Thrombolysis in acute myocardial infarction: the safety and efficiency of treatment in the accident and emergency department

J A Edhouse, M Sakr, J Wardrope, F P Morris

Abstract

Objectives—To assess the safety and efficiency with which the accident and emergency (A&E) department provides thrombolytic treatment for patients with acute myocardial infarction (AMI).

Methods—A prospective observational study based in a teaching hospital for one year. All patients who presented with the clinical and electrocardiographic indications for thrombolytic treatment were studied. Patients were grouped according to route of admission. After logarithmic transformation, the “door to needle times” of the groups were compared using a two tailed Student’s t test. Arrhythmias and complications after thrombolytic treatment were noted. The appropriateness of the treatment was assessed retrospectively by review of the clinical records and electrocardiograms, judged against locally agreed eligibility criteria.

Results—Data from 153 patients were analysed; 138/153 (90%) patients were admitted via the A&E department. The shortest door to needle times were seen in those patients thrombolysed by A&E staff within the A&E department (mean 43.8 minutes). The transfer of A&E patients to the coronary care unit (CCU) was associated with a significant increase in the door to needle time (mean 58.8 minutes, p = 0.004). Only one malignant arrhythmia occurred during the administration of thrombolysis in the A&E department, and this was managed effectively. No arrhythmias occurred during transfer of thrombolysed patients to the CCU. In every case, the decision to administer thrombolysis was retrospectively judged to have been appropriate.

Conclusions—The A&E department provides appropriate, safe, and timely thrombolytic treatment for patients with AMI. Transferring A&E patients to the CCU before thrombolysis is associated with an unnecessary treatment delay.


Keywords: thrombolytic treatment; acute myocardial infarction

The benefits of thrombolytic treatment in AMI are well established,1,2 and the greatest benefits are seen in patients treated early.3,4 In view of the considerable benefit from early thrombolysis it has been recommended that thrombolytic treatment be given at the first opportunity, and with the same degree of urgency as the treatment of cardiac arrest.6 Guidelines have been published calling for hospitals to develop fast track systems that allow for the prompt identification of those with obvious myocardial infarction.5

The interval between arrival at hospital and the start of treatment is known as the “door to needle time”, and the audit standard for patients presenting with obvious indications for thrombolysis has been set at 30 minutes.8 Duplication of medical assessment has been identified as a major factor causing in-hospital treatment delays.9 The shortest delays have been shown to occur when patients are thrombolysed within the accident and emergency (A&E) department.10 Nevertheless, a recent survey showed that only 35% of A&E departments give thrombolysis routinely.10 There may be a number of reasons why thrombolysis has not been widely adopted as a routine A&E procedure; there may be a lack of confidence in the ability of A&E staff to interpret electrocardiograms (ECGs) correctly, resulting in the inappropriate use of thrombolytic treatment. There may be concerns regarding potential complications and reperfusion arrhythmias, particularly if these occur during transfer to the coronary care unit (CCU). A lack of space to accommodate patients undergoing thrombolysis and insufficient numbers of nursing staff to provide supervision may also be a problem for some departments.

In Sheffield, patients with suspected AMI may be admitted to hospital via the A&E department or by general practitioner referral directly to the medical admissions ward. During the study period, A&E patients were thrombolysed immediately within the department, or after urgent transfer to the CCU. Patients admitted to the medical admissions ward were transferred to the CCU before thrombolysis.

The aim of the study was to assess whether the A&E department could provide thrombolytic treatment in a safe, appropriate, and timely manner when compared with the other delivery options available within the hospital.

Methods

We performed a study in a teaching hospital in Sheffield for one year (1996–97). We studied all patients who on presentation fulfilled the eligibility criteria for thrombolytic treatment. A questionnaire was completed prospectively for patients thrombolysed by A&E staff. The CCU
Box 1: Electrocardiographic criteria for thrombolysis

1. ST elevation >1 mm in two contiguous limb leads or >2 mm in two contiguous chest leads.
2. Proven new left bundle branch block.
3. Posterior myocardial infarction (tall R wave V1, ST segment depression V2 and V3).

Box 2: Contraindications to thrombolytic treatment

Absolute contraindications
- Active gastrointestinal bleeding or active internal bleeding
- Aortic dissection
- Neurosurgery or head injury within two months
- Cerebrovascular accident within two months
- Intracranial aneurysm/neoplasms
- Bleeding diathesis

Relative contraindications
- Traumatic cardiopulmonary resuscitation
- Proliferative diabetic retinopathy
- Abdominal aortic aneurysm
- Major surgery within 10 days
- Uncontrollable hypertension (systolic blood pressure >180 mm Hg or diastolic blood pressure >110 mm Hg)
- Gastrointestinal bleeding in previous six months or known ulcerative colitis
- Subclavian puncture
- Major trauma or childbirth within 10 days

and medical wards were visited daily in order to obtain data on all other patients. During the study period there was middle grade or consultant presence in the department for 13 hours a day (0800–2100 hours).

THROMBOLYSIS ELIGIBILITY CRITERIA

Patients were offered thrombolytic treatment if they presented within 12 hours of the onset of chest pain and fulfilled the required ECG criteria (box 1), provided there were no contraindications (box 2).

HOSPITAL PROCEDURES

Patients with suspected AMI received oxygen, aspirin, intravenous opiates, and antiemetics as appropriate.

The initial policy was to thrombolise all suitable patients within the A&E department.

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>No of patients</th>
<th>Mean age (years)</th>
<th>% presenting &quot;out of hours&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombolysis by A&amp;E staff in A&amp;E department</td>
<td>56</td>
<td>66</td>
<td>30 (53.5)</td>
</tr>
<tr>
<td>Thrombolysis by A&amp;E staff in CCU</td>
<td>43</td>
<td>61</td>
<td>29 (67)</td>
</tr>
<tr>
<td>A&amp;E patients referred for admitting team to thrombolysis</td>
<td>29</td>
<td>64</td>
<td>20 (69)</td>
</tr>
<tr>
<td>Patients &quot;missed&quot; by A&amp;E</td>
<td>10</td>
<td>66</td>
<td>9 (90)</td>
</tr>
<tr>
<td>Direct admission to medical ward</td>
<td>13</td>
<td>71</td>
<td>10 (77)</td>
</tr>
<tr>
<td>Thrombolysis inappropriately withheld</td>
<td>2</td>
<td>65.5</td>
<td>2 (100)</td>
</tr>
<tr>
<td>Total</td>
<td>153</td>
<td></td>
<td>100</td>
</tr>
</tbody>
</table>

**"Out of hours" = time of arrival between 0000–0800 hours weekdays, or during a weekend.

This took place in the resuscitation room, with continuous electrocardiographic monitoring. Transfer to the CCU occurred when a bed became available and was supervised by a doctor with a defibrillator. After a policy change, A&E patients were transferred to the CCU before thrombolysis if a bed was immediately available; the accompanying A&E doctor started the infusion on the CCU. If the CCU could not offer immediate access to a bed, the thrombolytic infusion started in the A&E department.

General practitioner referrals admitted directly to the medical admissions unit were transferred to the CCU before thrombolysis.

IDENTIFICATION OF PATIENTS ELIGIBLE FOR IMMEDIATE THROMBOLYSIS

All ECGs recorded before thrombolysis were obtained. The clinical records and ECGs were reviewed again after discharge, and patients with clear criteria for thrombolysis immediately on arrival were identified objectively, regardless of when they actually received thrombolysis.

Patients judged eligible for immediate thrombolysis were those with a clear history of chest pain, electrocardiographic criteria on their initial ECG, and no absolute or relative contraindications. We decided that the following patients could not reasonably be thrombolysed within the 30 minute target time; these patients were excluded from the analysis:
- Initial ECG did not fulfil eligibility criteria.
- Patients with history of recent infant and ECG changes of indeterminate age.
- Relative contraindication or possible absolute contraindication.
- Atypical presentation.
- Difficulty obtaining clear history, for example severe dyspnoea.
- ECGs with left bundle branch block.

Cases in which thrombolysis was inappropriately given or withheld were subject to further blind review by an A&E consultant and a cardiology consultant, who made the final decision.

OUTCOME MEASURES

- The door to needle times of the treatment groups. The door to needle time distribution was right skewed, and required logarithmic transformation before analysis with Student's two tailed t test for samples with equal variance.
- Inappropriate administration of thrombolysis. The decision to give or withhold thrombolysis was judged appropriate or inappropriate according to locally agreed electrocardiographic and clinical criteria (see boxes 1 and 2).
- Patients in whom thrombolytic treatment was inappropriately withheld.
- The nature and management of arrhythmia occurring within two hours of thrombolysis.
- Complications occurring within 24 hours of thrombolysis.
Thrombolysis was administered to 220 patients presenting with suspected AMI, but only 155 of these patients had the clinical and electrocardiographic indications for thrombolysis immediately on arrival at hospital. Data collection was complete in 153/155 (98.7%) of cases; this group of 153 patients was analysed in detail.

All patients had a straightforward mode of presentation, with clear indications for thrombolytic treatment; it was therefore appropriate to measure their door to needle times against the 30 minute standard. Other demographic data is summarised in table 1.

Ninety per cent of patients were admitted via the A&E department. A&E staff identified 92% of A&E patients requiring immediate thrombolysis, and administered thrombolysis to 72% of those eligible. Overall, 36% of A&E patients presented during periods when there was middle grade or consultant presence within the department.

**TIME TO THROMBOLYTIC TREATMENT**

The door to needle times are presented in table 2. The shortest door to needle times occurred when thrombolysis was given by A&E staff within the A&E department. Transferring A&E patients to the CCU before thrombolysis was associated with a significant increase in door to needle time, \( p = 0.004 \). Direct admission to the medical admission unit was associated with the longest in-hospital treatment delays.

**ACHIEVEMENT OF AUDIT STANDARD**

When thrombolysis was given by A&E staff within the A&E department, 32% of patients received treatment within the target time of 30 minutes (fig 1), but when they were transferred to the CCU before thrombolysis, this proportion fell to 14%. None of the A&E patients referred for thrombolysis by the senior house officer in cardiology received treatment within the 30 minute target time. Similarly, none of the patients admitted directly to the medical admissions unit started thrombolysis treatment within 30 minutes of arrival.

**ACCURACY OF ECG INTERPRETATION**

All thrombolytic administration was judged to have been given appropriately and in accordance with the clinical and electrocardiographic eligibility criteria.

A&E staff failed to identify 10/139 (7%) patients who presented with obvious indications for thrombolysis, and six of these were subsequently assessed on multiple occasions by the admitting physicians before the ECG changes were recognised. These patients had very long door to needle times (mean 234.5 minutes) compared with other groups (see table 2).

**COMPLICATIONS OF THROMBOLYSIS**

Complications occurred in 13% of thrombolysed patients (table 3), and the proportion was similar in all groups. Transient hypotension and allergic reactions were the most common complications, both occurring in 4% of patients. The frequency of allergic reaction is comparable with other published rates of 4.4% and 2.4%. One patient developed anaphylactic symptoms, but in the majority of cases the allergic reaction was mild; the infusion was discontinued, and all patients responded to standard treatment with steroids and antihistamines. Transient hypotension responded to the temporary cessation of the thrombolytic infusion in all cases.

Bleeding occurred in 3.3% of patients, similar to other published figures. There were four cases of minor bleeding and one major gastrointestinal haemorrhage requiring blood transfusion.

Cerebrovascular accidents occurred in three (1.9%) patients. Computed tomography was performed in two cases, and both demonstrated cerebral infarction. Thrombolysis trials have published stroke rates of 0.2%–1.0%.2 15

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**Table 2** Door to needle times of thrombolysed patients

<table>
<thead>
<tr>
<th></th>
<th>No of patients</th>
<th>Mean</th>
<th>Median</th>
<th>Interquartile range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombolysis by A&amp;E staff in A&amp;E department</td>
<td>56</td>
<td>43.1</td>
<td>42.5</td>
<td>28–51</td>
</tr>
<tr>
<td>Thrombolysis by A&amp;E staff in CCU</td>
<td>43</td>
<td>58.8</td>
<td>54</td>
<td>40–71</td>
</tr>
<tr>
<td>A&amp;E patients referred for admitting team to thrombolysé</td>
<td>29</td>
<td>94.2</td>
<td>82</td>
<td>55–118</td>
</tr>
<tr>
<td>Patients &quot;missed&quot; by A&amp;E</td>
<td>10</td>
<td>234.5</td>
<td>201.5</td>
<td>138–239</td>
</tr>
<tr>
<td>Direct admissions to medical ward</td>
<td>13</td>
<td>117.6</td>
<td>80</td>
<td>69–113</td>
</tr>
</tbody>
</table>

**Table 3** Complications of thrombolysis

<table>
<thead>
<tr>
<th>Complication</th>
<th>Outcome</th>
<th>Thrombolysis by A&amp;E staff (n=99)</th>
<th>Thrombolysis by cardiology staff (n=52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor haemorrhage</td>
<td>Complete recovery</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Major haemorrhage</td>
<td>Complete recovery</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Allergic reaction</td>
<td>Complete recovery</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>CVA</td>
<td>Residual problems</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Transient hypotension</td>
<td>Complete recovery</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>13</td>
<td>7</td>
</tr>
</tbody>
</table>

CVA = cerebrovascular accident.
Table 4  Reperfusion arrhythmias

<table>
<thead>
<tr>
<th>Arrhythmia</th>
<th>Treatment</th>
<th>Outcome</th>
<th>Thrombolysis by A&amp;E staff (n=99)</th>
<th>Thrombolysis by cardiology staff (n=52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus bradycardia</td>
<td>Atropine</td>
<td>Recovery</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>Ventricular fibrillation</td>
<td>DC shock</td>
<td>Recovery</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Atrial fibrillation/flutter</td>
<td>Drugs</td>
<td>Recovery</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>DC shock</td>
<td>Recovery</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Complete heart block</td>
<td>Atropine/pacing</td>
<td>Recovery</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>13</td>
<td>5</td>
</tr>
</tbody>
</table>

get time, prior transfer to the CCU is associated with an extremely low proportion of patients starting treatment within the target time (14%). Patients referred by general practitioners to the medical admissions unit experience much longer treatment delays than A&E patients; this may be due to a number of reasons. A pre-registration house officer may perform the initial assessment. There may be delays waiting for ECG technicians to attend, and inexperienced doctors may fail to recognise ECG changes. Patients may be subjected to multiple medical assessments and incur further delay awaiting transfer to the CCU before thrombolysis.

PARAMEDIC DIRECT ACCESS TO CCU

Paramedic direct access to the CCU is considered by some to be the "gold standard" of care for patients with AMI. In a recent large study in which paramedics were trained to interpret ECGs and select patients for direct admission to the CCU,4 a mean in-hospital treatment delay of 39 minutes was achieved. However, fewer than 25% of all thrombolysed patients were admitted by this route. While direct paramedic access to the CCU may confer an advantage on a small selected group, it does not appear to be a practical option for reducing door to needle times for the majority of patients.

APPROPRIATENESS OF A&E DEPARTMENT THROMBOLYSIS

There are reports in the literature raising doubts about the ability of A&E staff to interpret ECGs correctly,11-17 and this may partly explain why thrombolysis has not been widely adopted in A&E departments. However, these studies compare the ability of A&E senior house officers with those of cardiology consultants, registrars, or staff grade doctors. The relevant comparison is between A&E and medical/cardiology junior staff; when this is studied there appears to be no difference in the number of clinically significant errors made.28

In our study, all thrombolytic treatment was administered appropriately and in accordance with locally agreed clinical and ECG eligibility criteria. There is no evidence that A&E staff administer thrombolysis inappropriately. However, if the A&E department occasionally fails to identify patients with obvious indications for thrombolysis, very long door to needle times may result. The admitting physicians may assume that all candidates for thrombolysis have been selected out; A&E staff must be aware of their responsibility to examine ECGs carefully and seek advice if they are in doubt.

SAFETY OF A&E DEPARTMENT THROMBOLYSIS

Cardiac arrests are managed in most A&E departments on a daily basis, and A&E staff are therefore well practised in resuscitation techniques. Only one patient experienced a dangerous arrhythmia (ventricular fibrillation) in the A&E department, and this was managed effectively.

and in clinical practice in the UK a stroke rate of 2% has been described.16

REPERFUSION ARRHYTHMIAS

Arrhythmias that occurred during or within two hours of thrombolysis, and that required active treatment, were found in 11.9% of patients (table 4). Most commonly seen was a sinus bradycardia requiring a single dose of atropine.

Dangerous arrhythmias, for example ventricular fibrillation, sustained ventricular tachycardia, complete heart block or electromechanical dissociation, occurred in 3.3% of patients. There is no other strictly comparable published data, although the ISIS-2 study quotes a ventricular fibrillation rate of 3.3% and cardiac arrest rate of 7.2%.2

One life threatening arrhythmia (ventricular fibrillation) occurred in the A&E department, and the patient recovered completely after DC cardioversion. No arrhythmias requiring treatment occurred during the transfer of thrombolysed patients to the CCU. Adverse events during the transfer of thrombolysed patients have been audited previously,16 and as in our study, no events were documented.

Discussion

The importance of early thrombolysis in patients suffering AMI is well established, and the causes of in-hospital treatment delay have been analysed.10-12 16-20 It has been demonstrated that thrombolysis within the A&E department is associated with the shortest treatment delays.10 12 13 However, although most A&E consultants in the UK believe that thrombolysis should be given in A&E, only 35% of departments give thrombolytic treatment routinely.11

There may be a number of reasons why thrombolysis has not been widely adopted as a routine A&E procedure. These include concerns about the ability of A&E staff to interpret ECGs, or manage complications or arrhythmias, worries that patients may suffer reperfusion arrhythmias during transfer to the CCU, a lack of space to accommodate patients undergoing thrombolysis, and an insufficient number of nursing staff to provide supervision.

IN-HOSPITAL TREATMENT DELAYS

This study concurs with previous studies,10 12 13 16 which show that delays in the provision of thrombolytic treatment are significantly shorter when patients present to the A&E department and are thrombolysed there. Although only 32% of patients thrombolysed in A&E were treated within the 30 minute tar-
The risk of arrhythmias occurring during the transfer of thrombolysed patients is sometimes cited as a reason to confine thrombolysis to the CCU. Our study, along with a previous study, demonstrates that this is a theoretical concern rather than a practical problem. If patients are transferred in the company of a doctor and a defibrillator, the risk is likely to be extremely small.

Transient hypotension and allergic reactions were the only complications that occurred in the A&E department. Complications are a recognised risk of thrombolytic treatment, and this emphasis must be on early detection and appropriate management.

**Implications of providing thrombolysis in the A&E department**

**Immediate assessment and ECG based triage**

A high level of motivation is required among medical and nursing staff if patients are to be identified and thrombolysed with 30 minutes of arrival. Immediate assessment is essential in order to identify patients who may be infarcting. An ECG must be performed immediately and assessed by a member of the medical staff. Patients with the ECG criteria for thrombolysis are placed in the highest triage category and are seen immediately by a doctor.

**Training and guidelines**

In our study, 64% of patients requiring thrombolysis attended at times when there was no middle grade presence in the department. While the level of middle grade cover in A&E is increasing, it is still the case that senior house officers will see the majority of these patients. The education and training of senior house officers is therefore of paramount importance.

Training in the administration of thrombolysis must be given a high priority in the A&E induction programme, with emphasis on making an accurate diagnosis, checking carefully for contraindications, and most importantly, seeking senior advice when in doubt. The value of formal ECG training in reducing serious errors has previously been highlighted and ongoing training and feedback are required.

Written clinical guidelines, dosage and administration information, and instructions regarding the management of complications, are vital if relatively inexperienced doctors are to administer thrombolysis confidently and safely. A contraindications checklist, compiled for each patient, may be helpful as both an aide-memoire and a permanent record.

**Role of experienced A&E staff**

The mortality benefit from early thrombolysis is considerable, and justifies the involvement of experienced A&E staff whenever possible, both to support senior house officers and facilitate the patient’s management, just as they would in cases of major trauma or cardiac arrest. Departments lacking adequate staffing or facilities for training may not be in a position to provide safe and timely thrombolysis.

**Conclusions**

A&E staff can accurately select the vast majority of patients who require thrombolysis for AMI. Significantly shorter in-hospital treatment delays are seen when thrombolysis is administered by A&E staff within the A&E department, when compared with other delivery options available within the hospital. The transfer of A&E patients to the CCU before thrombolysis is associated with an important and unnecessary treatment delay.

Every effort should be made to shorten treatment delays for patients with AMI. The A&E department is best placed to deliver timely thrombolytic treatment. Where local facilities and conditions allow, A&E departments should develop the necessary education and training programmes in order to ensure the provision of safe and timely thrombolytic treatment for patients with AMI.

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