Relationship Between Asynchronous Myocardial Contraction and Left Ventricular Systolic and Diastolic Function

— Assessment Using the ECG-Gated Polar Map With 99mTc-Methoxy-Isobutyl Isonitrile —

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Background To quantitate the degree of 3-dimensional asynchronous myocardial contraction, an ECG-gated polar map method was developed with 99mTc-methoxy-isobutyl isonitrile, and used to investigate the relationship between asynchrony and left ventricular (LV) function.

Methods and Results Twelve normal subjects and 38 patients with an old myocardial infarction were studied with ECG-gated single-photon emission computed tomography (SPECT). In each frame, a myocardial perfusion polar map was reconstructed and the peak contraction phase in each pixel was displayed (phase map). The degree of asynchronous contraction was assessed from the standard deviations of the peak contraction phase (SDP) on the phase map. Ejection fraction (EF), peak ejection rate (PER), 1/3EF, peak filling rate (PFR) and 1/3 filling fraction (1/3FF) were calculated by the quantitative gated SPECT software, and E/A from Doppler echocardiography. The SDP was compared with these parameters. Correlation coefficients and p values between the SDP and parameters of cardiac function were as follows: EF, r=-0.69 (p<0.001); PER, r=-0.54 (p<0.001); 1/3EF, r=-0.57 (p<0.001); PFR, r=-0.29 (p<0.05); 1/3FF, r=-0.63 (p<0.001); E/A, r=-0.11 (p=0.51).

Conclusions There was a negative correlation between the SDP and LV systolic and diastolic function, which confirmed the functional significance of asynchrony on cardiac function. (Circ J 2005; 69: 183–187)

Key Words: Asynchrony; Diastolic function; Systolic function; Phase map; Polar map

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synchronous myocardial contraction occurs with myocardial disorders such as dilated cardiomyopathy, left bundle-branch block and ischemic heart disease, and is believed to decrease both systolic and diastolic cardiac function. However, there are few methods of quantitating the 3-dimensional (D) asynchronous myocardial contraction and the relationship between asynchrony and cardiac function has not been clarified quantitatively.

Left ventricular (LV) function has been evaluated clinically by echocardiography and by ECG-gated blood pool study and novel echocardiographic methods such as tissue Doppler imaging and ECG-gated single-photon emission computed tomography (SPECT) have been developed. In particular, quantitative gated SPECT software (QGS; Cedars-Sinai Medical Center, Los Angeles, CA, USA) enables evaluation of LV function by accurately determining the inner edge of the ventricle. However, we cannot use these methods to quantitate the 3-D heterogeneity of myocardial contraction, because the motion of the inner edge of the ventricle does not always concur with the regional wall thickening.

To evaluate asynchrony of regional myocardial contraction, we used 99mTc-methoxy-isobutyl isonitrile (MIBI) to construct an ECG-gated polar map and regional contraction curve based on the fact that the ventricular wall thickness correlated with the regional myocardial count. We then compared the results of QGS software and Doppler echocardiography in a patient with an old myocardial infarction (OMI) to test the hypothesis that asynchrony decreased cardiac function by disturbing the harmonic contraction and relaxation of the myocardium.

Methods

Patient Population

The study group comprised 12 normal subjects (11 males, one female, aged 64±10 years) and 38 patients with an OMI (ie, ≥3 months after onset; 34 males, 4 females, aged 67±9). Patients with arrhythmias, valvular heart disease, small ventricle (end-diastolic volume <50ml) and myocardial hypertrophy were excluded, as were patients with a complete perfusion defect.

Data Acquisition and Analysis

After injection of 1,000 MBq of 99mTc-MIBI, ECG-gated SPECT was performed using an L-shaped dual detector gamma camera (Optima NX; GE Medical Systems,
Milwaukee, WI, USA) with a low-energy, high-resolution collimator with a 64×64 matrix. Sixteen steps over a 90-degree acquisition of 50 beats for each projection was performed. The pixel size was 6.0 mm. After measuring the R–R interval, the length was divided into 12 frames. In each frame, after deciding the apical and basal site on the vertical long-axial image, a polar map formatted to 15×40 pixels (short-axial slices were reconstructed into 15 slices using linear interpolation) was reconstructed. The 15×40 pixels data from 12 serial polar maps were combined to obtain the time-course of regional count. The changes in the myocardial count during one cardiac cycle in each pixel was evaluated to construct a polar map of the peak contraction phase (ie, phase map) and the regional wall thickening curves. In the phase map, the frame number of the peak count was depicted by the array of a color bar. Further, the phase map was divided into 5 regions: apex (apical 3 slices), anterior, lateral, inferior and septal (4–12 slices were divided radially into 4 regions). The basal 3 slices were omitted from this calculation. Changes in the count (wall thickness) of each region were displayed with the volume curve of the left ventricle on the same figure (Fig 1). The regional count increase curve was represented by the fourth order harmonics of the Fourier series.

The peak count phase was regarded as the peak contraction phase because the regional myocardial counts correlates with wall thickness because of the partial volume effect. The mean phase and standard deviation of the peak contraction phase (SDP) were calculated as an index of asynchrony of myocardial contraction.

The QGS software was used for calculating the LV volume in each phase, and using that data, the volume curve of the left ventricle was calculated by fourth order harmonics of the Fourier series. Using the volume curve and its differential curve, parameters of LV function (ejection fraction (EF), peak ejection rate (PER) and 1/3 ejection fraction (1/3EF)) were calculated as the parameters of systolic function and the peak filling rate (PFR) and 1/3 filling fraction (1/3FF) as those of diastolic function. Those parameters were defined as follows and were compared with the SDP.

PER: peak dV/dt divided by the end-diastolic volume (EDV).
1/3EF: ejection fraction at one-third of the time to end-

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Table 1  Peak Contraction Phase (SDP) and Cardiac Function of Normal Subjects and Patients With an Old Myocardial Infarction (OMI)

<table>
<thead>
<tr>
<th></th>
<th>Normal group</th>
<th>OMI group</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>12</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>58±11</td>
<td>67±9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>SDP (frames)</td>
<td>0.71±0.26</td>
<td>1.15±0.40</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>EF (%)</td>
<td>59±7</td>
<td>52±11</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>PER (EDV/s)</td>
<td>2.53±0.51</td>
<td>2.40±0.63</td>
<td>NS</td>
</tr>
<tr>
<td>1/3EF (%)</td>
<td>26.6±5.1</td>
<td>23.9±6.7</td>
<td>NS</td>
</tr>
<tr>
<td>PFR (EDV/s)</td>
<td>1.78±0.39</td>
<td>1.70±0.49</td>
<td>NS</td>
</tr>
<tr>
<td>1/3FF (%)</td>
<td>28.5±8.9</td>
<td>19.8±7.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>E/A</td>
<td>0.84±0.40</td>
<td>0.74±0.24</td>
<td>NS</td>
</tr>
</tbody>
</table>

HR, heart rate; EF, ejection fraction; PER, peak ejection rate; EDV, end-diastolic volume; PFR, peak filling rate; FF, filling fraction; NS, not significant.
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Circulation Journal Vol.69, February 2005

systole divided by the stroke volume (SV).

PFR: peak -dV/dt divided by EDV.

1/3FF: filling fraction at one-third of diastole divided by SV.

Doppler Echocardiography
Doppler echocardiography was performed with a 2.5 MHz transducer (SSH-370A; Toshiba, Tokyo, Japan) as an evaluation of LV diastolic function. The E/A ratio was calculated by pulsed Doppler examination of mitral flow in the apical 2-chamber view, dividing the peak E-wave velocity by peak A-wave velocity.

Statistical Analysis
Values are expressed as means ± SD. Linear regression analysis was performed to determine the correlation coefficients between the distribution of the peak contraction phase and parameters that demonstrate cardiac function. Statistical significance of the correlation was determined using Pearson’s correlation coefficient test and p<0.05 was considered significant.

Results
The SDP and cardiac function of the normal subjects and patients with OMI are shown in Table 1. There were significant differences in heart rate (HR), SDP, EF and 1/3FF. The phase map and the changes in the regional count for a representative patient of each group are shown in Fig.1. With the map and the regional contraction curve, we could evaluate the extent and degree of dispersion of myocardial contraction and we confirmed that the volume curve of the left ventricle was a mirror image of the summation of regional myocardial contraction. In patients with MI, the phase of maximal myocardial contraction in the infarcted region was delayed compared with those of the non-infarcted region. On the other hand, the peak contraction phase existed for 1 or 2 frames in normal subject.

Fig 2. Relationship between the peak contraction phase (SDP) and the parameters of cardiac function. Scatter plots of SDP and (A) ejection fraction (EF), (B) peak ejection rate (PER), (C) 1/3EF, (D) E/A, (E) peak filling rate (PFR) and (E) 1/3 filling fraction (FF) are shown. There is a significant negative correlation between SDP and these parameters except for E/A.

Discussion
Asynchronous myocardial contraction has been observed in patients with OMI, cardiomyopathy1 Wolff-Parkinson-White syndrome12 and left bundle-blanch block2 and it has been suggested that asynchrony decreases cardiac function because resynchronization therapy by biventricular pacing improves cardiac function.13

To quantitate the asynchrony of myocardial contraction, we developed an ECG-gated polar map that focussed on the dispersion of the SDP by measuring the change in the regional myocardial count, and defined the degree of asynchrony as the standard deviation of the SDP. Furthermore, to clarify the relationship between the LV volume curve and regional myocardial contraction, these curves are displayed.
in the same figure.

In the curve analysis, we hypothesized that the contraction curves and the LV volume curve should be the mirror images. In normal subjects, the SDP of each region are concordant and these curves and the volume curve are symmetrical. In contrast, in patients with OMI, we observed a count increase, even in the infarcted region, except for the region showing complete perfusion defect, and observed a delay in the SDP in the infarcted region. In addition, in contrast to the contraction curves, a decrease in the early diastolic filling on the volume curve was also observed. Based on these findings, the regional SDP varied more than we expected, and the volume curve of the left ventricle was a mirror image of the summation of the wall thickening curves.

In the quantitative study, the SDP correlated inversely with the parameters of systolic function, such as EF, PER and 1/3EF, and with those of diastolic function, such as PFR and 1/3FF. These findings and the results of the curve analysis suggest that the regional delay of the SDP decreases systolic function because of a lack of harmonic myocardial contraction and a disturbance of reaching the minimal end-systolic volume, and also decreases diastolic function because the regional delayed contraction in the diastolic phase disturbs early ventricular filling and perhaps decreases myocardial relaxation by disturbing diastolic myocardial blood flow and metabolism.

Diastolic dysfunction has been mainly investigated in myocardial disorders and is suggested to be caused by abnormal calcium uptake of the sarcoplasmic reticulum and increased myocardial stiffness because of accumulation of collagen. Except for the myocardial dysfunction, the present findings suggest that dispersion of the contraction phase also decreased diastolic function.

Delayed myocardial contraction in the infarcted region is also observed by echocardiography as the so-called ‘tardokinesis’ although its mechanism has not been identified. One possible reason is prolongation of the action potential in the infarcted region, because dispersion of the QT interval, as an indicator of repolarization abnormality, increases during ischemia though no evidence has been found. Further experimental investigations are needed to clarify the mechanism.

In the present study, only the E/A, which is recognized as a parameter of diastolic function did not show a significant correlation with the SDP. One of the reasons is pseudonormalization of the E/A, which is a result of increased end-diastolic pressure of the left ventricle. In fact, a high E/A were observed in one of the present patient’s who had a dilated ventricle and low EF.

To evaluate cardiac function we performed echocardiography and ECG-gated SPECT; specifically, QGS software was used to detect the inner edge of the left ventricle. The accuracy of the LV volume calculated by the software was established by comparison with other modalities. In phase analysis, in contrast to evaluation of the change in the regional ventricular count, we assessed the change in the LV wall thickness by measuring the regional count per pixel based on the partial volume effect. A linear correlation between the regional count and wall thickness has been demonstrated by a phantom study in which the object size was 2-fold smaller than the spatial resolution (FWHM) of the SPECT image. As to the frame number, we performed 12-frame gating in this study because it has been reported that the EF calculated by 8-frame gating is smaller than 16-frame gating, and 16-frame gating requires more counts.

Using the data from the ECG-gated SPECT and our method, we were able to evaluate cardiac function in detail by separately evaluating ventricular volume, myocardial contraction and phase. We expect that our method will be useful for predicting the efficacy of resynchronization therapy, for evaluating diastolic heart failure and predicting lethal arrhythmia.

**Study Limitations**

First, there is the possibility that a pixel defined on a polar map shift to another site on the polar map in another frame because of the twisting and distortion caused by heterogeneous contraction. However, these phenomena would have influences the dispersion of the SDP because the area of the infarcted region was large enough to be compared with the distance of dislocation. Second, the spillover count from adjacent organs also influences the myocardial count and might reduce ventricular volume, but would not influence the phase analysis. Third, the HR of the OMI group was faster than that of the normal group, which might increase the SDP because the duration of each frame would be shorter. Thus, additional studies corrected with HR are needed.

**Conclusions**

We were able to assess the extent and degree of the phase delay of regional myocardial contraction using an ECG-gated polar map and regional contraction curve, which were calculated from the data by the usual ECG-gated SPECT without an additional procedure. Using this method we observed a negative correlation between the SDP and LV systolic and diastolic function, and confirmed the functional significance of asynchrony on cardiac function. Besides volumetrical analysis, the degree of asynchrony should also be assessed in the evaluation of cardiac function.

**References**

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