Perfusion and Contractile Reserve in Chronic Dysfunctional Myocardium: Relation to Functional Outcome After Surgical Revascularization

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Background—Chronic dysfunctional but viable myocardium may exhibit contractile reserve and/or intact perfusion. Segments with intact perfusion without contractile reserve are frequently observed in patients with ischemic cardiomyopathy. The clinical relevance of this observation is unclear; in particular, the functional outcome after revascularization is unknown. Thus, contractile reserve (using low-dose dobutamine echocardiography) and perfusion (using resting 99mTc tetrofosmin) were evaluated in 114 patients with ischemic cardiomyopathy and the findings were related to functional outcome (9 to 12 months after revascularization).

Methods and Results—Patients (n=114) with ischemic cardiomyopathy undergoing surgical revascularization were evaluated for perfusion (using 99mTc tetrofosmin) and contractile reserve (using low-dose dobutamine echocardiography). Contractile function (two-dimensional echocardiography) was assessed before and 9 to 12 months after revascularization. In the 1 336 dysfunctional segments, perfusion was preserved in 51% of the segments and contractile reserve in 31% (P<.05); 47% of the segments with perfusion did not exhibit contractile reserve. The majority (66%) of segments with recovery of function postrevascularization had intact perfusion and contractile reserve; the majority (58%) of segments without functional recovery lacked both perfusion and contractile reserve. Interestingly, 22% of segments with functional recovery and 25% of segments without functional recovery showed intact perfusion without contractile reserve.

Conclusion—Segments with intact perfusion/contractile reserve have a high likelihood of recovery of function postrevascularization; segments without contractile reserve/perfusion have a low likelihood of recovery and segments with intact perfusion without contractile reserve have an intermediate likelihood of recovery. (Circulation. 2002; 106[suppl I]:I-14-I-18.)

Key Words: myocardial viability ■ hibernating myocardium ■ heart failure ■ perfusion ■ contractile reserve

In patients with chronic ischemic left ventricular (LV) dysfunction, improvement of contractile function and favorable long-term prognosis after surgical revascularization have been demonstrated in those patients with dysfunctional but viable myocardium.1–6 Different techniques are available for the assessment of viable myocardium, based on the detection of different characteristics of viable myocardium.1–6 These characteristics include preserved glucose metabolism, intact cell membrane and mitochondria, preserved perfusion, and the presence of contractile reserve.1–6 The first 4 characteristics can be evaluated by nuclear imaging techniques: Glucose metabolism can be evaluated by F18-fluorodeoxyglucose (FDG) imaging,7,8 intact cell membranes can be evaluated by 201Tl imaging,9 intact mitochondria can be assessed by 99mTc sestamibi imaging,10 and preserved perfusion can be evaluated by either imaging with thallium-201 or 99mTc-labeled tracers.9,10 The presence of contractile reserve can be assessed during the infusion of low-dose dobutamine using two-dimensional (2D) echocardiography or magnetic resonance imaging.1–6 However, dysfunctional but viable myocardium does not always exhibit all characteristics. In particular, in a substantial percentage (approximately 25%) of the patients contractile reserve appeared absent, although other markers of viability (glucose metabolism, intact cell membrane, perfusion) were still present.11,12 The precise clinical relevance of this observation is thus far unclear and remains a matter of debate;13 in particular, the functional outcome after revascularization of these patients is uncertain. To further evaluate this phenomenon, we assessed contractile reserve (using low-dose dobutamine echocardiography).
TABLE 1. Patient Characteristics (n=114)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>61±7</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>106/8</td>
</tr>
<tr>
<td>Previous MI</td>
<td>109 (96%)</td>
</tr>
<tr>
<td>MVD</td>
<td>104 (91%)</td>
</tr>
<tr>
<td>Number stenosed coronary arteries</td>
<td>2.7±6</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>34±10</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>14 (12%)</td>
</tr>
<tr>
<td>Previous PTCA</td>
<td>16 (14%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>19 (17%)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>25 (22%)</td>
</tr>
<tr>
<td>COPD</td>
<td>19 (17%)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>18 (16%)</td>
</tr>
</tbody>
</table>

CABG: coronary artery bypass grafting; COPD: chronic obstructive pulmonary disease; LVEF: left ventricular ejection fraction; MI: myocardial infarction; MVD: multi-vessel disease; PTCA: percutaneous transluminal coronary angioplasty.

Assessment of Resting Contractile Function Before/After Revascularization

Resting contractile function was assessed by 2D echocardiography before and 9 to 12 months after revascularization. Four standard views of the LV were recorded (videotape and digitized in cine-loop format): parasternal long- and short-axis views and apical two- and four-chamber views. The prerevascularization and the postrevascularization images were reviewed (random order) off-line and consensus was achieved by 2 observers unaware of the other tests (low-dose dobutamine echocardiography, perfusion imaging). For analysis, a 16-segment model was used as suggested by American Society of Echocardiography.16 Both inward wall motion and wall thickening were analyzed. Each segment was assigned a wall motion score of 1 to 4: normal or mildly hypokinetic=1, severely hypokinetic=2 (decreased endocardial excursion and systolic wall thickening), akinetic=3 (absence of endocardial excursion and systolic wall thickening), and dyskinetic=4 (paradoxic outward movement in systole). Segments were considered dysfunctional when the wall motion score was 2 or more. Improvement of segmental wall motion score after revascularization by 1 grade or more was considered significant with the exception of improvement from dyskinesia to akinesis postrevascularization.

Assessment of Contractile Reserve

Contractile reserve was assessed using low-dose dobutamine echocardiography. Dobutamine was infused at 5 and 10 μg/kg/min, 5 minutes per stage. Images were acquired at the end of both stages (parasternal long- and short-axis views and apical two- and four-chamber views) and analyzed by 2 observers (blinded to the postrevascularization echocardiograms and unaware of the perfusion data) using the 16-segment model and the 4-point scoring system as described above. Dysfunctional segments (resting wall motion score 2 or more) were evaluated for the presence of contractile reserve, defined as improvement of wall motion score by 1 grade or more, with the exception of improvement from dyskinesia to akinesia.

Assessment of Perfusion

Perfusion was assessed at rest using 99mTc tetrofosmin (600 MBq) SPECT. Data acquisition was performed with a triple-head gamma camera system (Picker Prism 3000 XP, Cleveland, OH); the energy was centered on the 140 keV photon peak of 99mTc with a 15% window. Imaging was performed over 360 degrees (120 sectors of 3 degrees) with a total imaging time of 32 minutes. Data were stored in 64x64, 16-bit matrix. The raw scintigraphic data were reconstructed by filtered back projection using a Butterworth filter (cut-off frequency at 0.17 cycle/pixel, of order 3.5). No attenuation correction was used. Further reconstruction yielded standard long- and short-axis projections perpendicular to the heart axis. Reconstructed slices were 8 mm in all projections. The short-axis slices were displayed in polar map format, adjusted for peak myocardial activity (100%). The myocardium was divided into 16 segments, matching the echocardiographic segments (4 apical segments, 6 distal segments [anterior, anterolateral, inferolateral, inferior, inferoseptal, and anteroseptal], and 6 basal segments, comparable with the distal segments). Segments were divided into 4 categories: 1=normal tracer uptake (>75%), 2=moderately reduced tracer uptake (50% to 75%), 3=severely reduced tracer uptake (30% to 50%), and 4=absent tracer uptake (<30%). In dysfunctional segments, perfusion was considered preserved when activity was 50% or more (score 1 or 2).

Statistical Analysis

Descriptive results are expressed as mean±SD. Patient data were compared using the Student’s t test for paired and unpaired data when appropriate. Comparison of proportions was performed using chi-square analysis. McNemar testing was used to evaluate differences in positivity for contractile reserve (as assessed by low-dose dobutamine echocardiography) and perfusion (assessed by 99mTc tetrofosmin SPECT). P<.05 was considered significant.
Results

Contractile Function, Pre- and Postrevascularization
Six patients died during the study period (2 within 30 days after surgery (heart failure), 4 during the follow-up period (3 heart failure, 1 noncardiac death); 5 of these patients had absent perfusion and absent contractile reserve in all dysfunctional segments; 1 patient had 2 dysfunctional segments without perfusion/contractile reserve and 3 dysfunctional segments with preserved perfusion but without contractile reserve. In the remaining 108 patients, the symptoms improved significantly (mean CCS score reduced to 1.2 ± 0.3, mean NYHA score reduced to 1.9 ± 0.7, both P < 0.05 versus scores before revascularization).

Regional contractile function, as assessed by resting 2D echocardiography, demonstrated normal contraction in 392 (23%) segments and abnormal contraction in 1336 (77%) segments. Of the 1336 dysfunctional segments, 646 were severely hypokinetic, 629 akinetic, and 61 dyskinetic. Improvement of function postrevascularization occurred in 357 (27%) segments (63% severely hypokinetic, 37% akinetic, and 0% dyskinetic segments), whereas 979 (73%) segments did not improve (or even deteriorate in contractile function).

Recovery of function was not observed more frequently in the 41 patients with angina as compared with the 67 patients without angina (153 versus 204 dysfunctional segments).

LVEF was 34 ± 10% before revascularization and did not significantly improve after revascularization (36 ± 11%). However, an improvement in LVEF of 5% or more was observed in 38 patients (from 28 ± 8% before to 36 ± 4% after revascularization).

Presence of Contractile Reserve in Dysfunctional Myocardium
In the 1336 dysfunctional segments, low-dose dobutamine echocardiography demonstrated improvement of function (contractile reserve) in 412 (31%) segments. Of these 412 segments with contractile reserve, approximately two-third were hypokinetic 68% and one-third were akinetic (Figure 1). In the remaining 924 dysfunctional segments, no improvement of contraction occurred during infusion of low-dose dobutamine.

Preserved Perfusion in Dysfunctional Myocardium
In the 1336 dysfunctional segments, ⁹⁹ᵐTc tetrofosmin demonstrated preserved perfusion in 683 (51%) segments; 57% of the segments had perfusion score 1, and 43% of the segments had perfusion score 2. Of the segments with preserved perfusion, the majority was hypokinetic (Figure 2). In the remaining 653 dysfunctional segments perfusion was not preserved (72% of the segments with perfusion score 3 and 28% of the segments with perfusion score 4).

Intact Perfusion Versus Preserved Contractile Reserve in Dysfunctional Myocardium
In the 1336 dysfunctional segments, perfusion was more frequently preserved as compared with contractile reserve (31% versus 51%, P < 0.05). The exact distribution of segments according to the presence/absence of perfusion/contractile reserve is shown in Table 2. In the 683 segments with preserved perfusion, contractile reserve was present in 360 (53%) and absent in 323 (47%) segments. Conversely, in the 653 segments without preserved perfusion, contractile reserve was present in 52 (8%) segments and absent in 601 (92%) segments (Figure 3). Disagreement between the 2 techniques was 28%, with 86% being related to segments with preserved perfusion without contractile reserve.

The distribution of segments according to the presence/absence of perfusion/contractile reserve in relation to the absence/presence of angina is shown in Table 3.

TABLE 2. Characteristics of All 1336 Dysfunctional Segments

<table>
<thead>
<tr>
<th>Category</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P+</td>
<td>683</td>
</tr>
<tr>
<td>CR+</td>
<td>360 (53%)</td>
</tr>
<tr>
<td>CR−</td>
<td>323 (47%)</td>
</tr>
<tr>
<td>P−</td>
<td>653</td>
</tr>
<tr>
<td>CR+</td>
<td>52 (8%)</td>
</tr>
<tr>
<td>CR−</td>
<td>601 (92%)</td>
</tr>
</tbody>
</table>

P: perfusion; CR: contractile reserve; +: present; −: absent.
Perfusion and Contractile Reserve Versus Functional Outcome

The absence/presence of perfusion and absence/presence of contractile reserve in segments with and without improvement of contractile function after revascularization is shown in Figure 4. Of the 357 segments with recovery of function, the majority (66%) had both preserved perfusion and contractile reserve, whereas only 13% of the 979 segments without improvement of contractile function exhibited preserved perfusion and contractile reserve. The majority (58%) of the segments without improvement of contractile function postrevascularization exhibited neither intact perfusion nor preserved contractile reserve. In contrast, only 9% of the segments with improvement of contractile function postrevascularization lacked both perfusion and contractile reserve. Of interest, 22% of the segments with improvement of contractile function and 25% of the segments without improvement of contractile function postrevascularization showed intact perfusion without contractile reserve. Finally, small percentages of segments with and without improvement of function (3% and 4%, respectively) showed preserved contractile reserve without intact perfusion.

Of the 360 segments with preserved perfusion/contractile reserve, 66% exhibited recovery of function. Of the 601 segments without preserved perfusion/contractile reserve, 95% did not improve in function. Of the 323 segments with preserved perfusion without contractile reserve, 24% improved in function. Of the 52 segments with contractile reserve without perfusion, 79% did not improve in function.

Finally, the segments with higher levels of preserved perfusion demonstrated a higher likelihood of recovery; 225 of 389 segments with tracer uptake >75% improved in function postrevascularization as compared with 132 of 294 segments with tracer uptake 50% to 75%.

Discussion

In patients with ischemic cardiomyopathy, the assessment of residual viability in areas with chronic contractile dysfunction is important for prediction of improvement of function postrevascularization and prediction of long-term prognosis.1–6 Different techniques are available that rely on different characteristics of viable myocardium.1–6 Perfusion imaging (using 99mTc-labeled tracers or 201Tl) and assessment of contractile reserve (using low-dose dobutamine echocardiography) are widely used in the clinical setting for the assessment of viable myocardium. However, frequently chronic dysfunctional myocardium has preserved perfusion whereas contractile reserve is lacking.11,12 Data on the functional outcome of these segments are scarce.17 In the present study, perfusion imaging was compared with assessment of contractile reserve in a large number of patients with ischemic cardiomyopathy who were already scheduled for surgical revascularization. Both intact perfusion and the presence of contractile reserve were related to the severity of contractile dysfunction. Both perfusion and contractile reserve were more frequently observed in segments with severe hypokinesia as compared with akinetic segments, whereas dyskinetic virtually never exhibited intact perfusion of contractile reserve. Thus, the presence of these characteristics appears related to the severity of damage.

Moreover, perfusion was significantly more often preserved as compared with contractile reserve: 51% of the chronic dysfunctional segments showed intact perfusion and 31% showed contractile reserve. Head-to-head comparison of the individual segments revealed that the disagreement between the 2 imaging modalities was 28%, with 86% of these segments showing preserved perfusion without contractile reserve. Similar results have been reported by Panza et al.,12 who compared 201Tl imaging with dobutamine echocardiography and demonstrated that a large number of segments demonstrated 201Tl uptake but lacked contractile reserve. Studies comparing metabolic imaging with FDG to assessment of contractile reserve by dobutamine echocardiography have shown comparable results: A substantial percentage of the segments with FDG uptake did not exhibit contractile reserve.18,19 Pagano and colleagues20 demonstrated that segments with FDG uptake without contractile reserve had more ultrastructural damage and a higher percentage of fibrosis as
Compared with segments with preserved FDG uptake and intact contractile reserve, Nagueh and coworkers studied 20 patients with $^{201}$TI imaging and dobutamine echocardiography before surgical revascularization, and transmural biopsies were taken during surgery. The authors demonstrated a gradual increase of percentage fibrosis in different segments: 1% fibrosis in segments with both preserved $^{201}$TI uptake and contractile reserve, 9% fibrosis in segments with either preserved $^{201}$TI uptake or contractile reserve, and 28% fibrosis in segments without $^{201}$TI uptake and without contractile reserve. These findings further substantiate the suggestion that the severity of ultrastructural damage and fibrosis is related to the presence/absence of perfusion and contractile reserve. Segments with both characteristics have the least damage and fibrosis, segments with perfusion without contractile reserve have more damage/fibrosis and segments without perfusion/contractile reserve have the most severe damage/fibrosis.

An important issue is how these findings affect improvement of function postrevascularization. In the present study, the majority of the segments with improvement of contractile function postrevascularization showed both preserved perfusion and contractile reserve. Segments with both characteristics present may thus have a high likelihood of recovery of function post-revascularization (66% of the segments with both characteristics improved in function). In contrast, the majority of segments without recovery of function postrevascularization lacked both perfusion and contractile reserve. Segments without intact perfusion and contractile reserve may thus be considered to have a low likelihood of recovery of function postrevascularization (95% of the segments without perfusion/contractile reserve did not improve in function).

The segments with intact perfusion without contractile reserve pose a problem; 22% of the segments with recovery of function exhibited this pattern, but 25% of the segments without recovery of function also exhibited this pattern. Thus, segments with preserved perfusion without contractile reserve have an intermediate likelihood of recovery postrevascularization. However, from a clinical standpoint, it is important to emphasize that patients with preserved perfusion with contractile reserve may recover in function postrevascularization and should not routinely be denied surgical revascularization. Future studies are needed to identify which patients with this pattern are likely to improve and which patients will not improve in function postrevascularization.

**Limitations**

Functional follow-up was performed at 9 to 12 months, whereas longer follow-up may be needed for complete recovery of function. This may be of particular importance in patients with severely damaged myocardium. In addition, long-term survival may be a superior end-point than improvement of function.

Graft patency was not assessed; thus, graft occlusion may have prevented some viable segments from recovery of function.

Finally, although a similar 16-segment model was used for echo and SPECT data, misalignment may have influenced the results.

**Conclusions**

In chronic dysfunctional myocardium, perfusion is preserved more frequently than contractile reserve. Segments with both preserved perfusion and contractile reserve have a high likelihood of recovery of function postrevascularization; segments without preserved perfusion/contractile reserve have a low likelihood of recovery. Segments with preserved perfusion without contractile reserve have an intermediate likelihood of recovery after revascularization. Additional testing needs to be developed to predict which of these segments will improve and which segments will not improve in function.

**References**

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