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Relationship between fragmented QRS complex and early left ventricular dysfunction after mitral valve repair☆

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ABSTRACT

Background: Preoperative left ventricular (LV) ejection fraction (PreLVEF) and preoperative LV end-systolic diameter (PreESD) are known predictors for postoperative LV dysfunction after mitral valve repair (MVR). Fragmented QRS (fQRS) evaluated in 12-derivation electrocardiography has widely been accepted as a sign of myocardial fibrosis.

In the present study, we aimed to evaluate the relationship between fQRS in preoperative 12-lead electrocardiography (ECG) and postoperative LV dysfunction that develop after MVR in patients with severe primary mitral regurgitation (MR) due to mitral valve prolapse (MVP).

Methods: From 2019 to 2022, 49 patients who had undergone successful MVR surgery for severeMR caused by MVP were enrolled in the study. The preoperative and postoperative echocardiographic data were collected retrospectively. We analyzed the demographic, echocardiographic, operative and postoperative parameters to assess the relationship between fQRS and early postoperative LV dysfunction, defined as an LVEF<60%.

Results: PreLVEF of all patients were ≥ %65. A total of 22 patients had fQRS (44.9%) and postoperative LV dysfunction was found to be 36.7%. A significantly higher rate of fQRS was observed in the group with postoperative LV dysfunction compared to the group without (12 (66.7%) vs 10 (32.3%), p: 0.036). In multivariate analysis for fQRS, PreESD, preoperative pulmonary artery systolic pressure (PrePASP), preoperative atrial fibrillation (PreAF), and male gender, only fQRS was found to be a significant predictor of postoperative LV dysfunction (p: 0.003, OR: 4.28, 95% CI (1.15–15.96).

Conclusion: fQRS was found to be a predictor of postoperative LV dysfunction in the early period after MVR. fQRS may be a readily available and cost-effective test that can be used in clinical practice to predict postoperative LV dysfunction in patients undergoing MVR.

Introduction

Mitral regurgitation (MR) caused by mitral valve prolapse (MVP) is a common clinical condition that affects approximately 2% of the population [1]. Patients with chronic primary MR develop cardiac remodeling due to persistent volume overload, increased cardiac diameter, eccentric ventricular hypertrophy, and eventually left ventricular (LV) dysfunction [2]. Studies have shown that cardiac remodeling and myocardial fibrosis may develop in association with chronic MR [3,4]. Surgical mitral valve repair (MVR) is the recommended treatment for severeprimary MR. Preoperative LV ejection fraction (PreLVEF) and preoperative LV end-systolic diameter (PreESD) are known predictors for postoperative LV dysfunction after mitral valve repair [5].

Fragmented QRS complex (fQRS) includes the RSR' pattern within QRS of different morphology detected in 12-lead electrocardiography (ECG). fQRS is associated with myocardial scar, myocardial fibrosis, structural heart anomalies, ventricular dysrhythmia, and coronary artery disease [6–10].

In the present study, we aimed to evaluate the relationship between fQRS in preoperative ECGs and postoperative LV dysfunction that

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develop after MVR in patients with severeprimary MR due to MVP.

Methods

Study population

A total of 150 patients who underwent MVR due to severe MVP performed by a single surgical team between March 2019 and November 2022 were retrospectively evaluated. Preoperative ECGs of the patients were analyzed. Thirty-seven patients were excluded from the study due to atrial fibrillation (AF) [23], bundle branch block [5] and intraventricular conduction delay (QRS >120 ms) [9] on preoperative ECG while patients with previously documented AF who had sinus rhythm on preoperative ECG were not excluded from the study. The preoperative echocardiography results of the patients were analyzed and patients with LVEF below 65% (38) and those with moderate-to-severe aortic valve insufficiency or stenosis [7] were excluded from the study. Ten patients who underwent coronary artery bypass grafting (CABG) along with MVR were also excluded from the study. Postoperative, predischarge echocardiography results of the patients and echocardiography results at 1 month postoperatively were evaluated. Nine patients whose echocardiography results could not be obtained at 1 month postoperatively were excluded from the study. A total of 49 patients were enrolled in the study.

ECG analysis

Standard 12-lead surface resting ECGs (filter range0.5–150 Hz, 25 mm/s, 10 mm/mV) were recorded from all patients. These ECGs were reviewed blindly by 2 independent authors. fQRS was defined by the presence of various RSR′ patterns (QRS <120 ms) with or without a Q wave, which includes an additional R wave (R′) or notching of the R wave or S wave, or the presence of more than one R′ (fragmentation) without typical bundle-branch block in 2 contiguous leads corresponding to a major lead set for the territory of a major coronary artery. Coronary artery regions were defined as anterior: leads V1–V5; inferior: leads.

II, III, and aVF; and lateral: leads V6, I, and aVL. The QRS duration was determined by the longest QRS in any lead.

Patients had undergone MVR surgery using various techniques with a lesion-specific approach as previously described [11,12]. These techniques included commissuroplasty, quadrangular or triangular resection, leaflet sliding plasty, and neochordae replacement. A complete annuloplasty ring was implanted in the majority of patients, and an incomplete annuloplasty ring in a minority of patients. Tricuspid annuloplasty was applied to patients with moderate or severe tricuspid regurgitation, and complete left atrial or biatrial ablation was applied to patients diagnosed with paroxysmal AF with a previously documented AF episode was defined preoperative AF (PreAF).

Operative technique

During valve repair, myocardial protection was preserved using an induction dose of antegrade blood cardioplegia, with maintenance cardioplegia given mostly in a retrograde manner by means of a catheter in the coronary sinus. Cold blood cardioplegia was administered at 4 °C and consisted of a 4:1 ratio of blood to cardioplegia. The doses were administered approximately every 20 to 25 min. Before removal of the crossclamp, a dose of warm blood was administered through the retrograde catheter.

Echocardiographic analysis

All patients had preoperative transthoracic echocardiography. All echocardiographic measurements were performed according to the American Society of Echocardiography guidelines [13]. All patients had undergone transthoracic echocardiography before being discharged after MVR (mean, 4.5 days) and at 1 month postoperatively. LVEF <60% in postoperative echocardiography was considered LV dysfunction.

Statistical analysis

Statistical analysis was performed using the IBM SPSS Statistics for Windows, version 25 (IBM Corporation, Armonk, NY, USA). The results of continuous variables have been presented as mean ± standard deviation. The results of categorical data are reported as counts and frequencies (%). Categorical variables were compared using the chi-square test. Normality of the distribution of continuous variables was tested using the Kolmogorov–Smirnov test. Continuous variables were compared using the student *t*-test or the Mann–Whitney *U* test when applicable. The relationship of baseline variables with the occurrence of postoperative LV dysfunction was assessed using univariate and multivariable logistic regression analysis. Variables found to be significantly related to LV dysfunction following surgery in univariate analysis ($p \leq 0.1$) were entered into multivariable logistic regression model. The level of significance was set at $p < 0.05$.

Results

Table 1 shows the baseline characteristics of the 49 patients who had undergone MVR and were enrolled in the study. The mean age of the 49

Table 1
Baseline patient characteristics.

Demographics and comorbidity	
Age (years)	53 ± 13.1
Gender, n (male %)	30(61,2%)
Hypertension, n (%)	20 (40.8%)
Diabetes Mellitus, n (%)	6 (12.2%)
Hyperlipidemia	7(14.3%)
Coronary Artery Disease, n (%)	8(16.3%)
Peripheral artery disease, n (%)	4 (8.2%)
Obstructive lung disease, n (%)	4 (8.2%)
Renal failure n (%)	3(6.1%)
fQRS n (%)	22(44.9%)
preAF n (%)	17(34.7%)
Preoperative echocardiographic characteristics	
Pre ESD (mm)	39.6 ± 5.1
Pre EDD (mm)	58.4 ± 4
Pre LAD (mm)	46.3 ± 7.8
Pre PASP (mmHg)	43.8 ± 10.9
PreESD>40 mm n (%)	27(55.1%)
PrePASP >50 mmHg n (%)	17(34.7%)
Barlow's disease n (%)	24(28.6%)
Anterior leaflet prolapse n (%)	25(51%)
Posterior leaflet prolapse n (%)	38(77.6%)
Bileaflet prolapse n (%)	14(28.6%)
Operative Data	
Concomitant TVR n (%)	23(46.9%)
Surgical Ablation n (%)	17(34.7%)
PostopLVEF disfunction n (%)	18(36.7%)
CrossClamp time, (min)	128.1 ± 24.6
Cardiopulmonary bypass time, (min)	155.3 ± 35.6
Postoperative Data	
PostoperativeLVEF Predischarge	59.9 ± 7.5
PostoperativeLVEF after 1 months	60.1 ± 7.3
PostoperativeESD after 1 months	34.4 ± 7.3
PostoperativePASP after 1 months	36 ± 7

LVEF = left ventricular ejection fraction, LVEDD = left ventricular end-diastolic diameter, fQRS = fragmented QRS TVR = tricuspid valve repair. PreAF = preoperatif atrial fibrillation, PreESD = preoperatif left ventricular end-systolic diameter; PrePASP = preoperatif pulmonary artery systolic pressure, Postoperative LVEF dysfunction = LVEF<60%,

patients included in the study was 53 ± 13.1 years, 30 patients were male (61.2%), 20 patients had hypertension (40.8%), 6 had diabetes mellitus (12.2%), 7 had hyperlipidemia (14.3%), 8 had coronary artery disease (16.3%), 4 had peripheral artery disease (8.2%), 4 had obstructive lung disease (8.2%), and 3 patients had renal impairment (6.1%). A total of 22 patients had fQRS (44.9%) and 17 had PreAF (34.7%). The mean PreESD of the patients was 39.6 ± 5.1 mm, and the mean preoperative pulmonary artery systolic pressure (PrePASP) was 43.8 ± 10.9 mmHg. The rate of patients who developed postoperative LV dysfunction was found to be 36.7%. Surgical ablation was performed in 17 (34.7%) patients and concomitant TVR was performed in 23 (46.9%) patients. Postoperative LVEF in the pre-discharge period was 59.9 ± 7.5%. None of the patients died during the 1-month postoperative period.

Table 2 compares the clinical, echocardiographic, and operative parameters of patients with and without postoperative LV dysfunction. Age was found to be higher in the group with postoperative LV dysfunction compared to the group without (58.4 ± 15.02 vs. 49.87 ± 10.88, p: 0.03). Gender, hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease, peripheral artery disease, obstructive lung disease, renal impairment rates were similar across the two groups ($p > 0.005$ for all). A significantly higher rate of fQRS was observed in the group with postoperative LV dysfunction compared to the group without (12 (66.7%) vs 10 (32.3%), p: 0.036). Preoperative echocardiographic parameters were similar across the two groups ($p > 0.005$ for all). A significantly higher rate of concomitant tricuspid valve repair (TVR) was seen in the group with postoperative LV dysfunction compared to the group without postoperative LV dysfunction (14 (77.8%) vs. 9 (29%), $p < 0.001$).

In multivariate analysis for fQRS, PreESD, PrePASP, PreAF, and male gender, only fQRS was found to be a significant predictor of postoperative LV dysfunction (p: 0.003, OR: 4.28, 95% CI (1.15–15.96) (Table 3).

Table 2
Comparison of clinical, echocardiographic and operative parameters between patient groups based on postoperative LV dysfunction.

Variable	All patients ($n = 49$)	Postoperative LV Dysfunction		
		Yes ($n = 18$)	No ($n = 31$)	*P* value
Demographics and comorbidity				
Age (years)	53 ± 13.1	58.4 ± 15.02	49.87 ± 10.88	**0.03**
Gender, n (male %)	30(61.2%)	10 (55.6%)	20 (64.5%)	0.54
Hypertension, n (%)	20 (40.8%)	7(38.9%)	13 (41.9%)	0.83
Diabetes Mellitus, n (%)	6 (12.2%)	4(22.2%)	2(6.5%)	0.18
Hyperlipidemia	7(14.3%)	3(16.7%)	4(12.9%)	0.70
Coronary Artery Disease, n (%)	8(16.3%)	4(22.2%)	4(12.9%)	0.44
Peripheral artery disease, n (%)	4 (8.2%)	3(16.7%)	1(3.2%)	0.13
Obstructive lung disease, n (%)	4 (8.2%)	2(11.1%)	2(6.5%)	0.62
Renal failure, n (%)	3(6.1%)	1(5.6%)	2(6.5%)	1
Frag QRS (+)	22 (44.9%)	12(66.7)	10(32.3)	**0.036**
preAF	17(34.7)	9(50%)	8(25.8%)	0.09
Preoperative echocardiographic characteristics				
Pre ESD (mm)	39.6 ± 5.1	41.39 ± 4.51	38.58 ± 5.12	0.06
Pre EDD (mm)	58.4 ± 4	58.94 ± 3.87	58.03 ± 4.12	0.45
Pre LAD (mm)	46.3 ± 7.8	48.5 ± 4.57	45.08 ± 8.96	0.14
Pre PASP (mmHg)	43.8 ± 10.9	45.8 ± 9.74	42.65 ± 11.49	0.33
PreESD>40 mm n (%)	27(55.1%)	13 (72.2%)	14 (45.2%)	0.067
PrePASP >50 mmHg n (%)	17(34.7)	6(33%)	11(36%)	0.88
Barlow's disease n (%)	24(28.6)	6(33.%)	8(25.8%)	0.57
Anterior leaflet prolapse n (%)	25(51%)	10 (55.6%)	15 (48.4%)	0.63
Posterior leaflet prolapse n (%)	38(77.6%)	14 (77.8%)	24 (77.4%)	0.98
Bileaflet prolapse n (%)	14(28.6)	6(33.3%)	8(25.8%)	0.57
Operative Data				
Concomitant TVR n (%)	23(46.9)	14 (77.8%)	9(29%)	**<0.001**
Surgical Ablation n (%)	17(34.7)	9(50%)	8(25.8%)	0.09
CrossClamp time, (min)	128.1 ± 24.66	128.72 ± 27.98	127.74 ± 22.99	0.89
Cardiopulmonary bypass time, (min)	155.31 ± 35.6	158.06 ± 37.41	153.71 ± 35.09	0.69

LVEF = left ventricular ejection fraction, LVEDD = left ventricular end-diastolic diameter, fQRS = fragmented QRS, TVR = tricuspid valve repair. PreAF = preoperatif atrial fibrillation, PrePASP = preoperatif pulmonary artery systolic pressure, PreESD = preoperatif left ventricular end-systolic diameter, Postoperative LVEF dysfunction = LVEF<60%.

Discussion

In the present study, we investigated the relationship between fQRS on preoperative ECG and postoperative LV dysfunction in patients who underwent MVR surgery due to MVP.

a. Age, concomitant TVR and fQRS rates in the group with postoperative LV dysfunction were significantly higher compared to the group without postoperative LV dysfunction.
b. In multivariate analysis, fQRS was found to be an independent predictor of postoperative LV dysfunction while this was not the case for PreESD, PrePASP, PreAF and male gender.

LV dysfunction after mitral valve surgery has been demonstrated in various studies [14–16]. In our study, postoperative LV dysfunction was observed in 36.7% of the patients. Various explanations have been proposed for postoperative LV dysfunction. Starling and colleagues described that LVEF is overestimated in MR due to increased ventricular preload (end-diastolic volume) [17]. The fact that this increased preload disappears after MVR causes a decrease in end-diastolic volume and a decrease in LVEF [17]. Another proposed explanation for the decrease in LVEF in the early period is increased afterload after MVR and myocardial stress and/or injury after aortic crossclamp [16]. In the study conducted by Varghese et al., a significantly higher age, LVESD, PrePASP, LVEDD, PreAF, and concomitant maze procedure were found in the group with postoperative LV dysfunction after MVR, while a significantly lower preoperative EF was found [16]. In our study, similar to this study, the age rate was higher in the group with postoperative LV dysfunction and no differences were detected in other parameters except fQRS and TVR. Since patients with preoperative LVEF below 65% were excluded in our study, the similarity of preoperative LVEF in all patients may cause the similarity of other echocardiographic parameters to be similar as well. The higher TVR rate in the group with postoperative LV dysfunction may also be due to the effect of the tricuspid valve pathology on the right ventricular volume and function and indirectly on the postoperative LV function.

In the study by Suri and colleagues, increased LV diameter, worsening heart failure symptoms, PreLVEF, and AF were found to be predictive of LV dysfunction in the early postoperative period in 861 patients who underwent mitral valve replacement and MVR [14]. In the study conducted by Varghese and colleagues, PreAF, pulmonary hypertension, and PreESD were found to be independent predictors for the development of LV dysfunction in the early postoperative period in 632

Table 3
Predictors of postoperative LV dysfunction.

	Univariate		Multivariate	
	OR(95% CI)	p	OR(95% CI)	p
fQRS	4.2(1.22–14.45)	0.02	4.28(1.15–15.96)	0.03
PreESD>40 mm	3.16(0.9–11.03)	0.07	2.31(0.58–9.14)	0.23
PrePASP>50 mmHg	0.9(0.27–3.1)	0.89		–
Pre AF	2.88(0.84–9.79)	0.09	2.57(0.66–10)	0.17
Male gender	0.69(0.21–2.25)	0.54		–

fQRS = fragmented QRS, PreESD = preoperatif left ventricular end-systolic diameter; PrePASP = preoperatif pulmonary artery systolic pressure; PreAF = preoperatif atrial fibrillation. Postoperative LVEF dysfunction = LVEF<60%.

patients who underwent MVR [16]. In our study, the predictors reported in these studies were not detected in patients with postoperative LV dysfunction. Compared to these studies, our study consists of a more homogeneous group. All patients included in the study had normal LVEF and the study excluded patients undergoing concurrent CABG as well as those with AF detected on preoperative ECG. Of AF patients, only those with previously documented paroxysmal AF were included in the study. The preoperative characteristics of the patients that we included in our study were more homogeneous and the risk of developing postoperative LV dysfunction was relatively lower. As a result a higher threshold was set for postoperative LV dysfunction was defined as LVEF <60. Predictors of postoperative LV dysfunction may be different in a patient population with lower preoperative LVEF, which is likely to be at a relatively higher risk of developing LV dysfunction. This may be the reason of differences in results.

The relationship between myocardial fibrosis and LV dysfunction has been long known [18–20]. Histological data obtained from endomyocardial biopsies and autopsies indicate that myocardial fibrosis may develop in response to progressive cardiac remodeling due to chronic MR [3,4]. In a study in patients with primary MR conducted by Kitkungvan et al., LV fibrosis detected by cardiovascular magnetic resonance (CMR) was found to be higher in the MVP group compared to the non-MVP group (36.7% vs. 6.7%; $p < 0.001$) [21]. In our study, the study group consisted of patients with MVP, and the rate of fQRS, which we consider an indicator of myocardial fibrosis, was found to be 44.9% in the entire cohort. fQRS is defined as a variety of RSR' patterns with or without a Q wave in 12-lead resting ECG. There are clinical studies showing the relationship between myocardial scar that develops after myocardial infarction and fQRS [6,8]. Additionally, a relationship between regional fQRS and focal regional myocardial scar was detected with myocardial perfusion imaging [22]. Park and colleagues. Reported a strong correlation between fQRS and myocardial fibrosis detected by CMR [23]. To the best of our knowledge, there is no previous study showing the relationship between fQRS and postoperative LV dysfunction after MVR. In our study, fQRS detected on preoperative ECG in patients who underwent MVR was found to be an independent predictor of LV dysfunction in the early postoperative period. This finding may indicate that, in addition to factors such as postoperative preload reduction and postoperative myocardial stress/injury, which are implicated in postoperative LV dysfunction, myocardial fibrosis observed in MR due to MVP also contributes to the development of postoperative LV dysfunction. Although the effect of postoperative LV dysfunction at these threshold values, which are associated with fQRS, on long-term mortality and morbidity remains unknown, it may be appropriate to monitor these patients more closely in the clinic setting and surgery may be planned earlier in asymptomatic patients.

Limitations of the study

The main limitation of our study is the limited number of patients included in the study cohort; however, the exclusion of many patients served to obtain a more homogeneous patient group. The second limitation is the retrospective study design. Another limitation is that the effect of fQRS on long-term mortality and morbidity has not been evaluated prospectively. New prospective, randomized studies can be conducted to investigate this effect.

Conclusion

fQRS was found to be a predictor of postoperative LV dysfunction in the early period after MVR. fQRS may be a readily available and cost-effective test that can be used in clinical practice to predict postoperative LV dysfunction in patients undergoing MVR.

CRediT authorship contribution statement

Filiz Kizilirmak Yılmaz: Visualization, Validation, Supervision, Conceptualization. **Beytullah Cakal:** Visualization, Methodology. **Fatih Yılmaz:** Software. **Arzu Yazar:** Validation. **Umeyir Savur:** Formal analysis. **Aysel Akhundova:** Investigation. **Haci Murat Gunes:** Resources. **Ekrem Guler:** Data curation. **Atakan Dursun:** Writing – original draft. **Navin Yousufzai:** Writing – review & editing. **Mustafa Güden:** Supervision, Project administration.

Declaration of competing interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of paper.

References

[1] Nkomo Vuyisile T, Gardin Julius M, Skelton Thomas N, Gottdiener John S, Scott Christopher G, Enriquez-Sarano Maurice. Burden of valvular heart diseases: a population-based study. Lancet 2006;368:1005–11.
[2] Nishimura Rick A, Otto Catherine M, Bonow Robert O, Carabello Blase A, Erwin John P, Guyton Robert A, et al. 2014 AHA/ACC guideline for the Management of Patients with Valvular Heart Disease: a report of the American College of Cardiology/American Heart Association task force on practice guidelines. J American of Coll Cardiol 2014;63(22):e57–185.
[3] Fuster V, Danielson MA, Robb RA, Broadbent JC, Brown Jr AL, Elveback LR. Quantitation of left ventricular myocardial fiber hypertrophy and interstitial tissue in human hearts with chronically increased volume and pressure overload. Circulation. 1977;55(3):504–8.
[4] Edwards NC, Moody WE, Yuan M, Weale P, Neal D, Townend JN, et al. Quantification of left ventricular interstitial fibrosis in asymptomatic chronic primary degenerative mitral regurgitation. Circ Cardiovasc Imaging 2014;7(6):946–53.
[5] Zile Michael R, Gaasch William H, Carroll John D, Levine Herbert J. Chronic mitral regurgitation: predictive value of preoperative echocardiographic indexes of left ventricular function and wall stress. J Am Coll Cardiol 1984;235-242.
[6] 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):2495–501.
[7] Das MK, Saha C, El Masry H, Peng J, Dandamudi G, Mahenthiran J, 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):1385–92.
[8] Das MK, Suradi H, Maskoun W, Michael MA, Shen C, Peng J, 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.
[9] Peters S, Trümmel M, Koehler B. QRS fragmentation in standard ECG as a diagnostic marker of arrhythmogenic right ventricular dysplasia-cardiomyopathy. Heart Rhythm 2008;5(10):1417–21.
[10] Das MK, Zipes DP. Fragmented QRS: a predictor of mortality and sudden cardiac death. Heart Rhythm 2009;6(3):8–14.
[11] Castillo JG, Anyanwu AC, Fuster V, Adams DH. A near 100% repair rate for mitral valve prolapse is achievable in a reference center: implications for future guidelines. J Thorac Cardiovasc Surg 2012;144:308–12.
[12] Varghese RADH. Techniques for repairing posterior leaflet prolapse of the mitral valve. Oper Techniq Thor Cardiovas Surg 2011;16:293–308.
[13] Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committeeon standards, subcommittee on quantitation of two-dimensional echocardiograms. Journal of the American society. Echocardiography 1989;2(5):358–67.
[14] Suri Rakesh M, Schaff Hartzell V, Dearani Joseph A, Sundt Thoralf M, Daly Richard C, Mullany Charles J, et al. Determinants of early decline in ejection fraction after surgical correction of mitral regurgitation. Surg For Acqu Cardiovas Disease 2008;136(2):442–7.

[15] Tribouilloy C, Rusinaru D, Szymanski C, Mezghani S, Fournier A, Lévy F, et al. Predicting left ventricular dysfunction after valve repair for mitral regurgitation due to leaflet prolapse: additive value of left ventricular end-systolic dimension to ejection fraction. Eur J Echocardiogr 2011;702–710.
[16] Varghese R, Itagaki S, Anyanwu AC, Milla F, Adams DH. Predicting early left ventricular dysfunction after mitral valve reconstruction: the effect of atrial fibrillation and pulmonary hypertension. J Thorac Cardiovasc Surg 2014;148(2):422–7.
[17] Starling MR, Kirsh MM, Montgomery DG, Gross MD. Impaired left ventricular contractile function in patients with long-term mitral regurgitation and normal ejection fraction. J Am Coll Cardiol 1993:239–50.
[18] González A, Schelbert EB, Díez J, Butler J. Myocardial interstitial fibrosis in heart failure: biological and translational perspectives. J Am Coll Cardiol 2018;17;71(15):1696–706.
[19] Aoki T, Fukumoto Y, Sugimura K, Oikawa M, Satoh K, Nakano M, et al. Prognostic impact of myocardial interstitial fibrosis in non-ischemic heart failure. -comparison between preserved and reduced ejection fraction heart failure. Circ J 2011;75(11):2605–13.
[20] Sabbah HN, Sharov VG, Lesch M, Goldstein S. Progression of heart failure: a role for interstitial fibrosis. Mol Cell Biochem 1995;147(1–2):29–34.
[21] Kitkungvan D, Nabi F, Kim RJ, Bonow RO, Khan MA, Xu J, et al. Myocardial fibrosis in patients with primary mitral regurgitation with and without prolapse. J Am Coll Cardiol 2018;21;72(8):823–34.
[22] Mahenthiran J, Khan BR, Sawada SG, Das MK. Fragmented QRS complexes not typical of a bundle branch block: a marker of greater myocardial perfusion tomography abnormalities in coronary artery disease. J Nucl Cardiol 2007;14(3):347–53.
[23] Park Seung-Jung, On Young Keun, Kim June Soo, Park Seung Woo, Yang Ji- Hyuk, Jun Tae- Gook, et al. Relation of fragmented QRS complex to right ventricular fibrosis detected by late gadolinium enhancement cardiac magnetic resonance in adults with repaired tetralogy of fallot. Am J Cardiol 2012;109(1):110–5.