Improvement of myocardial function and perfusion after successful percutaneous revascularization in patients with chronic total coronary occlusion

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ABSTRACT

Background: Percutaneous coronary intervention (PCI) for chronic total occlusion (CTO) of a coronary artery can provide benefits in terms of myocardial function and survival but the procedure is complex and the success rate is relatively low. To assess these benefits, myocardial function, ischemia and viability should be clearly determined by means of a reliable diagnostic test. This study aimed to assess ventricular function and myocardial ischemia before and after PCI for CTO using cardiac magnetic resonance (CMR). NYHA functional class was also assessed before and after PCI.

Methods and results: CMR studies were performed in 43 consecutive patients (7 females; aged 64 ± 9.6 y.o.) with CTO scheduled for PCI and repeated 6 months post-PCI. PCI was successful in 33 (77%) of them. In this group CMR had shown inducible perfusion defects in 26 (79%) before PCI, while they were observed in 10 (30%) post-PCI CMR study (p < 0.001). The number of segments showing inducible perfusion defect (3.4 ± 2 prevs. 2.9 ± 4.5 post-PCI, p = 0.002) was significantly reduced in this group. Regional contractile function of segments showing viability also improved significantly in the group with successful CTO PCI compared to the group with an unsuccessful procedure. NYHA functional class for angina also improved in patients with successful revascularization while it remained unchanged in the group with unsuccessful procedures.

Conclusions: A successful CTO PCI leads to a reduction in inducible myocardial ischemia and to an improvement in regional wall motion, which results in clinical improvement.

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1. Introduction

The potential benefits of percutaneous coronary intervention (PCI) for chronic total occlusion (CTO) of a coronary artery are improvement in symptoms, left ventricular (LV) function, and survival. However, PCI is a complex procedure that has a high complication rate and a relatively low success rate in these patients. Current guidelines recommend PCI when symptoms are present and there is evidence of significant ischemia and viable myocardium in the territory supplied by the occluded vessel [1]. Thus, in both the selection of patients for PCI and the assessment of its benefits, an accurate evaluation of myocardial function, perfusion and viability is essential.

Most studies have evaluated results of CTO revascularization in terms of clinical outcome [2-5] or improvement of global left ventricular function assessed by contrast ventriculography [6-8]. However, the accuracy of ventriculography for measuring global and regional left ventricular function is limited [9]. Cardiac magnetic resonance (CMR) allows accurate and reproducible evaluation of myocardial function, perfusion, necrosis, and viability in a single test. A few studies [10,11] have assessed functional improvement in relation to myocardial perfusion and viability by CMR, but the number of patients studied is still low and there is a need for reliable, comprehensive information on the effects of PCI.

This study was performed to assess the improvement in left ventricular (LV) function and myocardial ischemia after CTO PCI using CMR.

2. Methods

2.1. Study population

The study population consisted of a series of consecutive patients recruited from February 2009 to November 2009, in whom a CTO of a coronary vessel was found and who were scheduled for PCI. All patients presented with symptoms and had been referred for a coronary angiography by their cardiologist. CTO was defined as occlusion existing for at least 3 months. Duration of the occlusion was based on a previous angiogram showing the occluded vessel or, in its absence, on clinical data indicating the occurrence of a clinical ischemic event potentially related to a coronary artery occlusion [12]. Exclusion criteria were: patients with >1 CTO and/or contraindication for CMR study. A complete CMR study protocol, including analysis of function, perfusion and myocardial viability, was scheduled prior to PCI. A second CMR was performed at least 6 months post-PCI. The study was conducted in accordance with the standards set by the “Declaration of
Table 1
Demographic and clinical characteristics of the study group.

<table>
<thead>
<tr>
<th></th>
<th>All patients (n = 43)</th>
<th>Successful revascularization CTO (n = 33)</th>
<th>Unsuccessful revascularization CTO (n = 10)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y.o.)</td>
<td>64 ± 9.6</td>
<td>66 ± 9.5</td>
<td>61 ± 9.7</td>
<td>0.28</td>
</tr>
<tr>
<td>Female</td>
<td>7 (16%)</td>
<td>7 (21%)</td>
<td>0 (0%)</td>
<td>0.17</td>
</tr>
<tr>
<td>Hypertension</td>
<td>34 (79%)</td>
<td>28 (84%)</td>
<td>6 (60%)</td>
<td>0.18</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>35 (81%)</td>
<td>25 (76%)</td>
<td>10 (100%)</td>
<td>0.17</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>1 (2%)</td>
<td>1 (3%)</td>
<td>0 (0%)</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes</td>
<td>15 (35%)</td>
<td>12 (37%)</td>
<td>3 (30%)</td>
<td>1</td>
</tr>
<tr>
<td>History of smoke</td>
<td>31 (72%)</td>
<td>23 (70%)</td>
<td>8 (80%)</td>
<td>0.70</td>
</tr>
<tr>
<td>Chronic renal disease</td>
<td>2 (5%)</td>
<td>1 (3%)</td>
<td>1 (10%)</td>
<td>0.42</td>
</tr>
<tr>
<td>Previous MI by medical history</td>
<td>17 (40%)</td>
<td>13 (39%)</td>
<td>4 (40%)</td>
<td>1</td>
</tr>
<tr>
<td>Previous MI by CMR</td>
<td>31 (72%)</td>
<td>22 (67%)</td>
<td>9 (90%)</td>
<td>0.24</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>5 (12%)</td>
<td>3 (9%)</td>
<td>2 (20%)</td>
<td>0.58</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>18 (42%)</td>
<td>12 (36%)</td>
<td>6 (60%)</td>
<td>0.28</td>
</tr>
<tr>
<td>Functional class</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>0–1</td>
<td>3 (7%)</td>
<td>3 (9%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>II–III–IV</td>
<td>40 (93%)</td>
<td>30 (91%)</td>
<td>10 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

CAD, coronary artery disease; MI, myocardial infarction; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention.

Fig. 1. Patient with CTO of an LAD coronary artery. A: perfusion study before PCI showing an inducible defect in the mid-septal, apical-septal and apical-anterior segments (arrows). B: no perfusion defects are seen in the study post-PCI.
Helsinki" and was approved by the ethics committee at our institution. Informed consent was obtained from all patients.

2.2. CMR studies

All studies were performed with a Siemens Avanto 1.5 T (Erlangen, Germany) scanner. After obtaining the usual scout planes, steady-state free-precession cine-MR images were acquired in individual long-axis planes and in multiple 8 mm-thick short-axis slices/2 mm gap from the atrio-ventricular groove to the apex of the left ventricle. Perfusion studies were performed using a hybrid echo planar gradient-echo sequence in 3 short-axis slices at basal, mid- and apical levels. These slices were imaged during the first-pass of 0.1 mmol/kg of gadoteridol (Gadovist 1.0, Bayer Schering Pharma, Berlin, Germany), injected at 4 mL/s into an antecubital vein. This study was performed during adenosine perfusion at 140 mcg/kg/min for 4 min and repeated after 10 min at rest. A 3D inversion-recovery segmented gradient echo sequence was acquired 10 min after contrast administration to assess delayed-enhancement (DE). Inversion times were adjusted to null the signal from normal myocardium (200–300 ms). This sequence was used in multiple short-axis planes using the same orientation as the cine-MR images and acquired during a patient breath-hold of approximately 20 s. The mean duration of the study was 45 min.

2.3. Image analysis

We analyzed cine loops and contrast-enhanced images on dedicated software (QMass MR 7.1, MEDIS, Leiden, The Netherlands). Left ventricular endo- and epicardial borders were traced manually on systolic and diastolic short-axis cine images. Left ventricular mass (LVM), end-diastolic (LVEDV) and end-systolic (LVESV) volumes, and ejection fraction (LVEF) were calculated for each patient. We used the American Heart Association 17-segment model[13]. Regional wall motion was assessed as follows: 1 = normal; 2 = hypokinetic; 3 = akinetic; and 4 = dyskinetic.

In a random sample of 20 patients LVEF was calculated by 2 experienced observers (S.P., G.P.) to assess interobserver variability.

Myocardial perfusion was evaluated during adenosine infusion and at rest. Visual analysis of CMR perfusion images was done by consensus of 2 experienced observers (S.P., G.P.) using 17-segment model. Segment number 17 was excluded for perfusion analysis. If the signal intensity on stress perfusion images was reduced in at least 2 contiguous myocardial segments, for at least three dynamic images, compared with remote myocardium, and this was not present in the rest study, it was considered to represent an inducible perfusion defect. If DE was present (see below) matching the area of the stress perfusion defect, it was considered a fixed perfusion defect and, therefore, no inducible ischemia was reported. Both the radial and the transmural extension of the defect were considered for this purpose. Regional distribution of perfusion defect and its correspondence to a particular coronary artery territory were determined according to the American Heart Association 17-segment model[13].

Delayed enhancement (DE) images were visually assessed by 2 experienced observers (S.P., G.P.) in consensus to determine myocardial necrosis and viability. Hyperenhanced areas were defined using the full-width at half-maximum method[14]. The distribution pattern and location of DE were noted. Necrotic mass, as identified by DE, was calculated by planimetry of the hyperenhanced areas on the set of short axis images of the left ventricle. The percentage of myocardial necrosis with respect to total LVM was also obtained. Myocardial viability was considered to be present in a segment when there is less than 50% of DE transmurality[15]. PCI attempt of the occluded vessel was deferred when absence of viability was found in ≥2 contiguous myocardial segments in the territory dependent from the vessel.

2.4. Invasive coronary angiography

Multiple angiographic projections were performed to visualize the coronary arterial tree. CTO of a vessel was considered to be present when angiography showed absent antegrade flow, defined as a thrombolysis in myocardial infarction (TIMI) flow grade of 0.
0. Collateral circulation was angiographically graded according to Rentrop classification as: 0 = no collateral filling; 1 = filling of side branches of the epicardial artery; 2 = partial filling of the epicardial artery; or 3 = complete filling [16].

2.5. Statistical analysis

Continuous variables are presented as mean ± SD when normally distributed, and median (interquartile range) when not. Differences in baseline characteristics between patients with successful PCI and non-successful PCI were evaluated using unpaired Student’s t-tests. Mann-Whitney rank sum test was performed when the variable had a non-Gaussian distribution. Comparisons between pre- and post-PCI CMRs were performed by paired t tests or Wilcoxon signed rank, as appropriate. Group differences for categorical variables were evaluated using Chi-square or Fisher’s exact test. McNemar’s test was used to compare NYHA functional class. A two-tailed p < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS (version 19.0, SPSS Inc., Chicago, Illinois).

3. Results

Of 68 selected patients, 25 were excluded (8 patients with 2 CTOs and 17 who refused a second CMR). Demographics and clinical characteristics of the 43 patients who completed the study are shown in Table 1. Distribution of coronary arteries with CTO was as follows: left anterior descending artery (LAD) = 15 (35%); circumflex artery (Cx) = 7 (16%); and right coronary artery = 21 (49%). Previous angioplasty was available in 19 patients (13 in the successful group and 6 in the unsuccessful group). The estimated duration of the occlusion was 13.7 ± 19.8 months (range 3–78 months). A good collateral coronary circulation was observed in all patients, this making PCI feasible. Successful PCI was defined as the restoration of thrombolysis by myocardial infarction (TIMI) grade 3 flow. PCI was performed in all patients and was successful in 33 (77%): 94% were drug eluting stents; 2.2 stents/patient (n = 33). During PCI, p = 0.001), whereas there were no changes in the groups with unsuccessful PCI (80% in pre-CMR vs. 70% in post-CMR, p = 0.3). A total of 688 segments were available for perfusion analysis and 731 for regional contractility and viability. Results of post-CMR exams in both groups are summarized in Tables 3 and 4. In the group of patients with successful revascularization a significant reduction in the number of segments showing an inducible myocardial perfusion defect was found (3.4 ± 2 pre- vs. 2.45 ± 2.5 post-PCI, p = 0.002) (Fig. 3). Also, there was a significant improvement in regional contractile function of those segments with DCE < 50% in the group with successful revascularization of patients showing ischemia was found in the group with successful CTO PCI (26% (95% CI: 0.876, 0.98). No differences were found in pre-CMR results of patients with successful and unsuccessful PCI (Table 2). A significant

### Table 2

<table>
<thead>
<tr>
<th>Pre-PCI CMR findings.</th>
<th>Successful revascularization CTO</th>
<th>Unsuccessful revascularization CTO</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular ejection fraction (LVEF), %</td>
<td></td>
<td></td>
<td>0.18</td>
</tr>
<tr>
<td>Mean</td>
<td>62 ± 12.2</td>
<td>57 ± 8.8</td>
<td></td>
</tr>
<tr>
<td>Left ventricular end-diastolic volume (LVEDV), ml</td>
<td>153 ± 38.9</td>
<td>150 ± 35.8</td>
<td>0.81</td>
</tr>
<tr>
<td>Mean</td>
<td>153 ± 38.9</td>
<td>150 ± 35.8</td>
<td></td>
</tr>
<tr>
<td>Left ventricular end-systolic volume (LVESV), ml</td>
<td>60 ± 34.9</td>
<td>67 ± 29.4</td>
<td>0.60</td>
</tr>
<tr>
<td>Mean</td>
<td>60 ± 34.9</td>
<td>67 ± 29.4</td>
<td></td>
</tr>
<tr>
<td>Left ventricular mass (LVM), g</td>
<td>130 ± 32.1</td>
<td>131 ± 28.3</td>
<td>0.90</td>
</tr>
<tr>
<td>Mean</td>
<td>130 ± 32.1</td>
<td>131 ± 28.3</td>
<td></td>
</tr>
<tr>
<td>Necrotic mass, g</td>
<td>5.5 ± 5.68</td>
<td>5.5 ± 8.20</td>
<td>0.94</td>
</tr>
<tr>
<td>Mean</td>
<td>3.7</td>
<td>3.8</td>
<td></td>
</tr>
<tr>
<td>Interquartile range</td>
<td>0–9.4</td>
<td>1–5</td>
<td></td>
</tr>
<tr>
<td>Number of ischemic segments per patient, n</td>
<td>3.42 ± 2.031</td>
<td>4.4 ± 2.68</td>
<td>0.22</td>
</tr>
<tr>
<td>Mean</td>
<td>3</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Interquartile range</td>
<td>2–5</td>
<td>2.25–7</td>
<td></td>
</tr>
<tr>
<td>Number of segments with DE ≤ 50% per patient, n</td>
<td>163 ± 189</td>
<td>163 ± 189</td>
<td>0.99</td>
</tr>
<tr>
<td>Mean</td>
<td>0.39 ± 0.864</td>
<td>0.70 ± 1.889</td>
<td></td>
</tr>
<tr>
<td>Number of dysfunctional segments with DE ≤ 50% per patient, n</td>
<td>2.45 ± 3.260</td>
<td>1.50 ± 1.716</td>
<td>0.42</td>
</tr>
<tr>
<td>Mean</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Interquartile range</td>
<td>1–3</td>
<td>0–1.25</td>
<td></td>
</tr>
</tbody>
</table>

### Table 3

<table>
<thead>
<tr>
<th>Comparison of CMR findings pre- and post-PCI in patients with successful CTO revascularization.</th>
<th>PRE-PCI CMR (n = 33)</th>
<th>POST-PCI CMR (n = 33)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular ejection fraction (LVEF), %</td>
<td>Left ventricular ejection fraction (LVEF), %</td>
<td>62 ± 12.2</td>
<td>65 ± 11.5</td>
</tr>
<tr>
<td>Mean</td>
<td>Mean</td>
<td>150 ± 35.8</td>
<td>149 ± 46.8</td>
</tr>
<tr>
<td>Left ventricular end-systolic volume (LVESV), ml</td>
<td>Mean</td>
<td>60 ± 34.9</td>
<td>56 ± 38.6</td>
</tr>
<tr>
<td>Left ventricular mass (LVM), g</td>
<td>Mean</td>
<td>130 ± 32.1</td>
<td>130 ± 29.8</td>
</tr>
<tr>
<td>Necrotic mass, g</td>
<td>Mean</td>
<td>5.3 ± 5.68</td>
<td>4.7 ± 5.68</td>
</tr>
<tr>
<td>Median</td>
<td>Median</td>
<td>3.7</td>
<td>1.9</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>Interquartile range</td>
<td>0–9.4</td>
<td>0–8.4</td>
</tr>
<tr>
<td>Number of ischemic segments per patient, n</td>
<td>Number of ischemic segments per patient, n</td>
<td>3.42 ± 2.031</td>
<td>1.82 ± 3.177</td>
</tr>
<tr>
<td>Mean</td>
<td>Mean</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>Interquartile range</td>
<td>2–5</td>
<td>0–2</td>
</tr>
<tr>
<td>Number of segments with DE ≤ 50% per patient, n</td>
<td>Number of segments with DE ≤ 50% per patient, n</td>
<td>16.8 ± 0.87</td>
<td>16.3 ± 1.89</td>
</tr>
<tr>
<td>Mean</td>
<td>Mean</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>Interquartile range</td>
<td>2.5–7</td>
<td>2.25–7</td>
</tr>
<tr>
<td>Number of dysfunctional segments with DE ≤ 50% per patient, n</td>
<td>Number of dysfunctional segments with DE ≤ 50% per patient, n</td>
<td>163 ± 189</td>
<td>151 ± 2.42</td>
</tr>
<tr>
<td>Mean</td>
<td>Mean</td>
<td>0.70 ± 1.889</td>
<td>1.40 ± 2.503</td>
</tr>
<tr>
<td>Number of dysfunctional segments with DE ≤ 50% per patient, n</td>
<td>Number of dysfunctional segments with DE ≤ 50% per patient, n</td>
<td>1.50 ± 1.716</td>
<td>1.10 ± 1.197</td>
</tr>
<tr>
<td>Mean</td>
<td>Mean</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>Interquartile range</td>
<td>0–1.25</td>
<td>0–1</td>
</tr>
</tbody>
</table>
revascularization that was not seen in the group with unsuccessful revascularization [Fig. 4].

No changes were observed in the necrotic myocardial mass before and after PCI in any of the groups.

3.2. Clinical follow-up

Functional class of the NYHA improved significantly in patients with successful revascularization: 29 (88%) of patients were in functional class ≥1 before PCI vs. 1 (3%) patient at follow-up (p < 0.001). Functional class did not improve when the procedure was unsuccessful: 9 (90%) patients were in functional class ≥1 before and after the procedure.

4. Discussion

This is the largest CMR perfusion study performed on a clinical basis showing benefits of successful CTO PCI. In our study most patients with a CTO had preserved left ventricular function, inducible myocardial perfusion defects, and myocardial necrosis of reduced extension, mostly non-transmural, indicating the presence of viable myocardial tissue. Patients undergoing successful CTO PCI show a significant reduction of myocardial ischemia and, also, a significant improvement in LV regional wall motion when viable myocardium is present. A significant improvement of functional NYHA class was also observed in these patients.

Few studies using CMR have shown the beneficial effect of PCI on CTO [10,11,17,18] and most of them included a lower number of patients. Cheng et al. [10] showed an increase in regional myocardial blood flow under adenosine-induced hyperemia in 17 patients with a successful CTO PCI. Other studies [11,19] have shown that an improvement in regional and global contractility is related to the extent of dysfunctional but viable myocardium assessed by DE. Findings in these studies, however, were based on quantification of myocardial blood flow [10] or calculation of wall thickening [11]. These methods of analysis to date are time-consuming and, therefore, not routinely used. Our study was performed on a routine clinical basis, consisting of a comprehensive CMR study – including adenosine stress perfusion imaging – with visual analysis of myocardial perfusion and regional contractility.

Recently Kirschbaum et al. [18] reported in a large series of patients with a CTO that a combination of various viability parameters, including low-dose dobutamine, improved the prediction of viability. However, in their study myocardial ischemia was not evaluated. Although we think that a low-dose dobutamine study might be particularly useful to determine viability in selected patients, in our study we did not include it as part of the evaluation pre-PCI. However, most of our patients presented with a reduced extension of scar, large perfusion defects, and with preserved LVEF. Thus, our patients had large extension of potentially viable tissue this making the dobutamine study less relevant, as opposed to the group of patients studied by Kirschbaum.

In our study, an improvement in LVEF, although of a small magnitude, was found in both groups. However, as mentioned before, in most of our patients – with successful or unsuccessful CTO PCI – LVEF was already preserved before the procedure. We also found a significant increase in LVEDV in the unsuccessful CTO PCI group. Previous reports have not analyzed results of unsuccessful CTO PCI.

Most of our patients presented with necrosis of reduced extension, as evidenced by a mean necrotic mass of 6 g, and a proportion of them (28%) showed no evidence of previous infarction. The relatively preserved left ventricular function and the absence of transmural necrosis in patients with CTO seem to indicate that during a gradually developing occlusion some myocardial protection mechanisms evolve, such as collateral circulation, that prevent extensive, irreversible myocardial damage.

Interestingly, and in contrast with previous reports [10,11], we found no increase in the amount of myocardial necrosis in the follow-up study, not even in the patients in whom PCI failed, supporting the safety of the procedure in terms of inducing new areas of necrosis.

One limitation of this study is that this series included only symptomatic patients, and it may not, therefore, represent the whole CTO population. Also, we did not perform a second angiography at 6 months post-PCI in all patients. The strength of the study, however, is that this is the largest series of patients to date and includes those in whom PCI could not be performed.

In conclusion, a successful PCI of CTO reduces inducible myocardial ischemia and improves regional wall motion, resulting in clinical improvements in terms of NYHA functional class.

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The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.
References


