Management of Acute Myocardial Infarction — Primary Angioplasty the Treatment of Choice!

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Abstract
The management goal of acute myocardial infarction is prompt revascularization. Recent years have seen improvements in both pharmacological and mechanical methods of revascularization of the infarct related arteries. This brief review summarises these developments and ongoing efforts.

Fibrinolytic Therapy : Current Status and Limitations
The components of pharmacological reperfusion are the fibrinolytic agent and the combination of anti-thrombotic and anti-platelet therapy. A number of well planned, prospective, large studies confirmed the efficacy, safety and feasibility of this mode of treatment.1,2 Several new fibrinolytic agents have undergone evaluation after the GUSTO I study3 which had showed the superiority of front loaded regimen with tPA over streptokinase. These include reteplase, tenectaplase and lanetoplase.4,5 However inspite of achieving modestly better TIMI 3 flow the overall outcome did not improve. Addition of glycoprotein (GP) IIb/IIIa receptor blocker abciximab to a reduced dose of fibrinolytic agents seemed to hold the promise to overcome the limitations of fibrinolytic therapy.4,5 The combination however did not show any improvement in the primary endpoints in the GUSTO V and ASSENT - 3 studies.6,7 The more potent pharmacological regimens and combination of anti-thrombotic and GP IIb/IIIa blockers also result in increase of stroke rates upto 3%.8 This is because systemic agents can not differentiate between coronary and non coronary vasculature.

Fibrinolytic therapy with its adjuncts has thus reached a plateau and despite its impact on improving the survival in general has been shown to have several limitations. These include inability to use in several situations, as mention below:
1. Inability to use in several situations.
2. Intra cranial bleeding.
3. Inability to achieve TIMI 3 flow in 40 - 45% patients.
4. Inability to achieve adequate ST segment resolution (>50% or 70%) within 60 to 180 minutes in a large number of patients and relatively high rates of recurrent ischemia and reocclusion.

Percutaneous Intervention (PCI)
PCI for managing AMI has several attractive features :
1. Nearly all patients are eligible.
2. A complete evaluation of coronaries is possible with confirmation of the acute occlusion.
3. It leads to prompt revascularization under vision with >90% TIMI 3 flow and with stent placement the residual stenosis is eliminated.
4. The reocclusion and stroke rates are very low.
5. Early discharge with full risk stratification.

PCI Versus Fibrinolysis
Primary PCI for treating AMI has been in use for more than 2 decades and has been compared with systemic thrombolysis in several trials. A recent meta analysis of 23 trials randomizing 7739 patients to receive fibrinolytic therapy [tissue plasminogen activator (tPA) in 76%] has shown the superiority of primary PCI10. The meta analysis has shown improved 30 days outcome which includes death, non fatal reinfarction and stroke (Table 1). These benefits were maintained during long term also (Table 2). These favorable results for PCI when compared to thrombolysis were seen when PCI was done often in hospitals without on-site surgery or the patients had to be transferred to PCI centers with significant time delays.

Reinfarction after thrombolytic therapy is a major problem. The fate of patients who develop reinfarction after a successful thrombolysis has been recently described in a meta analysis.11 There was a significant increase in mortality in patients with a reinfarction when compared with patients...
without reinfarction in all the TIMI risk categories. Low risk (7.9% vs. 3.0%; p<0.0001), intermediate risk (15.4% vs. 9.2%; p<0.0001) and high risk (39.5% vs. 25.1%; p<0.001). The reinfarction rates are known to occur significantly more often with thrombolytic treatment as compared to primary PCI. There is considerable interest in extrapolating recent advances in new devices and adjunct pharmacotherapies to the primary PCI scene. Use of GP IIb/IIIa blockers especially abciximab along with primary PCI has improved the outcome in a number of trials. It has been shown by Henriques et al. that there is a compromised long term survival in patients who had suffered apparent angiographic embolization during PCI for AMI. Thrombus aspiration techniques are increasingly being used during primary PCI to obviate this problem. A number of studies are evaluating the use of embolus protection measures with emergency coronary interventions during AMI. The data of some of the randomized studies (EMERALD & AIMI) however is not very encouraging.

The greatest benefit of PCI in AMI is the ability to achieve TIMI 3 flow in more than 90% patients even when the patient is treated in the late stages of infarction. On the other hand thrombolytic therapy instituted more than a few hours after symptom onset has significantly reduced efficacy (Fig. 1). Drug Eluting Stents

Drug eluting stents have received considerable attention during the last four years and have been reported to reduce the rates of repeat interventions significantly in randomized trials. Although patients with AMI have been excluded from these studies the data from registries have shown that these are safe and reproduce similar results with extremely low rates of re-intervention up to 1 year of follow up.

Pre-Hospital Thrombolysis

Pre-hospital thrombolysis is a very logical method of achieving early patency of the infarct related artery which is very relevant to countries like India. Patients within two hours of the onset of chest pain are ideal candidates with results even superior to primary angioplasty in the CAPTIM substudy with a 30 days mortality of only 2.5%. The CAPTIM study on prehospital thrombolysis vs. primary PCI (recruitment up to six hours of the onset of chest pain) found no statistical advantage of PCI. However it needs to be highlighted that the trial was not sufficiently powered to give this conclusion because of poor recruitment. It is also noteworthy that 26% of the recruited patients for pre-hospital thrombolysis underwent a ‘rescue PTCA’.

Patients presenting after two hours of onset of chest pain and being considered for primary PCI have been shown to have better results if thrombolysis is started before transferring them to a PCI center. The reported mortality is lower in patients where pre-hospital thrombolysis was started (3.2% vs. 5.8%; p<0.0001) presumably due to a higher patency rate of infarct related artery in comparison to patients transferred without thrombolytic therapy. The role of pre-hospital thrombolysis beyond 6 hours is very limited and it is best not given to these patients, who are clearly better candidates for primary PCI.

AMI: Thrombolysis or PCI?

The contemporary data thus clearly shows the benefits of primary PCI over thrombolysis. However the best strategy for treatment for a patient with AMI presenting to acute care services without catheterization facilities still is a matter of

Table 1: Primary angioplasty vs. Thrombolytic therapy for acute ST - segment elevation infarction : A qualitative (30 days outcome) review of 23 randomized trials

<table>
<thead>
<tr>
<th></th>
<th>Primary PTCA</th>
<th>Thrombolytic Therapy</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall short term death</td>
<td>7%</td>
<td>9%</td>
<td>0.0002</td>
</tr>
<tr>
<td>Death (excluding SHOCK trial data)</td>
<td>5%</td>
<td>7%</td>
<td>0.0003</td>
</tr>
<tr>
<td>Non fatal MI</td>
<td>2.5%</td>
<td>6.8%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Stroke</td>
<td>1%</td>
<td>2%</td>
<td>0.0004</td>
</tr>
<tr>
<td>Recurrent ischemia</td>
<td>6%</td>
<td>21%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Combined endpoint (death, non fatal reinfarction and stroke)</td>
<td>8%</td>
<td>14%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Table 2: Primary angioplasty vs. Thrombolytic therapy for acute ST - segment elevation infarction : A qualitative (12 months outcome) review of 23 randomized trials

<table>
<thead>
<tr>
<th></th>
<th>Primary PTCA</th>
<th>Thrombolytic Therapy</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall long term death</td>
<td>9.6%</td>
<td>12.8%</td>
<td>0.0019</td>
</tr>
<tr>
<td>Death (excluding SHOCK)</td>
<td>6.2%</td>
<td>8.7%</td>
<td>0.0053</td>
</tr>
<tr>
<td>Non fatal MI</td>
<td>4.8%</td>
<td>9.3%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Recurrent ischemia</td>
<td>22%</td>
<td>39%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Stroke</td>
<td>1%</td>
<td>2%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Combined endpoint (death, non fatal reinfarction and stroke)</td>
<td>12%</td>
<td>19%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Fig. 1: Mortality rates from randomized trials and relationship with time at presentation (PCI vs. Thrombolysis). Abbreviations :- PCI : Percutaneous Coronary Intervention, Lysis : Thrombolysis, hrs. : Hours
debate. The subject of immediate thrombolysis versus transfer for primary angioplasty has received attention during the last few years. In a meta-analysis of 6 clinical trials, it has been shown that upon a transfer time of ≤3 hours, the composite primary endpoint of death, reinfarction and stroke was significantly reduced by 42% (p<0.001) in the group transferred for primary PCI compared with the group receiving on site thrombolysis. When individual parameters of the combined endpoint were considered separately, reinfarction was reduced by 68% (p<0.001) and stroke by 56% (p=0.015). There was also a trend toward reduction in the all cause mortality of 19% (p=0.08). The role of combining low dose fibrinolytics, GP IIb/IIIa blockers/low molecular weight heparin followed by angioplasty (facilitated PCI) is being looked into by dedicated ongoing trials like FINESSE and ADVANCE-MI.

CONCLUSION

We need to develop specialized regional centers for the treatment of AMI. The goal should be to obtain ECG in the field and transferring patients with ST elevation from home directly to a “heart attack center” capable of handling emergencies with 24 hours facility of carrying out thrombolysis, primary PCI and emergency cardiac surgery with requisite infrastructure, personnel and hardware. This needs revamping of the existing facilities and the health care system.

REFERENCES


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