

# Trends in the provision of thrombolytic treatment between 1993 and 1997

J S Birkhead, on behalf of the Myocardial Infarction Audit Group

## Abstract

**Objective**—To evaluate trends in provision of thrombolytic treatment between 1993 and 1997.

**Design**—Observational study.

**Subjects**—3714 patients in 15 UK hospitals who had an admission diagnosis of myocardial infarction.

**Main outcome measures**—Changes in prehospital and hospital delay before thrombolytic treatment; use of emergency services.

**Results**—Between 1993 and 1997 the proportion of patients who called for help within 30 minutes of the onset of symptoms fell from 42.6% to 36.0%; difference 6.6% (95% confidence intervals (CI) 3.3% to 10%). The direct use of the emergency service by patients and by doctors sending an ambulance without seeing the patient increased by 18.9%. Patients given thrombolytic treatment within 90 minutes of calling for help increased from 28.2% to 39.1%; difference 10.9% (95% CI 7.2% to 14.7%). Over the same period the proportion of patients treated in emergency departments increased from 4.4% to 17.3%, and the median delay from arrival to treatment in emergency departments fell from 53 to 36 minutes. Median delays for patients treated in cardiac care units after assessment in the emergency department fell from 63 to 54 minutes.

**Conclusion**—Between 1993 and 1997 there was an increase in the proportion of patients with definite infarction having thrombolytic treatment within 90 minutes of a call for help. This was mainly the result of greater use of the emergency service and more rapid treatment of a larger proportion of eligible patients in emergency departments. Longer delays by patients have cancelled out some of this improvement.

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The benefit of early thrombolytic treatment for patients with myocardial infarction who have typical ECG changes of raised ST segment is now well established. The relation of 35 day mortality benefit to treatment delay is exponential.<sup>1</sup> The cusp of the curve relating benefit and delay lies between two and three hours with proportionally greater benefit from treatment occurring before that time. While

primary percutaneous coronary angioplasty may have a limited place in the management of acute myocardial infarction,<sup>2</sup> the effective use of thrombolytic agents will remain the first line treatment of acute myocardial infarction for the foreseeable future in the UK. The recently published National Service Framework includes a requirement for health authorities to monitor and improve the delay between a call for help and thrombolytic treatment for patients with clear cut myocardial infarction.<sup>3</sup>

In 1992 a pilot study examining delays in the provision of thrombolytic treatment showed a wide range of management strategy and delays.<sup>4</sup> Following this study a process audit was initiated in up to 60 UK hospitals starting in late 1992 which continues to the present time. Data from 15 hospitals who took part in this audit from the start have been used to examine changes in the provision of thrombolytic treatment which have occurred between 1993 and 1997, with particular emphasis on changes in early treatment.

## Methods

Data were analysed for two, eight month periods between December 1992 and July 1993, and between December 1996 and July 1997. Data were collected soon after arrival on the cardiac care unit by nursing staff and were stored using a preprogrammed hand held computer (Psion Series 2). Not all time points, such as the onset of symptoms, could be established with precision, but where possible times such as that of the call for help were recorded to within five minutes. Where treatment of patients with typical cardiographic changes was delayed for clinical reasons, such as hypertension, this was recorded. In this paper analysis of delays to the point of receiving thrombolytic treatment was limited to those patients without recorded delay. Data analysis was performed in Northampton and reports sent to collaborating centres at four month intervals. Reports provided collaborating hospitals with summary data for all centres anonymised so that each centre concerned could compare their own data with others.

The diagnostic criteria for definite infarction were a single episode of chest pain with the following ECG changes: ST elevation  $\geq 1$  mm in two limb leads, and/or ST elevation  $\geq 2$  mm in two contiguous chest leads, and/or new pathological Q waves. For a final diagnosis of definite infarction cardiac enzymes had to be twice the upper limit of normal.

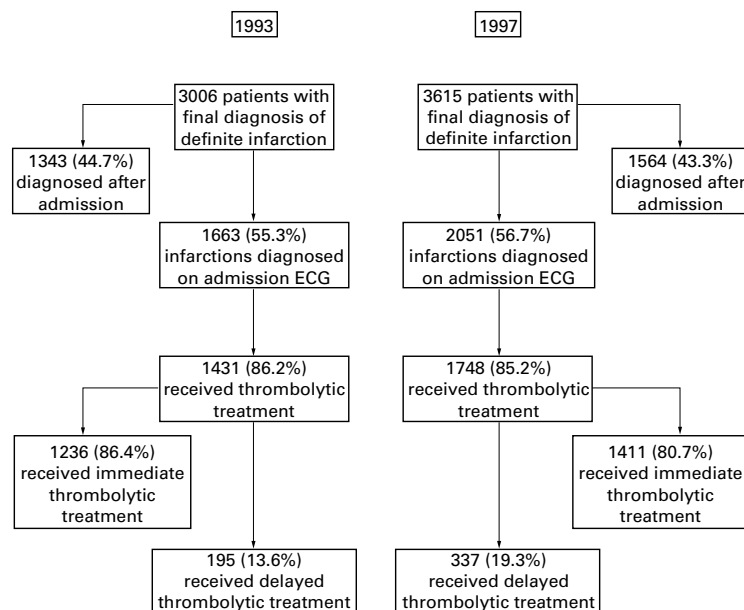


Figure 1 Patient population included in the study.

#### STATISTICAL ANALYSIS

Time delays are expressed as median (interquartile range) values in minutes. Differences in proportions are given with 95% confidence intervals (CI).

Comparisons are made throughout the paper between data from 1993 and 1997. In the text these dates are usually omitted to avoid repetition. In every case where comparisons are made data from 1993 precedes data from 1997.

## Results

#### PATIENT CHARACTERISTICS

These data concern 1663 patients in 1993, and 2051 patients in 1997 who received an electrocardiographic diagnosis of acute myocardial infarction at admission to hospital (fig 1). The proportion of women increased from 478/1663 (28.7%) to 676/2051 (33.0%); difference 4.3% (95% CI 1.2% to 7.2%). The mean age of patients increased from 64.1 years to 65.7 years ( $p < 0.001$ ), and the proportion of patients > 70 years old increased from 575/1663 (34.6%) to 827/2051 (40.3%); difference 5.7% (95% CI 2.6% to 8.9%).

#### COMPLETENESS OF DATA

The times for some events were not known. The following levels of data completeness were recorded: delay in calling for help 3298/3714 (88.8%), delay from call for help to arrival in hospital 3390/3714 (91.3%); for those who received thrombolytic treatment without a recorded delay, delay from admission to

Table 2 Median (interquartile range) delay in minutes for different calls for help: patients with a cardiographic admission diagnosis of myocardial infarction

	1993	1997
Patient calling and seeing doctor	79 (52, 115)	75 (51, 110)
Doctor called, patient not seen	60 (31, 91)	60 (40, 75)
Emergency call	41 (30, 60)	45 (33, 61)
Made own way	24 (5, 46)	34 (5, 60)
All patients	60 (33, 93)	55 (37, 81)

treatment 2566/2647 (96.9%), delay from call for help to treatment 2437/2647 (92.1%), and overall delay from onset of symptoms to treatment 2628/2647 (99.3%).

#### CALLING FOR HELP

Between 1993 and 1997 the proportion of patients who saw a doctor fell, and those who called the emergency service directly increased, as did the number of patients for whom an ambulance was sent by a doctor without seeing the patient. A small number of patients continued to make their own way to hospital (table 1).

#### DELAY IN CALLING FOR HELP

The median delay from onset of symptoms before a call for help increased from 55 (15, 170) minutes to 60 (25, 151) minutes. For those patients who saw a doctor the increase was from 60 (30, 195) to 75 (30, 215) minutes, and those who used the emergency service directly or for whom an ambulance was sent without being seen by a doctor the increase was from 30 (11, 105) to 45 (17, 120) minutes. The proportion of patients who called for help within 30 minutes of the onset of symptoms fell from 649/1492 (43.5%) to 666/1806 (36.9%); difference 6.6% (95% CI 3.3% to 10%). The fall was greater in patients older than 65 years. For younger patients the fall was from 337/741 (45.5%) to 324/797 (40.7%); difference 4.8% (95% CI -0.1% to 9.8%). For older patients the fall was from 312/751 (41.5%) to 342/1009 (33.9%); difference 7.6% (95% CI 3.1% to 12.2%).

#### DELAYS BETWEEN CALLING FOR HELP AND REACHING HOSPITAL

The median interval between a call for help and arrival in hospital fell from 60 (33, 93) to 55 (37, 81) minutes. There was an increase in the number of patients who reached hospital within 60 minutes of a call for help from 820/1522 (53.9%) to 1106/1868 (59.2%); difference 5.3% (95% CI 2.0% to 8.7%). Delay for different types of call has changed little with time but differences between different types of call remains wide (table 2).

#### CHANGES IN HOSPITAL PRACTICE

For patients treated without recorded delay the median time from arrival in hospital to thrombolytic treatment fell from 55 (35, 86) to 45 (26, 70) minutes. The range of median delay between individual hospitals was from 29 (18, 44) to 98 (85, 165) minutes in 1993, and from 25 (15, 30) to 93 (64, 131) minutes in 1997. The proportion having thrombolytic treatment within 30 minutes of arrival increased from 261/1206 (21.6%) to 452/1360 (33.2%);

Table 1 Calls made before reaching hospital: patients with a cardiographic admission diagnosis of myocardial infarction

	1993	1997	Difference (95% CI)
Patients calling and seeing a doctor	894 (53.8%)	754 (36.8%)	-17.0% (13.8% to 20.2%)
Doctor called, patient not seen	59 (3.6%)	210 (10.2%)	6.7% (5.1% to 8.3%)
Emergency call	531 (31.9%)	906 (44.2%)	12.2% (9.1% to 15.3%)
Made own way	179 (10.8%)	181 (8.8%)	-2.0% (0% to 3.9%)
Total	1663	2051	

Table 3 Proportional use of different departments for thrombolytic treatment, with median delays from arrival to treatment in minutes (interquartile range): patients having thrombolytic treatment without delay (see text)

	1993			1997		
	n	%	Median (IQR) (mins)	n	%	Median (IQR) (mins)
Accident & emergency department	54	4.4	53 (37, 80)	244	17.3	36 (20, 60)
Direct admission to CCU	292	23.6	30 (20, 50)	323	22.9	25 (15, 40)
Conventional treatment in CCU	849	68.6	63 (41, 95)	834	59.1	54 (36, 85)
Acute assessment/general ward	41	3.3	75 (53, 107)	10	0.7	45 (33, 70)
Total	1236	100	55 (35, 86)	1411	100	45 (33, 70)

CCU, Coronary care unit.

difference 11.6% (95% CI 8.3% to 15.0%). There was a shift from treatment in the cardiac care unit after initial assessment in emergency departments, to immediate treatment in emergency departments. In 1993 only one hospital treated more than 20% of patients in the emergency department. By 1997 4/15 hospitals, who between them contributed 224/244 (92%) of all patients treated in emergency departments, were using the emergency department for treatment of between 42–60% of patients with an admission diagnosis of definite infarction who were treated without delay. The proportion having direct admission to a cardiac care unit has not altered. The majority of patients continued to have thrombolytic treatment in the cardiac care unit after initial admission to an emergency department (table 3).

#### DELAY FROM CALL FOR HELP TO TREATMENT

The median delay from a call for help to treatment fell from 130 (90, 170) to 105 (77, 145) minutes. The median delay in individual hospital districts ranged from 95 (70, 135) to 145 (85, 195) minutes in 1993, and from 75 (60, 105) to 145 (110, 215) minutes in 1997. The number of patients who received thrombolytic treatment within 90 minutes of a call for help increased from 323/1146 (28.2%) to 505/1291 (39.1%); difference 10.9% (95% CI 7.2% to 14.7%). This increase was seen both for patients who saw a doctor before reaching hospital and for those who did not (table 4). The greatest reduction in delay was seen during the first three hours after a call for help (fig 2).

#### OVERALL DELAYS

The median delay from symptom onset to treatment fell from 195 (130, 315) to 180 (130, 290) minutes. The proportion having thrombolytic treatment within three hours of onset of symptoms was unchanged: 555/1236 (44.9%) v 681/1411 (48.3%); difference 3.4% (95% CI

–4.5% to 7.2%). The range of treatment within three hours of onset of symptoms in individual hospitals was from 25% to 53.7% in 1993, and from 28.7% to 64.6% in 1997.

#### Discussion

The real benefit of very early thrombolytic treatment is now firmly established.<sup>1</sup> An earlier analysis, which used pooled data from large trials each randomising at least 1000 patients, contained a smaller number of patients treated early after onset of symptoms. This described a linear relation between delay and 35 day mortality with a limited benefit of earlier treatment of 1.6 lives/1000 treated/hour.<sup>5</sup> This provided little incentive for clinicians to achieve earlier treatment.

#### DELAYS BEFORE ADMISSION

Of the components of delay before thrombolytic treatment, that attributable to the patient appears intractable. A recent examination of patient call delays showed little improvement over many years despite various interventions aimed at shortening this time.<sup>6</sup> During the period of this study the average age of patients admitted with infarction increased significantly, and a higher proportion were women. Older patients<sup>7</sup> and women, who present less often with typical symptoms,<sup>8,9</sup> are known to delay longer before a call for help.

Patient call delays increased between 1993 and 1997, both for calls made to a doctor and to the emergency service, and the proportion

Table 4 Proportions of patients having thrombolytic treatment within 90 minutes of a call for help: patients having thrombolytic treatment without delay (see text)

	1993	1997	Difference (95% CI)
Patients seeing a doctor	125/606 (20.6%)	134/463 (28.9%)	8.3% (3.1% to 13.6%)
Patients using the emergency service	131/408 (32.1%)	325/733 (44.3%)	12.2% (6.5% to 18.0%)
Patients making own way	67/132 (50.8%)	46/95 (48.4%)	–2.3% (10.8% to –15.5%)
All patients	323/1146 (28.2%)	505/1291 (39.1%)	10.9% (7.2% to 14.7%)

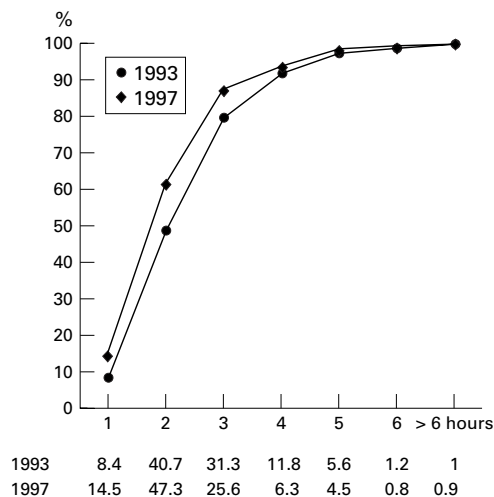


Figure 2 Cumulative percentage of patients having thrombolytic treatment after a call for help in 1993 and 1997. Lower panel indicates the proportion having treatment within each interval of one hour.

who made calls within 30 minutes of onset of symptoms fell. While this was most notable in those over 65 years old, this was also true of younger patients. At present there is no complete explanation for this; the small increase in mean age and the larger proportion of women in 1997 appear insufficient alone to explain this finding.

In 1997 fewer patients saw a doctor before coming to hospital. This was mainly because of the greater direct use of the emergency service by patients. In addition the number sent to hospital without being seen by a doctor increased, from 3.6% to 10.4% of all calls. Patients who used the emergency service reached hospital more quickly than those who saw a doctor; further reductions in delay may follow the shorter ambulance response times specified in the emerging findings of the National Service Framework.<sup>3</sup> The greater reliance on the emergency service not only resulted in more patients reaching hospital more quickly but also provided earlier access to a defibrillator, which has significant mortality benefit.<sup>10</sup> Although there has been an increase in use of the emergency service by patients with infarction, this remains smaller than the general increase in the use of the service; between 1992–93 and 1996–97 emergency ambulance journeys in England increased by 28.5%.<sup>11</sup>

#### DELAYS IN HOSPITAL

Some patients with clear cut electrocardiographic evidence of infarction received thrombolytic treatment after a delay for sound clinical reasons, such as hypertension requiring treatment. In 1993 13.6%, and in 1997 19.3%, were reported to have received treatment after a delay (fig 1). In the audit records it was not necessary to record the reason for the delay, and it is possible that delays for administrative reasons, or the need of a junior doctor to discuss the ECG with a more senior colleague before proceeding to treatment, were inappropriately included in this group. With this proviso the data for in-hospital delays were analysed only for those patients for whom no delay was reported.

The biggest fall in median delay before thrombolytic treatment, from 53 to 36 minutes, occurred in accident and emergency departments. Although treatment was given most rapidly after direct admission to the cardiac care unit, this approach may not be the best way to reduce delay for every hospital. Constraints of hospital geography, and the size of the cardiac care unit, may make it unsuitable for the triage of patients with chest pain, given that not all presumed infarctions are correctly diagnosed before an ECG has been recorded.

In this small group of UK hospitals only about one quarter (4/15) routinely gave thrombolytic treatment in emergency departments in 1997. With the increasing use of emergency services more patients will present to emergency departments with chest pain for diagnosis and treatment. When a diagnosis of definite infarction is made immediate initiation of

treatment in the emergency department should be encouraged. This will have implications for training of emergency department clinical staff, and effective and immediate liaison between on call medical teams and clinicians in emergency departments will be vital. The benefit of employing nurses specially trained in this role has been described and deserves further consideration.<sup>12</sup> There is little to commend the previous "slow track" policy of moving a patient to the cardiac care unit before treatment is commenced. The small increase in serious ventricular arrhythmias during use of thrombolytic treatment should not be considered a contraindication to treatment in emergency departments.<sup>13</sup> Accreditation of emergency departments requires evidence of effective provision of thrombolytic treatment, and provides an incentive for departments who have previously been unable to provide this service.<sup>14</sup>

#### DELAY FROM CALL FOR HELP TO TREATMENT, AND OVERALL DELAYS

In 1994 a target of 90 minutes was proposed for the delay between a call for help and thrombolytic treatment for patients with definite evidence of infarction at admission to hospital.<sup>15</sup> An increase from 28.2% to 39.1% in the number who reached the 90 minute target was recorded between 1993 and 1997. The National Service Framework now proposes a more stringent target of 60 minutes<sup>3</sup>; in 1997 only 14.5% of patients fulfilled this target.

Despite the improvement in delay from call to treatment the fall in median delay from onset of symptoms was small. There was no change in the proportion of patients who received treatment within three hours of the onset of symptoms, and the range between individual hospitals remains wide. A fall in the number making early calls for help appears to have cancelled out much of the reduction in delay achieved both before and after admission to hospital.

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## IMAGES IN CARDIOLOGY

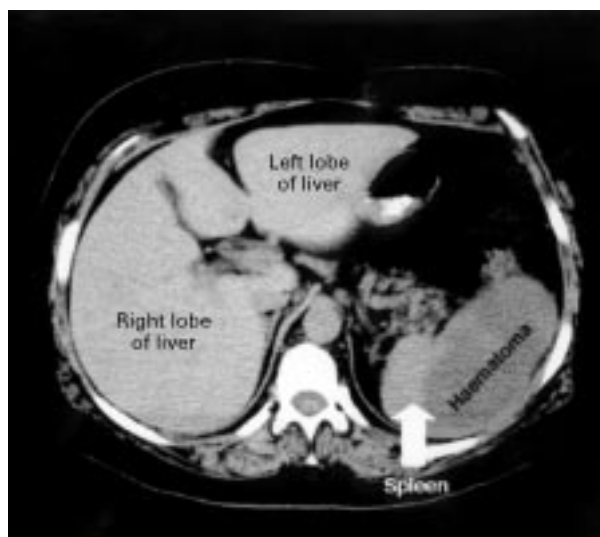
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### Spontaneous splenic haematoma after thrombolysis for acute myocardial infarction in a patient with von Recklinghausen's disease

A 51 year old woman was admitted with an 11 hour history of retrosternal and epigastric pain. She was known to have multiple neurofibromatosis and a large neurofibroma had been removed from the left sacral plexus in 1984. ECG showed changes of acute inferolateral myocardial infarction. There were no obvious contraindications to thrombolytic treatment and she received 1.5 MU of streptokinase over the following hour. She was given oral aspirin and subcutaneous heparin (she was obese and relatively immobile).

Over the next few days she complained of being generally unwell and developed a left sided pleuritic chest pain. Chest radiography and ventilation-perfusion scan were normal. Abdominal ultrasound revealed a moderate sized haematoma within the spleen with no evidence of free fluid in the abdomen and these findings were confirmed by computed tomography (CT). She was managed conservatively and repeat CT showed no progression of the haematoma. She was eventually discharged feeling well.

Splenic haematoma is a rare but a well recognised complication of thrombolytic treatment; this patient presented with left pleuritic chest pain mimicking pulmonary embolus.



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