SEVERITY OF THE REGIONAL WALL MOTION AND ITS EFFECTS ON GLOBAL LEFT VENTRICULAR DIASTOLIC FILLING IN PATIENTS WITH SINGLE-VESSEL CORONARY ARTERY DISEASE AND PREVIOUS MYOCARDIAL INFARCTION: ASSESSMENT WITH RADIONUCLIDE VENTRICULOGRAPHY

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The severity of the regional wall motion and its effects on the global left ventricular diastolic filling were analyzed with use of radionuclide techniques in 19 patients with isolated disease of the left anterior descending coronary artery with previous myocardial infarction. Regional maximum inward movements in the noninfarcted lateral region occurred at a time close to the global end-systole, but occurred far beyond the global end-systole in the infarcted septal and apical regions, resulting in the occurrence of the regional asynchronous wall motion between the infarcted and noninfarcted regions after the global end-systole. A positive correlation between this end-systolic asynchronous wall motion and the asynchronous filling in early diastole was found \( r = 0.69, p < 0.001 \). A negative correlation between the asynchronous filling in early diastole and the global peak filling rate was also found \( r = -0.58, p < 0.01 \).

Thus, the end-systolic regional asynchronous wall motion causes the subsequent regional asynchronous filling in early diastole, which may cause impairment of the global left ventricular filling in patients with single-vesel coronary artery disease with previous myocardial infarction.

**Impaired** left ventricular (LV) diastolic filling, assessed by radionuclide ventriculography, has been reported in many patients under resting conditions with coronary artery disease in whom there is evidence of previous myocardial infarction\(^1\)–\(^3\) However, changes in regional LV function after myocardial infarction and the mechanism of the diastolic filling abnormalities have not been fully studied in these patients. With the development of computer technology and gated radionuclide ventriculography, quantitative assessment of regional LV function has become an established method for the non-invasive evaluation of regional LV performance\(^4\)–\(^7,11\)–\(^13,17\). In the present study, regional time-activity curves of the infarcted and noninfarcted regions were analyzed by methods validated in our laboratory.\(^5\) From 19 patients

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**Key Words:**
- Single-vessel disease
- Myocardial infarction
- Regional asynchrony
- Regional diastolic filling

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with isolated disease of the left anterior descending coronary artery with previous transmural myocardial infarction, results were compared with those obtained previously from normal subjects.\textsuperscript{5}

The purposes of our study were to investigate the severity of the regional wall motion abnormalities and their effects on global LV diastolic filling, and to clarify the relationship between the regional LV asynchrony and global LV diastolic filling under resting conditions in patients with single-vessel coronary artery disease with previous transmural myocardial infarction.

**Patient Sample**

We studied 19 patients (17 men and two women, age range 35 to 67 years old, mean 53 ± 9 (± SD) years old) referred to the Yamaguchi University Hospital between 1981 and 1983. All had evidence of previous transmural myocardial infarction diagnosed by typical chest pain, typical rise and fall of the serum creatine kinase level, serial electrocardiographic changes, and resting images of thallium myocardial scintigraphy. The patients underwent diagnostic cardiac catheterization and electrocardiographically gated radionuclide ventriculography at least two months after the onset of typical chest pain. They had severe organic stenosis (\( \geq 75\% \) luminal diameter) of only the proximal left anterior descending branch. In 16 of the 19 patients, the luminal diameter was reduced by at least 80%. No patient had any other associated cardiac abnormality since those with additional coronary lesions had been excluded from the study. The tracer uptake defects seen on the resting myocardial images obtained with thallium-201 were in the anteropical or/and septal LV wall and there were no defects in other areas. Redistribution of thallium-201 in the infarcted areas was not present in any of the patients. There were functional collaterals to the involved vessel in 11 of the 19 patients. Radionuclide ventriculographic studies were performed at least 72 hours after treatment with calcium antagonists or beta-blockers had been stopped and at least 12 hours after treatment with nitrates was stopped. The test was performed during the 14 days before or after cardiac catheterization. All patients were in normal sinus rhythm and they had no conduction disturbances. Informed consent was obtained prior to the study.

Radionuclide ventriculographic results from 19 patients with previous myocardial infarction were compared with those obtained previously from 15 normal subjects (control group).\textsuperscript{5}

\begin{table}
\centering
\caption{CLINICAL AND HEMODYNAMIC DATA}
\begin{tabular}{lcccc}
\hline
 & \textit{N (n = 15)} & \textit{OMI (n = 19)} & \multicolumn{2}{c}{\textit{p value}} \\
\hline
Age (yr) & 50 ± 13 & 53 ± 9 & & NS \\
Heart rate (beats/min) & 72 ± 9 & 71 ± 11 & & NS \\
BSA (m\textsuperscript{2}) & 1.60 ± 0.14 & 1.66 ± 0.13 & & NS \\
EDV (ml) & 126 ± 19 & 154 ± 25 & & < 0.001 \\
ESV (ml) & 49 ± 9 & 83 ± 18 & & < 0.001 \\
SV (ml) & 72 ± 17 & 67 ± 15 & & NS \\
EF (%) & 61 ± 4 & 46 ± 9 & & < 0.001 \\
LVESP (mmHg) & 135 ± 14 & 134 ± 18 & & NS \\
LVEDP (mmHg) & 10 ± 4 & 11 ± 3 & & NS \\
Mean AO (mmHg) & 101 ± 9 & 100 ± 13 & & NS \\
\hline
\end{tabular}
\end{table}

Values are mean ± SD.

BSA = body surface area; EDV = end-diastolic volume; ESV = end-systolic volume; SV = stroke volume; EF = ejection fraction; LVESP = end-systolic pressure of LV; LVEDP = end-diastolic pressure of LV; Mean AO = mean aortic pressure; \( N \) = control subjects; OMI = patients with single-vessel disease with previous myocardial infarction.

The data obtained from the control subjects (\( N \)) have been reported previously.\textsuperscript{5}

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control subjects, aged 20 to 64 years (mean 50 ± 13 years old), underwent cardiac catheterization for the evaluation of atypical chest pain. They had normal left ventriculograms and coronary arteriograms and normal values for hemodynamic variables at rest and during a supine bicycle exercise test or ergonovine maleate test. There were no significant differences between the control group and the myocardial infarction group in mean age and mean resting heart rate (Table I).

Gated Radionuclide Ventriculography

Multi-gated equilibrium blood pool imaging was performed with a conventional gamma camera (PHO/GAMMA LFOV, Searle Inc., Des Plaines, IL) equipped with a high-resolution all-purpose parallel-hole collimator. The technique used in this study has been described in detail elsewhere. Briefly, all patients were given 15 to 20 mCi i.v. 99m-technetium-labeled human serum albumin. After the radionuclide had equilibrated with the intravascular space (about 10 min), the camera was positioned in the modified left anterior oblique projection (15 degrees caudal tilt). In all studies, low-count (500,000 counts) scintigrams were acquired with a digital computer (Scintview, Searle Inc.) until the camera obliquity that showed the greatest separation of the right and left ventricles was found (typically a 40 to 60 degree projection). Then, counts were acquired during 600 beats in a multiple-gated mode (framing rate up to 31 frames/cardiac cycle) on a magnetic disc with a digital computer (SCINTIPAC-1200, Shimadzu Seisakusho, Kyoto, Japan). These photo-events falling within a 20% window centered on the photoprobe of technetium-99m were recorded.

The original multiple-gated mode data were collected on a magnetic disc with a computer with 64 x 64 matrix. Each 30 to 40 msec frame contained more than 30,000 counts within the LV in the end-diastolic frame in patients with normal heart sizes. A LV longitudinal axis
Effects of the Regional Wall Motion on LV Filling

Fig. 1. The first-derivative curves derived from a control subject. GLB = global LV; SEP = septal region; LAT = lateral region; AX = apical region; ΔES = time difference from the end-systole in global LV to that in each of the three regions; TPFR = time to peak filling rate; PFR = normalized peak filling rate; Δt = time difference from the peak filling rate in global LV to that in each of the three regions; ST = systolic time; DT = diastolic time

Fig. 2. The positive correlation between the ΣΔES/systolic time and the total Δt/diastolic time suggests that the early diastolic asynchronous filling may be increased with progressive increase in the asynchronous regional wall motion beyond the global end-systole.

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connecting the midpoint of the base and apex was rotated parallel to the y-coordinate of the digital matrix and the heart was oriented vertically on the end-diastolic image. The first frame was defined as the end-diastolic frame. The end-systolic frame was defined as the frame with the minimum counts within the end-diastolic perimeter of the LV. Crescent-shaped global and regional background regions of interest were traced manually with an electronic cursor along the lateral, apical, and septal portions adjacent to and outside the LV end-systolic perimeter applied to the end-systolic frame, specifically avoiding regions of high-count activity. A computer program determined a geometric center of the area of the end-diastolic perimeter of the LV. Then, the computer program subdivided the end-diastolic perimeter of the LV into four regions (basal, septal, apical, and lateral), with two intersecting lines at an angle of 45 degrees to the longitudinal axis of the LV at the geometric center of the area. The background
correction for the four regions and the global LV was estimated with an average count per cell in each of the four background regions of interest obtained in the end-systolic frame. Background-corrected global and regional time-activity curves were generated from the global LV and each of three regions (septal, apical, and lateral) after three-point temporal smoothing using a fixed region of interest method. First-derivative curves (dV/dt) of these time-activity curves (V) were computed in each region and the global LV⁵ (Fig. 1). Since the basal region of the LV tended to overlie the regions of the mitral and aortic valves, left atrium, and great vessels, this region was excluded from study.

The following indices were obtained from the time-activity and the first-derivative curves in the global LV and in each of the three regions (septal, apical, and lateral) (Fig. 1).

Systolic Phase Indices (1) Ejection fraction (%) = 100 x (EDV – ESV) / (EDV – BG), where EDV, ESV, and BG were end-diastolic, end-

Fig. 3. Global normalized peak filling rate is reduced with progressive increase in the total Δt/diastolic time.

Fig. 4. Typical global and regional time-activity curves taken from a patient with isolated disease of the left anterior descending coronary artery with previous myocardial infarction, in which end-diastolic counts were expressed as 100% and minimum counts as 0%. As shown in this figure, regional LV ejections in the infarcted septal (SEP) and apical (AX) regions were delayed and ceased far beyond the global end-systole, during which period the noninfarcted lateral region (LAT) had begun to relax. GLB = global LV. The abscissa indicates the frame number.
systolic, and background counts, respectively. (2) $\Delta ES/\text{systolic time} = \text{to allow comparison of the time interval (}\Delta ES\text{) between global and regional end-systole (minimum counts on the time-activity curve), the relative value of the time interval was normalized to systolic time, the time from the R wave to the global end-systole. When regional end-systole occurred before global end-systole, this relative value was negative, and when regional end-systole occurred after global end-systole, this relative value was positive.}$

Diastolic Phase Indices: (1) Normalized peak filling rate (EDV/sec) = peak filling rate normalized to end-diastolic counts. (2) Time to peak filling rate/diastolic time = the time interval between the global end-systole and the peak positive dV/dt normalized to diastolic time (R-R interval minus global systolic time).$

Indices of Regional Asynchrony: (1) $\Sigma |\Delta ES/\text{systolic time}| = \text{sum of the absolute values of the}\Delta ES/\text{systolic time. This parameter is a quantification of the regional asynchrony at the global end-systole.}$ (2) Total $\Delta t/\text{diastolic time} = \text{sum of the absolute values of the normalized time differences} (\Delta t/\text{diastolic time}) \text{from the peak positive dV/dt in the global LV to that in each of the three regions.}$ This parameter is a quantification of the asynchronous filling in early diastole. Regional asynchrony is considered to increase with the increase in the values of the $\Sigma |\Delta ES/\text{systolic time}|$ or total $\Delta t/\text{diastolic time}$. 

Reproducibility of Radionuclide Technique

The reproducibility of radionuclide ventriculographic variables obtained in this study in measuring LV systolic or diastolic function has been reported and validated previously in patients with and without regional wall motion abnormalities.

Angiographic Study

Hemodynamic data were obtained during cardiac catheterization. Coronary angiographic examinations were performed by the Sones method. A Millar catheter-tip micromanometer was used for pressure measurement and cineangiography.

Statistical Analysis

The data are presented as mean $\pm$ SD. The lower and upper limits of the normal values were defined as the mean $\pm$ 2SDs determined previously in 15 control subjects. Statistical analysis was performed with the t-test for unpaired data. The level of statistical significance was $p < 0.05$.

Results

Clinical and hemodynamic parameters are listed in Table I and radionuclide parameters are listed in Table II. The values of these variables in 15 control subjects (control group) have been reported previously and are also presented in Tables I and II.

In the myocardial infarction group, global LV ejection fractions ranged from 29% to 54% and were reduced significantly compared with those of the control group. Regional LV ejection fractions were reduced not only in the infarcted septal and apical regions but also in the noninfarcted lateral region (Table II). Of the 19 patients in the myocardial infarction group, ejection fractions were outside the lower normal limits (<2SDs: global LV; 47%, septal; 54%, apical; 65%, lateral; 56%) in 15 patients (79%) in the global LV, 15 patients (79%) in the septal region, 16 patients (84%) in the apical region, and in 4 patients (21%) in the lateral region.

Maximum inward movement in the infarcted regions occurred significantly later than the global end-systole, so that the relative values of the $\Delta ES/\text{systolic time}$ in the myocardial infarction group were significantly greater in the septal and apical regions. There were no significant differences in this value between the control group and the myocardial infarction group in the noninfarcted lateral region (Table II). The relative values of the $\Delta ES/\text{systolic time}$ were outside the upper normal limits ($>2SDs$: septal; 0.06, apical; 0.05, lateral; 0.08) in 17 patients (89%) in the septal region and 14 patients (74%) in the apical region. Only four patients (21%) had abnormal values in the lateral region. Thus, $\Sigma |\Delta ES/\text{systolic time}|$, sum of the absolute values of the $\Delta ES/\text{systolic time}$, was significantly greater and was outside the upper normal limits ($>2SDs$; 0.17) in 17 patients (89%) in the myocardial infarction group (Table II).

Normalized peak filling rates in the myocardial infarction group were significantly lower in the global LV and in the infarcted septal and apical regions (Table II). These values were outside the lower normal limits (<2SDs: global LV; 2.2, septal; 2.2, apical; 2.4, lateral; 2.8 EDV/sec) in 12 patients (63%) in the global LV, 8 patients (42%) in the septal region, and in 11 patients (58%) in the apical region. A somewhat unexpected finding of the present study was that there was also a significant decrease in this
value in the noninfarcted lateral region and five patients (26%) of the 19 patients had a markedly decreased normalized peak filling rate (Table II).

The ratios of time to peak filling rate/diastolic time were significantly greater in the myocardial infarction group in the global LV and in the infarcted septal and apical regions. There were no significant differences in this ratio in the noninfarcted lateral region (Table II). These ratios were outside the upper normal limits (> 2SDs: global LV: 0.42, septal: 0.45, apical: 0.43, lateral: 0.38) in 6 patients (32%) in the global LV, 6 patients (32%) in the septal region, 7 patients (37%) in the apical region, and in one patient (5%) in the lateral region.

Total Δt/diastolic time in the myocardial infarction group was significantly greater than that in the control group (Table II), and was outside the upper normal limits (> 2SDs: 0.17) in 13 patients (68%).

A positive correlation was found between the ∑ΔES/systolic time and the total Δt/diastolic time (r = 0.69, p < 0.001) in the myocardial infarction group (Fig. 2). A negative correlation was also found between the global normalized peak filling rate and the total Δt/diastolic time (r = -0.58, p < 0.01) (Fig. 3).

Discussion

In this study, we used quantitative radionuclide techniques that are subject to a variety of potential errors. One of the major difficulties in analyzing regional time-activity curves in patients with hypokinesia, akinesia, or dyskinesia of the LV wall motion is the regional background correction. When regional time-activity curves were generated in these patients, crescent-shaped global and regional background regions of interest were traced manually along the lateral, apical and septal portions adjacent to and outside the LV end-systolic perimeter applied to the end-systolic frame, specifically avoiding high-count activity. This method is somewhat different from our previous method used in the control group or angina pectoris group in which the background regions of interest were traced along the lateral, apical and septal portions adjacent to and inside the LV end-diastolic perimeter applied to the end-systolic frame. In our method used in this study, there is an artificial limitation placed on their definition of end-systole by requiring the systolic area of interest to be within the end-diastolic perimeter of the LV. Since the background uncertainty is a principle determinant of the error involved in the fixed region of interest method, the regional background uncertainty in this study may be a critical variable. However, the percentages of the background counts per cell of the average global or regional regions of interest, obtained by this method, were as follows: global LV, 65 ± 4%; septal region, 75 ± 6%; apical region, 64 ± 8%; lateral region, 62 ± 4%. The values of the percent background in the global LV or in the infarcted septal and apical regions were slightly greater but not significantly different from the normal values determined previously in 15 control subjects. There was also no significant difference in this value between the control group and the infarction group in the noninfarcted lateral region.

Another difficulty in assessing regional wall movement in patients with regional wall motion abnormalities is the fixing of a reference point to which wall movement can be related. This has been discussed in earlier reports in which similar methods were used and will not be reviewed in detail here.

The present study demonstrated that regional asynchrony in early diastole was prominent in patients with previous myocardial infarction. This suggests that there was a progressive increase in the diastolic asynchrony in patients with severe manifestations of regional wall motion abnormalities of the LV. Our results confirm the earlier report of Holman et al. that there is progressively increasing regional asynchrony in patients with increasing severity of coronary artery disease. In the present study, when myocardial infarction developed, regional asynchronous filling became more severe in early diastole. Figure 4 shows typical global and regional time-activity curves obtained in a patient with single-vessel disease of the left anterior descending coronary artery with previous myocardial infarction. As shown in this figure, regional ventricular maximum inward movements in the infarcted septal and apical regions were delayed and ceased far beyond the global end-systole, during which period the noninfarcted lateral region had begun to relax. Similar radionuclide time-activity curves demonstrating the effects of regional systolic asynchrony on global LV relaxation and filling have been reported by Green et al. after coronary artery ligation in dogs. This delayed emptying in the affected regions does not contribute to the effective

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forward flow, since there is little to no change in global LV counts. In this figure, from frame 11 until frame 18, there is filling of the lateral region and emptying of the apical and septal regions and there is little change in global LV counts. This indicates that there is redistribution of blood in the LV during this period which probably corresponds to the isovolumic relaxation period, although our data give no support to this since the points of the aortic valve closure and the mitral valve opening could not be determined on the time-activity curves. The mechanism of this asynchronous regional wall motion beyond global end-systole and the redistribution of blood in the LV is unclear. One of possible explanations is that this event occurs during rapid pressure fall of the LV and is associated with the outward movement of the noninfarcted region, which may allow the infarcted regions to move passively in the inward direction. Another possible explanation is that the outward movement of the noninfarcted region may offset the abnormal inward movements of the affected regions to maintain the isovolumic status of the LV.\textsuperscript{14,15}

An unexpected finding of our present study was the demonstration of the depressed ejection fraction and the depressed normalized peak filling rate in the noninfarcted lateral region in the myocardial infarction group (Table II). There could be several possible explanations for this decreased function in the noninfarcted lateral region in the myocardial infarction group. First, the subdivision of the LV into smaller regions of interest was performed automatically by a computer program. This clearly did not take into consideration individual differences in LV anatomy, rotation, or magnitude of infarcted myocardium among patients. In some patients, there may be considerable overlap of the previously infarcted myocardium into the lateral region of interest. This would account for the significant reduction in ejection fraction and normalized peak filling rate in this lateral region in the myocardial infarction group. Similar findings that systolic function in noninfarcted regions was abnormal in patients with previous myocardial infarction and the several possible explanations for this depressed systolic function have been reported by other investigators.\textsuperscript{5–10} Second, the normalized peak filling rate is directly related to ejection fraction\textsuperscript{1} so that the abnormal normalized peak filling rate in the noninfarcted lateral region may be associated with a significant reduction in ejection fraction in that same region. Third, when the peak filling rate is normalized to end-diastolic counts, the enlarged LV, which was found in the myocardial infarction group (Table I), may appear to decrease the normalized peak filling rate.\textsuperscript{16} Hence, the enlarged lateral region of the LV may also appear to decrease the normalized peak filling rate in this region.

A positive correlation between the \(\Sigma(\Delta ES/\text{systolic time})\), a quantification of the asynchronous end-systolic wall motion, and the total \(\Delta t/\text{diastolic time}\), a quantification of the asynchronous filling in early diastole, suggests that the regional asynchronous filling may be increased with progressive increase in the asynchronous regional wall motion beyond the global end-systole (Fig. 2). A negative correlation between the total \(\Delta t/\text{diastolic time}\) and the global normalized peak filling rate, which had been reported previously in patients with single-vessel disease without previous myocardial infarction\textsuperscript{5} was also found in the myocardial infarction group (Fig. 3). This would indicate that the global peak filling rate is reduced with progressive increase in the asynchronous early diastolic filling\textsuperscript{5,12} Bonow et al.,\textsuperscript{1} using gated radionuclide ventriculography, also investigated the relationship between the regional systolic and diastolic function in patients with hypertrophic cardiomyopathy, and found that impaired global LV filling might result, in part, from nonuniformity of the systolic function.

Thus, in patients with single-vessel disease with previous myocardial infarction, asynchronous wall motion occurs between the infarcted and noninfarcted regions beyond the global end-systole, mainly due to the delay of the maximum inward movement in the infarcted regions. Such a regional end-systolic asynchronous wall motion increases asynchronous filling in early diastole, which may result in subsequent impairment of the filling of the global LV.

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