QRS duration is closely related to echocardiographic parameters in patients with ischemic mitral regurgitation

İskemik mitral yetersizlikli hastalarda QRS süresi ekokardiyografik parametrelerle yakından ilişkilidir

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Objectives: Prolonged QRS duration is associated with mechanical dyssynchrony. Ischemic mitral regurgitation (MR) results from geometric changes in left ventricular (LV) shape, which also causes mechanical dyssynchrony. The aim of this study was to define the correlation of QRS duration with echocardiographic parameters reflecting LV function, shape, and mitral deformation in patients with ischemic MR.

Study design: The study included 29 patients (19 males, 10 females; mean age 64±3 years) who had at least moderate ischemic MR and a history of myocardial infarction or coronary revascularization. All the patients underwent echocardiography where LV ejection fraction, LV volumes, effective regurgitant orifice, tethering distance, tethering area, end-systolic sphericity index, and pulmonary artery pressures were measured. The patients were assessed in two groups formed based on the cutoff value of 120 ms for QRS duration.

Results: The mean MR severity was 2.8±0.8. QRS duration was <120 ms in 19 patients, and ≥120 in 10 patients. Prolonged QRS duration (≥120 ms) was accompanied by significantly lower LV ejection fraction and higher LV volumes and mitral valve deformation indices. QRS duration was in correlation with the following: LV ejection fraction (r=-0.62, p<0.001), LV end-systolic volume index (r=0.58, p<0.0001), LV end-diastolic volume index (r=0.46, p=0.014), vena contracta (r=0.37, p=0.016), mitral annulus diameter (r=0.42, p=0.004), tethering distance (r=0.43, p=0.005), tethering area (r=0.44, p=0.003), and end-systolic sphericity index (r=-0.39, p=0.01). Multiple regression analysis showed that LV ejection fraction was the only independent variable affecting QRS duration (ß= -1.1, p=0.025).

Conclusion: QRS duration is closely correlated with LV systolic functions and geometry and mitral apparatus deformation in patients with ischemic MR.

Key words: Echocardiography; electrocardiography; heart conduction system; mitral valve insufficiency/diagnosis; myocardial ischemia; ventricular dysfunction, left/diagnosis.

Amaç: QRS süresinin uzaması, sol ventrikül (SV) mekanik senkronizasyon bozukluğunun bir göstergesidir. İskemik mitral yetersizlik (MY), mekanik senkronizasyon bozukluğuna da yol açan sol ventrikül geometrisinin bozulmasından kaynaklanır. Bu çalışmada, sol ventrikül sistolik fonksiyonlarını, geometrisini ve mitral aparat deformasyonunu gösteren ekokardiyografik parametrelerin QRS süresi ile ilişkisi araştırıldı.

Çalışma planı: Çalışmaya, en az orta derecede iskemik mitral yetersizliği ve miyokard infarktüsü veya koroner revaskülarizasyon öyküsü olan 29 hasta (19 erkek, 10 kadın; ort. yaş 64±3) alındı. Tüm hastalara yapılan ekokardiyografik incelemede SV ejeksiyon fraksiyonu, SV hacimleri, efektif regürjitan orifis, tethering mesafesi, tethering alanı, sistol sonu küresellik indeksi ve pulmoner arter basınçları ölçüldü. Hastalar, QRS süresi için kesim değeri 120 msn alınarak iki grupta değerlendirildi.

Bulgular: Ortalama MY derecesi 2.8±0.8 idi. QRS süresi 19 hastada 120 msn'den düşük, 10 hastada ise ≥120 msn bulundu. Uzamış QRS süresine (≥120 msn) anlamlı derecede düşük SV ejeksiyon fraksiyonu ve yüksek SV hacimleri ve mitral kapağı deformasyon indeksleri eşlik etmekteydi. QRS süresi şu parametrelerle yakın ilişki gösterdi: SV ejeksiyon fraksiyonu (r=-0.62, p<0.001), SV sistol sonu hacim indeksi (r=0.58, p<0.0001), SV diyastol sonu hacim indeksi (r=0.46, p=0.014), vena kontrakta (r=0.37, p=0.016), mitral anülüs çapı (r=0.42, p=0.004), tethering mesafesi (r=0.43, p=0.005), tethering alanı (r=0.44, p=0.003) ve sistol sonu küresellik indeksi (r=-0.39, p=0.01). Çoklu regresyon analizinde QRS süresini etkileyen tek bağımsız değişkenin SV ejeksiyon fraksiyonu olduğu görüldü (ß= -1.1, p=0.025).

Sonuç: İskemik MY'li hastalarda QRS süresi, SV sistolik fonksiyonları, geometrisi ve mitral aparat deformasyonu ile yakından ilişkili bir parametredir.

Anahtar sözcükler: Ekokardiyografi; elektrokardiyografi; kalp iletim sistemi; mitral kapağı yetersizliği/tanı; miyokard iskemisi; ventrikül disfonksiyonu, sol/tanı.

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Conduction delay, as manifested by a prolonged QRS complex duration, is common among patients with systolic dysfunction and heart failure and is associated with an increased prevalence of mechanical dyssynchrony, as opposed to patients with a narrow QRS complex.[1] Cardiac dyssynchrony results in a decrease in stroke volume, facilitation of mitral regurgitation, increased wall stress, and delayed relaxation.[2]

Ventricular dyssynchrony appears to have a deleterious impact on the natural history of heart failure, as a wide QRS complex has been associated with increased mortality in patients with heart failure.[3]

Ischemic mitral regurgitation (MR) results from geometric changes in left ventricular shape. Regional remodeling after myocardial infarction (MI) displaces papillary muscles and causes tethering of the mitral valve leaflets, which results in incomplete leaflet coaptation. Malcoaptation is aggravated further by dilatation of the mitral valve annulus.[4]

Coronary artery disease and MI together constitute a major cause of intraventricular activation delay and asynchrony, which may or may not manifest as bundle branch block on the surface electrocardiogram (ECG). Asynchrony is known for its direct effect on the duration of MR. Prolonged MR can abbreviate left ventricular filling, thus further compromising stroke volume and cardiac output. Activation delay usually causes a delay in the onset of segmental contraction of the left ventricle (LV), which in the presence of a regurgitant orifice can prolong the duration of MR with respect to cardiac cycle length.[5] Activation delay often is manifest on the surface ECG as a broad QRS complex, which itself is a known as an independent predictor of mortality.[2,3]

We hypothesized that QRS duration is strongly correlated with left ventricular systolic performance indexes as well as geometry and mitral apparatus deformation parameters assessed by echocardiography. The aim of this study was to find out specific echocardiographic parameters that may be associated with QRS duration in patients with at least moderate MR with relatively preserved left ventricular systolic functions.

PATIENTS AND METHODS

Patients. Forty-one patients who were found to have MR in echocardiographic examination were evaluated for eligibility to participate in the study. All the patients had either a history of MI or coronary revascularization. Patients with any stenotic valve lesion or having more than trivial aortic regurgitation were not included. In addition, 12 patients were excluded for the following reasons: pulmonary disease (n=2), renal failure (n=1), change in medication within one month prior to study (n=1), arrhythmias (n=2), unwillingness to participate (n=2), and inadequate echocardiographic images for the determination of proximal isovelocity surface area (n=4). Finally, the study group consisted of 29 patients (19 males, 10 females; mean age 64±3 years) with ischemic MR. All the patients had at least grade 2 MR. During the study period, all cardiac medications were continued and all the patients were in sinus rhythm. The study was approved by the local medical ethics committee, and all participants gave informed consent.

Echocardiography. All the patients underwent extensive echocardiographic and Doppler examinations using the Vivid 7 system (GE Vingmed Ultrasound, Horten, Norway). Left ventricular end-systolic and end-diastolic dimensions and volumes were measured according to the recommendations of the American Society of Echocardiography.[6] Left ventricular ejection fraction (LVEF) and volumes were measured by the biapical Simpson disk method.[6]

Mitral regurgitation index was defined as MR color jet area/left atrium area. Systolic pulmonary artery pressure was estimated from the systolic transtricuspid pressure gradient (in mmHg) using the simplified Bernoulli equation ($\Delta P=4V^2$, where V represents maximal tricuspid regurgitant velocity in m/sec).

Quantification of MR was performed by the proximal isovelocity surface area method as previously described.[7]

Sphericity index was calculated as the ratio of LV length to width in the apical four-chamber view.[8] To quantify mitral deformity, coaptation depth and tenting area of the mitral valve were measured. Coaptation distance was defined as the distance between the leaflet coaptation and the mitral annulus plane. Tenting area was defined as the area subtending the annulus and the two leaflets, and was calculated as half of the product of coaptation distance and annular diameter. These parameters were obtained at mid-systole in the apical four-chamber view.[9]

Mitral annular diameter, tenting area, and coaptation distance were considered to be the key features of mitral deformation, while LV ejection fraction, end-diastolic and end-systolic LV volumes were considered to be the markers of LV function. Left ventricular

end-diastolic and end-systolic sphericity indices were regarded as the markers of LV shape.

For each measurement, at least three nonconsecutive cardiac cycles were averaged.

QRS duration. A standard 12-lead computed resting ECG was obtained. All ECGs were interpreted by an experienced cardiologist, and the maximum QRS duration was recorded to the nearest 10 ms based on assessment of all the leads. The patients were assessed in two groups formed based on the cutoff value of 120 ms for QRS duration.[10]

Statistical analysis. Data were expressed as mean± the standard error of the mean (SEM) unless stated otherwise. Comparison of echocardiographic parameters between the two groups of QRS duration was made by the Mann-Whitney U-test. Correlations between QRS duration and echocardiographic parameters were sought by the Pearson's test. Multiple linear regression analysis by stepwise method was used for assessment of independent variables affecting QRS duration. A *p* value of less than 0.05 was considered significant. All statistical analyses were performed with the SPSS statistical software package (ver. 10.0) for Windows.

RESULTS

Clinical characteristics of the patients are summarized in Table 1. Patients with a prolonged QRS duration (≥120 ms) had significantly lower LVEF and higher LV volumes and mitral valve deformation indices (Table 2).

Table 1. Clinical characteristics of the patients (n=29)

Mitral regurgitation degree	2.8±0.8
Left ventricular ejection fraction (%)	45.9±2.5
Blood pressure (mmHg)	93.8±1.7
Heart rate (beat/min)	89.5±2.1

Univariate analysis showed that QRS duration was closely related to parameters of left ventricular function such as LVEF (r=-0.62, p<0.001; Fig 1a), LV end-systolic volume index (r=0.58, p<0.0001; Fig 1b), and LV end-diastolic volume index (r=0.46, p=0.014) (Table 3). QRS duration was also correlated with vena contracta (r=0.37, p=0.016), mitral annulus diameter (r=0.42, p=0.004), tethering distance (r=0.43, p=0.005), tethering area (r=0.44, p=0.003), and end-systolic sphericity index (r=-0.39, p=0.01). Multiple linear regression showed that LVEF was the only independent variable affecting QRS duration (ß= -1.1, SE: 0.67, p=0.025).

DISCUSSION

In this study we demonstrated that longer QRS duration was associated with alterations in LV structure and function as well as mitral apparatus deformation in patients with ischemic MR.

Ischemic MR is caused by changes in ventricular structure and function, ultimately but not necessarily directly related to the effects of ischemia. In the vast majority of cases, ischemic MR is essentially postinfarction MR, caused by progressive remodeling rather than reversible ischemia. Ischemic MR is associated with a poor prognosis independent of LV function.[11]

Table 2. Comparison of echocardiographic parameters in patients with a QRS duration of <120 ms and ≥ 120 ms

Echocardiographic parameters	QRS duration		*p*
	<120 ms (n=19)	≥120 ms (n=10)	
Left ventricular ejection fraction (%)	53.2±2.5	41.5±5.1	0.005
Left atrium diameter (cm)	4.3±0.1	4.7±0.3	0.337
Mitral regurgitation color jet area (cm^2)	6.1±0.5	10.0±2.5	0.082
Mitral regurgitation index	0.26±0.01	0.37±0.06	0.094
Vena contracta (mm)	0.37±0.01	0.50±0.03	0.004
Effective regurgitant orifice (mm^2)	24.8±1.9	28.4±3.1	0.862
Systolic pulmonary artery pressure (mmHg)	33.1±1.7	40.6±4.3	0.025
Mitral annulus (cm)	2.9±0.1	3.4±0.2	0.027
Tethering distance (cm)	1.1±0.1	1.3±0.1	0.044
Tethering area (cm^2)	1.8±0.2	2.8±0.4	0.047
Left ventricle end-diastolic volume (ml)	163.5±4.4	189.1±8.1	0.027
Left ventricle end-systolic volume (ml)	82.1±6.5	127.8±12.7	0.007
Systolic sphericity index	1.6±0.1	1.4±0.1	0.052
Diastolic sphericity index	1.5±0.2	1.4±0.0	0.145

Table 3. Correlations between QRS duration and echocardiographic parameters

Echocardiographic parameters	r	*p*
Left ventricular ejection fraction	-0.62	<0.001
Left atrium diameter	0.31	0.109
Mitral regurgitation index	0.39	0.011
Vena contracta	0.37	0.016
Effective regurgitant orifice	0.18	0.347
Mitral annulus	0.42	0.004
Tethering distance	0.43	0.005
Tethering area	0.44	0.003
Left ventricle end-systolic volume index	0.58	<0.0001
Left ventricle end-diastolic volume index	0.46	0.014
End-systolic sphericity index	-0.39	0.010
Systolic pulmonary artery pressure	0.23	0.129

Predictors of QRS widening in congestive heart failure (CHF) of ischemic etiology have been recently investigated. Functional MR is frequent among subjects with idiopathic dilated cardiomyopathy (IDC) and especially in patients with widened QRS. It is an independent predictor of death and CHF. In the setting of CHF, MR is the consequence of LV remodeling. Acute improvement after cardiac resynchronization therapy suggests that MR is in part due to intraventricular dyssynchrony that produces incomplete systolic valve closure.[12]

Barbieri et al.[13] studied the predictors of clinically relevant QRS widening in IDC. They observed that severe functional MR was a major determinant of electrical remodeling. They found that patients having severe MR at baseline showed more than 10% change in QRS duration during follow-up (10-33 months). They emphasized the role of severe MR in predicting electrical remodeling.

On physiological grounds, intraventricular delay is a determinant of functional MR, acting by prolonging isovolumic contraction time and interpapillary muscle activation time delay. Patients with CHF have chronically elevated filling pressures. In these patients, the energy of the regurgitant jet to the noncompliant left atrium further increases left atrial pressure and pulmonary pressure. The volume overload increases left ventricular wall stress. This causes subendocardial ischemia with further left ventricular dilatation, and hence conduction instability, which will ultimately contribute to ventricular dyssynhrony, leading to worsening heart failure. The association between QRS widening and other indicators of MR severity such as mean right atrial pressure, mean wedge pressure, and mean pulmonary artery pressure suggests the role of functional MR in the pathophysiology of electrical remodeling, whereas LVEF and cardiac output have less impact among patients with severe IDC. Cardiac resynchronization therapy eventually reduces duration and volume of functional MR, improves LV filling, and increases stroke volume.

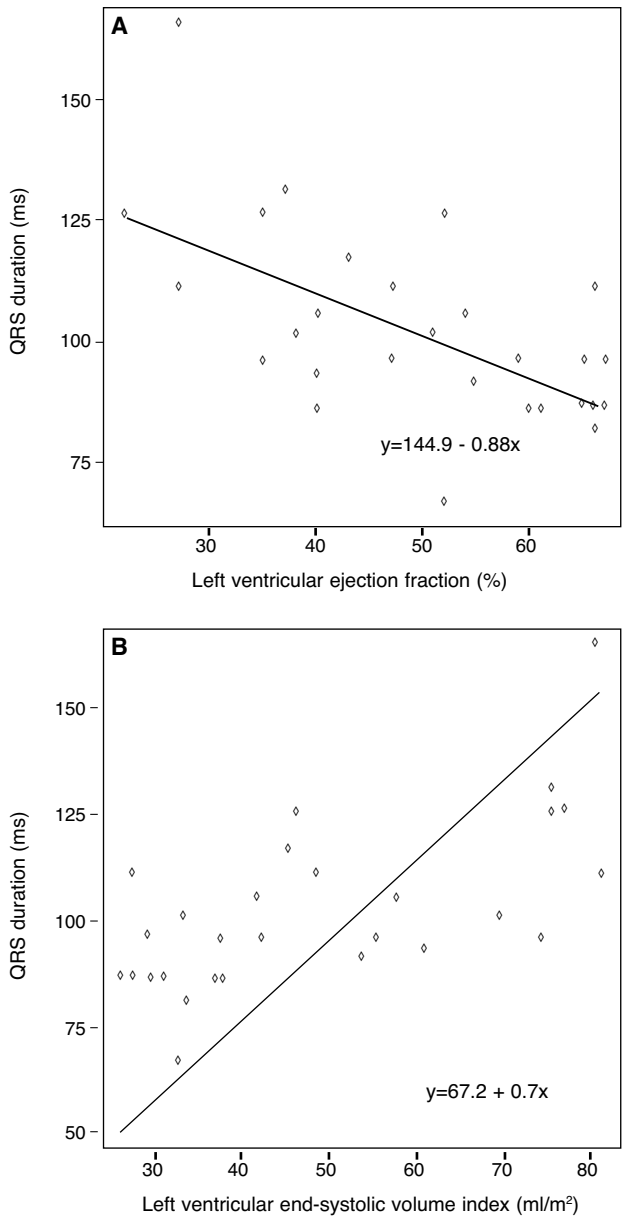

Figure 1. Correlaton between QRS duration and left ventricular **(A)** ejection fraction and **(B)** end-systolic volume index in patients with ischemic mitral regurgitation.

Longer QRS duration is associated with alterations in LV structure and function, and it has been shown that cardiac resynchronization therapy is effective in decreasing QRS duration and MR severity.[14]

The correlation between QRS duration and LV function has been studied in various patient populations. Yerra et al.[15] studied QRS duration and LV volumes and function in patients with acute myocardial infarction. They found that patients with longer QRS duration had higher LV end-diastolic and end-systolic volumes and lower LVEF. In another study, de Winter et al.[16] studied QRS duration and LV volumes and myocardial viability in patients with coronary artery disease and LV dysfunction. They also found increased LV volumes and decreased LVEF as well as decreased myocardial viability. In a study by Kruger et al.,[17] plasma brain natriuretic peptide levels and QRS duration were found to be the only independent predictors of LV systolic dysfunction assessed by LV end-systolic and end-diastolic volumes and LVEF. Similar to the aforementioned studies, we found significantly increased LV end-systolic and end-diastolic volumes and lower LVEF in patients with prolonged QRS duration (≥120 ms), suggesting that QRS duration is a marker of LV remodeling in patients with ischemic MR.

To our knowledge, this study is the first to investigate the relationship between echocardiographic parameters of mitral apparatus deformation and QRS duration and LV geometry. We found that the more the tethering distance and the area, the larger the mitral annulus, and the longer the QRS duration. We also found a weak correlation between systolic pulmonary artery pressure and QRS duration. In a recent study, van der Land et al.[18] studied patients with left bundle branch block (LBBB) with different stages of LV dysfunction and assessed the effect of LBBB on LV remodeling, MR, and mitral apparatus deformation by cardiac magnetic resonance imaging. It was found that LBBB was associated with functional MR and increased mitral tethering area regardless of QRS duration.

Sphericity index is a simple echocardiographic parameter reflecting the geometry of LV. The more closer it is to 1, the more sphere the LV is rather than being ellipsoid. In our study, we found that prolonged QRS duration was associated with a more spheric LV geometry.

Another important finding of our study is that LVEF is an independent predictor of QRS duration, which is consistent with findings of many studies assessing the relationship between LVEF and QRS duration in different patient groups.

However, we did not find any association between QRS duration and MR severity parameters such as MR color flow jet area, jet area/left atrial area, or effective regurgitant orifice. The *p* values were near to the statistical significance level. It would be better to validate these results with larger patient groups.

In this study, we demonstrated that LV functions and geometry as well as mitral deformation were better correlated with QRS duration rather than the presence of MR per se.

The main limitation to this study is that LV dyssynchrony was assessed by QRS duration in the surface ECG. Tissue Doppler and strain rate imaging would provide a more precise assessment of intraventricular dyssynchrony. Another limitation is the small size of the study group. Further studies with larger patient groups are needed to validate these results.

In conclusion, a simple electrocardiographic parameter, QRS duration, is closely correlated with LV systolic functions and geometry and mitral apparatus deformation in patients with ischemic mitral regurgitation, making QRS duration a reliable marker of LV remodeling which is associated with poor prognosis.

REFERENCES

1. Shenkman HJ, Pampati V, Khandelwal AK, McKinnon J, Nori D, Kaatz S, et al. Congestive heart failure and QRS duration: establishing prognosis study. Chest 2002;122:528-34.
2. Erlebacher JA, Barbarash S. Intraventricular conduction delay and functional mitral regurgitation. Am J Cardiol 2001;88:A7, 83-6.
3. Silvet H, Amin J, Padmanabhan S, Pai RG. Prognostic implications of increased QRS duration in patients with moderate and severe left ventricular systolic dysfunction. Am J Cardiol 2001;88: A6, 182-5.
4. Levine RA, Schwammenthal E. Ischemic mitral regurgitation on the threshold of a solution: from paradoxes to unifying concepts. Circulation 2005;112:745-58.
5. Soyama A, Kono T, Mishima T, Morita H, Ito T, Suwa M, et al. Intraventricular dyssynchrony may play a role in the development of mitral regurgitation in dilated cardiomyopathy. J Card Fail 2005;11:631-7.
6. 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 Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. J Am Soc Echocardiogr 1989;2:358-67.
7. Enriquez-Sarano M, Seward JB, Bailey KR, Tajik AJ. Effective regurgitant orifice area: a noninvasive Doppler development of an old hemodynamic concept. J Am Coll Cardiol 1994;23:443-51.

8. Borow KM, Lang RM, Neumann A, Carroll JD, Rajfer SI. Physiologic mechanisms governing hemodynamic responses to positive inotropic therapy in patients with dilated cardiomyopathy. Circulation 1988;77:625-37.
9. Boltwood CM, Tei C, Wong M, Shah PM. Quantitative echocardiography of the mitral complex in dilated cardiomyopathy: the mechanism of functional mitral regurgitation. Circulation 1983;68:498-508.
10. Shamim W, Francis DP, Yousufuddin M, Varney S, Pieopli MF, Anker SD, et al. Intraventricular conduction delay: a prognostic marker in chronic heart failure. Int J Cardiol 1999;70:171-8.
11. Rankin JS, Hickey MS, Smith LR, Muhlbaier L, Reves JG, Pryor DB, et al. Ischemic mitral regurgitation. Circulation 1989;79:I116-21.
12. Kanzaki H, Bazaz R, Schwartzman D, Dohi K, Sade LE, Gorcsan J 3rd. A mechanism for immediate reduction in mitral regurgitation after cardiac resynchronization therapy: insights from mechanical activation strain mapping. J Am Coll Cardiol 2004;44:1619-25.
13. Barbieri A, Grigioni F, Bursi F, Reggianini L, Bonatti S, Ricci C, et al. Role of severe functional mitral regurgitation in predicting electrical remodeling in idiopathic dilated cardiomyopathy. J Cardiovasc Med 2006;7:691-5.
14. Young JB, Abraham WT, Smith AL, Leon AR, Lieberman R, Wilkoff B, et al. Combined cardiac resynchronization and implantable cardioversion defibrillation in advanced chronic heart failure: the MIRACLE ICD Trial. JAMA 2003;289:2685-94.
15. Yerra L, Anavekar N, Skali H, Zelenkofske S, Velazquez E, McMurray J, et al. Association of QRS duration and outcomes after myocardial infarction: the VALIANT trial. Heart Rhythm 2006;3:313-6.
16. De Winter O, Van de Veire N, Van Heuverswijn F, Van Pottelberge G, Gillebert TC, De Sutter J. Relationship between QRS duration, left ventricular volumes and prevalence of nonviability in patients with coronary artery disease and severe left ventricular dysfunction. Eur J Heart Fail 2006;8:275-7.
17. Kruger S, Filzmaier K, Graf J, Kunz D, Stickel T, Hoffmann R, et al. QRS prolongation on surface ECG and brain natriuretic peptide as indicators of left ventricular systolic dysfunction. J Intern Med 2004; 255:206-12.
18. van der Land V, Germans T, van Dijk J, Zwanenburg JJ, Spreeuwenberg M, Marcus JT, et al. The effect of left bundle branch block on left ventricular remodeling, dyssynchrony and deformation of the mitral valve apparatus: an observational cardiovascular magnetic resonance imaging study. Int J Cardiovasc Imaging 2007;23:529-36.