Treatment of ST-elevation Myocardial Infarction: Need for a Better Reperfusion Strategy

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Treatment of ST-elevation Myocardial Infarction: Need for a Better Reperfusion Strategy

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The traditional definition of acute myocardial infarction (MI) is changing, largely because of the emergence of newer markers of myocardial damage. Using the conventional indicators of twice creatinine kinase rise, MI are now categorised as ST-elevation MI (Q wave MI) and non-ST elevation MI (non-Q MI). A recent chart review in Queen Mary Hospital shows that patients with ST-elevation MI were younger, mostly males, and had a higher in-hospital mortality than non-ST elevation MI (Table 1). Whilst a debate on the best management strategy for non-ST elevation MI remains, there are recent evidence and on-going trials on improving the treatment of ST-elevation MI, which still carries an in-hospital mortality of 6-8% in randomised trials, and up to 20% in "real" life cases in the United States.

Reperfusion therapy using fibrinolytic agents is the standard of care in the management of patients presenting with ST-elevation MI. The goal of reperfusion therapy is rapid, complete, and sustained restoration of normal flow in the infarct-related artery (IRA), thereby preserving left ventricular function and reducing mortality. Recent evidence have shown that re-establishment of normal epicardial flow does not mean successful myocardial reperfusion.1 Despite attaining Thrombolysis in Myocardial Infarction (TIMI) grade 3 flow in the IRA, myocardial reperfusion may still be impaired after primary percutaneous transluminal coronary angioplasty (PTCA). This is associated with large infarcts, poor left ventricular functional recovery, and increased mortality.2-6 Two methods have been developed recently to characterise myocardial reperfusion. The TIMI myocardial perfusion grade uses the clearance of the myocardial blush on the coronary angiogram to define different grades of myocardial reperfusion.7 This angiographic method of assessing myocardial reperfusion involves the performance of an invasive procedure and is not readily available. Resolution of ST elevation on the surface electrocardiogram (EKG) has been shown to correlate closely with myocardial contrast echocardiography findings8 and thus is a marker of myocardial reperfusion. Moreover, ST resolution carries prognostic implications in patients with acute MI receiving fibrinolytic agents or undergoing primary PTCA.9-16

Although new fibrinolytic agents have been developed and are starting to replace tissue plasminogen activator in the Western world, streptokinase is still used in many parts of the world as the fibrinolytic of first choice in ST-elevation MI. Using ST segment resolution as an endpoint for successful reperfusion strategy, a recent local study (Chen WH et al, unpublished observation) suggests that streptokinase resulted in complete ST resolution in only one-quarter of patients with ST-elevation MI. This strategy compared poorly to a third-generation fibrinolytic, lanoteplase, which

Table 1. Clinical characteristics and outcome of ST-elevation and non-ST elevation MI in Queen Mary Hospital in 1998 - 1999

<table>
<thead>
<tr>
<th></th>
<th>ST-elevation MI n=200</th>
<th>Non-ST elevation MI n=100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>65 ± 12</td>
<td>73 ± 11</td>
</tr>
<tr>
<td>% Female</td>
<td>20%</td>
<td>41%</td>
</tr>
<tr>
<td>Risk Factor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>50%</td>
<td>53%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>32%</td>
<td>40%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>22%</td>
<td>26%</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>18%</td>
<td>20%</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>16%</td>
<td>11%</td>
</tr>
</tbody>
</table>

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MYOCARDIAL INFARCTION, REPERFUSION THERAPY

resulted in ST resolution of 33% in 60 minutes. The better survival of patients treated with "front-loaded" tissue plasminogen activator and heparin, over streptokinase in patients with large anterior MI with early presentation was well documented in the GUSTO-I trial.

However, with the present fibrinolytic therapy, full myocardial reperfusion is only achieved in 30-45% of patients, and reocclusion occurs in about 30% by three months, which is associated with increased mortality. Resistance to thrombolysis results from the highly complex constituents of the clot that obstructs the IRA: a mixture of activated platelets, fibrin and thrombin. Thus fibrinolytics that act on the fibrin portion of the clot result in incomplete lysis. Worse still, exposure of clot-bound thrombin can cleave fibrinogen to fibrin, thus promoting re-thrombosis. In addition, platelet factors that result in vasoconstriction also limit recanalisation of IRA.

Thus to optimise myocardial reperfusion, two additional strategies may be considered in addition to fibrinolytics: anti-platelet and anti-thrombin therapy. Anti-thrombin therapy is already an integral element in current fibrinolytic treatment, especially with the tissue plasminogen activators. It is attractive to consider the low molecular weight heparins, with their more predictable bioavailability and factor Xa inhibition, which may be advantageously combined with these plasminogen activators. The glycoprotein IIbIIIa inhibitors, which blocks the final common pathway of platelet activation, has also been tested in pilot studies in combination with fibrinolytics in addition to aspirin. Early results suggest that these combinations may result in a higher percent of TIMI-3 flow than with conventional fibrinolytics. With proper dose reduction of fibrinolytic, the excessive bleeding risk may be acceptable. Whether these newer "cocktails" are translated into clinical benefits must await the results of currently ongoing large scale trials.

While fascinated by the newer chemical clot busters, one must not forget the more direct and proven approach: primary PTCA. Unfortunately at present, none of the Hospital Authority hospitals are equipped, both in equipment and personnel, to perform primary PTCA on a routine basis. This certainly is an area worth developing, as Hong Kong is a small area and a high percentage of patients with MI can reach the hospital within 4 hours, making PTCA a feasible option. As nearly half of the patients even with the newer fibrinolytics do not achieve optimal reperfusion, it is not unreasonable to adopt a "staged" strategy to perform rescue PTCA, perhaps using the non-invasive ST resolution method at 60 minutes as a triage. Finally, a "hybrid" approach may be considered in which lower dose lytics are given while getting ready to perform angioplasty, to optimise myocardial salvation.

A hypothetic scenario of the outcome of patients admitted to a hospital with MI is shown in the Figure 1.

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**Figure 1.** A hypothetical treatment path of 100 patients with acute MI admitted to a hospital, and the reasons for not achieving optimal myocardial perfusion therapy.
Roughly, only one quarter of these patients will derive optimal myocardial reperfusion. There remains many areas of improvement, including avoiding late presentation through public education and reducing the numbers of patients who are thrombolytic ineligible, in addition to the above mentioned strategies. Finally one must never forget that 1 in 4 patients who have a MI die before reaching hospital, emphasising that we need to pay attention to primary prevention of coronary risk factors, and improving our means to identify the plaque vulnerable to rupture.

References