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

İskemik mitral yetersizlikli hastalarda QRS süresi ekokardiyografik parametrelerle yakın olarak 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 (β=-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 fonksiyonlarının, geometrisini ve mitral aparat deформasyonunun gösteren ekokardiyografik parametrelerin QRS süresi ile ilişkili olduğu 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) alınmıştı. 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 grupa dağıtılmıştır.

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 etmektediydi. QRS süresi şu parametrelerde 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 anulus 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 süresinin etkilesen tek bağımsız değişkenin SV ejeksiyon fraksiyonu olduğu görüldü (β= -1.1, p=0.025).

Sonuç: İskemik MY’li hastalarda QRS süresi, SV sistolik fonksiyonları, geometrisi ve mitral aparat deformatasyonu ile yakından ilişkilidir bir parametredir.

Anchors sözcükler: Ekokardiyografi; elektrokardiyografi; kalp iletim sistemi; mitral kapağı yetersizliği; miyokard iskemisi; ventrikül disfonksiyonu, sol/tanı.
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 dysynchrony, as opposed to patients with a narrow QRS complex.\cite{1} Cardiac dyssynchrony results in a decrease in stroke volume, facilitation of mitral regurgitation, increased wall stress, and delayed relaxation.\cite{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.\cite{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.\cite{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.\cite{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.\cite{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.\cite{6} Left ventricular ejection fraction (LVEF) and volumes were measured by the biapical Simpson disk method.\cite{6}

Mitral regurgitation index was defined as MR color jet area/left atrium area. Systolic pulmonary artery pressure was estimated from the systolic tricuspid pressure gradient (in mmHg) using the simplified Bernoulli equation (ΔP=4V², 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.\cite{7}

Sphericity index was calculated as the ratio of LV length to width in the apical four-chamber view.\cite{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 anulus 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.\cite{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).

**DISCUSSION**

In this study we demonstrated that longer 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 ($B=-1.1$, SE: 0.67, $p=0.025$).

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

<table>
<thead>
<tr>
<th>Parameter</th>
<th>&lt;120 ms (n=19)</th>
<th>≥120 ms (n=10)</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral regurgitation degree</td>
<td>2.8±0.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td>45.9±2.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure (mmHg)</td>
<td>93.8±1.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (beat/min)</td>
<td>89.5±2.1</td>
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</tr>
</tbody>
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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 ($B=-1.1$, SE: 0.67, $p=0.025$).

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]
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 dyssynchrony, 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.

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.\textsuperscript{[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.\textsuperscript{[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.\textsuperscript{[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.\textsuperscript{[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 dysynchrony was assessed by QRS duration in the surface ECG. Tissue Doppler and strain rate imaging would provide a more precise assessment of intraventricular dysynchrony. 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**


