Delays to thrombolysis in the treatment of myocardial infarction

ABSTRACT—In-hospital delays to thrombolysis were significantly shorter when thrombolysis was available on admission to the accident and emergency department than after transfer to the coronary care unit (median 60 min v 84 min, $p < 0.0001$). With direct admission by general practitioners to a coronary care unit the subsequent in-hospital delay was shorter (median 39 min $p = 0.0004$), but overall delay to thrombolysis longer (median 220 v 170 min, $p = 0.0019$) because of longer pre-hospital delays. Overall delay was shortest with emergency ambulance referral and thrombolysis being administered in the accident and emergency department.

Thrombolytic drugs, given with aspirin, are now established treatment for myocardial infarction, and the sooner thrombolysis is administered after the onset of infarction the greater the benefit [1,2]. In the UK almost all thrombolytic therapy is given in hospital. Delays that occur in hospital before treatment is initiated are therefore important, and to reduce these delays hospital services need to develop policies for the acute management of myocardial infarction [3,4].

Patients with chest pain usually consult their general practitioner or call the emergency ambulance, and a small number go directly to the hospital. The route of admission of patients to coronary care units is determined by local hospital policy and facilities. Patients referred from general practitioners can be admitted either directly or through the accident and emergency department. Emergency ambulance and self-referred patients are usually first seen in the accident and emergency department, and subsequently transferred to the coronary care unit. How initial contact with the hospital is made depends upon the patient (ie whether through general practitioner, emergency ambulance or self-referral) and can be modified only by education of the population, which will take some time. It is quicker and easier to organise the subsequent in-hos-

pital management to ensure that where indicated the patient has smooth and rapid access to thrombolytic administration. The decisions that need to be made are these. Should thrombolysis be available in the accident and emergency department? Should all patients with chest pain be admitted directly to the coronary care unit, bypassing the accident and emergency department? Or should there be a combination of these alternatives so that thrombolytic therapy is administered at the site of initial contact, whether that is the accident and emergency department or the coronary care unit?

In an attempt to answer these questions, we analysed data collected prospectively at two coronary care units within the city of Newcastle upon Tyne.

Methods

Patients with out-of-hospital onset of myocardial infarction, who received thrombolysis, were identified from coronary care unit data, between July 1989 and November 1990, at two hospitals with catchment areas that overlap considerably. Protocols for thrombolytic therapy at both hospitals include the usual inclusion and exclusion criteria.

At the Royal Victoria Infirmary all patients, whatever the mode of referral, are first assessed in the accident and emergency department, with subsequent transfer to the coronary care unit if appropriate. In 1988 it was decided that thrombolytic therapy should be available in the accident and emergency department so that thrombolysis could be initiated before transfer to the coronary care unit where appropriate. However, the Royal Victoria Infirmary participated in the ISIS-3 trial between 21 October 1989 and 28 May 1990, and during this time (for pragmatic reasons) thrombolysis was administered solely in the coronary care unit after transfer from the accident and emergency department. This provided the opportunity to assess whether this change in policy would shorten the in-hospital delay to thrombolysis.

These two sets of data were compared with data collected at Freeman Hospital, where practically all patients are admitted via direct general practitioner referral, because that hospital has no accident and emergency department. Therefore at Freeman Hospital, thrombolytic therapy is administered in the coronary care unit—the first point of contact with hospital medical staff (Fig. 1).

Data collected prospectively included: (1) time from onset of symptoms to arrival in hospital (pre-hospital delay); (2) time from arrival in hospital to initiation of

GARETH PARRY, MRCP, Research Registrar
W. NEIL WRIGHTSON, RGN, Research Nurse
LOUISE HOOD, Research Assistant
PHILIP C. ADAMS, MRCP, Consultant Cardiologist, Departments of Cardiology, Royal Victoria Infirmary and Freeman Hospital, Newcastle upon Tyne
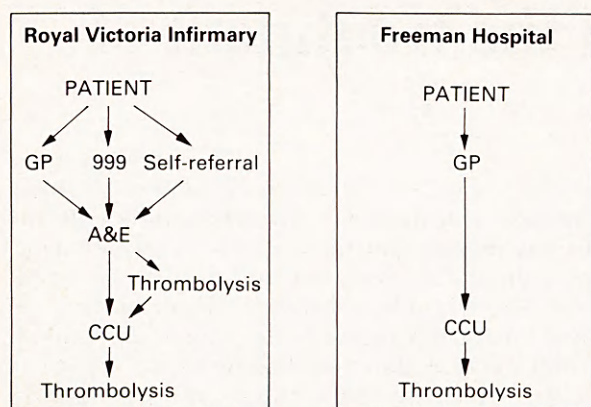DOUGLAS S. REID, FRCP, Consultant Cardiologist, Department of Cardiology, Freeman Hospital, Newcastle upon Tyne

Figure 1. *In-hospital organisation in the two hospitals*

thrombolytic therapy (in-hospital delay); (3) the total time from onset of symptoms to initiation of thrombolysis (overall delay). At the Royal Victoria Infirmary the in-hospital site of initiation of thrombolysis and source of referral were also recorded.

All time intervals are expressed as medians with interquartile ranges. Statistical analysis included analysis of variance for multiple group comparisons and Mann-Whitney U test for between group comparisons (as the populations were highly skewed).

Results

In all patients, myocardial infarction occurred before arrival in hospital. At Freeman Hospital, thrombolysis was administered to 109 patients referred directly by general practitioners to the coronary care unit. At the Royal Victoria Infirmary, 160 patients received thrombolytic therapy: 81 patients during the period when it was available in the accident and emergency department, and 79 patients when thombolysis was only available in the coronary care unit. These three patient populations were similar in terms of age, sex and site of infarction (Table 1).

Table 1. Patient characteristics—age, sex and infarct site

		Age (mean, years)	Sex (% male)	Infarct site (% inferior)
Freeman Hospital	n=109	63.5	61.5	44.0
Royal Victoria Infirmary	n=160	63.1	64.4	44.4
'A&E'	n=81	62.9	61.7	44.4
'CCU'	n=79	63.3	67.1	44.3

'A&E'=Thrombolysis available in the accident and emergency department
'CCU' = Thrombolysis in the coronary care unit only

Pre-hospital delay (Table 2)

Median pre-hospital delay in the three groups is shown in Table 2. It was significantly longer in patients referred by general practitioners to Freeman Hospital than in the patients who came to the Royal Victoria Infirmary. Of the 160 patients at the Royal Victoria Infirmary, 104 (65%) had called the emergency ambulance, 39 (24.5%) their general practitioner and 16 (10%) had attended after self-referral and self-transportation (Table 3). The source of one patient was not known. Patients attending by emergency ambulance or self-referral arrived at the Royal Victoria Infirmary significantly sooner after the infarction than those who were referred by their general practitioner—the latter delayed by a similar median time to those at Freeman Hospital.

In-hospital delay (Table 2)

At the Royal Victoria Infirmary availability of thrombolysis in the accident and emergency department reduced median in-hospital delay from 84 min to 60 min ($p < 0.0001$). In-hospital delay was shortest at Freeman Hospital (39 min $p < 0.0001$).

Overall delay from pain to thrombolysis

The overall delay from onset of symptoms to the initiation of thrombolysis was least at the Royal Victoria Infirmary during the period in which thrombolysis was available in the accident and emergency department (Table 2, $p = 0.008$).

Actual administration in the accident and emergency department

Although administration of thrombolytic therapy in the accident and emergency department was possible before and after the ISIS-3 trial, it was done in only 39 patients. The median in-hospital delay for these patients was 42 min (interquartile range 30–61 min), with an overall delay to thrombolysis of 135 min (interquartile range 100–195 min). These delays are not strictly comparable with those at the Freeman Hospital; those patients who had thrombolytic therapy in the accident and emergency department at the Royal Victoria Infirmary were cases where the diagnosis was immediately clear-cut, whereas the Freeman Hospital population is more heterogeneous.

Discussion

The proven value of thrombolytic therapy (and aspirin) in the treatment of acute myocardial infarction is undoubtedly the major advance of cardiology in the past decade. Dewar first reported the use of intracoronary thrombolysis in this city in 1977 [5], but it has taken many years to establish the benefit of intra-

Table 2. Components of the delay to thrombolysis.

		Pain to arrival in-hospital	Hospital to thrombolysis	Pain to thrombolysis
Freeman Hospital	n=109	160 (105–266)	39 (25–69)	220 (155–300)
Royal Victoria Infirmary	n=160	95 (55–187)	72.5 (50–96)	180 (120–280)
'CCU'	n=79	99 (55–210)	84 (65–107)	190 (150–320)
'A&E'	n=81	89 (55–154)	60 (35–90)	170 (108–240)
Analysis of variance		$p = 0.001$	$p < 0.001$	$p = 0.008$
Mann-Whitney		FRH longer than 'CCU' ($p = 0.0009$) and 'A&E' ($p < 0.0001$)	FRH shorter than 'CCU ($p < 0.0001$) and 'A&E' ($p = 0.0004$)	FRH longer than 'A&E' ($p = 0.0019$)
		'A&E' shorter than 'CCU' ($p < 0.0001$)	'CCU longer than 'A&E' ($p = 0.0134$)	

Delays expressed as median (interquartile range) in minutes.
'A&E' = thrombolysis available in the accident and emergency department.
'CCU' = thrombolysis in the coronary care unit only.
FRH = Freeman Hospital

venous thrombolysis—more recently from large-scale international clinical trials. Such trials have also confirmed that the sooner thrombolysis is administered the greater is the benefit in terms of survival [1,2]; the aim is therefore to treat as soon as possible after the onset of symptoms. The role of paramedics or general practitioners has yet to be clarified [6], although administration at the initial contact with health workers, which is advocated by some [7,8], would avoid subsequent in-hospital delays. Thus, optimisation of in-hospital delay is the current aim.

Site of administration

In many hospitals, patients are initially seen in the accident and emergency department (by the casualty officer or the resident medical officer, or both) and subsequently transferred to a ward (in this case the coronary care unit) for admission, as occurs at the Royal Victoria Infirmary. With this mode of admission, thrombolytic therapy can be initiated either in the accident and emergency department or after transfer to the coronary care unit. The policy of administering thrombolysis in the accident and emergency department, if clinically appropriate, led to a significant shortening of the in-hospital delay at the Royal Victoria Infirmary. We have not encountered any hazards with this policy, and have found it easier to establish

thrombolysis in the accident and emergency department than to arrange direct admission to the coronary care unit. In some hospitals with accident and emergency departments general practitioners can refer patients directly to the coronary care unit. However, it is still worthwhile having the facility for initiating thrombolytic therapy in the accident and emergency department for those patients who are not referred by general practitioners—which accounted for 75% of patients attending the Royal Victoria Infirmary in our study. We suggest, therefore, that all hospitals with accident and emergency departments should have the facility to administer thrombolysis at this point of first contact with the hospital.

Admission policy

Direct admission to the coronary care unit via the general practitioner has been proposed [9], as occurs at the Freeman Hospital. However, although this policy significantly shortens the in-hospital delay, overall delay from onset of pain to thrombolysis is longer because of longer pre-hospital delays. This suggests that patients with persistent unexplained chest pain should summon the emergency ambulance, as they then arrive in hospital more quickly than those who call their general practitioner. Travel in an emergency ambulance staffed by trained paramedics and

Table 3. Delays to thrombolysis according to source of referral at the Royal Victoria Infirmary

		Pain to arrival in-hospital	Hospital to thrombolysis	Pain to thrombolysis
RVI self	n=16	89.5 (44–220)	66 (50–87)	165 (105–291)
RVI GP	n=39	145 (108–316)	71 (49–90)	225 (156–390)
RVI 999	n=104	75 (46–127)	75.5 (50–107)	172.5 (120–240)
Analysis of variance		$p < 0.001$	$p = 0.327$	$p = 0.001$
Mann-Whitney		GP longer than 999 ($p < 0.0001$)	not significant	GP longer than 999 ($p = 0.0008$)

Delays expressed as median (interquartile range) in minutes
RVI = Royal Victoria Infirmary
GP = general practitioner referrals
self = self referrals
999 = emergency ambulance referrals

equipped with portable defibrillators is safer than self-transportation. The extra delay waiting for an ambulance should be minimal in an urban-suburban population, but we have no data regarding this delay in our population because of an industrial dispute at the time our survey was carried out.

At Brighton, rapid administration in the accident and emergency department has been achieved by 'fast tracking' [10] those patients with clear indications for thrombolysis. Their overall median delay after arrival in hospital following the adoption of such a policy (which included a checklist) was a commendable 17 minutes. In their patients who received streptokinase the median delay was 28 min, 9.5 min quicker than in an equivalent group of our patients at the Royal Victoria Infirmary. The difference is due to the fact that the resident medical officer (who had to be summoned) was responsible for making the decision regarding the administration of thrombolysis at our accident and emergency department. Instructing casualty officers (as in Brighton) in the indications and contraindications for thrombolysis would remove this added component of in-hospital delay. Alerting the accident and emergency department of potential candidates for thrombolytic therapy by ambulance paramedics *before arrival* (as occurs at Brighton) would also reduce this delay.

Conclusion

Substantial time savings can be achieved by administering thrombolysis in the accident and emergency department of a general hospital. Even more time is saved by patients attending hospital by emergency ambulance rather than by calling their general practitioner. These were also the conclusions of a recent paper by Birkhead [4]. Our data are somewhat different, however, in that our analysis defined patients according to whether thrombolysis was available in the accident and emergency department, and not whether it was given in that department. This may be an important distinction because thrombolysis may not be immediately indicated in all patients with suspected acute myocardial infarction when first seen in the accident and emergency department. Non-diagnostic symptoms or electrocardiographic changes, or contraindications may delay the decision to administer thrombolysis until arrival in the coronary care unit when subsequent clarification of the history, repeat ECG, or details regarding contraindications suggest that thrombolysis is indeed indicated [11]. The effect of this distinction is to reduce the difference in the in-hospital delay between the two sites of administration—primarily by prolonging the observed in-hospital delay in our accident and emergency group. This is, however, a more valid comparison for the population as a whole.

In a recent editorial [12] Petch advocated that patients 'take one aspirin and go as fast as possible to the nearest hospital coronary care unit'. Perhaps the best advice should be to swallow one aspirin and dial 999 to be taken to a hospital which administers thrombolysis in the accident and emergency department. All hospitals should reappraise their admission policy for patients with suspected myocardial infarction to minimise in-hospital delays; only then will the ultimate potential of thrombolytic administration be realised.

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Address for correspondence: Dr Gareth Parry, Department of Cardiology, Regional Cardiothoracic Centre, Freeman Hospital, Newcastle upon Tyne NE7 7DN.