Evaluation of Left Ventricular Function Three Years After Percutaneous Recanalization of Chronic Total Coronary Occlusions

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We investigated early and late effects of percutaneous revascularization for chronic total coronary occlusion on left ventricular (LV) function and volumes. Magnetic resonance imaging was performed in 21 patients before and 5 months and 3 years after recanalization. Global LV function and volumes and segmental wall thickening (SWT) were quantified on cine images. The 2 viability indexes used were the transmural extent of infarction (TEI) on delayed contrast enhancement images and end-diastolic wall thickness at baseline. Significant decreases in mean end-diastolic (86 ± 14 to 78 ± 15 ml/m²; p = 0.02) and mean end-systolic volume indexes (35 ± 13 to 30 ± 13 ml/m²; p = 0.03) were observed 3 years after recanalization. Mean ejection fraction tended to improve (60 ± 9% to 63 ± 11%; p = 0.11). SWT significantly increased at 5-months' follow-up (p <0.001), and an additional improvement was found at 3 years' follow-up (p = 0.04) in segments with TEI <25%. In segments with TEI of 25% to 75%, SWT was unchanged at 5-month follow-up (p = 0.89), but improved at 3 years (p = 0.04). SWT was unchanged in segments with transmural scars. For segmental functional recovery, TEI was a better predictor than end-diastolic wall thickness at baseline (odds ratio 5.6, 95% confidence interval 1.5 to 21.1, p = 0.01 vs odds ratio 2.5, 95% confidence interval 0.7 to 8.3, p = 0.14). In conclusion, a positive effect on LV remodeling and ejection fraction was observed up to 3 years after recanalization. Both early and late improvements in regional LV function were observed in the perfusion territory of chronic total coronary occlusion and were related to the transmural extent of infarction on pretreatment magnetic resonance imaging. © 2008 Elsevier Inc. All rights reserved. (Am J Cardiol 2008;101:179–185)

Chronic total coronary occlusions (CTOs) were observed in up to 30% to 35% of patients with suspected or known coronary artery disease who underwent diagnostic coronary artery catheterization.1 Myocardium in the perfusion territory of a CTO can be either functionally normal, dysfunctional and viable, or dysfunctional and nonviable. Dysfunctional but viable myocardium may recover function after percutaneous coronary intervention for CTO.2–4 It is currently unknown in what time span recovery of dysfunctional but viable myocardium can be seen. Several studies observed the beneficial effect of treatment of a CTO on left ventricular (LV) function with a follow-up of approximately 6 months.5–8 These early observations suggested that the time span of functional recovery of dysfunctional but viable myocardium may extend beyond 6 months, but no data were available for patients with a recanalized CTO.9,10 In the present study, we evaluated patients with dysfunctional myocardium caused by CTO early (5 months) and late (3 years) after percutaneous revascularization.

Methods

Patients scheduled for percutaneous revascularization of a CTO of a native coronary artery were prospectively studied. Of these patients, 75% had a positive exercise test result and the remaining 25% had progressive anginal symptoms. All successfully treated patients received a drug-eluting stent. Forty-seven patients were included in this study. In 34 patients, percutaneous coronary intervention was successful. Follow-up at 3 years was obtained in 21 patients; 1 patient died, 1 patient had a defibrillator implanted, 1 patient refused reinvestigation. Both early and late improvements in regional LV function were observed in the perfusion territory of chronic total coronary occlusion and were related to the transmural extent of infarction on pretreatment magnetic resonance imaging.

Patient characteristics are listed in Table 1. Exclusion criteria were any of the contraindications for magnetic resonance studies (pacemakers, claustrophobia, and cochlea implants). The institutional review board of the Erasmus Medical Center approved the study, and each subject gave written informed consent.

Magnetic resonance images were acquired using a 1.5-Tesla scanner. Patients were positioned supine with a car-

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Table 1
Baseline patient characteristics

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+ = Yes; 0 = No; ACE = angiotensin-converting enzyme; ASA = acetylsalicylic acid; LAD = left anterior descending artery; LCx = left circumflex artery; RCA = right coronary artery.
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dic 4- or 8-element phased-array receiver coil placed over the thorax (Signa CV/i; GE Medical Systems, Milwaukee, Wisconsin). Repeated breath holds and gating to the electrocardiogram were applied to minimize the influence of cardiac and respiratory motion on data collection. Cine magnetic resonance imaging was performed using a steady-state free-precessation technique (Fast Imaging Employing Steady State Acquisition). Imaging parameters were field of view 36 to 40 × 28 to 32 cm, matrix size 224 × 196, repetition time 3.4 ms, echo time 1.5 ms, flip angle 45°, 12 views/segment, and slice thickness 8.0 mm with a 2.0-mm slice gap. Using standard techniques to identify the major cardiac axes, 2- and 4-chamber cine magnetic resonance images were obtained. The 2- and 4-chamber end-diastolic images at end-expiration provided the reference images to obtain a series of short-axis views. This resulted in 10 to 12 cine breath-hold short-axis images to cover the entire left ventricle.

Delayed enhancement imaging was performed with a gated breath hold T1-inversion recovery gradient-echo sequence 20 minutes after infusion of gadolinium diethylenetriaminepentaacetic acid (0.2 mmol/kg intravenously; Magnevist; Schering, Berlin, Germany). Imaging parameters were repetition time 6.3 ms, echo time 1.5 ms, flip angle 20°, inversion pulse 180°, matrix 192 × 160, number of averages 1 to 2, and inversion time 180 to 280 ms (adjusted to null the signal of the remote myocardium). Slice locations of the delayed enhanced images were copied from the cine images.

All conventional angiograms before revascularization were evaluated by 2 experienced observers (TB, R-JMvG). Collateral function was scored using the Rentrop classification.11 The CTO was classified as a complete occlusion for which collateral function was scored 0. Friedberg et al.11 The CTO was classified as a complete occlusion for which collateral function was scored 0. The CTO was classified as a complete occlusion for which collateral function was scored 0. The CTO was classified as a complete occlusion for which collateral function was scored 0.

Results

The patient population consisted of 21 patients. In 11 patients, the CTO was located in the left anterior descending; in 8 patients, in the right coronary artery; and in 2 patients, in the circumflex artery. All images were good for analysis. Mean duration of occlusion was 7 ± 5 months. At follow-up, medication was similar to baseline except for clopidogrel, which was discontinued after 6 months.

A total of 336 myocardial segments were available for analysis, of which 106 were in the perfusion territory of a CTO. Of these 106 segments, abnormal contractile function (wall thickening <45%) was present in 49 segments (46%); 24 (49%) in the anterior area, 4 (8%) in the lateral area, and 21 (43%) in the inferior area. Of the 49 dysfunctional segments in the perfusion territory of a CTO, 21 (43%) had TEIs <25%, 25 (50%) had TEIs of 25% to 75%, and 3 (6%) had TEIs >75%. In this study, 19 segments had delayed enhancement before revascularization, whereas SWT was normal, although most had TEIs <25% (53%). EDWT was measured in these 49 dysfunctional segments at baseline: 11 segments had baseline EDWT <7 mm; 23 segments had EDWT of 7 to 9 mm, and 15 segments had EDWT >9 mm. Significant decreases in mean end-diastolic (86 ± 14 to 78 ± 15 ml/m²; p = 0.02) and mean end-systolic volume indexes (35 ± 13 to 30 ± 13 ml/m²; p = 0.03) were observed 3 years after recanalization. Mean ejection fraction tended to improve (60 ± 9% to 63 ± 11%; p = 0.11; Figure 1). At 3 years’ follow-up, 15 patients (71%) had normal ejection fraction, 13 (62%) had normal end-diastolic volume, and 14 (67%) had normal end-systolic volume values. SWT improved >10% in 27 dysfunctional segments (55%). Twenty-one segments (43%) developed normal wall thickening, whereas 12 segments (24%) had additional deterioration in wall thickening after 3 years of follow-up (Figure 2).

Mean SWT of all dysfunctional segments increased from 19 ± 21% at baseline to 31 ± 30% at 5 months’ follow-up and 47 ± 46% at 3 years’ follow-up. However, SWT of the revascularized dysfunctional segments was significantly lower compared with remote segments (47 ± 46% vs 82 ± 36%; p < 0.001). In segments with TEI <25%, mean SWT increased significantly at 5 months’ follow-up (18 ± 24% to 47 ± 28%; p < 0.001) with considerable additional improvement after 3 years (to 67 ± 48%; p = 0.04). In segments with TEI of 25% to 75%, SWT was unchanged at 5 months’ follow-up (22 ± 18% to 22 ± 22%; p = 0.89). Interestingly, after 3 years of follow-up, SWT improved significantly in these segments (to 39 ± 43%; p = 0.04). In segments with transmural scars (TEI >75%), SWT was unchanged at early (4 ± 33% to −9 ± 16%; p = 0.54) and late follow-up (to 13 ± 40%; p = 0.42; Figure 3).

When individual segments were stratified into EDWT at baseline, segments with EDWT <7 mm SWT were un-

\[ \text{baseline EDWT} <7 \text{ mm SWT} \]

\[ 19 \pm 21\% \]

\[ 31 \pm 30\% \]

\[ 47 \pm 46\% \]

\[ 82 \pm 36\% \]

\[ p < 0.001 \]

\[ 18 \pm 24\% \]

\[ 47 \pm 28\% \]

\[ p < 0.001 \]

\[ 67 \pm 48\% \]

\[ p = 0.04 \]

\[ 22 \pm 18\% \]

\[ 22 \pm 22\% \]

\[ p = 0.89 \]

\[ 4 \pm 33\% \]

\[ -9 \pm 16\% \]

\[ p = 0.54 \]

\[ 13 \pm 40\% \]

\[ p = 0.42 \]
changed at early (5 ± 17% to 8 ± 28%; p = 0.77) and late follow-up (to 15 ± 33%; p = 0.55). In segments with EDWT of 7 to 9 mm, SWT showed no improvement after 5 months (25 ± 16% to 33 ± 27%; p = 0.17), but showed remarkable improvement after follow-up of 3 years (to 51 ± 46%; p = 0.05). Segments with EDWT > 9 mm SWT showed marked improvement after 5 months (18 ± 26% to 44 ± 26%; p = 0.002) and tended to improve further after 3 years of follow-up (to 64 ± 44; p = 0.08; Figure 3).

Sensitivity, specificity, and positive and negative predictive values of viability indexes for predicting improvement >10% in SWT are listed in Table 2. Univariate logistic regression analysis for predicting SWT at 3 years was performed. For each level increase in TEI, the odds ratio (OR) was 0.63 (95% CI 0.40 to 0.98, p < 0.05). When a cut-off value of 25% TEI was chosen, the OR was 5.63 (95% CI 1.50 to 21.12, p = 0.01). The OR for each 1-mm increase in EDWT was 1.34 (95% CI 0.92 to 1.96, p = 0.13). When we used a cut-off value of 7 mm for EDWT, the OR was 2.5 (95% CI 0.74 to 8.31, p = 0.14). Multiple regression analysis showed no additive predictive value for EDWT in addition to TEI (p = 0.63).

Discussion

We report here that SWT improved in dysfunctional but viable segments 5 months after CTO recanalization, with even further improvement after 3 years of follow-up. Second, a reduction in remodeling was observed up to 3 years after recanalization, shown by decreased end-diastolic and end-systolic volumes. Third, improvement in regional function was related to the extent of myocardial fibrosis and could be predicted using delayed enhancement magnetic resonance imaging before revascularization.

Several investigators studied the effect of revascularization for CTO on global and regional LV function. In general, a positive effect on regional wall motion was observed and ejection fraction tended to improve at approximately 6 months’ follow-up. Long-term follow-up studies registered clinical end points. These nonrandomized studies showed a significant decrease in mortality and need for surgical revascularizations. One randomized study, the Total Occlusion Study of Canada 2, showed improvement in LV ejection fraction and remodeling in patients who underwent either optimal medical therapy or received percutaneous coronary intervention of the total occluded infarct-related vessel shortly after the acute myocardial infarct. However, no difference between the 2 treatment strategies was found. The positive effect in both groups can be ascribed to stunning of tissue early after the acute myocardial infarct, which will improve. In our group with a more chronic situation, recovery of function or reduction in remodeling can be related to hibernating in the targeted area, which can only improve after revascularization. Moreover, in the Total Occlusion Study of Canada 2, no assessment of myocardial viability was made before revascularization and viability was expected to be low where most of the patients presented with ST-elevated infarctions without thrombolysis treatment, which resulted in high levels of serum markers.

No previous study with pretreatment viability assessment on LV function after recanalization of a CTO was performed with a follow-up >6 months. Several investigators described additional improvement in LV function after the
general accepted 6-month follow-up period, but this was described in patients with surgical revascularization for coronary artery disease.\textsuperscript{21,22}

The recovery time of dysfunctional myocardium was related to the extent of damage on a cellular level\textsuperscript{23} that depended on different factors, including duration and severity of ischemia.\textsuperscript{24} Biopsies of hibernating myocardium showed defects in nearly all cells. The center of the cell lost its sarcomeres and myofibrils, the perinuclear area was absent of contractile material, and cellular debris occurred in the enlarged extracellular space.\textsuperscript{23,25} In a study of 19 patients with dysfunctional myocardium, myocardial biopsies showed a relation between the extent of structural changes and rate of recovery.\textsuperscript{26} Significant recovery could already be noted 1 week after revascularization when the dysfunctional myocardium showed no or little structural changes. In addition, when structural changes were widespread, recovery was delayed and the extent of recovery was incomplete at 6 months.

In the present study, improvement in SWT was observed beyond the 6-month period in segments with more extensive myocardial abnormalities (EDWT 7 to 9 mm or TEI 25% to 75%), suggesting that restoration of flow after revascularization may lead to late recovery of segments that did not depend on different factors, including duration and severity of ischemia.\textsuperscript{24} Biopsies of hibernating myocardium showed defects in nearly all cells. The center of the cell lost its sarcomeres and myofibrils, the perinuclear area was absent of contractile material, and cellular debris occurred in the enlarged extracellular space.\textsuperscript{23,25} In a study of 19 patients with dysfunctional myocardium, myocardial biopsies showed a relation between the extent of structural changes and rate of recovery.\textsuperscript{26} Significant recovery could already be noted 1 week after revascularization when the dysfunctional myocardium showed no or little structural changes. In addition, when structural changes were widespread, recovery was delayed and the extent of recovery was incomplete at 6 months.

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recover or incompletely recovered after 5 or 6 months. Conversely, dysfunctional segments with fewer abnormalities (EDWT >9 mm or TEI <25%) showed early improvement in function, possibly representing (chronic) stunned areas with less or no structural cellular changes.

In the present study, 2 previously described viability indexes were measured and the predictive value for possible systolic functional recovery was tested. The TEI per-indexes were measured and the predictive value for possible improvement in function, possibly representing (chronic) stunned areas.


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