Proximal embolic protection and biomarkers of reperfusion in ST-segment elevation myocardial infarction
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Introduction and outline

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Introduction and outline

General introduction

ST-segment elevation myocardial infarction
Acute coronary syndrome (ACS) is the leading cause of death worldwide.¹ Unstable angina, non ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI) are part of the continuum of ACS. Unstable angina and NSTEMI are “working diagnoses”, also called non-ST-segment elevation ACS, to distinguish these from STEMI. In patients with unstable angina and NSTEMI, new ST-segment elevation and pathologic Q-waves on the electrocardiogram (ECG) are usually absent. For patients presenting with ischemic chest pain compatible with ACS, the diagnosis of a STEMI can be confirmed by the ECG and typical rise and/or fall in serum cardiac biomarkers of myocyte injury (troponin or creatine kinase MB).² In the mid-1970s, acute myocardial infarction was identified, in the majority of cases, as being the result of a ruptured atherosclerotic plaque, causing thrombosis and occlusion of the coronary artery.³ Subsequently, rapid and effective reperfusion is the most important goal in the treatment of patients with STEMI.⁴ Over the last decades, several reperfusion strategies have been developed and used: from intracoronary infusion of streptokinase and intravenous thrombolytic therapy to primary percutaneous coronary intervention (PCI). Nowadays, primary PCI is the reperfusion therapy of choice because randomized trials have shown superior short- and long-term outcomes compared to fibrinolytic therapy. Furthermore, primary PCI is associated with better clinical outcomes than thrombolytic therapy irrespective of the type of thrombolytic regimen used, even when reperfusion is delayed because of transfer for primary PCI.⁵ Despite the value of primary PCI in patients with STEMI, myocardial salvage is frequently suboptimal after primary PCI (as determined by reperfusion biomarkers), and mortality remains substantial in high-risk subgroups.⁶ The outcome after primary PCI has remained essentially unchanged over the past decade, with neither new generation stents nor other novel devices or drugs improving survival beyond that achievable with balloon angioplasty alone.⁷, ⁸ One novel treatment strategy that might reduce myocardial microvascular dysfunction and infarct size and which eventually may improve the clinical outcomes in these patients with STEMI is to prevent distal embolization of atherothrombotic material during PCI and protect the heart from its detrimental consequences.
Distal embolization in acute myocardial infarction

Owing to the nature of the intervention and the atherothrombotic burden in the epicardial vessel, dislodgement of atherothrombotic debris may lead to distal embolization distal to the target lesion. This distal embolization may also arise from atherosclerotic disease and more specifically occur in acute coronary syndromes without any intervention. Embolization of atherothrombotic material during PCI is considered to be an important contributor to the ‘no reflow’ phenomenon. The concept of ‘no-reflow’ refers to a state of myocardial tissue hypoperfusion in the presence of a patent epicardial coronary artery. ‘No reflow’ appears to be a process rather than an immediate event occurring at the moment of reperfusion. Experimental studies demonstrated that the ‘no reflow’ area increases with time after reperfusion. Although it is clear that abnormalities at the level of the microvasculature cause the ‘no reflow’ phenomenon, the exact mechanism is uncertain. However, the underlying mechanism of ‘no reflow’ is microvascular dysfunction, which may be caused by endothelial swelling, tissue compression, myocyte edema, and neutrophil infiltration. In addition, microvascular plugging by macro- and micro-embolizations from the epicardial circulation is considered to be involved in this process.

Microvascular dysfunction following a PCI procedure is most commonly observed during primary PCI for acute myocardial infarction and SVG intervention. It is likely that all patients undergoing PCI for myocardial infarction or SVG disease experience embolization. Furthermore, it is likely that any manipulation of the epicardial coronary bed is accompanied by embolization. Also, treatment of the right coronary artery, thrombus burden, length and diameter of the infarct-related artery have been identified to be predictive for distal embolization in primary PCI patients.

Emboli are thought to be showered downstream after plaque rupture and/or lesion intervention, leading to the obstruction of small arteries and arterioles. Microemboli are likely to arise during PCI of lipid-rich vulnerable plaques. Liberation of plaque components, including platelet-fibrin complex, macrophages and cholesterol crystals, could provoke arteriole spasm, leading to further microvascular obstruction. The incidence of distal embolization after primary PCI in acute myocardial infarction patients ranges from 6 to 15%. The presence of distal embolization on coronary angiogram was associated with reduced myocardial blush grade and Thrombolysis
In Myocardial Infarction (TIMI) graded flow, less ST-segment resolution, higher incidence of new Q-waves, higher enzyme levels, and a higher incidence of re-infarction at one-year follow-up. Although angiographic evidence represents only the tip of the true embolization iceberg during PCI, visualization of distal embolization may have consequences for subsequent treatment and prognosis. Patients with angiographically visible distal embolization (Figure 1) had worse TIMI-graded flow and myocardial blush grade and less ST-segment recovery. However, with this potentially crude method of angiographic assessment of epicardial anatomy and flow, microembolizations due to thrombi and plaque components liberated by wiring, balloon inflation and stent placement, could easily be missed. Nonetheless, using a Doppler guide wire recording continuously coronary flow velocity is a technique that can detect those embolic particles.
Chapter 1

**Figure 1** Angiographic signs of distal embolization (red arrows) after primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction. Distal embolization in the left coronary artery in lateral view (A), in left coronary artery in right anterior oblique view (B), in the right coronary artery in right anterior oblique view (C), and again, in the right coronary artery in right anterior oblique view (D).
**Adjunctive therapy on the ‘no reflow’ phenomenon**

Several adjunctive therapies contribute to the prevention and treatment of distal embolization in acute myocardial infarction. In daily clinical practice, a combined antiplatelet and anticoagulation regimen consisting of aspirin, clopidogrel, and heparin is the recommended adjuvant pharmacotherapy in patients undergoing PCI, whereas the administration of a glycoprotein IIb/IIIa-receptor inhibitors is recommended in patients demonstrating poor ST-segment recovery or evidence of a ‘no reflow’ phenomenon.\(^{19,20}\) Over the last decade, promising mechanical and pharmacological adjunctive therapies to reduce distal embolization have been developed and investigated. A number of adjunctive pharmaco-therapies, including adenosine, α-blockers, calcium channel blockers, β-blockers, antithrombotics and antiplatelet agents, have been used to treat the ‘no reflow’ phenomenon. Accordingly, a series of adjunctive devices with different designs and mechanism of action have been developed and tested in clinical studies, however with conflicting results. These include distal and proximal embolic protection devices and thrombectomy devices. These devices have mostly been studied in primary PCI and SVG intervention. In patients with STEMI treated with primary PCI, several types of devices have been tested in small to large randomized, controlled trials (Table 1).
### Table 1: Overview randomized trials of embolic protection devices and thrombectomy devices in patients with acute myocardial infarction

<table>
<thead>
<tr>
<th>Author</th>
<th>Device</th>
<th>Number of patients</th>
<th>Successful procedure†</th>
<th>Debris retrieved</th>
<th>STR (D/C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Type</td>
<td>Name</td>
<td>PCI with device</td>
<td>PCI alone</td>
<td></td>
</tr>
<tr>
<td>Cura et al.</td>
<td>DP</td>
<td>SpiderRX</td>
<td>70</td>
<td>70</td>
<td>94%</td>
</tr>
<tr>
<td>Gick et al.</td>
<td>DP</td>
<td>FilterWire-EZ</td>
<td>100</td>
<td>100</td>
<td>95%</td>
</tr>
<tr>
<td>Kelbaek et al.</td>
<td>DP</td>
<td>FilterWire-EZ</td>
<td>312</td>
<td>314</td>
<td>99%</td>
</tr>
<tr>
<td>Matsuo et al.</td>
<td>DP</td>
<td>Guardwire</td>
<td>80</td>
<td>74</td>
<td>93%</td>
</tr>
<tr>
<td>Muramatsu et al.</td>
<td>DP</td>
<td>Guardwire</td>
<td>173</td>
<td>168</td>
<td>99%</td>
</tr>
<tr>
<td>Stone et al.</td>
<td>DP</td>
<td>Guardwire</td>
<td>252</td>
<td>249</td>
<td>97%</td>
</tr>
<tr>
<td>Tahk et al.</td>
<td>DP</td>
<td>Guardwire</td>
<td>60</td>
<td>56</td>
<td>97%</td>
</tr>
<tr>
<td>Ali et al.</td>
<td>T</td>
<td>AngioJet</td>
<td>240</td>
<td>240</td>
<td>95%</td>
</tr>
<tr>
<td>Antoniucci et al.</td>
<td>T</td>
<td>AngioJet</td>
<td>50</td>
<td>50</td>
<td>100%</td>
</tr>
<tr>
<td>Ikari et al.†</td>
<td>T</td>
<td>TVAC</td>
<td>180</td>
<td>175</td>
<td>86%</td>
</tr>
<tr>
<td>Beran et al.</td>
<td>T</td>
<td>X-Sizer</td>
<td>30</td>
<td>31</td>
<td>91%</td>
</tr>
<tr>
<td>Napodano et al.</td>
<td>T</td>
<td>X-Sizer</td>
<td>46</td>
<td>46</td>
<td>94%</td>
</tr>
<tr>
<td>Lefevre et al.</td>
<td>T</td>
<td>X-Sizer</td>
<td>100</td>
<td>101</td>
<td>87%</td>
</tr>
<tr>
<td>Dudek et al.</td>
<td>T</td>
<td>Rescue</td>
<td>40</td>
<td>32</td>
<td>87%</td>
</tr>
<tr>
<td>Kaltoft et al.</td>
<td>T</td>
<td>Rescue</td>
<td>108</td>
<td>107</td>
<td>89%</td>
</tr>
<tr>
<td>Burzotta et al.</td>
<td>T</td>
<td>Diver</td>
<td>50</td>
<td>49</td>
<td>98%</td>
</tr>
<tr>
<td>de Luca et al.</td>
<td>T</td>
<td>Diver</td>
<td>38</td>
<td>38</td>
<td>100%</td>
</tr>
<tr>
<td>Silva-Orrego et al.</td>
<td>T</td>
<td>Pronto</td>
<td>74</td>
<td>74</td>
<td>100%</td>
</tr>
<tr>
<td>Sardella et al.‡</td>
<td>T</td>
<td>Export</td>
<td>88</td>
<td>87</td>
<td>100%</td>
</tr>
<tr>
<td>Chevalier et al.</td>
<td>T</td>
<td>Export</td>
<td>120</td>
<td>129</td>
<td>98%</td>
</tr>
<tr>
<td>Svilaas et al.§</td>
<td>T</td>
<td>Export</td>
<td>536</td>
<td>536</td>
<td>89%</td>
</tr>
</tbody>
</table>

† successful procedure with embolic protection or thrombectomy device; †† Mortality was lower in the device group at 9 months follow-up (0% vs. 5%, p=0.02); § Mortality was lower in the device group at 1-year follow-up (4% vs. 7%, p=0.02); ¶ Major adverse cardiac events were lower in the device group at 8-month follow-up (13% vs. 21%, p < 0.05) ** significant improvement in rates of MBG ≥ 2; *** significant different in MBG 0 or 1; DP = distal embolic protection device; T = Thrombectomy device; STR = ST-segment resolution; D = device group; C = control group; TIMI = thrombolysis in myocardial infarction; MBG-3 = myocardial blush grade 3; LVEF = left ventricular ejection fraction; NS = not significant; * = p < 0.05; NA = not available; cTFC = corrected TIMI frame count.
### Table 1 Continued

<table>
<thead>
<tr>
<th>Author</th>
<th>TIMI-graded flow (D/C)</th>
<th>MBG-3 (D/C)</th>
<th>LVEF (D/C)</th>
<th>Infarct size (D/C)</th>
<th>Mortality at 30 days (D/C)</th>
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<tbody>
<tr>
<td>Cura et al.</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NA</td>
<td>NS</td>
</tr>
<tr>
<td>Gick et al.</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NA</td>
<td>NS</td>
</tr>
<tr>
<td>Kelbaek et al.</td>
<td>95%/85%*</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NS</td>
</tr>
<tr>
<td>Matsuo et al.</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NA</td>
<td>NS</td>
</tr>
<tr>
<td>Muramatsu et al.</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NA</td>
<td>NS</td>
</tr>
<tr>
<td>Stone et al.</td>
<td>NS</td>
<td>NS</td>
<td>NA</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Tahk et al.</td>
<td>TIMI-3 was more frequent in D*</td>
<td>NA</td>
<td>NS</td>
<td>NA</td>
<td>NS</td>
</tr>
<tr>
<td>Ali et al.</td>
<td>TIMI-3 was lower in D*</td>
<td>NS</td>
<td>NS</td>
<td>Tc 99 m sestamibi infarct size was greater in D*</td>
<td>5%/1%*</td>
</tr>
<tr>
<td>Antoniucci et al.</td>
<td>cTFC was lower in D*</td>
<td>NA</td>
<td>NA</td>
<td>Tc 99 m sestamibi infarct size was smaller in D*</td>
<td>NS</td>
</tr>
<tr>
<td>Ikari et al.*</td>
<td>NS</td>
<td>46%/21%*</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Beran et al.</td>
<td>cTFC was lower in D*</td>
<td>NA</td>
<td>NS</td>
<td>NA</td>
<td>NS</td>
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<tr>
<td>Napodano et al.</td>
<td>NS</td>
<td>72%/37%*</td>
<td>NS</td>
<td>NA</td>
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</tr>
<tr>
<td>Lefevre et al.</td>
<td>NS</td>
<td>NS</td>
<td>NA</td>
<td>NA</td>
<td>NS</td>
</tr>
<tr>
<td>Dudek et al.</td>
<td>NS</td>
<td>NS</td>
<td>NA</td>
<td>NA</td>
<td>NS</td>
</tr>
<tr>
<td>Kaltoft et al.</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>Tc 99 m sestamibi infarct size was larger in D*</td>
<td>NS</td>
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<tr>
<td>Burzotta et al.</td>
<td>NS</td>
<td>68%/45%**</td>
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<td>de Luca et al.</td>
<td>NS</td>
<td>37%/13%*</td>
<td>NS</td>
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<td>Silva-Orrego et al.</td>
<td>cTFC was improved in D*</td>
<td>88%/44%*</td>
<td>NA</td>
<td>NA</td>
<td>NS</td>
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<tr>
<td>Sardella et al.*</td>
<td>NS</td>
<td>89%/60%*</td>
<td>NS</td>
<td>gadolinium-enhanced CMR infarct size was smaller in T*</td>
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<tr>
<td>Chevalier et al.</td>
<td>NS</td>
<td>NS</td>
<td>NA</td>
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<td>NS</td>
<td>17%/26%***</td>
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Combined proximal embolic protection and thrombus aspiration in primary PCI

The Proxis system (St. Jude Medical, St. Paul, MN, USA; Figure 2) is indicated for use in the prevention of distal release of emboli in coronary vessels during a PCI. It is a unique device of combined proximal embolic protection and thrombus aspiration. The Proxis system is a single-operator full-length flexible catheter (6 or 7 French guiding catheter compatible) and based on a carbon dioxide gas (CO₂) inflation system. It is deployed proximal to the target lesion before crossing. To allow for sufficient antegrade flow around the Proxis catheter, lesion and vessel size recommendations for Proxis placement are a “landing zone” of generally more than 10 to 12 mm proximal to the target lesion and a native vessel size of more than 2.5 mm and a left main vessel of more than 3.0 mm. Inflation of the sealing balloon suspends antegrade flow during the period of lesion intervention. Stagnated blood and emboli liberated during intervention can be retrieved by aspiration. Crossing of the target lesion with the wire, balloon dilatation, and stent placement can be performed through the Proxis system and carried out under full proximal blockade of the vessel. Aspiration and embolic protection by temporary proximal vessel occlusion can be repeated during each step of PCI.

In contrast to distal embolic protection devices and manual thrombus aspiration devices, the Proxis system provides embolic protection before wire-crossing of the target lesion. The Proxis system has an advantage over the distal embolic protection devices in that they do not require a distal landing zone and they do not have the disadvantage of the need for placement of the device in the distal (tortuous) vessel or unknown anatomy, thereby passing the thrombotic lesion. Due to suspending the antegrade flow in the artery by inflation of the sealing balloon, the operator is able to manipulate the target lesion with wires, balloons, and stents. Hence, the Proxis system prevents both distal embolization during lesion crossing and protects side branches of target lesion proximally and distally. Furthermore, the Proxis system is also capable of aspirating stagnated blood and debris during every step of the procedure.

In the first part of the thesis, a study is described that was designed to evaluate the safety, feasibility, and effectiveness of combined proximal embolic protection and thrombus aspiration in patients with STEMI treated with primary PCI. Several reperfusion biomarkers, such as ST-segment resolution by continuous ST Holter monitoring, angiographic outcomes (myocardial blush grade, TIMI graded flow,
computer-assisted myocardial blush, angiographic signs of distal embolization), and intermediate outcomes determined by late gadolinium enhancement (LGE) cardiovascular magnetic resonance (CMR) imaging were used to evaluate the Proxis system.

**Figure 2** Proxis embolic protection system: (A) in native coronary artery, (B) in saphenous vein graft, and (C) full assembly.
Reperfusion biomarkers in acute myocardial infarction

Mortality is the ultimate parameter for measuring the efficacy of reperfusion strategies in patients with acute myocardial infarction. However, mortality after primary PCI for STEMI is low, usually below 10% at one year. Using mortality as a clinical end point in a primary PCI study, a large sample is necessary to test novel treatments in combination with the existing reperfusion strategies that are already highly effective. Furthermore, the prognosis of patients with STEMI varies widely, and clinical, biochemical, angiographic, and ECG markers of adverse prognosis are used to identify patients who are at risk of developing a life-threatening cardiac event and who have predominant benefit from intensive antithrombolytic and antiplatelet medical and interventional strategies.6, 7 Thus, early biomarkers of prognosis in patients that are candidates for reperfusion treatment efficacy are needed in order to select the optimal strategy and for the purpose of trial design.

In this regard, serum biomarkers of myocardial cell necrosis, most notably cardiac troponin T or I, have become valuable tools in the patients with ACS and have been implemented into the guidelines as part of the risk stratification in patients with ACS.21, 22 In addition, another extensively studied serum biomarker is high-sensitivity C-reactive protein (hsCRP). High-sensitivity CRP is an inflammatory biomarker that independently predicts future vascular events in patients who have had an episode of unstable patients as well in apparently healthy persons.23, 24 Interestingly, also plasma levels of N-terminal pro-brain natriuretic peptide (NT-pro-BNP) are elevated in patients with an acute myocardial infarction and provide unique prognostic information, independent of the presence of left ventricular dysfunction at presentation. NT-pro-BNP has been associated with long-term mortality in patients with stable coronary disease and ACS.25, 26 Thus, the prognostic value of these set of serum biomarkers, especially NT-pro-BNP, could provide complementary information on the patients’ prognosis at the time of primary PCI.

Angiographic predictors of outcome

The angiogram provides insight into epicardial flow of the infarct-related coronary artery and perfusion of the myocardium. For more than two decades now, the TIMI flow grade classification scheme has been successfully used to assess coronary
blood flow in ACS.\textsuperscript{27} It has been a valuable tool to compare angiographic outcomes following reperfusion, and the association of the TIMI flow grade with clinical outcomes (including mortality) has been well documented.\textsuperscript{28} However, restoration of epicardial flow does not necessarily lead to restoration of flow at the tissue level or microvascular perfusion.\textsuperscript{29} A method of assessing myocardial perfusion on the angiogram is the myocardial blush grade. A myocardial blush grade one or two represents diminished intensity in the myocardium and normal perfusion in the myocardium carries a score of three. A so-called “closed muscle” carries a score of zero in the myocardial blush grade system. Also, myocardial blush grade is independently related to long-term mortality in patients with STEMI undergoing primary PCI.\textsuperscript{30} Myocardial blush grading permits risk stratification even within epicardial TIMI grade 3 flow. Despite achieving epicardial patency with normal TIMI grade 3 flow, those patients whose microvasculature fails to open (myocardial blush grade 0-2) have a significant increase in mortality compared with those patients with both TIMI grade 3 flow in the epicardial artery.\textsuperscript{31} Because visual assessment of myocardial blush grade requires an experienced operator and is associated with inter-observer and intra-observer variabilities,\textsuperscript{30} computer analysis of myocardial reperfusion on the digital coronary angiogram could be less observer-dependent and may allow a more fine-grained assessment of reperfusion.\textsuperscript{32}

**Electrocardiographic predictors of outcome**
Whereas the angiogram may reflect the mechanical patency of the microvasculature and the integrity of the endothelium, the ECG may reflect the functional status of the supplied myocardium.\textsuperscript{33} The presence of incomplete ST-segment resolution after primary PCI is an important and immediately available diagnostic measure that might imply the presence of microvascular dysfunction. While ST-segment resolution is ultimately a surrogate electrocardiographic biomarker, ST-segment resolution reflects intensity and duration of myocardial ischemia and has consistently been associated with infarct size, left ventricular ejection fraction, and mortality in acute myocardial infarction patients.\textsuperscript{34-36} This relationship is known to be robust and constitutes the basis for guideline recommendations promoting re-assessment of ST-segments 90 minutes after initiation of therapy.\textsuperscript{37, 38} Even among patients with
angiographic successful procedures who on average enjoy a favourable prognosis, ST-segment recovery remains a strong predictor of mortality.34 Although most reports have documented this relationship between ST-segment resolution from 30 to 240 minutes after index procedure (with the use of several measures) in selected patient populations,34, 35, 39-41 it remains unclear whether ST-segment resolution measured immediately after PCI (early ST-resolution) could identify patients with continued high risk for a large infarct, impaired left ventricular function, and cardiac events. In research studies of new therapeutics in patients with STEMI, such as the PREPARE study, ST-segment recovery measured by continuous ST Holter monitoring (Figure 3) has proven to be one of the most robust and widely used measures to quantify the speed, stability, and quality of reperfusion.42, 43
Introduction and outline

Distal Embolization

Reperfusion

Peak

60 sec

30 min

12mm STE

98% Recov

(Reperfusion)

98% Recov
Figure 3 Continuous 12-lead ST-segment monitoring analysis: (A) antero-lateral ST-elevation (red) and reciprocal inferior ST-depression (blue), (B) temporal rotation shows three episodes of coronary occlusion: first two with complete reperfusion (left) and third with distal embolization (right), and (C) analogue anterior lead waveform examples of first reperfusion event and (D) distal embolization at 60 seconds and 30 minutes after events.

MRI measures of reperfusion and infarct size
Although LGE-CMR has limited availability in most hospitals and is time consuming, LGE-CMR is a well validated technique for the determination of the necrotic (subacute phase, Figure 4) and scarred (chronic phase, Figure 5) myocardium. Even when the diagnosis of myocardial infarction is certain, it is often useful to further characterize the infarct and identify the consequences. Infarct size can be measured accurately and with a high level of reproducibility in both acute and chronic settings. Furthermore, the high spatial resolution of LGE-CMR allows determination of the transmural extent of infarction, which provides supplemental information to infarct size in predicting improvement in contractile function with PCI or medical therapy.
LGE-CMR can distinguish acute myocardial infarcts with only necrotic myocytes from acute myocardial infarcts with necrotic myocytes and damaged microvasculature. The microvascular dysfunction (or microvascular obstruction) is important to detect because it appears to be associated with global and regional function recovery and poor clinical outcome.\textsuperscript{47, 48} Also, LGE-CMR is able to assess several functional parameters in great detail: left ventricular dimensions and global or regional left ventricular function.

In the second part of the thesis, these different modalities of reperfusion in relation to well-validated reperfusion biomarkers, LGE-CMR-derived outcomes and mortality are studied.

\textbf{Figure 4} Late gadolinium enhancement (LGE) cardiovascular magnetic resonance (CMR) images of a patient with a \textit{sub acute} right coronary artery related myocardial infarction: (A) three-chamber view and (B) two-chamber view. Both LGE-CMR images show transmural hypo-enhancement (‘microvascular obstruction’) in the infero-lateral region (red arrows).
Chapter 1

Figure 5 Late gadolinium enhancement (LGE) cardiovascular magnetic resonance (CMR) images of a patient with a chronic right coronary artery related myocardial infarction: (A) three-chamber view and (B) short-axis view. Both LGE-CMR images show transmural hyper-enhancement in the infero-lateral region (red arrows).

Outline of the thesis

The first part of the thesis concerns the evaluation of combined proximal embolic protection and thrombus aspiration using the Proxis system during primary PCI in patients with STEMI. The safety and feasibility of the Proxis system in STEMI is studied in Chapter 2. In Chapter 3, we evaluated the effect of combined proximal embolic protection and thrombus aspiration on continuous ST Holter parameters in patients with STEMI. The effect on infarct size and left ventricular function of the use of the Proxis system in patients with STEMI is investigated as assessed by LGE-CMR imaging in Chapter 4. As described in Chapter 5, an independent core-lab re-evaluated all angiographic outcomes of the PREPARE trial.

The second part of the thesis involves several biomarkers of reperfusion of patients with STEMI treated with primary PCI. In Chapter 6, we tested the usefulness of NT-pro-BNP as independent predictor for cardiac function among other cardiac serum biomarkers in acute myocardial infarction patients undergoing primary PCI. Also in Chapter 7, NT-pro-BNP on admission is tested as early predictor of ST-segment recovery after primary PCI and compared to other serum biomarkers. Chapter 8 describes the feasibility of computer-assisted myocardial blush quantification after primary PCI in
STEMI. In addition, Chapter 9 shows the association of computer-assisted myocardial blush quantification with LGE-CMR-derived outcomes. In Chapter 10, the effect of ST-segment recovery measured by continuous ST Holter monitoring on infarct size and left ventricular ejection fraction as determined by LGE-CMR is described. Furthermore, Chapter 11 studied the effect of ST-segment recovery immediately after primary PCI on the prognosis of patients with STEMI in the real world. Chapter 12 demonstrates the prediction of one-year mortality in patients with acute myocardial infarction with different measures of ST-segment recovery. Chapter 13 delineates the clinical and angiographic predictors of ST-segment recovery after primary PCI. Chapter 14 describes the presence of ST-segment recovery prior to primary PCI as an indicator of coronary patency in patients with acute myocardial infarction. Finally, Chapter 15 depicts the relation between microvascular dysfunction as assessed by coronary Doppler flow velocity measurements and LGE-CMR in patients with acute anterior wall myocardial infarction.
Chapter 1

Reference list


