Adjunctive Thrombectomy and Distal Protection in Primary Percutaneous Coronary Intervention
Impact on Microvascular Perfusion and Outcomes

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Abstract—A significant proportion of patients with ST-elevation myocardial infarction have persistent impairment of microvascular blood flow despite successful reperfusion of epicardial vessels. Microvascular dysfunction has been associated with larger infarct size, increased predisposition to ventricular arrhythmias, heart failure, cardiogenic shock, recurrent myocardial infarction, and death. It remains unclear whether this association is of direct mechanistic significance or whether the microcirculatory injury is an epiphenomenon and a manifestation of greater ischemic insult to the myocardium. Although several potential mechanisms have been proposed for the microvascular dysfunction, distal microembolization during mechanical reperfusion is likely to be an important contributor. Consequently, there has been increasing interest in the concept of adjunctive mechanical thrombectomy to improve outcomes in primary percutaneous coronary intervention. Until recently, randomized trials of thrombectomy and distal protection devices during primary percutaneous coronary intervention have provided conflicting results with no definitive evidence for efficacy. The recently published Thrombus Aspiration During Percutaneous Coronary Intervention in Acute Myocardial Infarction Study has rekindled the interest in this area. This trial is the largest randomized study of a thrombectomy device published to date and demonstrates that adjunctive treatment with aspiration thrombectomy during primary percutaneous coronary intervention improves surrogate and clinical end points. The aim of the present report is to review the evidence to date on the role of mechanical thrombectomy and embolic protection in native coronary arteries during primary percutaneous coronary intervention. (Circulation. 2009;119:1311-1319.)

Key Words: thrombus • percutaneous coronary intervention • thrombectomy • distal protection devices • myocardial infarction

A significant proportion of patients with ST-elevation myocardial infarction (STEMI) have persistent impairment of microvascular blood flow despite successful reperfusion of epicardial vessels.1–3 Microvascular dysfunction has been associated with larger infarct size, increased predisposition to ventricular arrhythmias, heart failure, cardiogenic shock, recurrent myocardial infarction, and death.4 It remains unclear whether this association is of direct mechanistic significance or whether the microcirculatory injury is an epiphenomenon and a manifestation of greater ischemic insult to the myocardium. Although several potential mechanisms have been proposed for the microvascular dysfunction, distal microembolization during mechanical reperfusion is likely to be an important contributor. Consequently, there has been increasing interest in the concept of adjunctive mechanical thrombectomy to improve outcomes in primary percutaneous coronary intervention (PCI). Until recently, randomized trials of thrombectomy and distal protection devices during primary PCI have provided conflicting results with no definitive evidence for efficacy. The recently published TAPAS (Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial Infarction Study) trial has rekindled interest in this area.5 This trial is the largest randomized study of a thrombectomy device published to date and demonstrates that adjunctive treatment with aspiration thrombectomy during primary PCI improves surrogate and clinical end points. The aim of the present report is to review the evidence to date on the role of mechanical thrombectomy and embolic protection in native coronary arteries during primary PCI.

Microvascular Perfusion and Injury
Restoration of perfusion and thereby myocardial salvage is the single most important objective in the management of STEMI to optimize outcomes. The immediate goal of reperfusion therapy has been to promptly restore normal (Thrombolysis In Myocardial Infarction [TIMI] grade 3) epicardial blood flow in the culprit vessel, which can now be achieved in 95% of cases.3 Tissue perfusion at the level of the myocardium is not restored in approximately one third of...
patients, even after successful primary PCI, owing to impairment in microvascular blood flow, and in these patients, the benefit of reperfusion is limited.6

Potential mechanisms of microvascular dysfunction include distal macroembolization or microembolization, local formation of thrombus, generation of oxygen free radicals, myocyte calcium overload, cellular and interstitial edema, endothelial dysfunction, vasoconstriction, and inflammation.6 Distal macroembolization of atheromatous and thrombotic debris can be detected by angiography in as many as 15% of patients,7 and in postmortem studies, ~80% of patients have evidence of microembolization.8 A recent study using Doppler flow wires to detect embolic particles (high-intensity transient signals) demonstrated that distal embolization is a universal phenomenon during primary PCI.9 The embolization occurred predominantly at the time of the first balloon inflation and stent deployment, and the magnitude correlated with the severity of the subsequent microvascular dysfunction. In the cardiac catheterization laboratory, impaired microvascular perfusion may manifest as the “no-reflow” phenomenon.10 Thrombus burden is a predictor of the no-reflow phenomenon and an independent predictor of adverse outcomes.11,12 Several techniques are available for detecting microvascular injury, but their precise role in clinical practice remains to be established.13 However, it is helpful to be familiar with them, because they commonly are used as surrogate end points in clinical trials of thrombectomy devices (Table 1).

**Table 1. Methods for Detecting Impaired Microvascular Perfusion**

<table>
<thead>
<tr>
<th>Technique</th>
<th>Indices</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG</td>
<td>ST-segment resolution</td>
<td>Widely available, simple, inexpensive,</td>
<td>Indirect marker of perfusion; no uniform method for assessment</td>
</tr>
<tr>
<td>Angiogram</td>
<td>Myocardial blush grade; corrected TIMI frame count</td>
<td>Available in the catheterization laboratory, inexpensive</td>
<td>Invasive, semiquantitative</td>
</tr>
<tr>
<td>Doppler wire</td>
<td>Coronary flow reserve; coronary wedge pressure</td>
<td>Available in the catheterization laboratory, quantitative</td>
<td>Invasive, expensive</td>
</tr>
<tr>
<td>Echocardiogram</td>
<td>Myocardial contrast echocardiography</td>
<td>Noninvasive, additional information on left ventricular function available</td>
<td>Limited availability; perfusion contrast agents relatively contraindicated in acute coronary syndromes; expensive</td>
</tr>
<tr>
<td>MRI</td>
<td>Perfusion imaging with gadolinium</td>
<td>Noninvasive, quantitative assessment of infarct size and microvascular injury</td>
<td>Limited availability, expensive</td>
</tr>
</tbody>
</table>

**Aspiration Thrombectomy**

Manual aspiration catheters are appealing because they are quick and easy to use, as well as relatively inexpensive. The early studies with these devices were small and therefore underpowered to detect differences in outcomes (Table 2). In the REMEDIA (Randomized Evaluation of the effect of MEchanical reduction of Distal embolization by thrombus aspiration In primary and rescue Angioplasty) trial, which enrolled 100 patients with STEMI, aspiration thrombectomy improved myocardial perfusion (myocardial blush grade and ST-segment resolution) but not clinical end points.17 De Luca and colleagues18 reported from a study of 76 patients with anterior STEMI that aspiration thrombectomy improved the indices of microvascular function (myocardial blush grade and ST-segment resolution), and this was associated with a reduced frequency of adverse left ventricular remodeling at 6 months; however, no difference was found in rates of major adverse cardiac events. The DEAR-MI (Dethrombosis to Enhance Acute Reperfusion in Myocardial Infarction) trial tested the efficacy of the Pronto aspiration extraction catheter. The thrombectomy group had better microvascular perfusion, less frequent no-reflow phenomenon (3% versus 15%, P<0.05), and less frequent angiographic embolization (5% versus 19%, P<0.05). Also, less myonecrosis was found, but no improvement was found in in-hospital outcomes.19 Finally, in a randomized study using the Rescue catheter, Kaltof and colleagues20 reported that no impact of thrombectomy was found on myocardial salvage, measured by sestamibi single-photon emission CT nuclear imaging. Of concern was the fact that the final infarct size was increased

**Thrombectomy Devices**

Because embolization occurs predominantly at the time of the initial balloon or stent inflation, the primary purpose of adjunctive thrombectomy is to reduce the thrombus burden and decrease the likelihood of distal embolization during subsequent angioplasty and stent deployment. Devices available for clinical use include aspiration and specifically designed thrombectomy catheters (Tables 2 and 3). Manual aspiration systems include the Diver CE (Invatec, Roncadelle, Italy), Export (Medtronic, Minneapolis, Minn), QuickCat (Kensey Nash, Exton, Pa), and Pronto (Vascular Solutions, Minneapolis, Minn) catheters. Devices that use a proximal vacuum pump include the Rescue PT system (Boston Scientific, Natick, Mass) and the thrombus vacuum aspiration catheter (TVAC, Nipro, Osaka, Japan). Specific thrombectomy devices include the AngioJet rheolytic thrombectomy system (Possis Medical Inc, Minneapolis, Minn) and the X-Sizer (ev3 Inc, Plymouth, Minn) catheters. The X-Sizer catheter is a unique device that has a helical distal cutter to break thrombus, which is removed by an external vacuum source. The device is no longer available for use in the coronary circulation, although 3 randomized trials of STEMI have demonstrated that it reduced distal embolization and improved microvascular perfusion (Table 3).14–16
which suggests possible harm. A potential explanation for this finding is that the introduction of catheters into the artery results in movement of thrombotic debris downstream. Although this is a distinct possibility, recent meta-analyses indicate the opposite, ie, that aspiration thrombectomy is associated with decreased angiographic evidence of distal embolization.

### TAPAS Trial

The TAPAS (Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial infarction Study) trial is the largest randomized study to date. A total of 1071 patients with STEMI were randomized to either aspiration thrombectomy with the 6F Export catheter with conventional PCI or conventional PCI alone. PCI could be performed by direct stenting or by balloon angioplasty followed by stent deployment, and bare-metal stents were used in all patients. Inclusion criteria were broad, with only those who had rescue PCI or a comorbid condition with a life expectancy of 6 months being excluded from the study. Treatment allocation was performed before angiography and hence without consideration of the thrombus burden. Fifty-four patients in the thrombectomy group (15% versus 8%, \( P = 0.004 \)), which suggests possible harm. A potential explanation for this finding is that the introduction of catheters into the artery results in movement of thrombotic debris downstream. Although this is a distinct possibility, recent meta-analyses indicate the opposite, ie, that aspiration thrombectomy is associated with decreased angiographic evidence of distal embolization.

### Table 2. Randomized Trials of Aspiration Thrombectomy in Primary PCI

<table>
<thead>
<tr>
<th>Reference</th>
<th>n</th>
<th>Study Device</th>
<th>GP IIb/IIIa Use, %</th>
<th>Primary End Point</th>
<th>Results</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Svilpaas (TAPAS)(^2) 2008</td>
<td>1071</td>
<td>Export catheter</td>
<td>93.4</td>
<td>MBG 0 or1</td>
<td>17.1% vs 26.3% (( P &lt; 0.001 ))</td>
<td>Thrombus aspiration improved microvascular perfusion and clinical outcomes in the thrombectomy group</td>
</tr>
<tr>
<td>Kaltoft(^20) 2006</td>
<td>215</td>
<td>Rescue catheter</td>
<td>96</td>
<td>Myocardial salvage</td>
<td>13% vs 18% (( P = 0.12 ))</td>
<td>Myocardial salvage measured by SPECT did not improve. Final infarct size greater in treatment group. No difference in STR between groups</td>
</tr>
<tr>
<td>DEAR-MI(^19) 2006</td>
<td>148</td>
<td>Pronto catheter</td>
<td>100</td>
<td>STR ( &gt; 70% ); MBG 3</td>
<td>68% vs 50% (( P = 0.05 )); 88% vs 44% (( P &lt; 0.0001 ))</td>
<td>Better microvascular perfusion with thrombectomy. Less distal embolization. No difference in rate of in-hospital MACE</td>
</tr>
<tr>
<td>DeLuca(^18) 2006</td>
<td>76</td>
<td>Device CE</td>
<td>Not reported</td>
<td>LV remodeling (end-diastolic volumes at 6 mo)</td>
<td>138.1 vs 152.5 mL (( P = 0.0001 ))</td>
<td>Better STR/MBG after procedure and lower incidence of LV remodeling at 6 mo in the thrombectomy group. No difference in MACE between groups</td>
</tr>
</tbody>
</table>

GP indicates glycoprotein; MBG, myocardial blush grade; SPECT, single-photon emission CT; STR, ST-segment resolution; MACE, major adverse cardiac events; and LV, left ventricular.

### Table 3. Randomized Trials of Rheolytic Thrombectomy and X-Sizer Devices in Primary PCI

<table>
<thead>
<tr>
<th>Reference</th>
<th>n</th>
<th>Study Device</th>
<th>GP IIb/IIIa Use, %</th>
<th>Primary End Point</th>
<th>Results</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIMI(^29) 2006</td>
<td>480</td>
<td>AngioJet</td>
<td>94.5</td>
<td>Infarct size</td>
<td>12.5±12% vs 9.8±11% vs (( P = 0.03 ))</td>
<td>Infarct size larger in thrombectomy group. No difference in TIMI flow grade, STR, 30-day MACE between groups</td>
</tr>
<tr>
<td>Antoniucci(^28) 2004</td>
<td>100</td>
<td>AngioJet</td>
<td>98</td>
<td>Early STR</td>
<td>90% vs 72% vs (( P = 0.022 ))</td>
<td>Improved STR in thrombectomy group; lower CTFC and smaller infarct size</td>
</tr>
<tr>
<td>X-Amine(^14) 2005</td>
<td>201</td>
<td>X-Sizer</td>
<td>60</td>
<td>STR ( \geq 50% )</td>
<td>68% vs 53% vs (( P = 0.037 ))</td>
<td>Better STR with thrombectomy group; no difference in MBG or 6-mo clinical outcomes between groups</td>
</tr>
<tr>
<td>Napodano(^15) 2003</td>
<td>92</td>
<td>X-Sizer</td>
<td>43.4</td>
<td>MBG 3; STR ( \geq 50% )</td>
<td>71.7% vs 36.9% (( P = 0.006 )); 82.6% vs 52.2% vs (( P = 0.001 ))</td>
<td>Thrombectomy improved myocardial perfusion</td>
</tr>
<tr>
<td>Beran(^16) 2002</td>
<td>66</td>
<td>X-Sizer</td>
<td>54</td>
<td>CTFC</td>
<td>18.3±10.2 vs 24.7±14.1 vs (( P &lt; 0.05 ))</td>
<td>Improved epicardial flow in thrombectomy group; better STR</td>
</tr>
</tbody>
</table>

GP indicates glycoprotein; STR, ST-segment resolution; MACE, major adverse cardiac events; and CTFC, corrected TIMI frame count.

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thrombectomy arm crossed over to conventional PCI because
the operator judged the target vessel to be too small or
tortuous to allow delivery of the aspiration catheter. Six
patients in the conventional PCI arm crossed over to throm-
bectomy on the basis of the operator’s judgment. No signif-
ificant differences in baseline characteristics were found be-
tween the 2 groups. Angiographically visible thrombus was
noted in 48.6% of the thrombectomy group and 44.0% of the
conventional PCI group ($P$=0.14). Successful aspiration of
the debris was confirmed by histopathological examination in
72.9% of cases. Postprocedural frequency of TIMI grade 3
epicardial flow did not differ between groups (86% versus
82.5%, $P$=0.12). The primary end point of postprocedural
myocardial blush grade 0 or 1 was present in 17.1% of
patients in the thrombectomy group compared with 26.3% in
the conventional PCI group (risk ratio 0.65, 95% confidence
interval 0.51 to 0.83, $P$<0.001; Figure 1). Other secondary
end points such as complete ST-segment resolution (56.6%
versus 44.2%, $P$<0.001) and absence of persistent ST-
segment deviation (53.1% versus 40.5%, $P$<0.001) were
more commonly achieved in the thrombectomy arm.

Importantly, improved myocardial perfusion was associ-
ated with a trend toward lower 30-day mortality (2.1% versus
4.1%, $P$=0.07). The differences in reinfarction (0.8% versus 1.9%,
$P$=0.11), target-vessel revascularization (4.5% versus 5.8%,
$P$=0.34), major bleeding (3.8% versus 3.4%, $P$=0.11), and
major adverse cardiac events (6.8% versus 9.4%, $P$=0.12)
were not statistically different at 30 days. At 1 year, cardiac
mortality was 3.6% in the thrombectomy group and 6.7% in
the conventional PCI group ($P$=0.020; Figure 2). The 1-year
composite end point of cardiac mortality or nonfatal
reinfarction was higher in the conventional PCI group.

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**Figure 1.** Microvascular perfusion according to treatment strategy in TAPAS. Percentages of patients are shown according to myocardial blush grade on the angiogram (**A**) and degree of resolution of ST-segment elevation (**B**) and persistent ST-segment deviation (**C**) on the ECG. Figure reproduced from Svilaas et al with permission from the publisher. Copyright © 2008, Massachusetts Medical Society; all rights reserved.
(hazard ratio 1.81, 95% confidence interval 1.16 to 2.84, \( P=0.009 \)).\(^{23}\) If confirmed, an event reduction of this magnitude would arguably represent the most important clinical advance in primary PCI since stents and glycoprotein IIb/IIIa inhibitors.

**Clinical Implications of TAPAS**

The TAPAS trial is the largest clinical trial of adjunctive thrombectomy and may be more representative of contemporary practice. It included a broad range of patients, most of whom were treated with stents and glycoprotein IIb/IIIa inhibitors. The improvement in myocardial perfusion with aspiration of thrombus confirms the findings of the majority of preceding smaller trials. The fact that this was associated with a reduction in mortality lends credence to the concept that microvascular protection is clinically relevant and technically feasible in STEMI; however, it is important to remember that the study was conducted at a single high-volume center with experienced operators. The median door-to-aspiration time (28 minutes, interquartile range 14 to 42 minutes) and door-to-balloon time (26 minutes, interquartile range 12 to 40 minutes) were remarkably short, and as such, the results may not be generalizable. A confounding factor that may have influenced outcomes is the fact that the majority of thrombectomy patients had direct stenting, whereas in the conventional PCI arm, the majority were treated with balloon dilation followed by stenting. An explanation for this is that aspiration of thrombus may facilitate direct stenting, likely by improving visualization of the lesion, which is associated with less distal embolization.\(^{24}\) In addition, better visualization of the culprit lesion may optimize sizing of stents.

Overall, the weight of evidence suggests that manual aspiration thrombectomy protects the microcirculation during primary PCI. Whether this is a direct result of a reduction in thrombus burden or is due to facilitation of direct stenting remains to be established. The data from the TAPAS trial are compelling and suggest that adjunctive thrombectomy in STEMI may also improve clinical outcomes. Additional data from further large, multicenter, randomized trials to confirm this finding would be helpful in establishing adjunctive thrombectomy as the standard of care. In the meantime, some authors advocate the use of aspiration catheters for primary PCI.\(^{25,26}\) A strategy based on the amount of thrombus burden may be difficult to apply in clinical practice, because 60% of patients with STEMI have totally occluded vessels at presentation, and the amount of thrombus is not visible initially in these patients.\(^{12}\) Moreover, angiographic assessment of thrombus burden is not accurate. This was highlighted in a recent study in which outcomes in patients who had primary PCI in lesions with no definite angiographic characteristics of thrombus were similar to those with a large thrombus burden.\(^{12}\)

Direct in vitro comparison of currently available aspiration catheters suggests that significant differences exist between them with regard to deliverability and the ability to extract thrombus.\(^{27}\) It is possible that further development in their design will lead to improvement in efficacy. The relatively small lumen size of currently available devices limits their utility in patients with very large or organized thrombi. Larger-lumen 7F catheters may be superior to 6F systems with regard to their extraction capacity.\(^{27}\)

**Rheolytic Thrombectomy (AngioJet)**

The AngioJet rheolytic system removes thrombus by using high-velocity saline jets around the catheter tip that entrain thrombus toward the inflow windows. The technique has the advantage of fragmenting the thrombus, and therefore, it may be useful in the presence of a large thrombus burden. An initial small, randomized trial of rheolytic thrombectomy as an adjunct to direct stenting in STEMI demonstrated improved myocardial perfusion and smaller infarct size (13.0±11.6% versus 21.2±18.0%, \( P=0.01 \)) with thrombectomy, but the clinical outcomes at 6 months were not different.\(^{28}\) However, this was not observed in the much larger AIMI (AngioJet rheolytic thrombectomy In patients undergoing primary angioplasty for acute Myocardial Infarction) trial that compared adjunctive thrombectomy and conventional primary PCI (Table 3).\(^{29}\) Potential limitations of the
study include the fact that patients were randomized after the coronary angiogram was performed, which may have introduced selection bias against enrolling patients with a large thrombus burden who might have been considered candidates for thrombectomy and hence inappropriate for randomization. Moreover, patients in the control arm had higher rates of TIMI grade 3 flow in the culprit artery before the PCI, a factor known to be associated with smaller infarcts. The area at risk was not measured, and hence, myocardial salvage could not be calculated. Finally, a retrograde thrombectomy technique was used (distal to proximal) without the device being activated while crossing the occlusion, which may have promoted embolization. Despite its limitations, the study has raised concerns about the safety of routine rheolytic thrombectomy in primary PCI, because its use was associated with a larger infarct size and greater 30-day mortality (4.6% versus 0.8%, \(P=0.02\)), although the mortality rate was unexpectedly low in the control group.

The ongoing JETSTENT (AngioJet thrombectomy and STENTing for treatment of acute myocardial infarction) trial has been designed to address the limitations of the AIMI trial.\(^3^0\) This randomized, multicenter, international trial will have a sample size of 500 patients and will compare rheolytic thrombectomy before direct stenting of the infarct artery with direct stenting alone during primary PCI. Patients with previous myocardial infarction and cardiogenic shock will be included, unlike the study by Antoniucci and colleagues.\(^3^0\) Another important difference is that the inclusion criteria will require an assessment of thrombus burden, with TIMI grade 3 to 5 thrombus being an inclusion criterion, and a reference vessel diameter \(\geq 2.5\) mm. Thrombectomy will be performed by an antegrade technique during the first pass in a proximal-to-distal direction. The 2 primary end points of this study are ST-segment resolution 30 to 45 minutes after PCI and infarct size at 30 days.

The current evidence does not support the routine use of the AngioJet system in primary PCI. It remains to be established whether the device facilitates microvascular protection or improves outcomes. The results of the JETSTENT trial will provide much needed information on the role of rheolytic thrombectomy as an adjunct to primary PCI.

### Embolic Protection Devices

Embolic protection devices that are in clinical use for PCI are deployed downstream from the culprit lesion and hence are known as distal protection devices. They include distal occlusive devices such as the GuardWire (Medtronic Inc) and the TriActiv system (Kensey Nash) and filters such as the FilterWire (Boston Scientific) and the SpideRx (ev3 Inc). The devices are designed to prevent the embolic material from entering the circulation beyond the lesion and thereby reduce macroembolization and microembolization. The filter-based systems have the advantage of maintaining antegrade flow, whereas the occlusive devices create a stagnant column of blood that has to be aspirated after PCI and before the protection balloon is deflated. The efficacy of distal protection, as an adjunctive therapy, in primary PCI has been investigated in several randomized clinical trials (Table 4).

### Distal Occlusive Devices

The occlusive systems have at least 2 theoretical advantages over the filters. First, they have a lower crossing profile, which may lead to less embolization of thrombus while crossing the lesion. Second, the aspiration of stagnant blood allows for the removal of humoral mediators released during PCI that may also contribute to microvascular dysfunction. The EMERALD (Enhanced Myocardial Efficacy and Recovery by Aspiration of Liberated Debris) trial is the largest (n=501) randomized trial of adjunctive embolic protection in primary PCI for patients who present within 6 hours of symptoms. Patients were randomized to either adjunctive distal protection with the GuardWire system or standard PCI.\(^3^1\) The primary end point of ST-segment resolution

### Table 4. Randomized Trials of Distal Protection Devices in Primary PCI

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Device</th>
<th>GP Ib/IIa Use, %</th>
<th>Primary End Point</th>
<th>Results</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMERALD(^3^3) 2005</td>
<td>GuardWire plus</td>
<td>83</td>
<td>STR (&gt;70%); infarct size</td>
<td>63.3% vs 61.9% (P=0.78); 12.0% vs 9.5% (P=0.15)</td>
<td>No difference in STR and infarct size between groups. No difference in MACE at 6 mo between groups</td>
</tr>
<tr>
<td>ASPARAGUS(^3^2) 2007</td>
<td>GuardWire plus</td>
<td>Not reported</td>
<td>STR (&gt;70%); MBG (&gt;3) (30 d)</td>
<td>38.2% vs 35.5% (P=0.81); 42.9% vs 30.4% (P=0.035)</td>
<td>Less distal embolization with treatment group. No difference in markers of myocardial damage between groups</td>
</tr>
<tr>
<td>PROMISE(^3^5) 2005</td>
<td>FilterWire-EX</td>
<td>100</td>
<td>Adenosine-induced flow velocity in IRA</td>
<td>34±17 vs 36±20 cm/s (P=0.46)</td>
<td>No improvement in coronary reperfusion with treatment group. No impact on infarct size</td>
</tr>
<tr>
<td>PREMIAR(^3^5) 2007</td>
<td>SpiderRX</td>
<td>26</td>
<td>STR (\geq 70%)</td>
<td>61.2% vs 60.3% (P=0.85)</td>
<td>No difference in STR between groups. No difference in MBG, in-hospital ejection fraction, or MACE at 6 mo</td>
</tr>
<tr>
<td>UPFLOW(^3^4) 2007</td>
<td>FilterWire-EX</td>
<td>75</td>
<td>Epicardial TIMI 3 flow; MBG 3; STR (\geq 70%)</td>
<td>88.2% vs 93.9% (P=NS); 68.1% vs 66% (P=NS); 65.6% vs 64.3% (P=NS)</td>
<td>No difference in angiographic or ECG evidence of reperfusion between groups</td>
</tr>
</tbody>
</table>

GP indicates glycoprotein; STR, ST-segment resolution; MACE, major adverse cardiac events; IRA, infarct-related artery; and MRG, myocardial blush grade.
>70% (63.3% versus 61.9%, \( P = 0.78 \)) and infarct size (12.0% versus 9.5%, \( P = 0.15 \)) did not differ between groups, even though embolic debris was retrieved from 73% of patients randomized to distal protection. No difference in mortality or major adverse cardiac events was observed at 6 months between the groups; however, several important findings were provided with regard to the use of distal protection. First, in high-risk subsets such as those with angiographically visible thrombus and totally occluded vessels, the distal protection group had larger infarcts. Second, in \( \approx 20\% \) of patients, the device could not be placed or was placed only after predilation of the infarct-related artery. Third, the median door-to-balloon time was significantly longer in the distal protection group (129 minutes, interquartile range 91 to 170 minutes) than in the conventional arm (108 minutes, interquartile range 84 to 142 minutes, \( P = 0.004 \)), which may have influenced outcomes. Another study that investigated the GuardWire occlusive device is the ASPARAGUS (ASPIrAtion of libeRated debris in Acute myocardial infarction with GuardWire pIUS) trial.\(^{32} \) In that study, adjunctive distal protection also did not improve the primary end point of myocardial blush grade and corrected TIMI frame count; however, a reduction was found in the frequency of slow flow and no-reflow phenomenon immediately after PCI in the distal protection arm (5.3% and 11.4%, \( P = 0.05 \)).

### Distal Embolic Filter Devices

These devices permit anterograde flow and hence are less likely to induce ischemia; they also allow contrast injections for imaging of the vessel during the procedure. The efficacy of the FilterWire has been investigated in 2 randomized trials, PROMISE (PROtection devices in PCI–treatment of Myocardial Infarction for Salvage of Endangered myocardium) and UPFLOW (Use of Protective filter wire to improve FLOW in acute myocardial infarction), neither of which demonstrated any benefit on microvascular function (Table 4).\(^{33,34} \) Of note, patients with non-STEMI were also included in the PROMISE trial. The PREMIAR (Protection of Distal Embolization in High-Risk Patients With Acute ST-Segment Elevation Myocardial Infarction) trial investigated the efficacy of the SpideRx system and reported no benefit on microvascular perfusion with adjunctive distal protection.\(^{35} \)

Overall, the larger clinical trials of distal protection devices have consistently demonstrated that this strategy for adjunctive thrombectomy does not improve microvascular perfusion or clinical outcomes during primary PCI. Several explanations are possible for the lack of efficacy. First, the devices themselves may promote distal embolization while crossing the culprit lesion. Second, the removal of debris may be insufficient, with inadequate ability to aspirate large particles with the occlusion devices or failure to capture particles <100 \( \mu m \) with the filter systems. Third, the potential exists for embolization into side branches that are proximal to the device. Fourth, predilation is often required to facilitate delivery of the device, which may negate the benefit because of the embolization that occurs during the initial balloon inflation. Although the precise reasons why such a promising concept has failed to prove effective remain unclear, what has been established is that distal protection is not an adjunctive strategy that can be recommended for primary PCI on a routine basis. Distal protection may still offer benefit in selected cases with high thrombus burden.

### Proximal Protection Device

A system for proximal (to the culprit lesion) embolic protection has been developed (Proxis system, St Jude’s Medical, Minneapolis, Minn).\(^{36} \) Proximal occlusion is based on the principle of suspending anterograde blood flow before PCI and then aspirating the stagnant column of blood that contains the embolic debris before restoring flow. This approach offers the theoretical advantage of protecting distal side branches. The Proxis system is not widely used in clinical practice, and its role in primary PCI has not been investigated. Preliminary experience suggests that the device requires further refinements to make it suitable for use in unstable patients.

### Conclusions

The evidence to date suggests that adjunctive thrombectomy with an aspiration catheter does offer microvascular protection during primary PCI, a conclusion supported by 2 recent meta-analyses\(^{22,21} \); however, both studies reported that no improvement in 30-day mortality. The data set continues to evolve. The recent TAPAS trial suggests that in a large study, it is possible to demonstrate that improved myocardial perfusion is associated with better clinical outcomes. The precise role of rheolytic thrombectomy in primary PCI remains to be established and is being investigated in an ongoing trial. Current embolic protection devices are not effective for microvascular protection in native coronary arteries and do not improve outcomes. Therefore, they should not be used routinely during primary PCI.

Several explanations are possible for the paradox between the improvement seen in the surrogate end points of myocardial perfusion and the lack of benefit in terms of clinical outcomes in the majority of aspiration and rheolytic thrombectomy studies conducted so far. First, with the exception of the TAPAS trial, the studies have been small and inadequately powered to investigate end points such as death and recurrent myocardial infarction. Second, the inclusion criteria have generally not incorporated an assessment of thrombus burden and culprit vessel size. It is likely that the greatest benefit will be seen in patients with moderate to large burden in larger vessels, who are at highest risk for distal embolization. Third, high-risk patients with cardiogenic shock and hemodynamic instability were excluded in many of the trials, and it is possible that this is a group that may benefit from adjunctive thrombectomy. Finally, there remains the possibility that the microvascular injury in STEMI is an epiphenomenon and not a determinant of infarct size or outcomes, although this seems less likely in light of the TAPAS trial.

On the basis of current evidence, we recommend aspiration thrombectomy as the primary adjunctive mechanical strategy of choice for the majority of patients undergoing primary PCI. We suggest that rheolytic thrombectomy with the AngioJet system and distal protection devices may be appro-
priate in a few selected patients with a very large thrombotic burden. Large, multicenter, randomized trials are needed to definitively establish the efficacy of these devices in reducing myocardial infarct size, heart failure, and mortality.

Disclosures

None.

References


