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Combined Fibrinolysis Using Reduced-Dose Alteplase Plus Abciximab With Immediate Rescue Angioplasty Versus Primary Angioplasty With Adjunct Use of Abciximab for the Treatment of Acute Myocardial Infarction: Asia-Pacific Acute Myocardial Infarction Trial (APAMIT) Pilot Study

Aaron Wong,[1]* Koon-Hou Mak,[1] Charles Chan,[1] Tian-Hai Koh,[1] Kean-Wah Lau,[1] Tai-Tian Lim,[1] MD, Soo-Teik Lim,[1] Philip Wong,[1] Ling-Ling Sim,[1] Yean-Teng Lim,[2] Huay-Cheem Tan,[2] and Yean-Leng Lim,[3] PhD

We conducted a randomized feasibility pilot study comparing combined fibrinolysis with immediate rescue angioplasty vs. primary angioplasty with adjunctive abciximab in patients with acute myocardial infarction (AMI). Seventy patients with ST segment elevation AMI of ≤ 6 hr were randomized to either 50 mg of alteplase and abciximab (n = 34) or primary angioplasty with adjunctive abciximab (n = 36). Coronary angiography was performed at 60 min in the combined lytic group and TIMI 3 flow was present in 65% of patients as compared to 25% (*P* = 0.001) in the primary angioplasty group prior to intervention. Treatment success, defined as TIMI 3 flow, was achieved in 83% of patients in the primary angioplasty group (*P* = 0.075 compared to 65% in combined lytic group before rescue angioplasty). There was no difference in overall treatment success between primary angioplasty and combined lytic group with rescue angioplasty (83% vs. 94%; *P* = NS). Major adverse cardiac events at 1 month were not significant (15% vs. 11%; *P* = NS), but there was a trend toward more events in the combined lytic group at 6 months (32% vs. 14%; *P* = 0.066), particularly in target vessel revascularization. In this feasibility pilot study, high rate of TIMI 3 flow was attained in patients with AMI with both combined fibrinolysis and primary angioplasty with adjunctive abciximab. A larger randomized trial is currently ongoing to compare these two strategies. *Catheter Cardiovasc Interv 2004;62:445–452.*

Key words: fibrinolysis; myocardial infarction; angioplasty; platelets

INTRODUCTION

The goal of modern therapy of acute myocardial infarction (AMI) is to achieve rapid and complete reperfusion of ischemic myocardium. Although not the best surrogate marker, Thrombolysis in Myocardial Infarction (TIMI) grade 3 flow is still commonly used as clinical indicator of normal reperfusion and its presence is associated with improved clinical outcomes after AMI [1].

Many currently available fibrinolytic agents can be administered safely and rapidly but only 30–55% achieved TIMI 3 flow in the infarct-related artery (IRA) 60–90 min after administration [2]. Bleeding complications, especially intracranial hemorrhage, remain a significant limitation to fibrinolytic therapy [3]. With the recent understanding of the role of platelets in the initiation of atherothrombosis in AMI, the combination of reduced-dose alteplase and abciximab has been tested. Fibrinolytic agents induce thrombin generation and platelet activation [4,5], and the addition of potent anti-

[1]Department of Cardiology, National Heart Centre, Singapore
[2]Cardiac Department, National University Hospital, Singapore
[3]Centre for Cardiovascular Therapeutics, Western Health, University of Melbourne, Australia

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*Correspondence to: Aaron Wong, National Heart Center, 17 Third Hospital Avenue, 168752, Singapore. E-mail: aaron_wong@nhc.com.sg

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platelet agents, such as glycoprotein (GP) IIb/IIIa receptor inhibitors, which can negate these deleterious effects, had been found to be efficacious in improving TIMI 3 flow rate [6].

Primary angioplasty is regarded not only as an effective alternative therapy to fibrinolysis for AMI, but superior clinical outcomes had been reported when compared to pharmacological therapy in AMI [7–9]. The use of coronary stents in primary angioplasty, with concomitant use of antiplatelet agents such as aspirin, thienopyridine derivatives, and GP IIb/IIIa inhibitors, has enhanced immediate and long-term clinical outcomes [10,11].

A randomized trial designed to compare two state-of-the-art strategies of combined pharmacological strategy, using alteplase and abciximab, versus mechanical reperfusion strategy, using intracoronary stenting with adjunctive abciximab, in an Asian population is being developed as the Asia-Pacific Acute Myocardial Infarction Trial (APAMIT). This pilot study aims to demonstrate the feasibility of comparing these two treatment strategies.

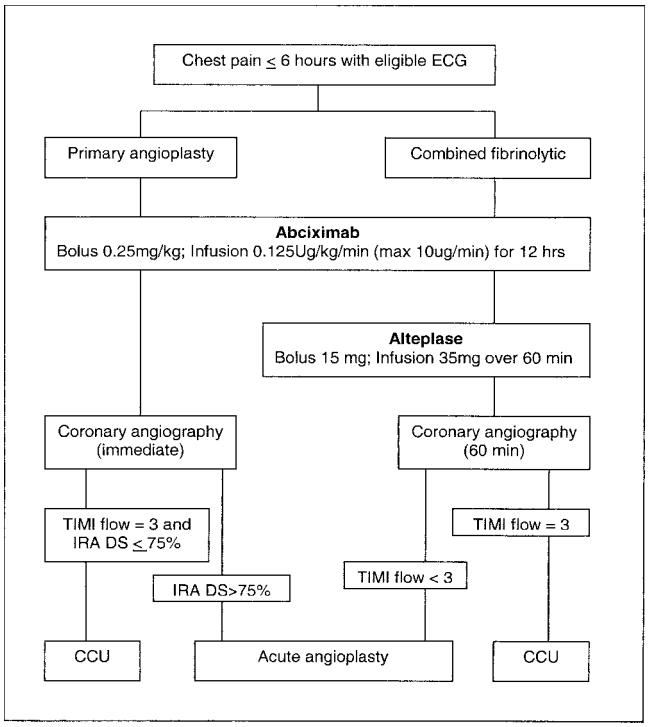

Fig. 1. APAMIT pilot study protocol. DS, diameter stenosis; CCU, coronary care unit.

MATERIALS AND METHODS

The APAMIT pilot study was conducted between February 1999 and June 2000 at two centers: National Heart Centre and National University Hospital of Singapore. Ethic committees of both institutions approved the protocol.

Study Population

All patients age over 21 with the following inclusion criteria were eligible for the study after obtaining written informed consent: chest pain $\geq$ 30 min, suggestive of AMI, presenting within 6 hr of onset; and electrocardiography findings of new left bundle branch block or ST segment elevation of $\geq$ 1 mm in two or more limb leads or $\geq$ 2 mm in two or more contiguous precordial leads.

Patients were excluded if they had any one of the following exclusion criteria: the use of fibrinolytic agents was contraindicated due to increased risk of bleeding (active or recent gastrointestinal bleeding, hemorrhagic diathesis, prolonged cardiopulmonary resuscitation, systolic blood pressure $>$ 200 mm Hg not responding to urgent standard treatment, or recent organ biopsy or major surgery or trauma); cardiogenic shock on presentation to emergency room (ER); previous known allergic reaction to aspirin, ticlopidine, clopidogrel, or a glycoprotein IIb/IIIa inhibitor; patient actively participating in any other clinical studies; coronary angiography cannot be performed within 60 min because of logistic or other reasons.

Treatment Regimens

Randomization was performed using sealed envelopes after informed consent was obtained. All patients received a loading dose of 300 mg aspirin and abciximab, which was given as a bolus dose of 0.25 mg/kg and 12-hr infusion of 0.125 μg/kg/min (up to maximum of 10 μg/min) in the ER (Fig. 1). Unfractionated heparin, 40 U/kg bolus (up to a maximum of 4,000 U), and 5 U/kg/hr infusion was given in patients randomized to combined fibrinolytic to keep an activated prothrombin time (aPTT) of 50–70 sec for a recommended time of 24 to 48 hr. Patients in the primary angioplasty group received 50 U/kg bolus heparin and, if required, additional bolus doses in the catheterization laboratory to keep the activated clotting time (ACT) between 200 and 250 sec during coronary intervention.

In the combined fibrinolytic group, alteplase was administrated as a 15 mg bolus followed by an infusion of 35 mg over 60 min immediately after randomization. The dose of alteplase infusion was reduced to 20 mg after the occurrence of three bleeding events. Coronary angiography was performed at completion of alteplase. If the TIMI flow was 3, no intervention was attempted irrespective of the severity of the underlying lesion. These patients were managed medically and continued with heparin infusion 1 hr after the vascular sheath was removed. However, if the TIMI flow in the IRA was $<$ 3,

rescue angioplasty was performed. The initial six patients who had TIMI grade 3 flow had rescue angioplasty because the initial protocol allowed for angioplasty to lesion ≥ 75% stenosis on visual estimation. In the primary angioplasty group, coronary angiography was performed immediately. Primary angioplasty of the IRA was performed if there was significant narrowing of ≥ 75% by visual estimation irrespective of the TIMI flow grade.

For both primary and rescue angioplasty, procedures were performed in accordance with institutional guidelines. Coronary artery stenting was performed if stent-like result was not obtained after balloon angioplasty. The NIR Primo stent (Sci-Med, Boston Scientific) was used in all patients and deployed with high-pressure inflation of ≥ 12 atm. The arterial sheath was removed 4–6 hr later when ACT was < 170 sec or aPTT was < 50 sec. Oral ticlopidine 250 mg twice daily or clopidogrel 75 mg daily was administered and continued for 4 weeks following the procedure.

Long-term aspirin and β-blockers are recommended, and angiotensin-coverting enzyme inhibitors in patients who had anterior MI, reduced left ventricular systolic function (< 40%), or previous documented heart failure. Other adjunctive therapies may be used at the discretion of the attending physician.

Angiographic Analysis

Coronary angiograms were reviewed independently by two interventional cardiologists. TIMI flow grade and corrected TIMI frame counts (cTFC) were determined from all films using previously described techniques [12,13].

Endpoints

The primary endpoint of this study was the angiographic occurrence of TIMI 3 flow in the IRA 60 min after treatment in the combined fibrinolytic group and immediately postprocedure in the primary angioplasty group. The secondary clinical endpoint was a composite of major adverse cardiac events (MACE), including all-cause mortality, recurrent ischemia (included residual ischemia on functional testing), recurrent MI, target vessel revascularization (TVR), and stroke at 30 days. Major bleeding complications were defined as those requiring blood transfusion or intracranial bleeding confirmed on computer tomography scan or magnetic resonance imaging.

Statistical Analysis

Categorical variables were summarized as frequencies with percentages and continuous variables as mean ± SD or medians with interquartile ranges. Analysis was on an intention-to-treat basis. Statistical comparison was made by either the chi-square or Fisher's exact test for discrete variables, and Student's *t*-test or Wilcoxon signed rank test, as appropriate, for continuous variables.

TABLE I. Baseline Characteristic According to Treatment Arm*

	Primary angioplasty (n = 36)	Combined fibrinolytic (n = 34)	*P*
Mean age, years	56 ± 10	55 ± 11	0.776
Male	30 (83)	26 (76)	0.473
Previous AMI	3 (8)	4 (12)	0.706
Diabetes mellitus	10 (28)	12 (35)	0.498
Hypertension	12 (33)	19 (56)	0.058
Current smoker	22 (61)	16 (47)	0.238
Hyperlipidaemia[a]	32 (94)	29 (81)	0.152
Killip class			0.905
I	29 (81)	27 (79)	
II	7 (19)	7 (21)	
Infarct location			0.147
Anterior	20 (56)	13 (38)	
Inferior	16 (44)	21 (62)	
Symptom-to-hospital, min	145 (94, 204)	135 (82, 204)	0.883
Door-to-treatment,[b] min	114 (102, 134)	70 (55, 91)	< 0.001

*Data are shown as mean ± SD, n (%), and median (25th, 75th percentiles).

[a]Patients required lipid-lowering therapy at discharge.

[b]Door-to-balloon time for primary angioplasty and door-to-needle time for combined fibrinolytic.

RESULTS

A total of 70 patients were enrolled in this pilot study. Baseline characteristics were similar in both groups (Table I). The mean age of enrolled patients was 55.7 years and 80% were male. Diabetes mellitus and hypertension were present in 31% and 44% of patients, respectively.

Angioplasty was not performed in two patients in the primary angioplasty group: one had left main disease requiring urgent coronary artery bypass graft (CABG) and the other had an IRA which was too small and distal for intervention. One patient in the combined fibrinolytic group did not receive alteplase due to miscommunication but was included in the intention-to-treat analysis.

Angiographic Findings

Angiography was performed in all patients and TIMI flow grade was assessed at a median time of 67 and 50 min after randomization in the combined fibrinolytic group and primary angioplasty group prior to procedure, respectively ($P = 0.001$). The median door-to-needle time in the combined fibrinolytic group was 70 min compared to a door-to-balloon time of 114 min in the primary angioplasty group ($P < 0.001$).

Combined Fibrinolytic vs. Primary Angioplasty

TIMI 3 flow occurred in 22 patients receiving the combined fibrinolytic and 9 patients in the primary angioplasty

TABLE II. Angiographic Findings*

	Primary angioplasty (n = 36)	Combined fibrinolytic (n = 34)	*P*
Time to angiography, min	50 (40, 66)	67 (58, 84)	0.001
Infarct-related artery			0.345
LAD	20 (56)	14 (41)	
LCx	1 (3)	3 (9)	
RCA	15 (42)	17 (50)	
TIMI flow at angiography			0.001
0 or 1	22 (61)	7 (20)	
2	5 (14)	5 (15)	
3	9 (25)	22 (65)	
Corrected TIMI frame count			
Preprocedure	100 (34, 100)	29 (22, 63)	< 0.001
Postprocedure	21 (17, 30)	21 (16, 27)	0.707
Treatment success	30 (83)	22 (65)	0.075
Overall success[a]	30 (83)	32 (94)	0.261

*Data are shown as n (%) and median (25th, 75th percentile).
[a]Including rescue angioplasty in the combine fibrinolytic group.

TABLE III. In-Hospital Clinical Events*

Outcomes	Primary angioplasty (n = 36)	Combined fibrinolytic (n = 34)	*P*
Death	2 (6)	1 (3)	
Recurrent ischemia	0	0	
Reinfarction	0	0	
Stroke	1 (3)	0	
Severe pump failure	2 (6)	0	
TVR			
CABG	1 (3)	1 (3)	
percutaneous coronary	1	1	
intervention	0	0	
Major bleeding	2 (6)	1 (3)	
Composite	5 (14)	1 (3)	0.199

*Data are shown as n (%).

group receiving only abciximab ($P = 0.001$; Table II). Rescue angioplasty was successful in the first 6 patients in the combined fibrinolytic group who had TIMI 3 flow and in the subsequent 11 patients with TIMI flow < 3, except for 1 who had persistent TIMI 2 flow due to distal embolization. There was one patient in whom the IRA TIMI flow was assessed to be 3 by the attending interventional cardiologists, and therefore no rescue angioplasty was performed, but was graded < 3 by independent reviewers. The procedure success rate with combined fibrinolytic ± rescue angioplasty was therefore 94%.

The preprocedural cTFT of the IRA was significantly lower (29 vs. 100; $P < 0.001$) in the combined fibrinolytic group but no difference was seen between the two groups at the end of the procedure when rescue angioplasty performed in the combined fibrinolytic group was included.

Primary angioplasty was performed in 34 of the 36 patients randomized to primary angioplasty. The procedure was successful in 30 of the 34 (88%) patients. Three patients had persistent TIMI 2 flow and one developed no-reflow phenomenon. The overall treatment success rate on an intention-to-treat basis was 83% in the primary angioplasty group ($P = 0.075$ compared to 65% in combined fibrinolytic group). All patients who had angioplasty received coronary stents except for one in whom the IRA was considered too small for stenting.

Clinical Events and Bleeding Complications

In-hospital composite clinical events were listed in Table III. There were three in-hospital deaths, resulting in the overall in-hospital mortality rate of 4%. The two deaths in the angioplasty group were both associated with major bleeding (one also had an embolic stroke). In the primary angioplasty group, two patients developed severe pump failure and another required urgent CABG for left main disease. The only death in the combined fibrinolytic group had successful fibrinolysis but developed major gastrointestinal bleeding during the coronary angiography. He had severe triple-vessel disease and underwent CABG. He died of sudden cardiac death 4 days after the operation.

The incidence of thrombocytopenia was similar in both groups, occurring in three patients in each group. Four patients had a decrease of platelet count > 25% from baseline, of whom two had platelet counts of < 100,000/ml. No bleeding occurred and no platelet transfusion was required in these patients.

There was no significant different in the composite endpoint at 30 days between the groups (Table IV). However, MACE rate was marginally higher in the combined fibrinolytic group at 6 months (32% vs. 14%; $P = 0.066$). Target vessel revascularization accounted for most of this increase in MACE rate in the combined fibrinolysis group. Functional tests, which include exercise treadmill ECG, stress echocardiography, and nuclear perfusion scan, were performed at physicians' discretion after discharge. Out of the seven that had recurrent ischemia, six were on functional testing, of whom four had TVR and two were treated medically.

Sixteen patients in the combined fibrinolytic group had patent IRA with significant underlying lesion (mean diameter stenosis, 72.8%; range, 54.0–86.3%) and visible thrombus angiographically but did not received angioplasty or CABG, and none of these patients had any in-hospital cardiac event, in particular recurrent ischemia or infarction. At 6-month follow-up, 8 of these 16 patients were still event-free. However, of the other 17 patients in the lytic group who had rescue angioplasty, only one had an event at 6 months.

TABLE IV. MACE Rate at 30-Day and 6-Month Follow-Up*

Outcomes	Primary angioplasty (n = 36)	Combined fibrinolytic (n = 34)	*P*
30 days			
Death	1[a] (3)	1 (3)	
Recurrent ischemia	0	4 (12)	
Reinfarction	1 (3)	0	
Major bleeding	2 (6)	1 (3)	
Stroke	1 (3)	0	
TVR			
CABG	1 (3)	3 (9)	
Percutaneous coronary	1	1	
intervention	0	2	
Composite	4 (11)	5 (15)	0.731
6 months			
Death	2 (6)	1 (3)	
Recurrent ischemia	1 (3)	7 (21)	
Reinfarction	1 (3)	3 (9)	
Major bleeding	2 (6)	1 (3)	
Stroke	1 (3)	0	
TVR	2 (6)	8 (24)	
CABG	2	2	
Percutaneous coronary	1	6	
intervention	2 [2/1] (6)	8 [2/6] (24)	
Composite	5 (14)	11 (32)	0.066

*Data are shown as N (%).
[a]One patient died in hospital after > 30 days therefore not included.

DISCUSSION

Great advancements were made since the last randomized trial comparing fibrinolysis to primary angioplasty in the treatment of AMI. The limitations of fibrinolytic agents, which include inability to dissolve platelet-rich thrombus [14], have been overcome by addition of potent antiplatelet agents, which improved IRA patency rate [4,6,15] and lowered the incidence of recurrent ischemia and infarction [16]. Conversely, the feared complications of abrupt vessel closure and coronary dissection during angioplasty can be alleviated by coronary stenting, which has also been shown to improve short- and long-term clinical outcomes [10,17].

This randomized pilot study was conducted to test the feasibility of comparing combined fibrinolysis using reduced-dose alteplase plus abciximab and primary angioplasty plus abciximab in patients presented with AMI. The only reported randomized trial comparing these two strategies was published after the completion of our study and enrolled 162 patients with AMI < 12 hr. Routine angiography was not performed in the combined lytic group and IRA patency rate in this group was therefore not known. However, primary angioplasty was found to be superior to combined fibrinolytic when myocardial salvage was used as the endpoint in that study [18].

Combined Fibrinolytic vs. Primary Angioplasty

In this pilot study, the occurrence of TIMI 3 flow in 65% and 22% of patients in the combined fibrinolytic group and primary angioplasty group after abciximab, respectively, supported previous reported results [4,15]. Although the TIMI flow grade was assessed later in the combined fibrinolytic group (67 vs. 50 min; $P = 0.001$), the higher patency rate in this group is unlikely to be accounted for by the time difference as abciximab alone in other studies only achieved TIMI 3 flow of 15–20% at 60 min [6]. These data again support the additional beneficial effect of abciximab on clot lysis in combination with reduced-dose alteplase in AMI.

There were less LAD infarcts (41% vs. 56%) in the combined fibrinolytic group and this may contribute to a higher treatment success rate since it is more difficult to establish TIMI 3 flow in the LAD with pharmacologic therapy. Indeed, there was significantly higher treatment success rate in non-LAD compared LAD infarcts (80% vs. 43%; $P = 0.04$) within the combined fibrinolytic group and primary angioplasty tends to achieve a higher TIMI 3 flow rate in LAD infarcts (75% vs. 43%; $P = 0.06$) compared to combined fibrinolytic.

The in-hospital MACE rate was relatively low in the combined fibrinolytic group as compared to other studies [8] because rescue angioplasty was performed in all our patients with TIMI flow < 3 in the IRA. Notably, there was no in-hospital recurrence ischemia or infarction in the 16 patients in the combined fibrinolytic group who had patent IRA with high-grade underlying lesions but was left untreated. The administration of abciximab prevents platelet aggregation [4,5] and this may reduce the rate of reocclusion in these IRA [4,5,16]. Half of these 16 patients were event-free at 6-month follow-up, suggesting that not all patients after successful fibrinolysis required TVR. As we know that a significant portion of AMI was due to plaque rupture in noncritically stenotic lesion [19], more effective thrombolysis, which may be achieved with combined antiplatelet and fibrinolytic agents, may result in more complete dissolution of platelet-rich thrombus and therefore restoring a larger lumen.

Although there was a trend toward higher MACE rate at 6 months in the combined fibrinolytic group, especially TVR, the majority was performed because of significant residual ischemia after functional tests and not of acute coronary syndromes. In this pilot study, abciximab appeared to shift a high-risk intervention in the setting of AMI with a highly thrombogenic milieu to a low-risk elective procedure. Passivation of the plaque by GP IIb/IIIa receptor inhibition and inhibition of vibronectin or MAC-1 receptor by abciximab may contribute to this clinical benefit.

The overall procedural success rate of 88% in primary angioplasty in this study is comparable to other larger series [7–9]. Coronary stenting was optional in this trial as the benefit of stenting over balloon angioplasty in AMI was still doubtful when this trial was conducted [11]. Nonetheless, all patients except one received intracoronary stents and the practice was corroborated by recent findings that coronary stenting in AMI yields better results when compared to balloon angioplasty alone [17]. There were three patients who had persistent TIMI 2 flow despite successful stenting and distal embolization of atherosclerotic plaque and/or thrombus was the most likely cause. No-reflow phenomenon occurred in one patient due to high thrombus load. Recent introduction of distal protection or thrombectomy devices may help in these situations to prevent microvascular occlusion secondary to atherothrombotic embolization during balloon inflation or stenting.

The median door-to-balloon time of 114 min in the primary angioplasty group in our study was just within the recommended time frame by the American College of Cardiology of 90 ± 30 min [20] and 70-min door-to-needle time in the combined fibrinolytic group was relatively longer compared to other studies [9,18]. There are two important and peculiar reasons for this delay in our part of the world. First, medical consent to participate in clinical trials or even specific treatment for a patient is usually decided jointly after the arrival of and lengthy discussion among the family members. Second, language barrier is common in our multilingual society, especially in the elderly. One or both problems could make the time required to obtain proper informed consent considerably longer.

Bleeding Complications

Major bleeding complications appeared infrequently in this small pilot study. More importantly, although there was one delayed nonhemorrhagic stroke in the primary angioplasty group, there was no intracranial bleeding. However, there were three patients who developed gastrointestinal bleeding, resulting in one death, paradoxically, in the primary angioplasty group. Although two of the three major bleedings occurred in the primary angioplasty arm, these events had led the APAMIT investigators to reduce the alteplase infusion dosage from 35 to 20 mg after 50 patients were enrolled in the study. Nevertheless, 6 of the subsequent 10 patients receiving the lower alteplase infusion regime had TIMI 3 flow in the IRA. There was no subsequent major bleeding after the three events.

The incidence of thrombocytopenia in our population appeared to be comparable to that of the Caucasian population in other similar studies [21]. Although there was no definite evidence, in view of the reported difference in coagulation profiles of Asian population [22] with greater tendency to bleeding, the dose of unfractionated heparin used in this study was slightly lower than the standard recommended weight-adjusted dose, which appeared to be as effective in our study population [23].

Facilitated Angioplasty and Rescue Angioplasty

Primary angioplasty or rescue angioplasty was performed in a total of 51 patients in this study and the overall procedural success rate was 92% (46 of 51). Recent studies have shown that procedural success rate as well as clinical outcomes were improved when TIMI 2 or 3 flows was achieved before primary angioplasty [24–26]. This may represent lower thrombus load in a patent IRA prior to procedure and subsequent lower incidence of distal embolization and no-reflow phenomenon.

At the moment, it seems that pharmacological therapy alone is not an optimal strategy because the best agents can only achieve a patency rate of 65–70% limited by bleeding complications. One the other hand, although primary angioplasty has much higher patency rate, the inherent delay in implementing this strategy generates concern and makes one wonders if clinical outcomes could be further improved if complementary treatments had been given during the delay.

Thus, fibrinolysis and primary angioplasty may not be mutually exclusive. If combined fibrinolytic could safely achieve high recanalization rate of IRA, and patency of IRA is desirable prior to primary angioplasty, it is logical to propose an attractive alternative treatment for AMI, facilitated angioplasty, i.e., combined fibrinolysis followed by coronary angioplasty [27,28]. The early administration of widely available combined lytic agents may overcome the delay in activating the catheterization laboratory in primary angioplasty and maximize myocardial salvage by establishing normal coronary flow in a high percentage of patients. Subsequent angioplasty with stenting will obliterate any underlying high-grade lesions and, in combination with potent antiplatelet agent, reduce the high rate of reocclusion observed among patients treated with fibrinolytic alone. However, these combination strategies would be extremely costly and may potentially increase bleeding complications if performed in all patients, especially in the elderly [16].

Another treatment strategy is to perform rescue angioplasty if there is no clinical indication of reperfusion at 60 min after initiation of pharmacological therapy. The crucial determinant of this strategy is the recognition of successful reperfusion noninvasively at a critical time span. The currently ongoing main APAMIT study utilizes this strategy in the combined fibrinolytic group, using ST segment resolution as clinical marker for successful reperfusion. In this pilot study, using the presence of TIMI 3 flow on coronary angiography performed routinely as successful reperfusion, the rate of TIMI 3

flow of combined fibrinolysis followed by rescue angioplasty, if required, was 94%. It is hoped that not only the speed and rate of TIMI 3 flow in the IRA and therefore clinical outcomes will be improved, but the number of patient with AMI requiring initial intervention will be reduced using this strategy as well.

Study Limitations

The major limitation of this pilot study is the small number of patients and, as such, limited power to observe statistical significant differences. The conclusions of this pilot study are therefore preliminary at best. Another limitation is that two key changes in the protocol occurred in the middle of the trial in the combined fibrinolytic arm: rescue angioplasty was not allowed if TIMI flow was 3, irrespective of lesion severity, and alteplase infusion was reduce from 35 to 20 mg. The former change did not affect the primary endpoint but created heterogeneity, and therefore limitation on the interpretation, in the outcomes of patients who were successfully treated with combined fibrinolytic alone. Although the use of stenting was not mandatory, the use of coronary stents was liberal in the trial due to increasing evidence that showed superiority of stenting over balloon angioplasty in AMI during the course of the trial. Distal protection and thrombectomy devices were not available at the time of the trial and ongoing studies are evaluating the role of these devices in AMI, especially in patients with high thrombus load.

CONCLUSIONS

Combined fibrinolysis and primary angioplasty were both highly efficacious in achieving TIMI 3 flow in the IRA. In-hospital events after procedure were rare following both strategies, irrespective of underlying lesion severity. There was more intervention performed in the combined fibrinolytic group but the majority was performed after functional testing. A larger multicenter trial, the main APAMIT, with a modified protocol to compare the efficacy of these two treatment strategies is current being conducted.

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