

**MYOCARDIAL INFARCTION & ISCHEMIA THERAPY UPDATE**

# Primary PCI in STEMI: The Role of Thromboaspiration

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## INTRODUCTION

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Acute myocardial infarction is a potentially life-threatening disease that even in the current device-oriented era remains a challenge for the interventional cardiologist. The underlying pathological mechanism has been shown to be atherosclerotic plaque rupture or erosion with subsequent thrombus formation, which leads to coronary artery occlusion and myocardial necrosis.<sup>1</sup> In order to restore blood flow in the artery and prevent the detrimental effect of myocardial muscle loss, two strategic approaches have been shown to be mandatory. First of all it is pivotal to open the occluded artery and secondly it is imperative to prevent further fibrin deposition and platelet activation and aggregation. The latter is mainly achieved by giving oral antiplatelet therapy with aspirin and a P2Y<sub>12</sub> receptor inhibitor and administering an intravenous antithrombotic agent, such as heparin or bivalirudin.<sup>2</sup> However, thrombus removal from the infarct related artery and reperfusion of the damaged myocardium has been proven to be a more complex issue. This is due to the fact that, even though the hypothesis of thrombotic material extraction which could result in better clinical outcome seems appealing and logical, the available studies have shown surprisingly conflicting results.<sup>3-5</sup> Several mechanisms have been proposed to explain reperfusion failure during primary percutaneous coronary interventions (pPCI), despite the use of dedicated devices that remove thrombotic debris, leading to microvascular obstruction and myocardial injury.<sup>6-12</sup>

**KEY WORDS:**

**ABBREVIATIONS**

MACE = major cardiovascular events  
PCI = primary percutaneous coronary  
intervention  
pPCI = primary percutaneous coronary  
intervention  
STEMI = ST elevation myocardial  
infarction

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## THROMBECTOMY DEVICES

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Currently, there are four different types of devices that are designed to prevent distal embolization of atherothrombotic particles, distal occlusion/aspiration systems, filters, proximal occlusion/aspiration devices, and thrombectomy catheters.<sup>13-15</sup> Thus far, there has been an abundance of evidence suggesting that during pPCI, the utilization of filters and occlusion devices prior to stent implantation compared with stent implantation alone, does not offer any benefit regarding the extent of myocardium salvaged and the long term clinical outcome.<sup>16-20</sup> On the other hand, devices that remove thrombotic material have shown promising results, with the more recent TAPAS (Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial infarction Study) trial exhibiting reduction of mortality in the thrombus aspiration population compared with the stent alone patients.<sup>3</sup>

To date various thrombectomy devices have been developed, that facilitate manual or mechanical removal of intracoronary thrombus. Mechanical thrombectomy devices,

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such as the X-Sizer and AngioJet devices, can remove large thrombi and effectively reduce the thrombotic burden, but are considered to be technically demanding to handle, time consuming to prepare, bulky and relatively expensive. Furthermore, the AIMI (AngioJet in Acute Myocardial Infarction) trial failed to show infarct size reduction or survival benefit in patients treated with rheolytic thrombectomy.<sup>21</sup> These unfavorable results, which came from a poorly designed trial, limited the use of mechanical thrombectomy in the subsequent years. The recently published JETSTENT (AngioJET Rheolytic Thrombectomy Before Direct Infarct Artery STENTing with Direct Stenting Alone in Patients with Acute Myocardial Infarction) trial,<sup>22</sup> which included 501 patients, showed a strong clinical benefit of rheolytic thrombectomy in the setting of pPCI for acute myocardial infarction and rekindled the interest in rheolytic thrombectomy especially in the presence of large thrombus, where its use has been demonstrated to be a significant independent predictor of reduced risk of stent thrombosis and major adverse cardiac events (MACE).<sup>23,24</sup>

In contrast to mechanical thrombectomy that still needs to prove its efficacy in the high risk setting of pPCI and for this reason is not widely utilized, *manual thrombectomy* with aspiration catheters has been extensively employed, since the majority of trials exhibited favorable results.<sup>3,25-27</sup> During the last few years, several catheters with different characteristics have been introduced in clinical practice. These catheters include the Export<sup>®</sup> AP Aspiration Catheter (Medtronic, MN, USA), the Fetch<sup>®</sup> 2 Aspiration Catheter (MEDRAD, Inc.), the Diver<sup>™</sup> CE (Invatec, Roncadelle, Italy), the Pronto<sup>™</sup> (Vascular Solutions, MN, USA), the QuickCat<sup>™</sup> (Spectranetics Inc., CO, USA), the Thrombuster II (Kaneka Corp. Japan), the Nipro's TransVascular Aspiration Catheter (Osaka, Japan), the Eliminate aspiration catheter (Terumo Medical Supply, Japan) and the Hunter<sup>®</sup> (IHT Cordynamic, Barcelona, Spain). However, all the aforementioned aspiration catheters have similar design incorporating two lumens – one lumen for passage of the catheter over a coronary wire and a second lumen for manual aspiration of thrombus and atheromatous debris.

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#### ASPIRATION THROMBECTOMY

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The first large scale randomized trial that compared aspiration thrombectomy followed by stenting versus stenting alone in patients with acute myocardial infarction was the TAPAS trial.<sup>3,28,29</sup> A total of 1,071 patients were randomly assigned to the thrombus-aspiration group or the conventional-PCI group before undergoing coronary angiography. The investigators evaluated angiographic and electrocardiographic signs of myocardial reperfusion and assessed clinical outcome. Successful aspiration was confirmed in 72.9% of patients. A myocardial blush grade of 0 or 1 occurred in 17.1% of the patients in the thrombus-aspiration group and in 26.3% of

those in the conventional-PCI group ( $P < 0.001$ ). Complete resolution of ST-segment elevation occurred in 56.6% and 44.2% of patients, respectively ( $P < 0.001$ ).<sup>29</sup> Moreover, at one year follow-up cardiac death was 3.6% in the thrombectomy group and 6.7% in the conventional PCI group (hazard ratio - HR 1.93; 95% confidence intervals-CI 1.11-3.37;  $p = 0.020$ ). Additionally, 1-year cardiac death or non-fatal reinfarction occurred in 5.6% of patients in the thrombus aspiration group and 9.9% of patients in the conventional PCI group (HR 1.81; 95% CI 1.16-2.84;  $p = 0.009$ ).<sup>3</sup>

The favorable results observed in the TAPAS trial were confirmed by a meta-analysis that included 30 studies with 6,415 patients.<sup>16</sup> The investigators compared catheter thrombus aspiration, mechanical thrombectomy, and embolic protection with pPCI alone.<sup>16</sup> The meta-analysis showed that manual thrombectomy improved myocardial perfusion and was associated with lower mortality (2.7% for the catheter thrombus aspiration group vs. 4.4% for pPCI alone,  $P = 0.018$ ).<sup>16</sup> In another meta-analysis, De Luca and colleagues assessed nine randomized trials with 2,417 patients comparing PCI with aspiration thrombectomy versus pPCI alone.<sup>30</sup> This meta-analysis also found that patients treated with thrombectomy had less distal emboli (7.9 vs. 19.5%,  $P < 0.0001$ ), a higher frequency of TIMI 3 flow (87.1 vs. 81.2%,  $P < 0.0001$ ) and Myocardial Blush Grade 3 (52.1 vs. 31.7%,  $P < 0.0001$ ) post-PCI, and lower 30-day mortality (1.7 vs. 3.1%,  $P = 0.04$ ).<sup>30</sup> The beneficial effect of thrombectomy on myocardial microcirculation may be due to the preservation of microvascular integrity.<sup>31</sup> In a separate meta-analysis, Burzota and colleagues further investigated the impact of thrombectomy on long-term clinical outcome in a collaborative individual patient-data pooled analysis of 11 randomized trials.<sup>32</sup> Subgroup analysis was planned according to the type of thrombectomy device (manual or non-manual), diabetic status, IIB/IIIa-inhibitor therapy, ischemic time, infarct-related artery and pre-PCI TIMI flow. The study demonstrated that manual thrombectomy significantly improved one-year survival in patients undergoing pPCI. Furthermore, after subgroup analysis, manual thrombectomy was associated with improved survival in patients treated with IIB/IIIa-inhibitors.<sup>32</sup> The results of the aforementioned study suggest that manual thrombectomy significantly improves the clinical outcome in patients with pPCI and its effect may be additional to that of IIB/IIIa-inhibitors.

A more recent prospective, non-randomized trial from Leiden sought to investigate whether there is an adjunctive effect of thrombus aspiration among patients with acute myocardial infarction and angiographic evidence of thrombus, receiving prehospital abciximab.<sup>27</sup> ST-segment resolution was significantly higher in the thrombectomy-facilitated group, and multivariate analysis identified thrombectomy as an independent predictor of ST-segment resolution. Additionally, distal embolization was higher in the conventional pPCI group among patients with higher thrombus grades and at 12

month clinical follow-up, thrombus aspiration was associated with reduced all-cause mortality (log-rank  $p = 0.032$ ).<sup>27</sup> In contrast, the INFUSE-AMI randomized trial demonstrated that, in patients with large anterior ST-segment elevation myocardial infarction (STEMI) undergoing primary PCI with bivalirudin anticoagulation, bolus intracoronary abciximab significantly reduced infarct size at 30 days but not manual aspiration thrombectomy.<sup>33</sup> However, the investigators observed that from randomization to 1 year, thrombus aspiration compared with no aspiration was associated with lower rates of new-onset severe heart failure (0.9% versus 4.5%;  $P=0.02$ ) and of rehospitalization for heart failure (0.9% versus 5.4%;  $P=0.0008$ ), but with non-significantly different rates of mortality.<sup>34</sup> Therefore, the results of INFUSE-AMI further support the use of thrombus aspiration combined with intrasession abciximab in patients with anterior STEMI undergoing pPCI with bivalirudin anticoagulation.<sup>34</sup>

Subsequent to the previous favorable results, both the European Society of Cardiology (ESC) and the recently updated 2013 ACCF/AHA STEMI guidelines endorsed the use of aspiration thrombectomy with pPCI in STEMI, with a Class IIa (Level of Evidence: B) recommendation.<sup>35,36</sup> Even so, the use of aspiration thrombectomy during pPCI has remained controversial. This is perhaps due to the fact that, even though removal of some thrombus at the culprit lesion site may prevent distal embolization, improve epicardial coronary flow, and therefore reduce microvascular obstruction and no-reflow, the thrombectomy catheter itself may cause distal thrombus embolization. Moreover, its use adds to procedural time. Hence, there are still concerns regarding its unrestricted application in all patients undergoing pPCI and it has been argued that the majority of evidence is based on small scale trials that did not have the power to determine survival benefit.<sup>37</sup>

The recently published TASTE trial (Thrombus Aspiration before PCI in STEMI) was undertaken in order to shed more light in the role of manual thrombectomy.<sup>38</sup> TASTE was a multicenter, prospective, randomized, controlled, clinical open-label trial based on the Swedish angiography and angioplasty registry platform with blinded evaluation of end points.<sup>38</sup> The investigators observed that death from any cause occurred in 2.8% of the patients in the thrombus-aspiration group, as compared with 3.0% in the pPCI alone group (HR 0.94; 95% CI, 0.72 to 1.22;  $P=0.63$ ). The rates of hospitalization for recurrent myocardial infarction at 30 days were 0.5% and 0.9% in the two groups, respectively (HR 0.61; 95% CI, 0.34 to 1.07;  $P=0.09$ ), and the rates of stent thrombosis were 0.2% and 0.5%, respectively (HR 0.47; 95% CI, 0.20 to 1.02;  $P=0.06$ ). The study did not show any significant differences between the groups with respect to the rate of stroke or neurologic complications.<sup>5</sup> The results of TASTE do not support routine thrombus aspiration before pPCI in patients with STEMI and raise more questions regarding the optimal management of those patients.

Ongoing are two more trials that compare manual thrombus aspiration with pPCI alone, PATA STEMI and TOTAL. The PATA STEMI (The Randomized Physiologic Assessment of Thrombus Aspiration in Patients with Acute ST-Segment Elevation Myocardial Infarction Trial) study aims to determine whether manual thrombus aspiration increases myocardial perfusion assessed by index of microcirculatory resistance.<sup>39</sup> The multicenter, prospective, open, international, randomized TOTAL trial (Thrombectomy with percutaneous coronary intervention versus PCI ALone) is designed to evaluate the efficacy of routine upfront manual aspiration thrombectomy and will recruit 10,700 patients.<sup>40</sup>

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## CONCLUSION

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Manual thrombectomy is easily applicable and several studies have confirmed its favorable effect on myocardial perfusion, especially when it is combined with adjunctive pharmacotherapy, such as the intracoronary administration of IIb/IIIa agents. However, there is no doubt that the TASTE trial will impact everyday clinical practice at least up to a point and until the newer randomized trials further clarify the role and the indications of manual thrombectomy in patients with STEMI submitted to pPCI.

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