Reperfusion strategy for ST-segment elevation myocardial infarction: trend over a 10-year period

Objectives To review the 10-year trend of reperfusion strategies in patients with ST-segment elevation myocardial infarction, and the adoption rate of percutaneous coronary interventions as opposed to thrombolytic therapy. Also to explore why some patients did not receive reperfusion therapy, and document changes in reperfusion strategies after the introduction of primary percutaneous coronary intervention programmes.

Design Case series.

Setting A regional hospital, Hong Kong.

Patients All patients with ST-segment elevation myocardial infarction from January 2000 to December 2009.

Results There were 1835 patients with ST-segment elevation myocardial infarction in that period, of which 1179 (64.3%) received reperfusion therapy (thrombolytic therapy, 46.0%; primary percutaneous coronary intervention, 17.5%; emergency coronary artery bypass graft, 0.7%). After introduction of the primary percutaneous coronary intervention programme, significantly more ST-segment elevation myocardial infarction cases underwent that particular intervention (1.6% in 2000 increasing to 30.6% in 2009), while the proportion receiving thrombolytic therapy declined (57.4% in 2000 decreasing to 35.0% in 2009). Seven reasons for no reperfusion therapy were identified. The commonest ones were delayed presentation (45.1%), succumbed before reperfusion (16.0%), multiple medical co-morbidities (15.2%), and contra-indication to thrombolytic therapy (14.8%). The proportion without reperfusion therapy due to a contra-indication to thrombolytic therapy declined (22.7% in 2000 decreasing to 4.9% to 2009), whilst an increasing proportion received primary percutaneous coronary interventions.

Conclusions Primary percutaneous coronary intervention is increasingly used as the reperfusion therapy in ST-segment elevation myocardial infarction and is replacing thrombolytic therapy, though the latter still remains a mainstay of therapy. A significant proportion of ST-segment elevation myocardial infarction cases received no reperfusion due to various reasons.

New knowledge added by this study

• In the era of widespread reperfusion therapy for ST-segment elevation myocardial infarction (STEMI), a significant proportion of patients still did not receive this therapy in our locality.
• The commonest cause of non-reperfusion in STEMI was delayed presentation.

Implications for clinical practice or policy

• Education of the public to improve awareness of ischaemic symptom is necessary, in order to improve the chance of reperfusion.
• Contra-indication to thrombolytic therapy, once a common reason for non-reperfusion, can be dealt with primary percutaneous coronary intervention (PCI). Therefore PCI capability should be developed in more centres in our locality.

Introduction

Current guidelines recommend attempting reperfusion therapy for all patients presenting with electrocardiograms (ECGs) showing ST elevation myocardial infarction (STEMI)
within 12 hours of symptom onset. Although it takes a longer time to undertake primary percutaneous coronary intervention (PCI) than to give thrombolytic therapy, it is the preferred option if performed in a timely fashion. Normalisation of coronary blood flow can be better achieved by primary PCI, and the rates of death, re-infarction, recurrent ischaemia, and stroke are also lower.4-7

Nevertheless, a significant proportion of STEMI patients are not offered any reperfusion therapy. In the Euro Heart Survey (EHS), only 56% of STEMI patients received reperfusion therapy,8 in the TETAMI (Treatment with Enoxaparin and Tirofiban in Acute Myocardial Infarction) registry, 28% of patients presenting within 12 hours of symptom onset did not receive reperfusion therapy.9

This retrospective study reviews the 10-year trend of the reperfusion strategy for STEMI patients in a single regional hospital. Among those who received such therapy, we set out to review the adoption rate of PCI in comparison to thrombolytic therapy. Among those who did not receive reperfusion therapy, we explored the various reasons, and the changes that ensued in this respect after the introduction of hospital’s primary PCI programme. The aim was to assess the likelihood of achieving reperfusion therapy in our hospital setting, as local data were lacking. This forms the basis for identifying targets and strategies for improvement.

Methods

Case selection

All hospitalised patients of Pamela Youde Nethersole Eastern Hospital with a coding of ‘acute myocardial infarction (AMI)’ as the diagnosis in the Clinical Data Analysis and Reporting System over the 10-year period from 1 January 2000 to 31 December 2009 were identified. This hospital was opened in 1993 and served as a major acute hospital providing a full range of specialist services to Hong Kong citizens. Cases coded with the diagnosis of subendocardial infarction or non-Q wave myocardial infarction (non-Q MI) were therefore excluded.

For the remaining cases without a specific type of myocardial infarction coded, the electronic or written records were reviewed to identify patients with STEMI, which formed the cohort for this study. All ECGs of this final cohort were reviewed to ensure that the diagnostic criteria of STEMI were fulfilled. These criteria consisted of: new ST elevation at the J-point in two contiguous leads with the cut-off points of ≥0.2 mV in leads V2-V3 and/or ≥0.1 mV in other leads, and also presumed new-onset left bundle branch block. In this cohort of STEMI cases, the baseline demographic characteristics, type of reperfusion therapy, and reasons for no reperfusion therapy were entered in a pre-designed data sheet.

Statistical analysis

Data were presented as means, medians, ranges, and standard deviations (SDs), together with P values as appropriate. Categorical data included proportions of reperfused and non-reperfused cases before and after the implementation of the primary PCI programme, gender distribution in the reperfused and non-reperfused cases, and mortality rates. These were compared using the Chi squared test. Continuous data such as ages in the reperfused and non-reperfused cases were compared using Student’s t test.

Results

A total of 3317 cases with the coding of AMI were retrieved, of which 945 coded with ‘subendocardial
‘acute myocardial infarction’ or ‘non-Q MI’ were excluded. A further 537 were excluded after study of their discharge summaries, of which 483 were non-STEMI or unstable angina, and 54 were elective admissions (for coronary angiogram, PCI, or convalescent care after coronary artery bypass graft [CABG], or open heart surgery in other hospitals). The remaining 1835 patients formed the cohort that was analysed in this study. The number of STEMI cases per year is illustrated in Table 1.

The respective mean and median ages of these STEMI patients were 71 (SD, 13; range, 28-101) years and 73 years. In all, 1206 (65.7%) cases were males. Of 1835 STEMI cases, 1179 (64.3%) received reperfusion therapy. They included 322 (17.5%) who received primary PCI, 12 (0.7%) who underwent an emergency CABG procedure, and 845 (46.0%) who received thrombolytic therapy.

Regarding the 656 (35.7%) cases who did not receive any reperfusion therapy, in 651 there were clearly documented underlying reasons, whereas in five (0.3%) there was no identifiable reason as the medical record was unavailable. These five patients all succumbed shortly after admission, which was a postulated reason for no reperfusion.

Anterior STEMI accounted for 1043 (56.8%) of the cases, 727 (39.6%) cases were inferior, 47 (2.6%) had presumed new-onset left bundle branch block, and 13 (0.7%) had posterior myocardial infarction. The infarct territory was not identified for the five patients whose medical information was unavailable.

The number and proportion of cases who received and did not receive reperfusion therapy throughout the 10 years are illustrated in Table 1 and Figure 1, respectively.

### TABLE 1. Patients with ST-segment elevation myocardial infarction per year having various or no reperfusion procedures (2000 to 2009)*

<table>
<thead>
<tr>
<th>Year</th>
<th>Total No. of patients</th>
<th>No. (%) having primary PCI</th>
<th>No. (%) having emergency CABG</th>
<th>No. (%) having thrombolytic therapy</th>
<th>No. (%) having no reperfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>183</td>
<td>3 (1.6)</td>
<td>0</td>
<td>105 (57.4)</td>
<td>75 (41.0)</td>
</tr>
<tr>
<td>2001</td>
<td>158</td>
<td>3 (1.9)</td>
<td>0</td>
<td>89 (56.3)</td>
<td>66 (41.8)</td>
</tr>
<tr>
<td>2002</td>
<td>167</td>
<td>7 (4.2)</td>
<td>1 (0.6)</td>
<td>94 (56.3)</td>
<td>65 (38.9)</td>
</tr>
<tr>
<td>2003</td>
<td>182</td>
<td>17 (9.3)</td>
<td>3 (1.6)</td>
<td>89 (48.9)</td>
<td>73 (40.1)</td>
</tr>
<tr>
<td>2004</td>
<td>205</td>
<td>48 (23.4)</td>
<td>1 (0.5)</td>
<td>94 (45.9)</td>
<td>62 (30.2)</td>
</tr>
<tr>
<td>2005</td>
<td>166</td>
<td>40 (24.1)</td>
<td>2 (1.2)</td>
<td>74 (44.6)</td>
<td>50 (30.1)</td>
</tr>
<tr>
<td>2006</td>
<td>189</td>
<td>49 (25.9)</td>
<td>1 (0.5)</td>
<td>76 (40.2)</td>
<td>63 (33.3)</td>
</tr>
<tr>
<td>2007</td>
<td>197</td>
<td>47 (23.9)</td>
<td>3 (1.5)</td>
<td>75 (38.1)</td>
<td>72 (36.5)</td>
</tr>
<tr>
<td>2008</td>
<td>208</td>
<td>53 (25.5)</td>
<td>0</td>
<td>86 (41.3)</td>
<td>69 (33.2)</td>
</tr>
<tr>
<td>2009</td>
<td>180</td>
<td>55 (30.6)</td>
<td>1 (0.6)</td>
<td>63 (35.0)</td>
<td>61 (33.9)</td>
</tr>
<tr>
<td>Total</td>
<td>1835</td>
<td>322 (17.5)</td>
<td>12 (0.7)</td>
<td>845 (46.0)</td>
<td>656 (35.7)</td>
</tr>
</tbody>
</table>

* PCI denotes percutaneous coronary intervention, and CABG coronary artery bypass graft

![FIG 1. The proportion of cases who received and did not receive reperfusion therapy from 2000 to 2009](image)

STEMI denotes ST-segment elevation myocardial infarction, CABG coronary artery bypass graft, and PCI percutaneous coronary intervention.
The adoption rate of thrombolytic therapy decreased from 57.4% in 2000 to 35.0% in 2009, while the adoption of primary PCI increased from 1.6% in 2000 to 30.6% in 2009.

We started a primary PCI programme on 1 November 2003. The adoption rate of primary PCI before then was 2.6%, which increased to 26.3% after its initiation (P<0.001). The adoption rate of thrombolytic therapy before the PCI programme was 56.7%, which decreased to 46.3% after its implementation (P=0.14). The percentage of patients not receiving reperfusion therapy before the programme was 39.9%, which decreased to 33.4% after its implementation (P=0.34).

Patients with ST-segment elevation myocardial infarction without reperfusion

Of all STEMI patients, 656 (35.7%) did not receive reperfusion therapy, of whom 318 (48.5%) were male. The respective mean and median ages in these 656 patients were 75 (SD, 13; range, 31-101) years and 77 years. Compared with the entire cohort of STEMI patients, this group had more elderly patients (aged >80 years) [P=0.003].

Seven reasons for no reperfusion were identified as follows: (1) delayed presentation; (2) death before reperfusion could be implemented; (3) multiple medical co-morbidities rendering the patient ineligible; (4) contra-indication to thrombolytic therapy; (5) spontaneous reperfusion; (6) delayed diagnosis; and (7) patient refusal. The number and proportion of cases in these categories over the 10-year period are illustrated in Table 2 and Figure 2, and are analysed below.

### TABLE 2. Patients with ST-segment elevation myocardial infarction (STEMI) per year having no reperfusion according to reason (2000 to 2009)

<table>
<thead>
<tr>
<th>Year</th>
<th>Total No. of patients</th>
<th>STEMI without reperfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Delayed presentation</td>
</tr>
<tr>
<td>2000</td>
<td>183</td>
<td>75 (41.0)</td>
</tr>
<tr>
<td>2001</td>
<td>158</td>
<td>66 (41.8)</td>
</tr>
<tr>
<td>2002</td>
<td>167</td>
<td>65 (38.9)</td>
</tr>
<tr>
<td>2003</td>
<td>182</td>
<td>73 (40.1)</td>
</tr>
<tr>
<td>2004</td>
<td>205</td>
<td>62 (30.2)</td>
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</tr>
<tr>
<td>2009</td>
<td>180</td>
<td>61 (33.9)</td>
</tr>
<tr>
<td>Total</td>
<td>1835</td>
<td>656 (35.7)</td>
</tr>
</tbody>
</table>

FIG 2. Proportions of different reasons for no reperfusion therapy (2000 to 2009)
Delayed presentation
This was the commonest reason for non-reperfusion, and accounted for 296 (45.1%) of such cases. The cut-off delay after symptom onset was 12 hours. The number of cases per year remained similar. A significant number of these patients presented with atypical symptoms; in 69 dyspnoea was the reported symptom, whilst 19 others complained of epigastric pain, vomiting, and syncope. Diabetes mellitus was present in 122 (41.2%) of these cases. Moreover, eight patients had STEMI diagnosed either in mainland China (n=7) or in Macau (n=1), but refused reperfusion therapy there. When they reached our hospital, more than 12 hours had elapsed since their symptoms and therefore reperfusion therapy was not performed. Possible inadequate social support may also have contributed to delays, in that 64 (22%) patients were either old-age home residents or living alone.

Death before reperfusion
This ensued in 105 (16.0%) of the non-reperfusion cases, and the numbers per year remained similar. Their mean and median ages were 78 and 79 years, respectively. This subgroup was in general older than the whole STEMI cohort (mean and median ages being 71 and 73 years, respectively). These patients had all lapsed into ventricular fibrillation or pulseless electrical activity before prompt reperfusion was given, and resuscitation had failed. Among them, 17 (16.2%) had cardiac tamponade; prompt pericardiocentesis was performed in 14 of them but did not alter the outcome.

Multiple medical co-morbidities
Multiple co-morbidities rendered reperfusion therapy ineligible in 100 (15.2%) of the cases. The number of cases per year also remained similar. Their mean and median ages were 82 and 84 years, respectively; 86 patients in this subgroup were aged ≥75 years. The common relevant co-morbidities included hypoxic brain damage post-resuscitation (n=21), history of malignancy (n=11), poor pre-morbid status due to previous cerebrovascular accident (n=10), and a history of dementia (n=7). In this subgroup, 62 patients succumbed during the index hospitalisation, and a further nine within 6 months, yielding an overall 6-month mortality of 71%.

Contra-indications to thrombolytic therapy
These were present in 97 (14.8%) of the cases. The rate of no reperfusion due to any contra-indication to thrombolytic therapy declined over the 10 years, from 22.7% in 2000 to 4.9% in 2009 (P=0.038). The common contra-indications to thrombolytic therapy included: history of intracranial haemorrhage, gastro-intestinal bleeding, haemoptysis, significant anaemia (haemoglobin level, <80 g/L), and being postoperative.

Spontaneous reperfusion
This ensued in 25 (3.8%) of the cases. The definition of spontaneous reperfusion was spontaneous resolution of ST-segment elevation in the 12-lead ECG before initiation of reperfusion therapy. No patient in this group succumbed during their index admission, but one succumbed within 6 months because of community-acquired pneumonia. Therefore, the in-hospital and 6-month mortality rates in this subgroup were 0 and 4%, respectively.

Delayed diagnosis
Delayed diagnosis was the reason in 23 (3.5%) of the non-reperfusion cases. The diagnosis was missed on the initial 12-lead ECG. In this subgroup, ECGs of five patients were misinterpreted in the Accident and Emergency (A&E) Department, four in the Department of Medicine, 13 in other departments (Surgery, Orthopaedics and Traumatology, Neurosurgery, and Psychiatry), and one seen by a private general practitioner.

Patient refusal
Patient refusal of thrombolytic therapy accounted for five cases. In the year 2000, two patients refused for fear of bleeding complications and were discharged against medical advice; no further information on them was available. In 2006 and again in 2009, single patients refused thrombolytic therapy for the same reason; they had PCI performed 2 days later, survived, and were followed up till 2008 and 2010, respectively. The remaining patient (in 2006) refused both thrombolytic therapy and PCI despite detailed explanations (for fear of bleeding complications and acute renal impairment, respectively), and succumbed during the index admission.

Mortality experiences
In-hospital mortality in patients who did not have reperfusion therapy was 39.8%, which was significantly higher than the 16.7% rate in patients who received primary PCI (P=0.017). Corresponding 6-month mortality rates were 45.4% and 20.8% (P=0.043).

Discussion
The mainstay treatment for STEMI is timely reperfusion, with primary PCI being superior to
thrombolytic therapy in terms of efficacy and safety. The primary PCI programme in this hospital has operated since November 2003. For this purpose, the A&E Department was to contact the Cardiac Catheterization Laboratory directly for feasibility of primary PCI for the particular patient with STEMI, when he/she arrived to the A&E Department between 08:30 and 17:00 hours on weekdays other than public holidays. This time frame was extended to 07:30 to 19:30 hours from October 2010. Outside this time frame, primary PCI would nevertheless be performed if there was a specific indication (eg contra-indication to thrombolytic therapy or haemodynamic instability). Otherwise thrombolytic therapy was offered as first-line therapy.

This retrospective study demonstrated that after the introduction of the primary PCI programme, a significantly greater proportion of STEMI patients underwent this form of reperfusion therapy over the 10-year period. This was accompanied by a decrease in the proportion of cases that received thrombolytic therapy or no reperfusion (Fig 1).

A significant proportion of cases (35.7%) did not receive reperfusion therapy for various reasons, which was consistent with EHS findings that reported a figure of 44%. The proportions of female and elderly patients having no reperfusion were higher than in the whole STEMI cohort, in which the finding was consistent with the GRACE (Global Registry of Acute Coronary Events) analysis, and the studies from Mehta et al and Berton et al. Apparently, female and elderly patients were more likely to have atypical symptoms and present later.

Delayed presentation was the most common reason for no reperfusion therapy. The current STEMI guidelines do not recommend attempting reperfusion in patients who present more than 12 hours after symptom onset. There was a relatively high proportion of diabetic patients in this group, who might not have prominent ischaemic symptoms and therefore might not seek medical advice immediately. Ribeiro et al reported that diabetes mellitus was an independent predictor of delayed reperfusion. The study by Marchant et al indicated that subclinical autonomic neuropathy was an important cause of silent myocardial ischaemia in diabetic patients.

In eight patients who developed STEMI in mainland China, the patients refused reperfusion therapy there. This finding was unique to our locality. Due to the geographical and economic relationship between mainland China and Hong Kong, a significant number of Hong Kong citizens live or work in mainland China. We anticipate that we shall continue to encounter this type of patient in the future. Education to promote early treatment in the nearest hospital is needed for those who are often in mainland China or overseas.

A significant number of patients with delayed presentation were old-age home residents or living alone. The study from Sheifer et al suggested a causal relationship between delayed presentation and poor social support. This group often lived in an unfavourable environment, where communication might also be limited by low education levels and impaired cognition. More training should be provided to the health providers of elderly homes to increase awareness of ischaemic symptoms.

A significant proportion of patients were ineligible for reperfusion therapy because of multiple medical co-morbidities. In the AMI-Florence Italian Registry, the proportion of patients receiving reperfusion progressively decreased with increasing numbers of chronic co-morbidities. Elderly patients are less likely to receive reperfusion even if eligible. Many trials of reperfusion therapy excluded those aged >75 years. Besides, the elderly more often had relative contra-indications for thrombolytic therapy (eg poorly controlled hypertension and history of stroke). In the absence of other contra-indications, we should not preclude patients from reperfusion therapy because of advanced age. The Fibrinolytic Therapy Trialists’ Collaborative Group demonstrated a greater absolute reduction of mortality in elderly patients (>75 years old) treated with thrombolytic therapy.

Contra-indication to thrombolytic therapy was once a common reason for no reperfusion in this hospital, and in the early years accounted for about 16% of such cases. The absolute and relative contra-indications of thrombolytic therapy are well-defined in current guidelines. In our series, the rate of non-reperfusion in this group declined significantly over the 10 years, because an increasing proportion received primary PCI, especially after the introduction of the primary PCI programme. Even if these patients were admitted to our hospital after the office hours, they might receive primary PCI by the on-call cardiac team.

Lack of PCI capability in some hospitals in our locality is a significant factor affecting clinical outcomes in those with a contra-indication to thrombolytic therapy. Development of PCI facilities in more hospitals and a well-structured triage system to hospitals with PCI capability is desirable. The latest guideline contains a Class IC recommendation to establish protocols for STEMI patients who are ineligible for thrombolytic therapy to be transferred to PCI-capable hospitals.

In STEMI patients who subsequently undergo spontaneous reperfusion, none succumbed during their index hospitalisation. Evidently, this group had better clinical outcomes than the whole STEMI cohort. An analysis in a sub-study of the ASSENT-4 PCI trial suggested that ‘electrocardiographic
spontaneous reperfusion’ was associated with a lower mortality. Resolution of ST-segment elevation might reflect both the recanalisation of the culprit epicardial vessel and better microvascular flow at the cellular level.21

A number of cases did not receive reperfusion therapy because the diagnosis was not made from the initial ECG. This was a practical issue also observed by others, and may be avoided by exercising greater care in ECG reading, including seeking a cardiologist’s opinion early. More training for health care workers on ECG interpretation could be beneficial.

The relatively static proportions of non-reperfusion cases during the 10-year study period were largely related to static numbers in the following three categories: delayed presentation, death before reperfusion, and multiple medical co-morbidities rendering patients ineligible. These three accounted for 76.3% of such cases, for which corrective strategies should be implemented.

Education to improve public awareness of ischaemic symptoms and motivation to seek early medical advice is warranted, and could be promoted through mass media and educational campaigns. The earlier the diagnosis is established, the earlier can reperfusion therapy be given, and hopefully improve outcomes greatly. On the contrary, reperfusion therapy should not be withheld solely because of advanced age. If scientific evidence and clinical guidelines are strictly applied, the majority of STEMI patients should receive reperfusion therapy. The ESTIM registry illustrated that it was possible to implement revascularisation in as many as 89% of all patients.23

Limitations
First, this was a retrospective study, and thus important data may have been lost or not well-documented, and some medical records were not retrieved. Second, although the reasons for no reperfusion therapy were predefined before starting data collection, adjustments were considered necessary throughout the study, which could have resulted in inaccuracies or incomplete data abstraction. Third, this study reported experience with the management of STEMI in a single tertiary hospital only, which may not be applicable to the entire population of Hong Kong. Hence any general recommendations to optimise receipt of reperfusion therapy may apply to our locality only.

Conclusions
Prompt restoration of myocardial blood flow is essential in STEMI, for which PCI can offer better clinical outcomes and is preferable to thrombolytic therapy. With the introduction of the primary PCI programme, more STEMI cases underwent this form of reperfusion throughout the 10-year period. This was accompanied by a decrease in the proportions that received thrombolytic therapy and no reperfusion. For various reasons however, a significant proportion of patients still received no reperfusion therapy—delayed presentation, death before reperfusion, and multiple medical co-morbidities being the commonest. In general these patients were older, presented with atypical symptoms, and a large proportion had poor social support. Public education to improve awareness of ischaemic symptoms may facilitate early presentation. Providing more social support might benefit those who are socially vulnerable. Concerning patients with multiple medical co-morbidities, physicians can judge on an individual basis what constitutes the best interest for each patient, instead of routinely pursuing less aggressive treatment. Contra-indication to thrombolytic therapy is another reason for no reperfusion, which can be overcome by primary PCI. It is desirable for PCI programmes to be developed on a larger scale and in more centres, so as to increase the percentage of eligible patients that can be offered reperfusion therapy.


