Rheolytic Thrombectomy in Patients with Acute Coronary Syndrome and Large Thrombus Burden: Initial and Mid-Term Results from a Single Centre Experience

Petros Dardas¹, Nikos Mezilis¹, Vlasis Ninios¹, Georgios K. Efthimiadis¹, Dimitrios Tsikaderis¹, Efstatios Pagourellas³, Christodoulos Plakos²

¹Department of Cardiology and Cardiothoracic Surgery, St. Luke’s Hospital, ²Cardiology Department, AHEPA Hospital, Thessaloniki, Greece

Original Research

Introduction: The presence of a large intracoronary thrombus burden is a major complicating factor during percutaneous coronary intervention (PCI) in patients with an acute coronary syndrome (ACS). The use of rheolytic thrombectomy (RT) has been proposed to prevent thrombus-related complications, with conflicting results. The purpose of this study was to identify the feasibility and safety of this approach.

Methods: We conducted a single-centre, retrospective, observational case-control study, comparing the outcomes of PCI in 26 consecutive patients with ACS and a large thrombus burden who underwent RT to those of a control group of 26 patients, matched with regard to artery location and initial TIMI flow grade.

Results: Despite the higher prevalence of acute ST-elevation myocardial infarction and the larger thrombus burden in the RT group, there was less incidence of distal embolisation/no-reflow and less use of vasoactive intracoronary agents. The final TIMI flow was identical in both groups. There was no difference between the two groups in the in-hospital and mid-term incidence of major adverse coronary events.

Conclusions: In this study, the use of RT in patients with a large thrombus burden during acute PCI was both feasible and safe and reduced the incidence of initial no-reflow phenomenon.

Percutaneous coronary intervention (PCI) involving balloon angioplasty and stenting is an effective treatment for acute coronary syndrome (ACS), including ST-elevation myocardial infarction (STEMI) and unstable angina. Despite the technique’s efficacy, procedural complications such as reduced coronary flow/no-reflow and distal embolisation frequently occur, especially when a large amount of intracoronary thrombus is present.¹² Plugging of the distal microvasculature causes mechanical obstruction of flow and also induces a secondary inflammatory response in the injured myocardium.³⁴ These phenomena may occur even with attainment of thrombolysis in myocardial infarction (TIMI) grade 3 flow.

Mechanical treatment of thrombotic lesions by means of thrombectomy and distal or proximal protection devices has been proposed to prevent the complications caused by thrombi. Early studies demonstrated superior procedural and clinical outcomes in patients treated with the Angiojet rheolytic thrombectomy (RT) device (Possis Medical, Inc., Minneapolis, Minnesota, USA), in terms of reducing thrombus burden and improving coronary flow.⁵⁻⁷ However, in a recent randomised trial, patients with STEMI who were treated with Angiojet application followed
by stent implantation had a larger mean final infarct size and higher mortality compared with controls.\(^8\) It is possible that thrombectomy might be beneficial in the subgroup of patients with a large thrombus burden, but these patients made up only a small portion of the previous study population. A possible benefit from the use of RT in patients with a large thrombus burden who underwent primary PCI for STEMI was also described by another survey.\(^9\)

The purpose of the present study was to evaluate the safety and efficacy of RT in patients undergoing PCI (primary and rescue) for ACS and presenting with a large thrombus burden.

**Methods**

**Study population**

Since August 2004, 520 patients have undergone primary or rescue PCI for ACS in our institution. We retrospectively identified 26 patients (5\% of the whole population) with a large thrombus burden (≥TIMI grade 3 classification) and ACS, who underwent RT before their planned angioplasty (RT group, n=26). ‘Large thrombus burden’ was defined according to the classifications outlined in Tables 1 and 2. It should be emphasised that the most commonly used classification scheme for thrombus burden is the TIMI thrombus grade scale outlined in Table 1.\(^{10}\) Although this classification facilitates thrombus definition for the purpose of conducting clinical trials, it lacks the qualitative elements of thrombus description, which are also important in determining the potential for embolisation during PCI. In particular, grade 5 of this classification (total occlusion) has no value in quantifying the underlying thrombus burden, because a total occlusion can be caused by either a small or large thrombus burden. Yip et al\(^{11}\) proposed an alternative classification scheme that may be clinically useful for estimating the potential for embolisation during PCI (Table 2). Indicators of large thrombus burden according to this classification have been shown to be independent predictors of slow flow during PCI.\(^{11}\)

The control group comprised 26 patients from the above total population (control group, n=26) who presented with ACS, showing similar artery lesions and initial TIMI flow grades, but did not undergo RT.

**Cardiac catheterisation and coronary intervention**

All patients received dual antiplatelet therapy (aspirin 100 mg and a loading dose of clopidogrel 300-600 mg) before the planned procedure. Dual antiplatelet therapy (aspirin 100 mg/day and clopidogrel 75 mg/day) was continued for at least 12 months. At the time of the procedure, heparin was administered to maintain an activated clotting time >250 seconds. The use of glycoprotein IIb/IIIa receptor inhibitors was at the operator’s discretion. An intra-aortic balloon pump was used or not depending on the patient’s haemodynamic status.

Angiojet RT was performed as a default strategy for angiographically large thrombus, or if there was a high risk of distal embolisation in the operator’s view.

---

**Table 1. TIMI thrombus grade scale.**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No cineangiographic characteristics of thrombus are present.</td>
</tr>
<tr>
<td>1</td>
<td>Possible thrombus is present, with reduced contrast density, haziness, irregular lesion contour, or a smooth convex “meniscus” at the site of total occlusion suggestive but not diagnostic of thrombus.</td>
</tr>
<tr>
<td>2</td>
<td>Definitive thrombus, with greatest dimensions half of the vessel diameter.</td>
</tr>
<tr>
<td>3</td>
<td>Definitive thrombus but with greatest linear dimension &gt;0.5 but &lt;2 vessel diameters.</td>
</tr>
<tr>
<td>4</td>
<td>Definitive thrombus, with the largest dimension &gt;2 vessel diameters.</td>
</tr>
<tr>
<td>5</td>
<td>Total occlusion.</td>
</tr>
</tbody>
</table>

**Table 2. Thrombus burden classification.**

<table>
<thead>
<tr>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete obstruction with an angiographic thrombus with the greatest linear dimension more than three times the reference lumen diameter (Type II lesion).</td>
</tr>
<tr>
<td>Cut-off pattern (i.e. lesion morphology with an abrupt cut-off at the obstructive level).</td>
</tr>
<tr>
<td>Presence of accumulated thrombus (i.e. 5 mm of linear dimension) proximal to the occlusion.</td>
</tr>
<tr>
<td>Presence of floating thrombus proximal to the occlusion.</td>
</tr>
<tr>
<td>Persistent dye stasis distal to the occlusion.</td>
</tr>
<tr>
<td>Reference lumen diameter of the infarct related artery of 4.0 mm.</td>
</tr>
</tbody>
</table>
Rheolytic Thrombectomy in Patients with ACS

RT was performed using either the Angiojet XMI or XVG catheter (Possis Medical). Prior to thrombectomy, a temporary pacemaker was inserted in all patients, in view of the high rates of bradycardia associated with the use of the Angiojet. The Angiojet RT System consists of a drive unit, a disposable pump set and an RT catheter (Possis Medical). The dual-lumen catheter tracks over a guidewire. High velocity saline jets are directed back into the catheter, creating a low-pressure zone at the distal tip (Bernoulli principle), which results in suction, break-up and removal of thrombus through the outflow lumen. The device was activated during antegrade passage and predilation was avoided except in rare circumstances.

Coronary angioplasty and stent placement were performed using standard techniques. The use of intracoronary nitroprusside, verapamil and/or adenosine was at the operator’s discretion.

Angiographic analysis

Angiograms were reviewed by two investigators blinded to clinical information and outcomes. TIMI flow was graded as previously reported.12 No-reflow after PCI (requiring intracoronary injection of nitroprusside, verapamil and/or adenosine) was defined as reduced antegrade flow (TIMI flow grade ≤2), in the absence of occlusion at the treatment site. The initial injection of the infarct-related artery was used to determine initial TIMI flow grade and final TIMI flow grade was assessed following guidewire removal.13 The culprit coronary lesion was classified using American College of Cardiology (ACC)/American Heart Association (AHA) criteria.14

Study endpoints and definitions

The primary study endpoint was the incidence of in-hospital and mid-term major adverse cardiac events (MACE), including death, non-fatal myocardial infarction, target vessel revascularisation (re-intervention in the related artery), and stroke. Secondary endpoints included the incidence of TIMI III flow after PTCA and in-laboratory complications (ventricular tachycardia or fibrillation (VT/VF), coronary artery perforation). Angiographic success was defined as restoration of TIMI III flow in the infarct-related artery with <50% residual stenosis. Clinical success was defined as angiographic success with freedom from MACE.

Clinical follow up

Information regarding baseline clinical characteristics, procedural details and in-hospital events was obtained from the electronic database maintained at St. Luke’s Hospital. Post discharge survival status was obtained from the Municipal Civil Registry. A questionnaire was mailed to all living patients focusing on re-hospitalisation and MACE. Patients were contacted when necessary for additional information. Written consent was obtained from all living patients.

Statistical analysis

The normality of data distributions was tested with the Kolmogorov-Smirnov criterion for p>0.05. Data are expressed as mean ± standard deviation or as total (percentage), accordingly. Baseline characteristics were compared using Student’s t-test for continuous variables or the Mann-Whitney u-test as a non-parametric alternative. Categorical variables were tested using χ². The latter test was also performed in order to reveal significant differences in event incidence between groups, since the small number of endpoints recorded did not allow the construction of survival curves. A p-value <0.05 was considered statistically significant. Analyses were performed using the XLSTAT statistical software (version 2007 for Microsoft Excel).

Results

Clinical data

The baseline clinical characteristics of the two study groups are shown in Table 3. There were no significant demographic differences between the RT and control groups, apart from age: patients in the RT group were younger. On clinical presentation, more patients from the RT group suffered from acute myocardial infarction (30.8% vs. 11.5%, p=0.02), whereas more patients from the control group presented with unstable angina (73.1% vs. 57.7%, p<0.05). More patients in the RT group had an ejection fraction <40% (p=0.02). Glycoprotein IIb/IIIa receptor inhibitors were used more frequently in the control group (76.9% vs. 57.7%, p=0.02).

Angiographic and procedural characteristics

These are shown in Table 4. Vessel involved, pre-procedural stenosis, and reference vessel diameter did not differ between the two groups. ACC/AHA type C
Lesions were more frequent in the RT group (76.9% vs. 66.7%, p<0.05). At initial angiography, there was a higher prevalence of large thrombus burden in the RT group, according to the classification by Yip et al\textsuperscript{11} and as indicated by the higher thrombus grade (thrombus grade 4.5 ± 0.7 in the RT group and 2.2 ± 1.3 in the control group, p<0.01). However, there was no difference in the distribution of initial TIMI flow between the two study groups. Distal protection devices and intra-aortic balloon pump were equally but not fre-
quenty used in the two study groups, while the use of drug-eluting stents and stent length also did not differ between the two groups. Distal embolisation/no-reflow immediately post PCI, requiring intracoronary use of nitroprusside/ adenosine and/or verapamil, were more frequent in the control group (p=0.01). Final TIMI flow was similar in the two groups. It was not possible to remove the quantity of thrombus in one patient from the RT group and the procedure was abandoned. However, clinical and angiographic success were practically the same in both groups. In-laboratory events were minimal in both groups.

**In-hospital and mid-term MACE**

One patient from the RT group developed non-Q myocardial infarction before hospital discharge (Table 5). During PCI, 2 patients (one from each group) developed VF arrest which was successfully treated using DC shock. The rest of the patients in both groups had an uneventful hospital stay. Mean follow up was more than 30 months for both groups. One patient from the RT group died (from cancer) and one patient from the control group needed target lesion revascularisation (repeat PCI) because of restenosis. The rest of the patients in both groups had event-free survival (absence of non-fatal myocardial infarction, target lesion revascularisation and stroke, p: NS). The rate of dual antiplatelet continuation for more than 12 months was 69.2% for the RT group and 65.4% for the control group (p: NS).

**Discussion**

In acute coronary syndromes, the presence of visible thrombus is an important predictor of PCI-related complications, including distal embolisation and the no-reflow phenomenon. Furthermore, even in patients who achieve TIMI grade 3 flow after angioplasty, residual thrombus has been associated with worse outcomes. When visible thrombus embolises to the distal circulation during primary PCI, outcomes are compromised. The Zwolle group found that macro-embolisation occurred in 14% of patients with STEMI treated with primary PCI. These had worse TIMI flow in the infarct-related artery, worse myocardial reperfusion, as evidenced by less frequent grade 2-3 myocardial blush at angiography, and less complete ST-segment resolution, larger infarct size, worse left ventricular function and higher mortality. Even in patients without macro-embolisation, myocardial reperfusion following primary PCI is often suboptimal, as evidenced by persistent ST-segment elevation and abnormal myocardial blush. Patients with suboptimal myocardial reperfusion have limited myocardial salvage and increased mortality. Distal micro-embolisation with primary PCI may contribute to poor myocardial reperfusion. This has stimulated great interest in attempts to remove thrombus, prevent distal micro-embolisation, improve myocardial reperfusion, reduce infarct size and improve outcomes. The recently presented TAPAS study indicated that thrombus aspiration during primary PCI is associated with an improvement in survival at 1 year.

There have been a number of thrombectomy devices that have been used as adjunctive therapy with primary PCI. Those that have been most thoroughly studied are the X-Sizer Catheter System (ev3, Inc., Plymouth, Minnesota, USA), several manual aspiration devices and the Angiojet System (Possis Medical, Minneapolis, Minnesota, USA). Most recently, there is evidence that a novel mesh-covered stent together with a conventional embolic protection system may prevent distal embolisation in degenerated vein grafts.

<table>
<thead>
<tr>
<th>Table 5. In hospital and long term major adverse cardiac events (MACE).</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RT group (n=26)</strong></td>
</tr>
<tr>
<td>In-hospital MACE (%)</td>
</tr>
<tr>
<td>Follow up (months)</td>
</tr>
<tr>
<td>Cumulative death (%)</td>
</tr>
<tr>
<td>Non-fatal myocardial infarction (%)</td>
</tr>
<tr>
<td>Target vessel revascularisation (%)</td>
</tr>
<tr>
<td>Stroke (%)</td>
</tr>
<tr>
<td>Event-free survival</td>
</tr>
<tr>
<td>Dual antiplatelet continuation</td>
</tr>
</tbody>
</table>

RT – rheolytic thrombectomy
Several studies have demonstrated the safety and feasibility of adjunctive RT in patients with ACS. In the vein graft Angiojet study (VeGAS-1) trial and the VeGAS-2 acute myocardial infarction registry, RT significantly reduced thrombus burden in patients with acute myocardial infarction before definitive treatment \( (73.2 \pm 64.6 \text{ vs. } 15.5 \pm 30.1 \text{ mm}^2) \) and was associated with a high rate of final TIMI 3 flow.\(^5\) There are five registries providing important observational data regarding the use of the Angiojet in “real world” ACS patients with a large thrombus burden who are treated with PCI.\(^9\) Patients treated with RT had better resolution of thrombus, better TIMI flow post PCI, better myocardial blush post PCI, and better MACE-free survival.

In addition, there have been one small and one large multi-centre randomised trial evaluating RT using the Angiojet with primary PCI for STEMI. Antoniucci et al performed a randomised trial comparing RT before stenting with direct stenting alone.\(^7\) Patients randomised to RT had a significantly higher rate of early ST-segment resolution and improved corrected TIMI frame count. In addition, patients treated with RT had a significantly smaller infarct size measured with sestamibi scintigraphy at 1-month \( (13.0\% \text{ vs. } 21.2\%, \text{ p}<0.01) \). In aggregate, these data suggested that adjunctive RT improved early angiographic outcomes, myocardial perfusion, and also limited the extent of infarction.

On the basis of these promising results, a larger multi-centre randomised trial was designed. In the Angiojet rheolytic thrombectomy in patients undergoing primary angioplasty for acute myocardial infarction (AiMI) trial, 480 patients were randomised to primary PCI with or without RT before stent implantation.\(^8\) In contrast to the Antoniucci trial, the primary endpoint (infarct size by single photon emission computerised tomography imaging) was higher in the RT group \( (12.1\% \text{ vs. } 10.9\%, \text{ p}<0.02) \), and there was no difference in myocardial blush, TIMI frame count or ST-segment resolution between the study groups. A lower incidence of TIMI 3 grade flow post PCI was also observed in the Angiojet group \( (92\% \text{ vs. } 97\%, \text{ p}=0.02) \). Moreover, there was a significantly higher mortality at 30 days in the RT arm \( (4.6\% \text{ vs. } 0.8\%, \text{ p}<0.02) \). The investigators concluded that RT does not reduce infarct size and cannot be recommended for routine use in patients with STEMI undergoing primary PCI. The reasons for the worse outcomes with RT in the AiMI trial are not clear. The study was not powered to detect differences in clinical endpoints, so the differences in mortality were quite unexpected. These differences were not due to a high mortality in the Angiojet arm, but rather to an unexpectedly low mortality in the control arm. The 30-day mortality in the control arm \( (0.8\%) \) was lower than in any previous primary PCI trial and occurred in a patient population that was selected to be high risk. The data safety and monitoring committee and the executive committee, after reviewing the data, did not find any indication that any of the 11 deaths in the Angiojet group were directly attributed to the device. The differences in mortality remain unexplained, but could be related to chance.

But why did the AiMI trial find no improvement in myocardial perfusion and no reduction in infarct size with RT? There are several possible explanations. The larger infarct size did not translate into worse LV ejection fraction. Ejection fraction measured by sestamibi imaging at 14-28 days was similar in the Angiojet and control groups \( (51.3\% \text{ vs. } 52.3\%, \text{ p}=0.38) \). The frequency of TIMI 3 flow pre PCI was higher in the control group \( (27\% \text{ vs. } 19\%, \text{ p}=0.05) \), and it is possible that this could influence infarct size, favouring a smaller infarct size in the control group. Secondly, it is possible that the greater infarct size could be related to the technique used for performing RT. In AiMI, there was no effort to systematically perform thrombectomy with the Angiojet from proximal to distal, and predilation was sometimes performed to facilitate passage of the Angiojet catheter. Both predilation and advancement of the Angiojet catheter across the thrombus laden lesion without activation of the device could predispose to distal embolisation. In Antoniucci’s trial, which reported superior results with the Angiojet, the device was activated during antegrade passage and predilation was avoided except in rare circumstances.

It is also possible that RT may be beneficial in the subgroup of patients with a large thrombus burden, but these patients made up only a small proportion of the patients in AiMI and any benefit may have been lost when outcomes were examined for all patients. Finally, distal embolisation may not be the major cause of impaired microvascular reperfusion. Other factors, such as reperfusion injury or delayed reperfusion with irreversible damage to the microvasculature, may be the major factors in impaired myocardial reperfusion.

The findings of the current study, in concordance
with prior published results, suggest that Angiojet RT appears to be safe and effective for the treatment of ACS patients in the presence of a large thrombus burden (Figure 1), even when these patients have a higher risk profile (more patients with acute myocardial infarction, lower ejection fraction, more ACC/AHA lesions, larger thrombus burden). The use of Angiojet RT was associated with a significantly lower incidence of the no-reflow phenomenon immediately post PCI, despite the higher thrombus burden in this group of patients (Figure 2). As a result, there was less frequent need for the intracoronary use of nitroprusside, adenosine and/or verapamil. Reducing the occurrence of no-reflow is clearly beneficial, given the detrimental effects of no-reflow on clinical outcome. In addition, there were no cases of coronary artery perforation and, apart from 2 cases of VF arrest (one in each group) which were successfully treated by DC shock, no other major adverse in-laboratory events, indicating the safety of Angiojet RT during PCI in this high-risk group of patients, as compared to the control group.

The most important finding of our study was that in-hospital and mid-term mortality and MACE were not significantly different in patients treated with the Angiojet. While the AiMI trial enrolled patients with thrombus burden of any size, with <25% incidence of large thrombus burden (≥TIMI 3 grade classification), the patients enrolled in our study all had a large thrombus burden (≥3). Therefore, it is reasonable to conclude that Angiojet RT is valuable in the setting of ACS with a large thrombus burden, but should not be used in cases with a small or no thrombus burden, possibly because it may cause distal embolisation of small, non-visible, adherent thrombus and may add to procedural time.

More recently, Sianos and colleagues emphasised the role of a large thrombus burden as an independent predictor of MACE and infarct-related artery stent thrombosis in patients treated with drug-eluting stents for STEMI. RT was found to be a significant independent predictor for infarct-related artery stent thrombosis (hazard ratio 0.11, p=0.03).

Some of the answers to the questions raised by the results of the AiMI trial may come from the Angiojet thrombectomy and stenting for treatment of acute myocardial infarction (JETSTENT) trial, which is ongoing. Pending the results of JETSTENT, the interventional cardiologist currently faces the decision of how to manage ACS patients with a large thrombus burden. We know that patients with a large thrombus burden are at increased risk for distal embolisation and poor procedural and clinical outcomes. Overall, our data suggest that the use of adjunctive RT in the...

**Figure 1.** Primary PCI during acute inferior myocardial infarction. A. Occlusion of the right coronary artery with large thrombus burden. B & C. TIMI 3 flow distally after rheolytic thrombectomy with Angiojet, without balloon inflation. D. TIMI 3 flow and full vessel patency after primary stenting.
setting of ACS with a large thrombus burden is feasible, safe, and does not increase the risk of adverse clinical outcomes. Until further data are available, it seems that the most reasonable strategy is to perform Angiojet RT in patients with a large thrombus burden, prior to PCI in the setting of ACS.

**Study limitations**

This report presents a single-centre, observational, retrospective study of consecutive patients undergoing PCI for ACS, treated in a single institution by a single group of interventional cardiologists, and therefore may have all the limitations arising from such an approach—especially in the determination of angiographic parameters, such as thrombus burden, that require great discipline in angiographic documentation. Another limitation is the relatively small size of the study. The use of Angiojet RT was not pre-specified, but was applied at operator discretion for large thrombus-containing lesions.

**Conclusions**

Angiojet RT in patients with ACS and a large thrombus burden is safe and effective in the removal of thrombus, while reducing the occurrence of the no-reflow phenomenon. Both the immediate and long-term results appear to be equally good. Studies have shown that macro-embolisation is harmful and leads to impaired myocardial reperfusion and worse clinical outcomes, and macro-embolisation is more likely to occur in patients with a large thrombus burden. Thrombectomy devices have proven to be very effective in removing thrombus. Therefore, physicians should consider Angiojet RT in the setting of significant angiographic thrombus.

**References**

4. Thielmann M, Dörge H, Martin C, et al. Myocardial dysfunc-
Rheolytic Thrombectomy in Patients with ACS


