Platelet GPIIb/IIIa receptor blockers for failed thrombolysis in acute myocardial infarction, alone or as adjunct to other rescue therapies

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Early and complete restoration of myocardial blood flow is the therapeutic goal for treatment of patients with acute myocardial infarction (MI). After fibrinolytic therapy patients who fail to achieve Thrombolysis in Myocardial Infarction (TIMI) grade 3 epicardial blood flow are at high risk of death and congestive heart failure[1]. With currently available thrombolytic therapies less than two-thirds of patients have TIMI grade 3 flow in the infarct related artery 90 min after initiation of thrombolytic therapy[2]. Thus in patients who fail to reperfuse following thrombolytic therapy, there is a need for rescue therapies.

To identify candidates for rescue therapy, clinicians use information from the ECG and patient history. While ST resolution is a highly accurate predictor of infarct artery patency, restoration of normal epicardial flow is not sufficient to ensure adequate myocardial perfusion[1]. Percutaneous coronary intervention (PCI) has been shown to be successful in restoring vessel patency in up to 90% of patients undergoing a rescue procedure[3,4]. In addition in the ADMIRAL study, early use of a platelet glycoprotein IIb/IIIa inhibitor (GPIIb/IIIa), abciximab, started prior to primary stenting for acute MI, has shown greater initial TIMI 3 flow before stenting with greater success rate of the stenting procedure and lower combined end point of death, reinfarction or urgent target vessel revascularisation at 30 days[5]. Furthermore at 6 months improvement in coronary patency and left ventricular function was maintained.

Abciximab, as part of rescue therapy with PCI, has been shown to improve clinical outcomes[6,7] and left ventricular function[7]. In this issue Ronner et al.[8] have presented a single centre retrospective study of patients who were admitted or transferred with a myocardial infarction and underwent rescue therapy within 24 h for failed thrombolysis. Since treatment strategies were not randomised they have emphasised bleeding rates rather than mortality. Rescue therapy for failed thrombolysis included PCI, further lytic therapy and GPIIb/IIIa inhibitors often in combination. Of the 154 with primary admission to the Thoraxcenter and who had thrombolysis for acute MI, rescue therapy was given in 36%. This compares with an earlier study where the rescue PCI rate was 22%[3]. In this study, of the patients treated with rescue PCI, 38% were in Killip class 3 or 4 compared with 4·6% of patients who had an entry Killip class greater than 2 and had a rescue PCI performed in the GUSTO I angiographic substudy[4].

Major bleeding, defined as intracerebral, decrease of haemoglobin greater than 3·1 g. dl\(^{-1}\) or bleeding requiring surgery or transfusion, occurred following rescue therapy in 21·6% of patients in this study. Of the patients who had PCI with the administration of a GPIIb/IIIa inhibitor as rescue therapy in this study, major bleeding occurred in 26·6%, which is higher than 16% for moderate and 3·6% severe bleeding seen in patients receiving similar therapies in the GUSTO III trial[6]. Patients receiving a GPIIb/IIIa agent as part of any rescue strategy in this study had a major bleeding rate of 31%. In a recently published small study (89 patients) by Petronio et al., patients randomised to receive abciximab before rescue PCI had an overall bleeding rate of 20% with no significant difference when compared with placebo and no severe bleeding in the abciximab group based on GUSTO III definitions[7]. Bleeding associated with intra-aortic balloon pump (IABP) use in the present study was 48%. From the Benchmark registry, although not strictly comparable, any access site bleeding was only 4·4% in patients undergoing cardiac catheterisation and PCI with IABP usage[8]. But, even in the absence of treatment with GPIIb/IIIa agents, rescue PCI is known to increase the need for blood transfusion[3].

In the GUSTO III trial, patients receiving abciximab along with early rescue PCI (within 24 h) for failed lytic therapy following acute MI have been shown to have better 30 day outcomes but increased bleeding[6]. Recently, for patients receiving abciximab compared with placebo in association with early rescue PCI (within 24 h), a significant reduction occurred in major adverse cardiac events at 6 months for the combined end-point of death, reinfarction, congestive heart failure and target vessel revascularisation and recurrent ischaemia[7]. This could be explained by reduction in microembolization with improvement in the coronary microcirculation using GPIIb/IIIa inhibitors. In the present study[8] mortality after rescue therapy was lower (2%\(a\)) in the
group receiving rescue PCI and a GPIIb/IIIa inhibitor. PCI after failed lysis (TIMI 0–1 flow) has also been shown to improve survival at 1 year in patients with a moderate to large MI[10]. Poor outcomes have been noted, with mortality rates up to 30% after failed thrombolysis and failed rescue PCI[4]. This is more likely due to these patients being in extremis rather than related to the procedure itself[4].

A significant proportion of major bleeding in this study (70%) occurred at arterial and venous access sites. With smaller size catheters and better arterial access management techniques these will probably be reduced in the future. No data have been given in this study regarding platelet counts and the use of antiplatelet agents such as clopidogrel or ticlopidine. It is likely that many of these patients would have received these medications, which again increase the bleeding risks. Close platelet count monitoring is necessary when patients receive multiple antiplatelet agents.

While there is evidence that abciximab improves outcomes when used as an adjunct to rescue PCI it is associated with increased bleeding risks. Other GPIIb/IIIa agents, such as eptifibatide and tirofiban, have not been studied extensively in the setting of rescue therapy. It is possible that bleeding complications may be reduced in view of their shorter duration of action.

While primary PCI has been shown to be superior to thrombolytic therapy[11,12], lytic therapy still remains the easiest and quickest available treatment for acute MI. At least one study has shown that mortality at 1 year for failed primary PCI is as high as 26% similar to that of failed rescue PCI[3]. Ronner et al[3] have suggested local criteria for rescue PCI should be provided. However, the suggestion that patients who might be suitable for rescue therapy for failed lysis should have a primary PCI will have significant logistic and resource implications. Unless primary PCI can be guaranteed within a definite time frame, lytic therapy should still be considered as first choice treatment for all patients with acute MI. The important point is not to delay the restoration of myocardial reperfusion in candidates suitable for either of the two alternatives. The limitations of retrospective data need to be recognised. Ongoing randomised trials comparing various therapies for rescue procedures should define the best management strategy to improve outcomes in patients failing to reperfuse adequately with thrombolytic therapy.

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References