Thrombolysis in acute myocardial infarction: an audit of practice

ABSTRACT—A retrospective casenote audit of the use of thrombolysis in 212 of 335 patients with acute myocardial infarction (63%) was carried out on the coronary care unit of a Sheffield teaching hospital. The overall inpatient mortality was 17%, 12% in the thrombolysis group and 26% in the remainder (p < 0.005). Patients aged 75 years or older were less likely to die if they received thrombolytics (p < 0.05) despite an excess of anterior myocardial infarctions in the thrombolysis group (p < 0.01). The infusion of streptokinase had to be stopped in five patients (4%) because of allergy or arrhythmias. Thrombolytic therapy was considered in all patients with acute myocardial infarction; it was withheld inappropriately in eight cases and given inappropriately in two. Thrombolysis produced clear benefits in mortality for all patients, including those over 75 years old. There was a high rate of use of thrombolysis which was generally safe and appropriate, although adjustments to the guidelines may allow even more patients to receive this therapy.

At the time when the present generation of house officers entered medical school, patients with acute myocardial infarctions admitted to most hospitals in Britain were primarily treated with bed rest and pain relief. In the few intervening years there has been a revolution in the management of the condition. Large multicentre trials have confirmed that thrombolysis, aspirin, and beta blockade [1-5] significantly reduce mortality. These measures must, therefore, be considered in all patients with suspected acute myocardial infarction.

Between 1987 and 1989 the reported routine use of fibrinolytic agents by consultant physicians and cardiologists rose from 2% to 68% [6]. However, it seems that a large number of eligible patients (estimated at between 20,000 and 60,000 a year) [7] may not receive potentially life-saving treatment.

Bed space permitting, all patients with a diagnosis of acute myocardial infarction are admitted to our coronary care unit by nine different 'take' teams, but while on the coronary care unit their management is supervised by a single cardiologist. However, the decision to give thrombolysis is often made by the resident medical officer, who may be an inexperienced senior house officer.

We wanted as many as possible of our patients with acute myocardial infarction to receive thrombolytic therapy. But in view of the harm that thrombolytic agents can cause in the wrong setting [8] we also wished to be sure that they were not being prescribed inappropriately. In order to assist the junior doctor in deciding when to administer thrombolytics, simple guidelines (Table 1) were provided, based on the major thrombolytic studies [2-5].

Aspirin is routinely prescribed in this hospital for patients with suspected acute myocardial infarction. But, as it is frequently started by general practitioners or in the accident and emergency department, we have not considered its use as we were principally interested in coronary care practice.

In this audit we have assessed the adherence to the guidelines, and determined the impact of thrombolysis in our practice on inpatient mortality and on heart failure on discharge. Also, as the use of thrombolysis in the elderly is still ill defined [9], we paid particular attention to the effect of thrombolysis in patients aged 75 years and over.

Methods

A retrospective casenote audit was carried out on patients admitted to the coronary care unit between 1 Aug '90 and 1 Aug '91. We reviewed the medical notes of all patients who had received thrombolysis, or in whom the diagnosis of acute myocardial infarction, chest pain, acute cardiac failure, or arrhythmias had been recorded. The diagnosis of acute myocardial infarction was based on the following criteria: a rise of serum creatinine phosphokinase to at least double the upper limit of normal, and/or a typical evolution of electrocardiographic changes within a consistent clinical setting. For all patients with a definite acute myocardial infarction the site was noted, as was age and sex and whether they were known to have had diabetes mellitus, hypertension, or a previous myocardial infarction. Outcome measures included death, the use of inotropic support, and cardiac failure requiring diuretic therapy on discharge.

If a patient with an acute myocardial infarction received thrombolysis, the time from the onset of pain...
and any complications were noted. Where thrombolytic therapy was not used, we established the reason for it, and whether prohibition of treatment was according to the guidelines. In a proportion of cases thrombolysis had been withheld because the admitting doctor did not consider that the electrocardiogram demonstrated diagnostic ST segment elevation. These electrocardiograms were reassessed.

We made a note of any patients who had been given thrombolysis inappropriately. Statistical analysis was by Chi square with Yates correction and Fishers exact test. Significance was accepted at \( p < 0.05 \).

**Results**

During the study period 335 patients with acute myocardial infarction were admitted to the Royal Hallamshire Hospital coronary care unit. Thrombolytic therapy was used in 212 patients (63.3\%) (Table 2), of whom 207 received 1.5 mega units of streptokinase, and five were given 100 mg of tissue plasminogen activator. Of these five patients two had been treated with streptokinase within the previous six months, and one patient had an anaphylactic reaction shortly after streptokinase infusion had been started; on recovery, he received tissue plasminogen activator without incident. The remaining two patients were initially treated with streptokinase, but shortly afterwards suffered a further episode of prolonged cardiac pain with new ST segment elevation consistent with reinfarction; they were therefore given tissue plasminogen activator.

**Mortality and heart failure** (Table 2)

The overall inpatient mortality was 17\%, 12\% in the thrombolytic group and 26\% in the remainder (\( p < 0.005 \)). At the time of discharge from hospital heart failure was present in 33\% of patients in both groups. In other respects, the two sets were significantly different: anterior and inferior myocardial infarctions were more common in patients who had been given thrombolysis, whereas the site was more often subendocardial or unknown in those who had not. This difference is a reflection of the initial selection process (ie the requirement for ST elevation on the admission electrocardiogram). Diabetes and a history of previous myocardial infarction were also significantly more common in those who did not receive streptokinase.

**Table 2. Characteristics of patients admitted with acute myocardial infarction and treatment allocation**

|                  | No thrombolysis | Thrombolysis |
|------------------|-----------------|--------------|
|                  | All cases       | < 6 hrs      | > 6 hrs      |
| Number           | 123             | 212          | 130          | 80            |
| Age              |                 |              |              |               |
| average          | 64.2            | 63.3         | 61.7         | 66.1 x        |
| SD               | 10.6            | 10.3         | 10.0         | 10.5          |
| range            | 36–87           | 36–88        | 36–82        | 36–88         |
| Sex              |                 |              |              |               |
| male             | 79(64)          | 141(67)      | 93(71)       | 47(58)        |
| female           | 44(36)          | 71(33)       | 37(29)       | 33(42)        |
| Death**          | 32(26)          | 25(12)       | 13(10)       | 12(15)        |
| Heart failure    |                 |              |              |               |
| (on discharge)   | 41(33)          | 71(33)       | 36(28)       | 33(41)x       |
| Inotropes        | 20(16)          | 20(9)        | 13(10)       | 7(10)         |
| Previous MI*     | 37(30)          | 41(19)       | 25(19)       | 16(20)        |
| Diabetes*        | 21(18)          | 20(9)        | 10(8)        | 10(12)        |
| Hypertension     | 29(24)          | 63(30)       | 31(24)       | 31(29)x       |
| Site**           |                 |              |              |               |
| anterior         | 46              | 99           | 51           | 48xx          |
| inferior         | 47              | 108          | 77           | 30            |
| posterior        | 2               | 4            | 2            | 1             |
| subendo          | 14              | 1            | 0            | 1             |
| unknown          | 14              | 0            | 0            | 0             |

* \( p < 0.05 \) Between the thrombolytic and non-thrombolytic groups
** \( p < 0.005 \)

x \( p < 0.05 \) Between the early and late thrombolytic groups
xx \( p = 0.01 \)

The timing of thrombolytic treatment was unknown in two patients.

MI = myocardial infarction.
Timing of thrombolysis

Of the 212 patients who received thrombolysis, 130 (61%) did so within six hours of the onset of chest pain. Timing of thrombolysis did not significantly influence mortality but heart failure on discharge was significantly more common in patients treated after six hours. However, those who presented late were significantly older and more likely to have had hypertension than the patients attending within six hours (Table 2). Also, anterior acute myocardial infarction was more prevalent than inferior acute myocardial infarction in the group who were treated later.

Elderly patients

The outcome for 56 patients aged 75 years or older is shown separately (Table 3). Mortality was significantly less ($p < 0.05$) in those given streptokinase despite a large excess of patients with anterior myocardial infarction ($p < 0.01$). Heart failure on discharge appeared to be more common in patients given thrombolysis, but the difference was not significant. In other respects the two groups were comparable.

Comparison of old and young patients (Table 4)

There was no difference in the rates of use of thrombolysis between those aged 75 years and over (34/56; 61%) and younger patients (178/279; 64%) ($p = ns$). Although the reduction in mortality from 50% to 21% in the elderly group appears to be much greater than the fall from 21% to 10% in the younger patients, this difference was statistically not significant.

Complications of thrombolysis

One patient suffered a cerebrovascular event within 24 hours of thrombolytic treatment, but a computed tomography head scan was normal and he made a swift and full recovery. Infusion of streptokinase was stopped in five (4%) patients because of allergic reaction or arrhythmias (in two), but there were no serious bleeding problems.

Failure of the treatment guidelines

Two patients with a final diagnosis of pericarditis were given streptokinase without complications. They were the only cases where thrombolysis was used in the wrong setting.

The reason for withholding streptokinase from patients with suspected acute myocardial infarction was documented in every case (Table 5). The commonest reason was absence of diagnostic ST segment elevation (46/123: 37%). On subsequent review, seven of these electrocardiograms were thought to show ST segment elevation consistent with acute myocardial infarction (sites: anterior 1, inferior 3, posterior 1,

| Table 3. Thrombolysis in patients aged 75 and over |
|-----------------------------------------------|
| Age | No thrombolysis | Thrombolysis |
|-----|-----------------|--------------|
| mean | 78.4 | 77.8 |
| SD | 3.1 | 3.0 |
| range | 75–87 | 75–88 |
| Sex | | |
| male | 11 | 21 |
| female | 11 | 13 |
| Death* | | |
| 11 (50%) | 7 (21%) |
| Heart failure (on discharge) | | |
| 7 (32%) | 21 (62%) |
| Site** | | |
| anterior | 3 | 25 |
| inferior | 13 | 9 |
| posterior | 1 | 0 |
| subendo | 3 | 0 |
| unknown | 2 | 0 |
| Diabetes | | |
| 3 (14%) | 2 (6%) |
| Hypertension | | |
| 6 (27%) | 10 (29%) |
| Previous MI | | |
| 8 (36%) | 8 (24%) |

*p = < 0.05
**p = 0.002
MI = myocardial infarction

lateral 2). Cardiac massage and presentation after 24 hours were the next most likely reasons for not giving thrombolysis (11% each). The reason for not giving thrombolysis was inconsistent with our guidelines in only one case (of hypotension).

Discussion

At present, particularly as guidelines vary from place to place, it is not clear what percentage of patients with acute myocardial infarction should receive thrombolysis. Following a six-months coronary care unit study, Jagger et al [10] concluded that 51% (67 out of 131) of patients with a proven acute myocardial infarction were eligible for thrombolysis but their guidelines included ST segment elevation of at least 2 mm in two or more electrocardiograph leads, and excluded patients aged over 70 years and those presenting six hours or more after the onset of pain. This proportion of suitable patients was still higher than previous reports had suggested [11,12]. The practice in a district general hospital was similar [13], with 58% (112 out of 193) of patients with proven acute myocardial infarction receiving thrombolysis. In that study 15 patients who had not suffered an acute myocardial infarction had also been given thrombolytics, and one of them died of a thoracic aortic dissection. In our
Thrombolysis in acute myocardial infarction: an audit of practice

Table 4. Comparison of young and elderly

|                      | <75y (n = 279) |                      | 75y+ (n = 56) |
|----------------------|----------------|----------------------|---------------|
|                      | Thrombolysis % | No Thrombolysis %    | Thrombolysis % | No Thrombolysis % |
| Uptake of treatment  | 178(64)        | 101(36)              | 34(61)        | 22(39)            |
| Death                | 18(10)         | 21(21)               | 7(21)         | 11(50)            |
| Heart failure on discharge | 44(25)   | 26(25)               | 21(62)        | 7(32)             |

Mean, % in brackets, no significant differences between the young and elderly

study, 63% of all patients admitted to the coronary care unit with an acute myocardial infarction were treated with thrombolysis, but in only two patients (each with a final diagnosis of pericarditis) were thrombolytic agents prescribed inappropriately.

On our coronary care unit the consultant cardiologist carries out a ward round every morning with the resident medical officer of the preceding night. This serves to supervise the management of patients and acts as a teaching exercise for junior doctors. We believe this has heightened the awareness of the role of thrombolysis within the guidelines, contributing to the high uptake without loss of safety. In Plymouth [14], by simply asking nursing staff to remind junior doctors of the option of thrombolysis, the proportion of eligible elderly patients who actually received treatment rose from 12% to 46%, reinforcing the view that patient management can readily be improved by frequent feedback and teaching.

As expected, thrombolytic therapy reduced inpatient mortality, but there was no improvement in heart failure on discharge. Because of the selection process the incidence of anterior and inferior infarctions was greater in those given thrombolysis. However, the untreated group had a higher prevalence of diabetes and previous myocardial infarctions, and this may have influenced outcome. We did not audit the use of aspirin, which may also have affected mortality figures, but because we routinely prescribe aspirin for patients with suspected acute myocardial infarction, it is likely that its rate of use was similar in all classes of patients.

In our study, mortality was significantly reduced in patients over the age of 75 years who were given thrombolysis, despite a preponderance of anterior myocardial infarctions in this group which itself carries an increased risk of death. Indeed, the figures suggest that the elderly benefited more than the young. Neither GISSI nor ISIS 2 excluded patients on the grounds of age [2,5]. In the former study, no clear improvement in mortality in those aged over 65 years was demonstrated although there was a trend at 21 days. In ISIS 2, however, the reduction in mortality was significant and the benefit in absolute terms was greater than for younger patients. In a review of the literature, Witry and his colleagues [9] concluded that the elderly should receive thrombolitics after careful screening for contraindications. Our results reinforce the view that age in itself is not a contraindication to thrombolysis.

In our audit, the largest group of patients who had no contraindication to thrombolysis but did not receive it were those whose admission electrocardiogram was not judged to be diagnostic of acute myocardial infarction. In expert hands the electrocardiogram is still the most accurate diagnostic aid in the first 24 hours of an acute myocardial infarction [15,16]. Seven (2%) patients failed to receive thrombolysis because diagnostic electrocardiographic abnormalities were missed. None of the abnormalities was gross, three being subtle posterior or lateral changes. Emerson et al [17] assessed the ability of junior doctors to interpret the electrocardiograms of 604 patients attending with chest pain at Westminster Hospital emergency department. They concluded that errors in electrocardiogram interpretation led to the wrong management decision in 1.5% of cases, a rate similar to that in our study.

In common with previous reports [2,3,5], adverse events due to thrombolysis were low in our study.

Table 5. Reasons for withholding thrombolysis

| Reason                              | No. |
|-------------------------------------|-----|
| Equivocal electrocardiogram         | 46  |
| Cardiopulmonary resuscitation       | 14  |
| Presentation 24 hours after onset of pain | 14  |
| Arterial or central venous puncture | 10  |
| Active or potential bleeding        | 10  |
| Death before administration possible | 5   |
| Previous cerebrovascular accident   | 4   |
| Miscellaneous                       | 20  |

Proposed changes

Although the proportion of patients with acute myocardial infarction receiving thrombolysis was higher in our study than usually reported, it was still denied to 37%. However, in only eight (2%) cases was thrombolysis withheld incorrectly according to our guidelines. In the case of equivocal electrocardiograms, the
guidelines now make it clear that the tracing should be repeated in case of evolving changes. Also, in keeping with the findings of the GISSI group [5], contraindication is limited to stroke within the previous two months rather than at any time (Table 1). However, it seems that the only way significantly to increase the proportion of patients given thrombolysis on the coronary care unit is to revise the guidelines, making them less restrictive. We have now divided the contraindications into absolute and relative categories, as suggested by Thomas and Sheridan [18], so that each case may be judged on its own merits. In practice, especially in patients who are particularly at risk and likely to gain most from thrombolysis (ie patients with anterior infarctions, women, older patients, and those with hypotension or who have had a previous myocardial infarction [2]), it would be appropriate to err on the side of treatment when there is no absolute contraindication.

Conclusions

A decision regarding the use of thrombolysis was recorded in the case notes of every patient with suspected acute myocardial infarction admitted to the coronary care unit during the study period. In those receiving thrombolysis there was a clear reduction in mortality. Despite the high rate of usage, only two patients (0.9% of those receiving thrombolysis) were given treatment in the wrong setting (specificity of 99% according to our guidelines). Thrombolysis was withheld inappropriately in eight patients, giving a sensitivity of 96%. We believe that frequent feedback to junior doctors made an important contribution to these figures.

Our results are consistent with previous trial data, confirming that thrombolysis is of benefit at all ages.

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