

# Thrombus aspiration in acute myocardial infarction

Rupture of an atherosclerotic plaque is the principal mechanism responsible for the development of an acute coronary syndrome. Thrombus formation ensues rapidly on the surface of the injured endothelium. When the infarct vessel is completely occluded, ST-elevation myocardial infarction is diagnosed and urgent reperfusion is required. While infarct artery patency can be restored in most patients, adequate reperfusion at the tissue level is achieved much less often because of distal embolization of plaque and thrombus. Manual thrombus aspiration has been shown to reduce thrombus burden and improve markers of reperfusion, such as epicardial flow (thrombolysis in myocardial infarction flow), myocardial blush grade and ST-elevation resolution, compared with conventional balloon angioplasty and stenting. In one study, mortality was also reduced, but this result could not be duplicated in other series. Additional research is needed to clarify the exact role of manual thrombectomy in the management of ST-elevation myocardial infarction.

**KEYWORDS:** mortality ■ myocardial blush grade ■ pathophysiology ■ ST-elevation myocardial infarction ■ ST-segment elevation ■ thrombectomy ■ thrombolysis in myocardial infarction flow

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Cardiovascular disease accounts for the majority of nonaccidental adult deaths in the USA. According to 2011 mortality data, an acute coronary event (acute coronary syndrome [ACS]) occurs every 30 s and is fatal in half of these cases [1]. Most of the deaths are related to acute plaque disruption in the coronary tree, which causes ACS.

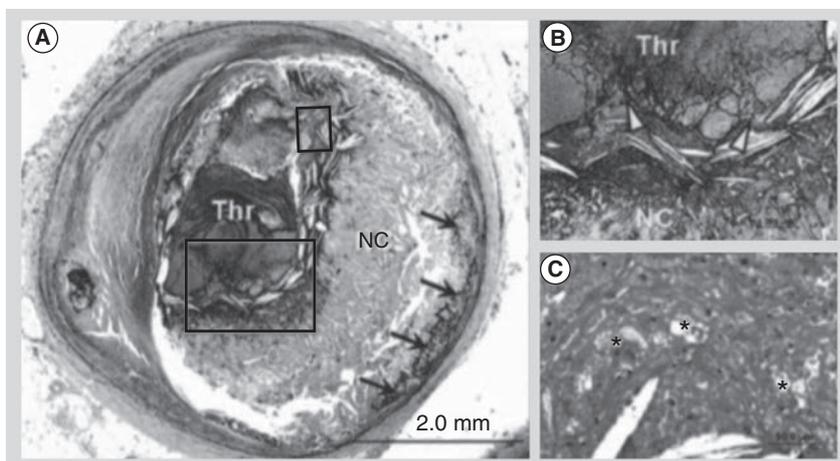
Overall, mortality from ACS has decreased in the last 20 years because of improved detection and treatment, particularly with the introduction of potent antithrombotic therapy and early reperfusion [2]. Since ACS is caused by acute coronary thrombosis, percutaneous coronary intervention (PCI) is superior to medical therapy alone in nearly all patients with high-risk ACS. The benefit of PCI, particularly in patients with ST-elevation myocardial infarction (STEMI), may be enhanced by thrombus removal. In this article, we will discuss the indications, outcomes and recommendations for the use of adjunctive thrombectomy, as well as the relationship between the composition of the aspirated thrombus material and clinical outcome after primary PCI.

## Pathophysiology of ACS

Atherosclerosis is a systemic disease of medium and large arteries characterized by multifocal, lipid-rich plaque development [3,4], predominantly at predilection sites characterized by low and oscillatory endothelial shear stress [5]. The disease

begins to develop early in life, but progression varies greatly and is difficult to predict. However, it usually takes decades to develop the advanced lesions that are responsible for clinical disease. While most plaques remain asymptomatic (sub-clinical disease), some become obstructive, causing stable angina, and a few become thrombosis-prone (vulnerable) and may lead to ACS.

Most data suggest that ACS occurs as a result of some degree of physical disruption to the atherosclerotic plaque with subsequent exposure of the highly thrombogenic subintimal tissue to the blood stream, which leads to the activation of platelets and thrombus formation [6]. There are several forms of plaque disruption that can be identified microscopically. The most frequent type of plaque disruption presents as a gap in the fibrous cap that separates the lipid-rich necrotic core of a plaque from the lumen of the artery (FIGURE 1). In a worldwide survey [7], plaque rupture was the most frequent cause (~70%) of coronary thrombosis, regardless of clinical presentation, including patients dying from the syndrome and those who survive the acute event [8]. The second form of plaque disruption is plaque fissuring, defined as a lateral tear in an eccentric plaque with underlying small necrotic core. The superficial tear lifts a layer of the intima from the underlying fibrous tissue and the intraplaque hemorrhage extends into the necrotic core, creating a tract usually lined by macrophages. This form of plaque disruption is



**Figure 1. Plaque rupture.** (A) Occlusive thrombus with underlying large NC and almost total absence of a fibrous cap. The medial wall is destroyed and near the base of the NC there is calcification (arrows). (B) Higher magnification image of the rupture site (large box in (A)). Thin fibrous cap is disrupted (arrow heads).

(C) Higher magnification of thrombus with cholesterol clefts (small box in (A)), red cells and foamy macrophages (asterisks).

NC: Necrotic core; Thr: Thrombus.

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seen in 10–15% of sudden coronary death cases [9]. Other less common forms of physical disruption of the atherosclerotic plaques include intraplaque hemorrhage and rupture of calcified nodules [10]. In any form of plaque disruption, exposure of the underlying thrombogenic material leads to a cascade of chemical and biological events that result in thrombus formation.

The initial coronary thrombus consists predominantly of platelets and is subsequently strengthened by fibrin deposition and entrapment of red blood cells [11]. An additional stagnation thrombus may form proximally and distally to the original thrombus, thus greatly increasing thrombus burden. As ACS develops, the patency of the culprit artery may change over time, manifesting intermittent occlusion and recanalization [12,13]. There is frequently microembolization from the rupture plaque into the distal microcirculation, which is partially mitigated by endogenous t-PA secretion from the endothelium. When occlusion persists for a significant time, STEMI presentation is more likely. By contrast, a nonocclusive thrombus or intermittent patency tend to present as ACS without ST-segment elevation (NSTEMI). The severity of ischemia is influenced by the extent of collateral flow to the affected territory and by adjacent vascular tone.

### Why use adjunctive thrombectomy in STEMI patients?

Restoration of normal coronary flow and myocardial salvage are the principal objectives in the

management of STEMI. The immediate goal of mechanical reperfusion is to promptly restore normal (thrombolysis in myocardial infarction [TIMI] grade 3) epicardial blood flow in the culprit vessel. This can be achieved nearly universally with current technology [14]. By contrast, tissue reperfusion at the level of the myocardium is not normalized in nearly a third of patients, even after successful primary PCI, limiting the benefit of epicardial reperfusion [15].

Potential mechanisms for microvascular dysfunction include distal macro- or micro-embolization, *in situ* formation of thrombus, generation of oxygen free radicals, cellular and interstitial edema, endothelial dysfunction, vasoconstriction, inflammation, and microvascular hemorrhage or destruction [15]. It is likely that distal embolization occurs predominantly after stent deployment and may result in no-reflow or slow flow in the infarct-related artery. This has led to growing interest in reducing the thrombus burden as an initial step during primary PCI. The two principal strategies to achieve this goal are thrombus aspiration and intracoronary administration of glycoprotein IIb/IIIa inhibitors (GPIs). A third modality, prevention of distal embolization by proximal or distal occlusion devices, has not been shown to be beneficial [16]. Several large randomized trials evaluated the use of GPIs in STEMI with conflicting results [16,17]. Patients with the highest risk profile and most abnormal baseline characteristics benefit the most from the use of GPIs [18]. Currently, it is a class IIa American College of Cardiology/American Heart Association (ACC/AHA) recommendation to use GPIs for selected patients with high thrombus burden [19]. Routine use of GPIs in STEMI does not appear to be beneficial, although direct intralumen administration of abciximab may reduce infarct size [17,20]. This review will focus on thrombus aspiration and evacuation.

### Thrombectomy devices

Several thrombectomy devices have been designed to reduce thrombus burden and prevent distal embolization. These can be divided into mechanical thrombectomy devices (e.g., AngioJet™ [Medrad Interventional/Possis, MN, USA], Rescue™ [BSC, MN, USA], X-Sizer™ [ev3, MN, USA]); and manual thrombectomy devices.

#### ■ Mechanical thrombectomy

The AngioJet thrombectomy system consists of a hollow catheter through which saline is infused under pressure and forced to exit retrogradely just before the catheter tip. These jets create a

localized vacuum, drawing thrombus into the hollow catheter (Venturi effect), where it is mechanically disrupted and evacuated from the body. The US FDA approved the device in 1998 based on its performance among patients with ACS enrolled in the VeGAS-1 and -2 trials [21]. In the subsequent AIMI trial, patients randomized to adjunctive thrombectomy had a larger infarct size compared with conventional PCI, a lower rate of TIMI flow grade 3 and a higher incidence of 30-day major adverse clinical events [22].

The X-Sizer catheter has a helical distal cutter to break the thrombus, which is suctioned out by an external vacuum source. The device is no longer available for coronary use, although it improved microvascular reperfusion in three randomized STEMI trials [23–25].

### Manual aspiration thrombectomy

STEMI guidelines predominantly recommend the use of manual, rather than mechanical, aspiration devices. Examples, among more than 15 brands available, include: Diver CE™ (Invatec, Roncadelle, Italy), Export™ (Medtronic, MN, USA), QuickCat™ (Kensey Nash, PA, USA), Xpress-Way™ (Atrium Medical Corporation, NH, USA), and Pronto™ (Vascular Solutions, MN, USA) catheters. The maximal tip diameter for these catheters (fitting 6-F guiding catheters) varies between 1.34 m (Pronto) and 1.73 m (Export). The Diver CE is equipped with side holes (in one version) for fresher thrombus aspiration, and some are available in 7-F (Xpress-Way, Export and Pronto) and even 8-F size (Pronto). Manual aspiration catheters are easy to use and are inexpensive. Based on the pathophysiological considerations described above, they address three distinct objectives in the management of STEMI patients: evacuate as much thrombus as possible to prevent (further) distal embolization of plaque and thrombus material; eliminate circulating pro-inflammatory and -thrombotic substances

secreted by activated platelets and injured endothelium; and provide a conduit for intralesion and intracoronary selective administration of vasoactive substances and antithrombotic agents. The early studies with these devices were small and lacked statistical power to detect differences in clinical outcomes. They used surrogate markers of reperfusion as primary end points (TABLE 1).

In the 100 STEMI patients of the REMEDIA trial, aspiration thrombectomy with the Diver CE device improved myocardial reperfusion (ST-segment resolution [STR]  $\geq 70\%$ : 44.9 vs 36.7%;  $p = 0.02$  and myocardial blush grade [MBG]  $\geq 2$ : 68.0 vs 58.0%;  $p = 0.034$ ). Despite the favorable effect on surrogate markers, the REMEDIA trial failed to show a benefit in 30-day major adverse cardiac events (MACE – death, stroke, reinfarction and target vessel revascularization) for the aspiration arm, but the study lacked power for MACE [26]. In a 50-patient substudy using myocardial contrast echocardiography, thrombus aspiration reduced early microvascular obstruction and marginally improved 6-month adverse left ventricular remodeling [27].

De Luca and colleagues analyzed data from 76 patients with anterior STEMI who had aspiration thrombectomy and found that it improved microvascular function (MBG and STR) and reduced frequency of adverse left ventricular remodeling at 6 months; again, there was no difference in MACE rate [28].

The DEAR-MI trial evaluated the Pronto aspiration catheter. The thrombectomy group had improved microvascular perfusion, less frequent no-reflow (3 vs 15%;  $p < 0.05$ ), and reduced angiographic embolization (5 vs 19%;  $p < 0.05$ ). There was also less myonecrosis (lower peak CK-MB), but no improvement was seen in in-hospital outcomes [29].

The EXPIRA trial randomized 175 patients with STEMI to primary PCI alone versus primary PCI with manual thrombectomy and showed a

**Table 1. Trial of manual aspiration thrombectomy using surrogates of reperfusion as primary end points.**

Study (year)	Patients (n)	Device (manufacturer, location)	End point(s)	Ref.
REMEDIA (2005)	99	Diver CE™ (Invatec, Roncadelle, Italy)	MBG $>2$ , STR	[26]
DEAR-MI (2006)	148	Pronto™ (Vascular Solutions, MN, USA)	STR, MBG 3	[29]
Kaltoft <i>et al.</i> (2006)	215	Rescue™ (BSC, MN, USA)	Myocardial salvage	[31]
De Luca <i>et al.</i> (2006)	76	Diver CE™ (Invatec, Roncadelle, Italy)	MBG $>2$ , STR	[28]
EXPIRA (2009)	175	Export™ (Medtronic, MN, USA)	MBG $>2$ , STR	[30]
VAMPIRE (2008)	355	TVAC™ (Nipro, Osaka, Japan)	SR or NR	[48]
TAPAS (2008)	1071	Export™ (Medtronic, MN, USA)	MBG	[35]

MBG: Myocardial blush grade; NR: No-reflow; SR: Slow reflow; STR: ST-segment resolution.

significant improvement in the rates of MBG 3 and complete STR. This study was unique in that it evaluated infarct size by MRI and also found that microvascular obstruction extent was lower in the acute phase with aspiration (1.7 vs 3.7 g;  $p = 0.0003$ ). An improvement in infarct remodeling (size reduction) at 3 months was also seen with aspiration (from 17 to 11% of left ventricular mass;  $p = 0.004$ ), but not in the control group (from 14 to 13%;  $p =$  not significant) [30].

The INFUSE-AMI trial was a multicenter, randomized, single-blinded trial with a  $2 \times 2$  factorial design (intralesion abciximab vs no abciximab [Clearway™ catheter; Atrium Medical Corporation] and aspiration thrombectomy [Export catheter] vs no aspiration) and included 452 patients with anterior STEMI at 37 sites in six countries. The study used infarct size as a percentage of left ventricular mass measured by cardiac MRI after 30 days as the primary end point. There was no significant difference between patients randomized to aspiration thrombectomy versus no aspiration in infarct size (median: 17.0 [interquartile range (IQR): 9.0–22.8%] vs 17.3% [IQR: 7.1–25.5%], respectively;  $p = 0.51$ ), absolute infarct mass (median: 20.3 [IQR: 9.7–31.7 g] vs 21.0 g [IQR: 9.1–34.1 g], respectively;  $p = 0.36$ ), or abnormal wall motion score (median score 7.5 in both groups;  $p = 0.89$ ) [17].

Finally, in a randomized study using the Rescue catheter, Kaltoft and colleagues reported that thrombectomy had no impact on myocardial salvage, measured by sestamibi single-photon emission computed tomography (SPECT) nuclear imaging. In fact, infarct size was increased in the thrombectomy group (15 vs 8%;  $p = 0.004$ ) [31]. It is possible that bulky catheters cause distal embolization of thrombotic debris before aspiration occurs. Two recent meta-analyses refute this speculation, showing that aspiration thrombectomy is associated with a lower rate of angiographically visible distal embolization (AVDE) [32,33].

### TAPAS trial

The TAPAS trial is the largest randomized study to date evaluating the effects of manual thrombectomy [34]. It was performed at a single center in The Netherlands and included 1071 patients with STEMI. Patients were randomized to either aspiration thrombectomy with the 6-F Export catheter before conventional PCI ( $n = 535$ ) or to conventional PCI alone ( $n = 536$ ). PCI could be performed by direct stenting or by balloon angioplasty followed by stent deployment, and bare-metal stents were used in all patients. The primary end point was final MBG. Secondary

end points included the degree of STR, and clinical outcomes (death or death/MI) at 30 days and 1 year. Inclusion criteria were very broad. Treatment allocation was performed before angiography, independent of thrombus burden. Less than 10% of patients crossed over from one arm to the other. There were no significant differences in baseline characteristics between the two groups. Angiographically visible thrombus was noted in 48.6% of the thrombectomy group and in 44.0% of the conventional PCI group ( $p = 0.14$ ). Successful aspiration of debris was confirmed by histopathological examination in 72.9% of cases. The primary end point of postprocedural MBG 0 or 1 occurred in 17.1% of patients in the thrombectomy group compared with 26.3% in the conventional PCI group (risk ratio [RR]: 0.65; 95% CI: 0.51–0.83;  $p < 0.001$ ; FIGURE 2). Frequency of postprocedural TIMI grade 3 flow was similar between groups (86 vs 82.5%;  $p = 0.12$ ). Other secondary end points such as complete STR (56.6 vs 44.2%;  $p < 0.001$ ) and absence of persistent ST-segment deviation (53.1 vs 40.5%;  $p < 0.001$ ) were more common in the thrombectomy group (FIGURE 2).

Importantly, improved myocardial perfusion was associated with a significantly lower 30-day mortality (1.1 vs 2.9 vs 5.7% for MBG 3, 2 and 0/1, respectively;  $p = 0.001$ ). The early mortality benefit associated with MBG 3 persisted at 1 year (3.7 vs 4.7 vs 11%, respectively;  $p = 0.001$ ). There were no significant differences in reinfarction (0.8 vs 1.9%;  $p = 0.11$ ), target vessel revascularization (4.5 vs 5.8%;  $p = 0.34$ ), major bleeding (3.8 vs 3.4%;  $p = 0.11$ ) and MACE (6.8 vs 9.4%;  $p = 0.12$ ) at 30 days between the thrombectomy and conventional PCI groups, respectively. At 1 year, cardiac mortality was 3.6% in the thrombectomy group and 6.7% in the conventional PCI group ( $p = 0.020$ ) (FIGURE 3) [10]. The 1-year composite end point of cardiac mortality or nonfatal reinfarction was higher in the conventional PCI group (hazard ratio [HR]: 1.81; 95% CI: 1.16–2.84;  $p = 0.009$ ) [35].

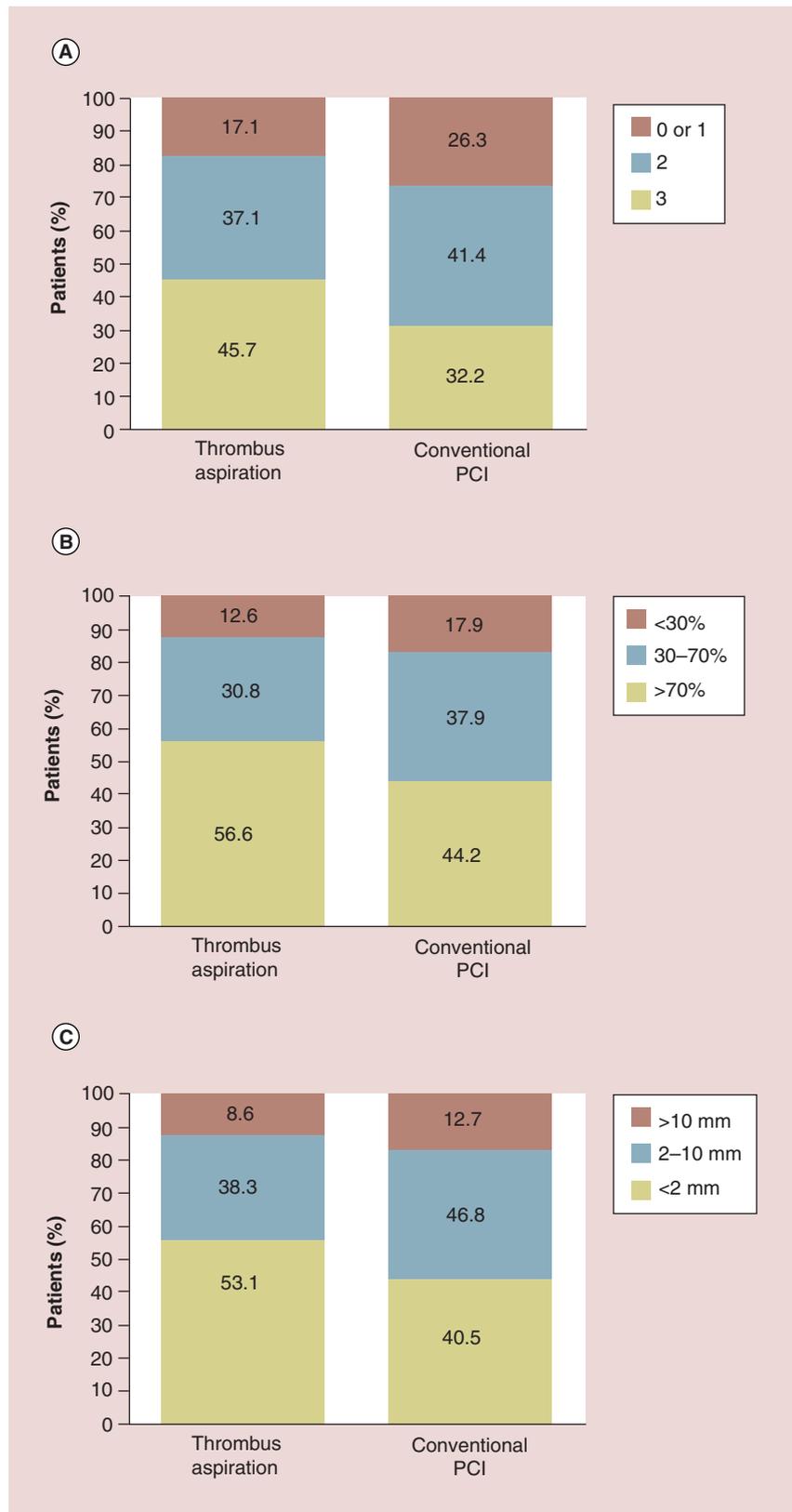
### ■ Clinical significance of the TAPAS trial

The TAPAS trial is the largest clinical trial of adjunctive manual thrombectomy to date and may be more representative of contemporary practice than other studies because of its broad inclusion criteria. Most patients were treated with stents and GPIs. TAPAS confirmed the observations from other small randomized trials regarding the improvement in myocardial perfusion after adjunctive aspiration thrombectomy. The

association with a reduction in mortality supports the concept that microvascular protection is technically feasible and clinically relevant in STEMI; however, TAPAS was a single, high-volume center with experienced operators and very short door-to-aspiration time (28 min; IQR: 14–42 min), and thus may overestimate the true advantages of this intervention. Recently, the TASTE trial reported that manual thrombus aspiration did not reduce mortality at 30 days among 7012 Scandinavian patients with STEMI (2.8 vs 3.0% in conventional PCI arm; HR: 0.94; 95% CI: 0.72–1.23;  $p = 0.63$ ) [36]. Currently, the TOTAL trial is randomizing approximately 4000 patients with STEMI to PCI alone versus PCI with adjunctive aspiration thrombectomy. The primary end point of the study is the first occurrence of cardiovascular death, recurrent myocardial infarction, cardiogenic shock, or new or worsening New York Heart Association Class IV heart failure within 180 days [102]. The study should provide clear data as to whether aspiration thrombectomy should be routinely performed during primary PCI. Another trial, ‘Effect of Thrombus Aspiration in Patients With Myocardial Infarction Presenting Late After Symptom Onset’, is being conducted in Germany and uses microvascular obstruction by cardiac MRI as its primary end point [103].

### Meta-analysis of randomized controlled trials

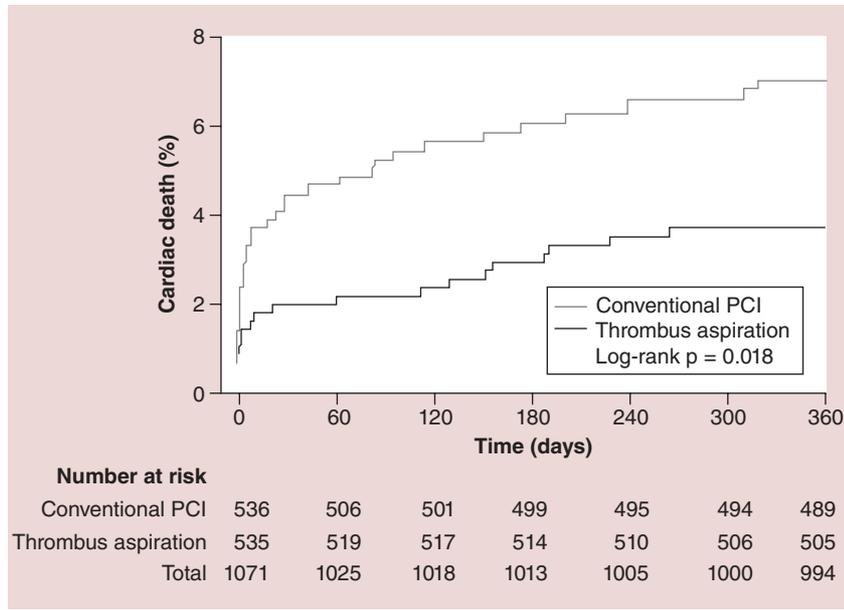
As most of the trials testing adjunctive thrombectomy were not powered to detect differences in clinical outcome, several meta-analyses have been conducted to evaluate its role in primary PCI. Bavry *et al.* analyzed 30 trials (6415 patients) that tested adjunctive thrombectomy or emboli protection devices during primary PCI, among which 13 trials used manual thrombus aspiration (47% of the total populations) [37]. In this meta-analysis, manual thrombectomy resulted in better MBGs (the incidence of MBG 3 after revascularization was 53% for adjunctive devices vs 40% for PCI alone [RR: 1.38; 95% CI: 1.20–1.58;  $p < 0.0001$ ]) and improved STR (the incidence of complete STR was 63% for adjunctive devices vs 53% for PCI alone [RR: 1.27; 95% CI: 1.15–1.41;  $p < 0.0001$ ]). Importantly, the 3–6 month mortality was significantly lower in patients receiving manual aspiration compared with the control group (2.7 vs 4.4%;  $p = 0.018$ ) [37]. In the same meta-analysis, manual aspiration was superior to emboli protection devices and mechanical thrombectomy, neither of which showed clinical benefit (FIGURE 4).



**Figure 2. Markers of myocardial reperfusion in the two treatment groups of the TAPAS trial. (A) Myocardial blush grade; (B) the degree of ST-segment resolution; and (C) persistent ST-segment deviation.**

PCI: Percutaneous coronary intervention.

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**Figure 3. Cumulative rate of cardiac death at 1-year follow-up in the TAPAS trial.**

PCI: Percutaneous coronary intervention.

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In another meta-analysis of 18 prospective randomized controlled trials, Burzotta and colleagues used patient-level data that allowed evaluation of outcomes in subgroups [32]. No statistically significant difference was found between adjunctive device therapy and PCI versus standard PCI for early death or reinfarction (odds ratio [OR]: 0.85; 95% CI: 0.54–1.33; 13 RCTs; n = 2818). Subgroup analyses found a statistically significant effect in favor of treatment with thrombectomy in reducing AVDE (OR: 0.51; 95% CI: 0.28–0.92; seven RCTs; n = 1281), absence of STR (OR: 0.46; 95% CI: 0.32–0.66; 12 RCTs; n = 1934) and absence of MGB <3 (OR: 0.42; 95% CI: 0.23–0.75; nine RCTs; n = 1562). All the benefit was confined to aspiration thrombectomy, while none was observed with distal emboli protection devices. This meta-analysis has the advantage of a patient-level analysis, but also has the potential for bias, as only 11 of 18 trial investigators agreed to participate and provide data for the study. There was also significant heterogeneity among studies and statistical evidence for small trial bias. In a subsequent meta-analysis from the same group, using patient-level data from 2686 patients enrolled in 11 trials, adjunctive thrombectomy was associated with reduced 1-year mortality (p = 0.049). Subgroups analysis showed that thrombectomy is associated with improved survival in patients treated with GPIs (p = 0.045) and that the survival benefit is confined to patients treated with manual thrombectomy (p = 0.011) [38].

In the meta-analysis performed by De Luca and colleagues in 2008, which included nine randomized trials with 2417 patients (1209 patients in the manual thrombectomy device group and 1208 in the control group), PCI preceded by manual thrombectomy was compared with PCI alone. Adjunctive manual thrombectomy was associated with significantly improved post-procedural TIMI grade 3 flow (87.1 vs 81.2%; p < 0.0001) and postprocedural MBG 3 (52.1 vs 31.7%; p < 0.0001), less distal embolization (7.9 vs 19.5%; p < 0.0001), and a significant reduction in 30-day mortality (1.7 vs 3.1%; p = 0.04) [39].

Finally, in a Bayesian meta-analysis of 21 randomized trials, thrombectomy (performed in 16 studies) resulted in significantly less no-reflow (OR: 0.39; 95% credible interval [CrI]: 0.18–0.69), more complete STR (OR: 2.22; 95% CrI: 1.60–3.23) and higher rates of TIMI grade 3 flow (OR: 2.50; 95% CrI: 1.48–4.41). There was no reduction in death (OR: 0.94; 95% CrI: 0.47–1.80), or in the composite of death, recurrent MI or stroke (OR: 1.07; 95% CrI: 0.63–1.92) with thrombectomy. Restriction of the analysis to trials that used manual aspiration thrombectomy devices yielded similar results [40].

A special clinical scenario that may be particularly well suited for thrombus aspiration is the treatment of acute stent thrombosis, because of the large thrombus burden present in these patients. In a propensity-adjusted analysis of 205 patients from multiple centers with angiographically proven stent thrombosis, manual aspiration was used in 56% of the subjects. After adjustment for clinical and angiographic characteristics, aspiration thrombectomy resulted in higher rates of final TIMI grade 3 flow and improved procedural success (96 vs 83% for conventional PCI; p < 0.001). There was no significant difference in long-term mortality (adjusted HR: 0.99; 95% CI: 0.44–2.24) [41].

### Current guidelines for adjunctive thrombectomy

Based on these data, the ACC/AHA guidelines have given aspiration thrombectomy a class IIa (level of evidence B) indication in primary PCI for STEMI. The European Society of Cardiology guidelines also conferred manual thrombus aspiration a class IIa indication (level of evidence A) [42,43]. Some authors advocate aspiration thrombectomy only in patients with high thrombus burden [44,45]. Such a strategy may be difficult to implement as at least 75% of patients with STEMI have no-flow (TIMI 0) on initial

angiogram, rendering evaluation of thrombus burden difficult or impossible.

### Aspirated thrombus composition & its relation to clinical outcome

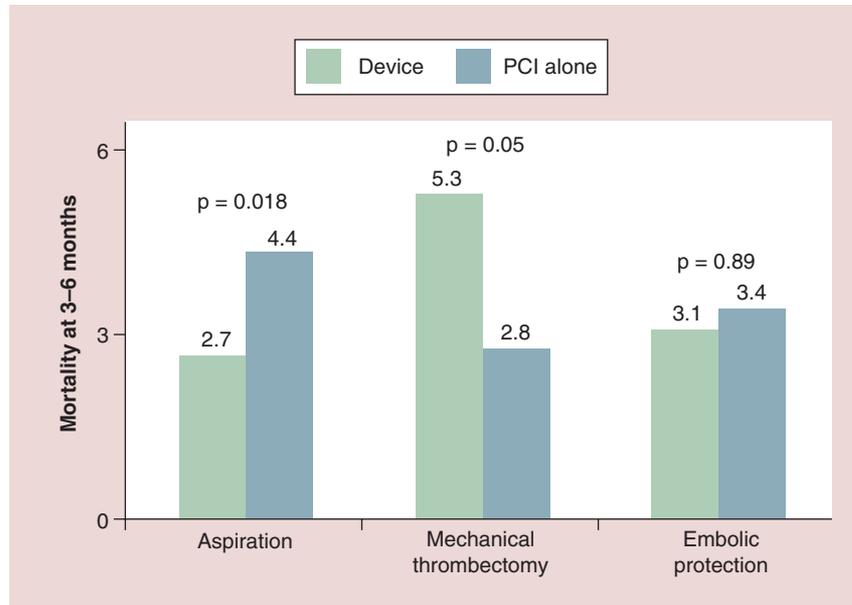
Investigators at a high-volume STEMI center in The Netherlands correlated thrombus age with outcome in 1315 consecutive STEMI cases undergoing primary or rescue PCI [46]. Aspirated material was assessed by histopathology for thrombus presence. When found (75.3% of the cohort), thrombus was classified as either fresh (<24 h, containing mostly erythrocytes, granulocytes, platelets and fibrin) or older thrombus (characterized by the presence of necrotic fragments from red and white blood cells, as well as smooth muscle growth, neovascularization and connective tissue deposition). Fresh thrombus was present in 552 patients (42.0%), while older thrombus was seen in 372 patients (28.2%). Patients with older thrombus had a significantly higher 4-year mortality (16.0 vs 7.4%; HR: 1.82; 95% CI: 1.17–2.85;  $p = 0.008$ ), potentially related to less myocardial salvage. A more recent study assessed the association between composition of aspirated thrombi and the incidence of AVDE during PCI in patients with STEMI treated with thrombus aspiration. The study included 164 patients (126 men; mean age  $65 \pm 12$  years). In aspirated samples, histopathological analysis revealed thrombus components alone in 118 patients (72%), and both thrombus and plaque fragments (containing macrophage-derived foam cells and occasional smooth muscle cells) in 46 patients (28%). The authors concluded that an erythrocyte-rich component in aspirated coronary thrombi and plasma glucose levels on admission were closely associated with the incidence of AVDE [47].

### Conclusion

Manual thrombus aspiration, but not distal embolic protection devices or mechanical thrombectomy, improves markers of reperfusion during primary PCI. One single-center study and a meta-analysis of smaller trials indicated the possibility that manual thrombectomy reduced mortality. Large-scale multicenter randomized trials are needed to confirm its utility in all STEMI patients.

### Executive summary

- Atherosclerotic plaque rupture results in thrombus formation and acute myocardial infarction.
- Manual thrombus aspiration improves infarct vessel reperfusion and prevents distal embolization of plaque and thrombus material.
- There is conflicting evidence regarding the effect of thrombectomy on short- and long-term survival.



**Figure 4. Mortality at 3–6 months in patients treated with primary percutaneous coronary intervention with or without adjunctive devices for the treatment of thrombus from the meta-analysis by Bavry et al.**

PCI: Percutaneous coronary intervention.

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### Future perspective

The data presented in this review suggest that we have a fairly mature understanding of the pathophysiological processes leading to STEMI. The disparity between the effect of thrombus aspiration on mortality in older versus newer trials suggests that we need to better identify the patient and vessel characteristics that are most likely to benefit from this intervention. We predict that in the next few years we will be able to better image the thrombus, identify its components and select the patients best suited for thrombectomy. Better and more selective delivery of antithrombotic medications may further assist in improving outcome in STEMI.

### Financial & competing interests disclosure

*The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.*

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