Deceleration Time in Ischemic Cardiomyopathy
Relation to Echocardiographic and Scintigraphic Indices of Myocardial Viability and Functional Recovery After Revascularization

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**Background**—In patients with heart failure secondary to left ventricular (LV) systolic dysfunction, a short deceleration time (DT) successfully predicts clinical outcome. The impact of myocardial viability and revascularization on the mitral inflow velocities, however, is unknown.

**Methods and Results**—Forty patients with ischemic cardiomyopathy underwent 201Tl scintigraphy (SPECT) and 2D, Doppler, and dobutamine echocardiography (DE, to 40 μg·kg⁻¹·min⁻¹) 2 days before CABG. Echocardiography was repeated 3 months after revascularization to determine recovery of function. Significant correlations were present between DT and LV contractile reserve by DE (r=0.72), scar perfusion defect by SPECT (r=0.69), and the change in ejection fraction (ΔEF) after surgery (r=0.77) (all P<0.01). DT >150 ms effectively identified (sensitivity 79%, specificity 81%) patients with ΔEF ≥5%. The population was divided into 2 groups according to DT: group 1 (DT >150 ms, n=21) and group 2 (DT ≤150 ms, n=19). At baseline, NYHA class, LV EF, age, and use of cardiovascular drugs were similar between the 2 groups. The number of viable segments by both DE and SPECT, however, was higher in group 1 (both P<0.01), and only patients in group 1 had an increase in EF (29±4.8% to 40±8%, P<0.01) after surgery. Death and heart transplantation occurred in 7 patients from group 2 and 1 patient from group 1 (P=0.017).

**Conclusions**—In patients with ischemic cardiomyopathy, the reduced amount of viable myocardium results in a restrictive mitral inflow pattern, which in turn predicts poor survival. (Circulation. 2001;103:1232-1237.)

**Key Words:** echocardiography  ■  scintigraphy  ■  cardiomyopathy  ■  hibernation  ■  diastole

**Methods**
The Baylor College of Medicine Institutional Review Board approved the investigation, and all patients provided written, informed consent before their participation. The study population was composed of 40 patients with LV systolic dysfunction secondary to IC who were scheduled to undergo CABG. None of the patients had evidence of an acute coronary syndrome, valvular heart disease, or primary cardiomyopathy, and all had moderate to severe LV systolic dysfunction at rest.

**Echocardiographic Studies**
Echocardiographic studies were performed with either a Hewlett-Packard (5500) or an Acuson (Sequoia) ultrasound system an average of 2 days before revascularization. All patients were able to lie supine without dyspnea and were imaged in a left lateral position. Standard parasternal and apical views were acquired first, and mitral inflow was recorded by pulse Doppler in the apical 4-chamber view, with the sample volume positioned at the valve tips.3 Dobutamine infusion (DE) was initiated at a dose of 2.5 μg·kg⁻¹·min⁻¹ and advanced at 3-minute intervals to 5, 7.5, 10, 20, 30, and 40 μg·kg⁻¹·min⁻¹.8 Continuous monitoring of ECG and blood pressure was performed throughout the infusion. Images were recorded on both

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videotape and digital format for later analysis. Three months after surgery, the patients’ LV systolic function and mitral inflow velocities were reevaluated with a resting echocardiographic study.

Echocardiographic Analysis

Analysis was performed by 2 observers blinded to the clinical, scintigraphic, and each other’s data. Observer A (Y.Y.) measured only the following parameters: mitral inflow peak E velocity, peak filling velocity at atrial contraction (A velocity), E/A ratio, acceleration time and DT of peak E velocity, isovolumic relaxation time (IVRT), A duration, and the atrial filling fraction (AFF). Measurements were made in 3 cardiac cycles and averaged by previously reported techniques.7 Observer B (S.F.N.), who was unaware of the Doppler data and sequence of studies, interpreted the 2D echocardiogram. LV ejection fraction (EF) was calculated with the multiple disk method9 at baseline, during DE (at 10 μg · kg⁻¹ · min⁻¹), and 3 months after surgery. The numbers of viable and nonviable segments were derived from the response to dobutamine. Segments with any response were considered viable, including segments with a biphasic, sustained, and ischemic response.8 We recently observed10 that segments defined as viable by the above criteria have significantly less interstitial fibrosis (2% to 3%) than segments without any contractile response to dobutamine (28%). LV contractile reserve was computed as the difference between the highest EF measured during low-dose DE and that at baseline.

SPECT Myocardial Scintigraphy

Rest-redistribution ⁹⁹mTc scintigraphy (single photon emission CT, SPECT) was performed as previously reported from our laboratory.10 A large-field-of-view rotating gamma camera with a high-resolution parallel-hole collimator was used. Thirty-two frames were acquired over a 180° arc. The images were reconstructed with a filtered back-projection algorithm and a Butterworth filter with a cutoff frequency of 0.5 Nyquist and an order of 5. Reconstructed tomograms were reoriented in the standard short, horizontal long, and vertical long axes for interpretation and quantification. Experienced nuclear cardiologists who had no knowledge of any other patient data quantified SPECT images. Defect size was derived by the polar map method. The raw polar maps for each patient were statistically compared with a corresponding normal data bank to determine the perfusion defect size. Segments with a maximal uptake (rest or redistribution) of ≥60% were considered viable.10

Statistical Analysis

Unpaired Student’s t or χ² tests were used to compare the clinical, echocardiographic, and scintigraphic data between the 2 groups of patients as divided by DT. Paired t testing was applied to compare the changes in EF and mitral velocities after revascularization in each group. The 3 groups of patients divided by baseline DT and change in EF (ΔEF) after surgery were compared by ANOVA and Bonferroni-corrected t tests for pairwise comparisons. Regression analysis was used to relate DT to both DE and SPECT indices of viability, ΔEF, and duration of stay in the intensive care unit (ICU). Significance was set at a value of P<0.05.

Results

All 40 patients had symptoms of heart failure before surgery, and the majority complained of angina (62%). Before the baseline echocardiographic study and after clinical evaluation, attempts were made to maximize cardiac medications, and doses were advanced as tolerated. Typical medication regimens included ACE inhibitors (captopril, average daily dose 90 mg; lisinopril, 20 mg), nitrates (isosorbide dinitrate 90 mg), diuretics (furosemide 80 mg, metolazone 2.5 mg), β-blockers (metoprolol 75 mg), and digoxin (0.25 mg).

Relation of Mitral Inflow Pattern to DE Indices of Viability

Significant correlations were observed between DT and LV contractile reserve (r=0.72, r²=0.52, P<0.01; Figure 1, left) and the number of viable segments (r=0.84, r²=0.71, P<0.01; Figure 1, right). Other Doppler parameters with significant correlation to LV contractile reserve included IVRT, r=0.46; AFF, r=0.5; and the E/A ratio, r=−0.58 (all P<0.01). The number of viable segments by DE was also related to IVRT (r=0.5, P<0.01), AFF (r=0.44, P<0.01), and E/A ratio (r=−0.58, P<0.01). The mitral inflow pattern (DT >150 ms) was similar in patients in whom ≥50% of the segments showed a biphasic or ischemic or sustained response (P>0.1).

Relation of Mitral Inflow Pattern to SPECT Indices of Viability

Significant correlations were observed between DT and the perfusion defect size by SPECT (total defect, r=−0.5; % scar, r=−0.69; both P<0.01) (Figure 2, right). Furthermore, a direct relation was noted between the number of viable segments by SPECT and DT (r=0.76, P<0.01; Figure 2, left). Other Doppler parameters likewise had significant relations with SPECT indices of viability (number of viable segments by SPECT versus AFF, r=0.45; IVRT, r=0.4; and E/A ratio, r=−0.5; P<0.05). DT was >150 ms in patients with ≥50% of segments having ≥50% or ≥60% thallium uptake (P>0.1) but was ≤150 ms in patients in whom ≥50% of the segments had thallium uptake <50% (P=0.03).
Relation of Functional Recovery to the Mitral Inflow Pattern, DE, and SPECT Indices of Viability

Significant relations were also observed between ΔEF at 3 months and DT as well as the number of viable segments by both DE and SPECT (r=0.77, r=0.83, r=0.82, respectively, all P<0.01; Figure 3). With a receiver operating characteristic curve, a DT >150 ms provided the best separation of patients with a ΔEF >5% and <5% (sensitivity 79%, specificity 81%).

Several models were constructed to predict ΔEF after revascularization by DT and echocardiographic and scintigraphic indices of myocardial viability. These variables in different combinations accounted for 71% to 77% of the variance in the ΔEF (number of viable segments by DE and DT accounted for 71%, r=0.84; number of viable segments by SPECT and DT accounted for 72%, r=0.85; and number of viable segments by DE plus number of viable segments by SPECT accounted for 77%, r=0.88).

Patient Groups and Clinical Outcome

Subsequently, we divided the patient cohort into 2 groups based on DT: group 1, DT >150 ms and group 2, DT ≤150 ms. At baseline, age, NYHA class, LVEF, heart rate, and cardiac medications were similar in both groups (Table 1). By design, the 2 groups differed significantly in all parameters derived from the mitral inflow velocity. Group 2 patients had a higher E/A ratio, a shorter DT, and a lower AFF than group 1 patients (Table 2). Importantly, DE indices of viability were different between the 2 groups; group 1 patients had a significantly higher contractile reserve and a greater number of viable segments than did group 2 patients (both P<0.001). Likewise, the total defect size by SPECT (P=0.015) and the scar percentage (P=0.002) were larger in group 2. At follow-up 3 months later, LVEF by echocardiography increased significantly in group 1 (29±4.8 to 40±8, P<0.001) yet remained unchanged in group 2 (27±8.6 to 27±10, P=0.42).

The clinical course also differed remarkably in the 2 groups (Table 3). Group 1 patients had a shorter ICU stay, fewer admissions for exacerbation of heart failure, and lower use of diuretics after surgery (all P<0.05). At 1 year, of the 19 patients with a DT ≤150 ms, 3 had died of progressive heart failure, 1 had died of sudden death, and 3 had undergone heart transplantation. Among the 21 patients with a DT >150 ms, only 1 died of sepsis (P=0.017). In the 40 patients

TABLE 1. Baseline Clinical Characteristics of the Patient Population

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (21 Patients) DT &gt;150 ms</th>
<th>Group 2 (19 Patients) DT ≤150 ms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>64±9</td>
<td>62±11</td>
</tr>
<tr>
<td>Men/women</td>
<td>14/7</td>
<td>15/4</td>
</tr>
<tr>
<td>NYHA class</td>
<td>2.2±0.7</td>
<td>2.6±1</td>
</tr>
<tr>
<td>Angina</td>
<td>13/21 (62)</td>
<td>12/19 (63)</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>29±4.8</td>
<td>27±8.6</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>13/21 (62)</td>
<td>12/19 (63)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>15/21 (71)</td>
<td>15/19 (79)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>7/21 (33)</td>
<td>6/19 (32)</td>
</tr>
<tr>
<td>Smoking</td>
<td>9/21 (43)</td>
<td>9/19 (47)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>16/21 (76)</td>
<td>14/19 (74)</td>
</tr>
<tr>
<td>Positive family history</td>
<td>5/21 (24)</td>
<td>5/19 (26)</td>
</tr>
<tr>
<td>Cardiovascular drugs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>21/21 (100)</td>
<td>18/19 (95)</td>
</tr>
<tr>
<td>Nitrates</td>
<td>19/21 (91)</td>
<td>16/19 (84)</td>
</tr>
<tr>
<td>β-Blockers</td>
<td>7/21 (33)</td>
<td>6/19 (32)</td>
</tr>
<tr>
<td>Digoxin</td>
<td>6/21 (29)</td>
<td>6/19 (32)</td>
</tr>
<tr>
<td>Diuretics</td>
<td>13/21 (62)</td>
<td>13/19 (68)</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>14/21 (67)</td>
<td>13/19 (68)</td>
</tr>
<tr>
<td>Calcium blockers</td>
<td>4/21 (19)</td>
<td>3/19 (16)</td>
</tr>
</tbody>
</table>

Values are n (%) except as noted. There were no statistically significant differences between the 2 groups.
TABLE 3. Clinical Outcomes of the Patient Population

<table>
<thead>
<tr>
<th>Clinical Outcome</th>
<th>Group 1 (21 Patients)</th>
<th>Group 2 (20 Patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DT &gt;150 ms</td>
<td>DT ≤150 ms</td>
</tr>
<tr>
<td>Duration of ICU stay, d</td>
<td>1.8±1.3</td>
<td>4.2±2.3</td>
</tr>
<tr>
<td>Change in NYHA class after surgery</td>
<td>−1.7±0.7</td>
<td>−0.7±0.8</td>
</tr>
<tr>
<td>Use of intravenous inotropes after surgery</td>
<td>(2/10)</td>
<td>(9/19)</td>
</tr>
<tr>
<td>Use of diuretics after revascularization</td>
<td>4/21 (19)</td>
<td>15/19 (79)*</td>
</tr>
<tr>
<td>Admission for CHF after bypass</td>
<td>3/21 (14)</td>
<td>8/19 (42)</td>
</tr>
<tr>
<td>Admission for unstable angina</td>
<td>2/21 (10)</td>
<td>2/19 (11)</td>
</tr>
<tr>
<td>Percutaneous revascularization</td>
<td>2/21 (10)</td>
<td>1/19 (5)</td>
</tr>
<tr>
<td>AICD implantation</td>
<td>0/21 (0)</td>
<td>2/19 (11)</td>
</tr>
<tr>
<td>Postrevascularization angina</td>
<td>2/21 (10)</td>
<td>2/19 (11)</td>
</tr>
<tr>
<td>Death or heart transplantation</td>
<td>1/21 (5)</td>
<td>7/19 (37)*</td>
</tr>
</tbody>
</table>

AICD indicates automated internal cardioverter-defibrillator. Values are n (%).

*P<0.01, †P<0.02, ‡P<0.03, §P<0.05.

combined, significant relations were present between DT (r=−0.73) and change in EF after revascularization. Patients with short DT had a smaller number of viable dysfunctional segments, whereas patients with a long DT had a larger number of viable dysfunctional segments. This finding is consistent irrespective of the imaging modality used or change in DT.

Doppler Velocities After Revascularization and Their Relation to Viability and Clinical Outcome

Six group 2 patients (baseline DT ≤150 ms, 2a) had an increase in DT after surgery of ≥40 ms (> mean±2 SD of interobserver difference), whereas 13 patients had a shorter or unchanged DT (2b). In the former 6 patients, DT increased from 113±27 to 184±31 ms (P<0.004). Similarly, consistent with an increase in the diastolic filling pattern and lower filling pressures, E/A ratio decreased (2.5±1.4 to 1.1±0.5, P=0.06) and AFF (0.2±0.09 to 0.35±0.14, P=0.06) and IVRT (70±16 to 97±34, P=0.03) increased. Each patient in this subset had viable dysfunctional segments and an improvement in LVEF (Table 4). Furthermore, 5 of the 6 patients had a 2-grade decrease in NYHA class, and 1 patient improved by 1 grade. In this subset, there were no admissions for CHF, no deaths, and no heart transplantations (P=0.04 versus the remaining 13 group 2 patients).

Conversely, the remaining 13 patients (2b) had further shortening in DT (110±24 to 97±19 ms, P<0.01) and IVRT (67±19 to 55±20 ms, P=0.002), along with an increase in E/A ratio (2±0.8 to 3±1.4, P=0.009) and a decrease in AFF (0.21±0.14 to 0.17±0.1, P=0.035). The number of viable dysfunctional segments was small, and LVEF was minimal (range −6% to 1%). Importantly, the 7 events of death or heart transplantation occurred in this subgroup.

In group 1, overall DT was essentially unchanged (258±65 to 250±103 ms). Only 2 patients had shortening of DT (276 to 78 and 219 to 100 ms, respectively), 1 in the context of unstable angina and symptoms of pulmonary congestion and the other in the setting of acute myocardial infarction.

All 40 patients were then divided into 3 groups based on baseline DT and change in EF after revascularization. Patients with short DT had a smaller number of viable dysfunctional segments (number of segments 1 to 3 by both DE and SPECT) had a short DT at baseline and failed to recover systolic function after surgery. As the number of viable segments increased (5 to 7 segments by DE and SPECT), EF increased after surgery, but DT was still ≤150 ms at baseline. With further increase in the indices of viability (9 to 10 viable segments by DE and SPECT), DT became >150 ms (baseline value), and after revascularization the majority (19 of 21) of these patients exhibited an improvement in EF (ANOVA, P<0.001; all pairwise multiple comparisons with P<0.03 for number of viable segments by both DE and SPECT).

As expected, ΔEF after surgery also was different between the 3 groups: patients with 1 to 3 viable segments had no increase in EF, those with 5 to 7 segments had an increment of 6.8±1.8%, and the patients with 9 to 10 segments had the largest increase: 9.6±4% (ANOVA, P<0.001; all pairwise multiple comparisons, P<0.05).

Discussion

Our study shows a strong association of the mitral inflow pattern with indices of myocardial viability in patients with IC undergoing CABG. These results help explain the association of DT with survival. As shown, when DT was ≤150 ms, DE and SPECT indices of viability were reduced. Another important and novel finding of our investigation is the ability of DT to predict functional recovery after revascularization.

Relation Between DT, Myocardial Viability, and Survival in Patients With IC

We observed a strong inverse correlation between DT and the number of viable segments by both DE and SPECT. The presence of a short DT was associated with a smaller number of viable segments, a lack of recovery of LV systolic function, and a worse clinical outcome after revascularization. These results were derived from a population undergoing CABG and may not be applicable to patients who are deemed unsuitable for mechanical revascularization. Nevertheless, we believe that the associations between DT and viability indices help elucidate the mechanism linking the mitral inflow pattern to survival in IC patients. There is currently strong evidence that the presence and extent of myocardial viability have a significant impact on the clinical outcome of patients with IC. These observations have been consistent irrespective of the imaging modality used or whether viability is defined as preserved cellular metabolism by PET,11 perfusion by either SPECT12 or contrast echocar-
diography,¹³ or contractile reserve.¹⁴,¹⁵ Therefore, the reduced amount of viable myocardium accounts for the worse survival in those patients with IC who exhibit a restrictive mitral inflow pattern.

A particularly interesting observation in this study is the interaction of myocardial viability, mitral inflow velocities, and functional recovery after revascularization in patients with a short DT. As noted above, in the presence of 5 to 7 viable segments (by both DE and SPECT), LV systolic function can improve despite the presence of a DT ≤150 ms. In these patients, the mitral inflow pattern improves after surgery corresponding to a reduction in filling pressures. It is probable that the relief of ischemia and the improvement in systolic function after revascularization lead to the observed changes in diastolic function. It is also possible that myocyte (and myocardial) elasticity normalizes with successful revascularization of the hibernating myocardium, leading to a reduction in LV stiffness and filling pressures and hence the changes in the mitral inflow pattern.

**Reasons for a Short DT in Patients With IC**

In patients with IC, replacement fibrosis occurs secondary to myocardial necrosis that develops because of prolonged repetitive ischemia and/or infarction. We have previously shown⁹ that nonviable segments by DE have a larger amount of fibrosis. Likewise, we¹⁰,¹⁶ and others¹⁷,¹⁸ have noted a strong relationship between viability assessed by SPECT (both ⁹⁹mTc and ⁹⁹mTc) and regional fibrosis. Therefore, IC patients with large amounts of nonviable myocardium have more extensive fibrosis.

In patients with IC, DT has been shown to be highly predictive of filling pressures.¹⁹,²⁰ In addition, Himura et al⁹ showed a good correlation between the mitral inflow pattern and late diastolic LV stiffness in patients with a reduced EF. Data from an animal model of pacing-induced heart failure indicate that DT has a strong relation with LV stiffness.²²,²³ Therefore, the short DT in IC patients is the result of increased chamber stiffness. We believe that the increased interstitial fibrosis is in all likelihood the cause of the abnormal stiffness of IC hearts. There is ample evidence relating LV stiffness and fibrosis in animal models and in patients. For example, animal data show that regression of interstitial collagen is accompanied by an improvement in LV compliance.²⁴ Likewise, in the clinical arena, studies have shown a strong relation of fibrosis to LV stiffness in patients with aortic valve disease.²⁵ Similar to the findings in animal studies, a long-term reduction in filling pressures was associated with a decrease in LV fibrous tissue content after valve replacement. Therefore, it is reasonable to conclude that advanced interstitial fibrosis plays an important pathophysiological role in increasing both stiffness and filling pressures in patients with IC and that this results in a restrictive mitral inflow pattern.

**Conclusions**

The reduced amount of viable myocardium may be the link that explains why the restrictive mitral inflow pattern is a powerful predictor of survival in patients with IC.¹–⁶ More importantly, our study identifies the mitral inflow pattern as a potential predictor of viability and functional recovery in patients with myocardial hibernation. In the presence of ≥5 to 7 viable segments, however, EF may still improve after revascularization despite a short DT.

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**References**


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