------------|----------------|-----------|
| GLS (%)       | 20.30±0.51         | 19.60±1.88    | 19.94±2.21     | 0.841     |
| EF (%)        | 61.40±3.50         | 56.80±1.78    | 59.70±3.12     | 0.071     |

Data were presented as mean±sd, a; Extracted from ANOVA. GLS: global longitudinal strain. EF: ejection fraction.
Table 3. Comparison of echocardiographic parameters between case and control groups

|                | - fQRS      | + fQRS      | P value |
|----------------|-------------|-------------|---------|
| ANTSEPT Base   | 17.20±2.69  | 14.85±3.90  | 0.032   |
| ANTSEPT Mid    | 20.25±3.54  | 18.15±3.96  | 0.085   |
| POST Base      | 19.45±2.28  | 18.90±2.61  | 0.483   |
| POST Mid       | 20.80±2.31  | 20.20±2.59  | 0.444   |
| ANT Base       | 17.10±2.65  | 17.40±3.07  | 0.743   |
| ANT Mid        | 20.35±2.96  | 20.25±3.82  | 0.927   |
| Apex           | 25.60±3.55  | 23.90±4.27  | 0.179   |
| INF Base       | 19.00±1.78  | 17.25±2.02  | 0.006   |
| INF Mid        | 21.15±2.08  | 20.00±2.60  | 0.131   |
| INF Apex       | 25.85±2.70  | 24.35±4.13  | 0.182   |
| LAT Base       | 18.95±2.67  | 17.35±3.54  | 0.115   |
| LAT Mid        | 20.20±2.61  | 19.55±3.89  | 0.538   |
| Apex           | 24.60±3.91  | 23.55±4.26  | 0.422   |
| SEPT Base      | 17.15±1.93  | 15.35±2.06  | 0.007   |
| SEPT Mid       | 20.80±1.77  | 18.65±2.37  | 0.002   |
| Apex           | 25.90±3.13  | 23.25±3.46  | 0.015   |

A3C_GLS 21.07±2.28  19.44±2.92  0.057
A2C_GLS 21.67±1.95  20.74±1.96  0.143
A4C_GLS 21.44±1.81  19.86±2.58  0.031
GLS   19.94±1.78  21.41±1.59  0.009

ANTSEPT: anteroseptal; POST: posterior; ANT: anterior; INF: inferior; LAT: lateral; SEPT: septal; A3C_GLS: GLS in apical three-chamber view; A2C_GLS: GLS in apical two-chamber view; A4C_GLS: GLS in apical four-chamber view. Bold values imply statistical significance.