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Thrombolytic therapy for myocardial infarction facilitated by mobile coronary care

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SUMMARY

Background: **The benefit of Thrombolytic Therapy (TT) for acute myocardial infarction is time sensitive. In Northern Ireland widespread availability of mobile coronary care units facilitates delivery of TT to heart attack victims. This region-wide prospective observational study assessed the efficacy of various methods of delivery of TT.**

Methods: **All 15 acute hospitals providing acute coronary care in Northern Ireland participated and data were collected prospectively over six months on all patients admitted with acute myocardial infarction or who received TT. The information was analysed regarding appropriateness of TT, methods and timeliness of delivery of TT and mortality rates. Performance was measured against National Service Framework standards.**

Findings: **Of 1638 patients with acute myocardial infarction 584 were considered eligible for TT and 494 (85%) received it, in addition to 18 patients without infarction. Of the 512 thrombolysed patients 282 (55%) were treated in hospital coronary care units, 131 (26%) were treated pre-hospital, 97 (19%) in accident and emergency departments, and two in general medical wards. Overall median call-to-needle time was 87 (7-1110) mins and this was shortest for pre-hospital treatment when 55% of call-to-needle times were ≤ 60 mins. For patients treated in hospital median door-to-needle time was 46 (0-1065) mins and this was shortest when TT was administered by accident and emergency staff, when 65% of door-to-needle times were ≤ 30 mins. In patients with ST elevation myocardial infarction TT was associated with lower mortality, especially when administered pre-hospital.**

Interpretation: **NSF targets for TT are unlikely to be met in Northern Ireland without increasing pre-hospital delivery of TT and by improving collaboration between coronary care and accident and emergency staff with TT availability in accident and emergency departments.**

INTRODUCTION

The introduction of thrombolytic therapy (TT) for acute myocardial infarction in the 1980's contributed greatly to improvement in both short[1-5] and long term [6,7,8] survival rates. Early studies showed that the benefit achieved was inversely related to the delay between onset of symptoms and delivery of the thrombolytic drug.[1,3,5,9]

Throughout Northern Ireland mobile coronary care became widely available following the pioneering work of Pantridge and Geddes in Belfast in 1966 [10] and reduction of community mortality rate for myocardial infarction achieved by a mobile coronary care unit was clearly demonstrated in the pre-thrombolytic era.[11] With the advent of TT it appeared that the availability of mobile units should facilitate its rapid delivery to victims of myocardial infarction outside hospital. The benefit of prompt pre-hospital TT has been demonstrated when provided by general

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practitioners[12] and by paramedics.[13,14] Numerous studies have demonstrated a superiority of primary angioplasty over TT in reducing mortality[15] but it is unlikely to become widely available in the near future so TT continues to be the mainstay of reperfusion therapy.

In order to assess the efficiency of delivery of TT in a region where mobile coronary care is widely available we conducted a prospective study of the timeliness of administration, appropriateness and effectiveness of this therapy throughout Northern Ireland over a six-month period.

PATIENTS AND METHODS

All fifteen hospitals providing acute coronary care in Northern Ireland (population 1.69 million) participated in the study and data were collected over six months from 1/04/01 to 30/09/01. Documentation was carried out by designated members of medical staff or senior nursing staff with the assistance of audit department staff. All patients admitted to hospital who received TT or who had a final diagnosis of myocardial infarction were included. Information relating to previous history, risk factors, indications and contraindications for TT, delay times for provision of coronary care and TT, sites where TT was administered, diagnostic tests and mortality rates was collected. A copy of the electrocardiograph (ECG) relevant to the decision for TT (usually the admission ECG) was retained to allow the accuracy of the diagnosis and appropriateness of the clinical decision to be checked by an independent assessor (C.W.) in consultation with the patient's consultant physician. The final diagnosis of myocardial infarction was at the discretion of the patient's consultant physician and depended on ECG changes and the results of cardiac enzymes and/or troponin levels as used in the local hospitals. The variable use of troponin levels throughout the hospitals led to a considerable variation in thresholds for diagnosis of non- ST elevation infarction.

Eleven of the fifteen hospitals operated mobile coronary care units of various types; ten were staffed by a doctor, nurse and driver and one was nurse led. The nurse led unit did not routinely provide pre-hospital TT. All patients in Northern Ireland had access to a mobile coronary care unit at the request of themselves, their general practitioner or emergency ambulance personnel. Patients were admitted via mobile coronary care units, or via accident and emergency departments, or directly to hospital at the request of a general

TABLE I

Sex, age and medical history of patients with confirmed myocardial infarction whether or not thrombolytic therapy (TT) was administered.

		TT patients (494)	*Non TT patients (1144)*
Gender	Male	357(72%)	652(57%)
	Female	137(28%)	492(43%)
Mean age (years)	Male	62	69
	Female	72	75
Medical history	Myocardial infarction	111(22%)	377(33%)
	Angina	123(25%)	442(39%)
	Hypertension	177(36%)	447(39%)
	Diabetes	61(12%)	210(18%)
	Cigarette smoking (current)	180(36%)	255(22%)
	Cigarette smoking (ex)	113(23%)	260(23%)
	Family history of IHD	161(33%)	273(24%)
	None of the above	44(9%)	104(9%)

practitioner. The timeliness of administration of TT was related to the various methods of delivery of care and performance was measured against targets for call-to-needle and door-to-needle times as recommended by the National Service Framework for England and Wales (NSF).[16]

Statistics

We considered that statistical analysis of our data would not be appropriate because patients selected or not selected for TT had quite different prognostic indicators and severity of presenting symptoms greatly influenced their selection for the various routes of admission. Comparison of the outcomes of these groups of patients would therefore be inappropriate.

RESULTS

Over a six-month period 1638 patients with a final diagnosis of acute myocardial infarction were admitted to acute hospitals in Northern Ireland. The age, sex and previous medical history of these patients, whether or not they received TT, are shown in Table I. Those who received TT were more likely to be younger, male, current smokers, with a family history of ischaemic heart disease, and with less previous cardiovascular disease.

There was significant ST segment elevation consistent with acute myocardial infarction without left bundle branch block on the presenting ECG in 775 (47%) patients and 77 (5%) had left bundle branch block. Sixty-nine of the patients with left bundle branch block, seven with ventricular pacing rhythm and one with broad complex tachycardia did not receive TT due to the well-recognised diagnostic difficulty in the presence of left bundle branch block[17] although this ECG abnormality is not a contra-indication to TT when there is strong clinical suspicion of myocardial infarction. An additional 191 patients had at least one clinical contra-indication to TT (Table II). Therefore 584 patients were considered eligible for and 494 (85%) received TT. Three patients refused TT and 87 did not receive TT due to difficulties with ECG interpretation.

TABLE II

Clinical contra-indications to TT among 1638 patients with myocardial infarction.

Clinical Contraindications	*Frequency*
Late presentation	125(7.6%)
Potential bleeding risk	56(3.4%)
On anti-coagulant	34(2.1%)
Recent CVA/TIA	31(1.9%)
Age	27(1.6%)
Uncontrolled hypertension	7(0.4%)
Primary Angioplasty	2(0.1%)
Other	30(1.8%)

An additional 18 patients received TT but were later shown to have no evidence of myocardial infarction. Eleven of these patients had acceptable criteria for the diagnosis of acute myocardial infarction on the presenting ECG, eight with ST segment elevation and three with left bundle branch block. Seven patients received TT inappropriately due to incorrect ECG interpretation but no untoward effects of treatment were noted.

The frequency of TT for patients with myocardial infarction varied from 18% to 55% among the 15 hospitals mainly due to local differences in the criteria used for final diagnosis of myocardial infarction in relation to serum enzyme or troponin levels in patients with chest pain without ST segment elevation on ECG. This caused variability of inclusion of patients with non-ST elevation infarction who were ineligible for TT.

Of the 512 patients who had TT 282 (55%) were treated in hospital coronary care units, 130 (25%) were treated pre-hospital by mobile coronary care units, 97 (19%) were treated in accident and emergency departments, two were treated in general medical wards and one patient was treated by his general practitioner.

Timeliness of TT

Of 478 patients whose time of onset of symptoms was recorded the median delay from symptom onset to initiation of TT was 175 minutes. The median time from the patients first request for medical assistance to onset of thrombolytic therapy i.e. call to needle time, was 87 (7-1110) minutes and call to needle time of ≤ 60 minutes was achieved in 152 patients (32%). The shortest median call to needle time was seen in patients treated by mobile coronary care units when call to needle time of ≤ 60 minutes was achieved in 55% compared with 47% in accident and

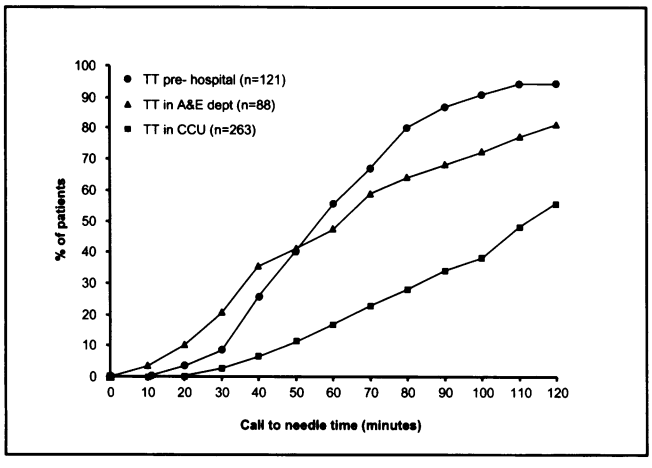

Fig 1. Cumulative distribution of call-to-needle times (times were indeterminate for 40 patients).

emergency departments and 17% in hospital coronary care units (Figure 1). Of 123 patients who received TT pre-hospital and had reliably documented times the median delay from arrival of the mobile unit to initiation of TT was 20 mins. Among 62 patients who were attended by mobile units but were transferred to hospital before TT was administered the median call to needle time was extended by 58 minutes.

Of 394 patients who activated out-of-hospital medical attention by either a general practitioner or emergency ambulance or mobile coronary care unit, the median call-to-needle times were 60 minutes for those treated pre-hospital, 100 minutes for those treated in accident and emergency departments and 126 minutes for those treated in hospital coronary care units (Figure 2). The NSF target call-to-needle time of ≤ 60 minutes was achieved in only 20% and 7% of patients treated in accident and emergency departments

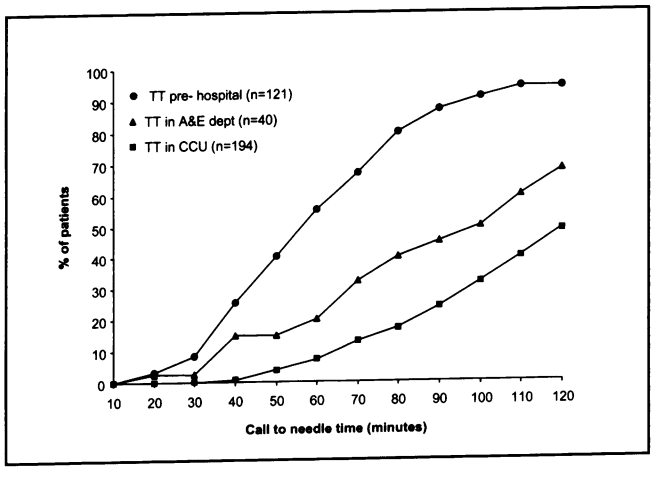

Fig 2. Cumulative distribution of call-to-needle times for patients who initially activated out-of-hospital medical attention (times were indeterminate for 38 patients)

and in coronary care units respectively compared with 55% of those treated pre-hospital.

For patients treated in hospital the median time from arrival at hospital to the onset of TT, i.e. door-to-needle time was 46 (0-1065) minutes. Patients treated in accident and emergency departments had the shortest median door-to-needle time, especially when treated by accident and emergency staff rather than waiting for cardiac unit staff (Figure 3). Door to needle time of ≤ 30 minutes was achieved in 65% of patients treated by accident and emergency staff compared with

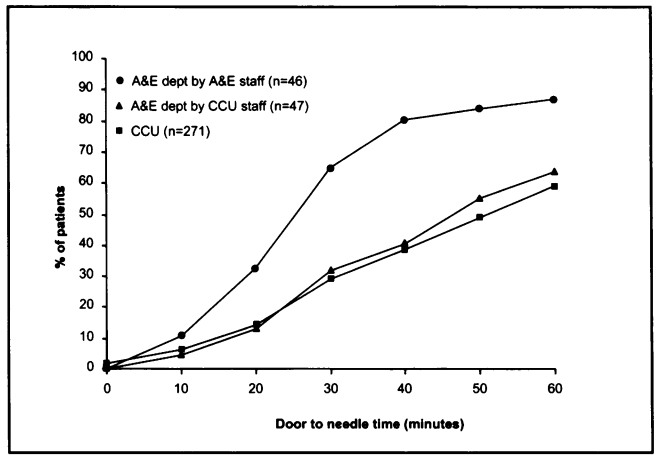

Fig 3. Cumulative distribution of door-to-needle times for patients whose TT was given in hospital (times were indeterminate for 7 patients)

only 32% when treated by cardiac unit staff in accident and emergency departments and 29% when treated in coronary care units.

Among patients whose call-to-needle time was more than 60 minutes important reasons noted for the delay were slow response by the general practitioner in 31(6%) or request by the general practitioner for the patient to attend the health centre in 13(3%), distance from hospital in 24(5%), non-diagnostic initial ECG necessitating repeat ECGs in 38(7%), initial clinical condition requiring stabilization before administering TT in 31(6%), uncertainty of the diagnosis requiring investigations such as echocardiography before administering TT in 8(2%), and consultation with a senior member of staff in 19(4%). In 31(6%) the delay time could not be defined and in 40(8%) no particular reason was identified.

Mortality Rates

Of the 1638 patients with a final diagnosis of acute myocardial infarction 165(10%) died in hospital and 204(12%) had died by six weeks

after infarction. Among patients with ST segment elevation on their presenting ECG who received TT the in-hospital and six week mortality rates were 10% (49/494) and 11% (56/494) respectively, compared with 18%(60/331) and 20% (67/331) respectively for those who did not receive TT. However the higher frequency of adverse factors among those who were not given TT may have contributed to this difference in outcome making statistical comparison inappropriate. When TT was given pre-hospital or in accident and emergency departments mortality rates tended to be lower than when it was given in coronary care units (Table III).

TABLE III

Mortality rates according to the site of administration of TT for patients with confirmed myocardial infarction.

Site of TT	*Hospitl mortality*	*6-week mortality*
Pre-hospital (123)	10(8.1%)	12(9.8%)
A&E dept (92)	8(8.7%)	10(10.9%)
Coronary care (277)	31(11.2%)	34(12.3%)
Other (2)	0	0

DISCUSSION

With the advent of TT for acute myocardial infarction it appeared that, within the UK, Northern Ireland was in a uniquely advantageous situation to achieve the maximum benefit because of widespread availability of mobile coronary care. This provided the means to deliver TT promptly to the coronary patient in addition to providing all other necessary acute treatment to stabilise the patient. The time delay from coronary occlusion, presumed to be onset of symptoms, to TT determines the likelihood of successful reperfusion but its largest component is patient delay before summoning help[18, 19] which, in this study, was about 90 mins. Unfortunately this cannot easily be altered [17] but call-to-needle and door-to-needle times should be amenable to improvement by changes in strategy. In this study pre-hospital TT, which accounted for a quarter of all TT, was associated with shorter call-to-needle times compared with in-hospital administration. Delaying administration of TT by transfer to hospital extended delay to TT by about an hour. Patients treated in accident and emergency departments received TT earlier than those treated in hospital coronary care units but call-to-needle time ≤ 60 minutes as recommended by the NSF was achieved in the majority of patients only when TT was given pre-hospital. Similar reductions in call-to-needle times have previously been achieved when TT was administered pre-hospital by general practitioners,[12] paramedics with hospital based support,[13, 14, 20] and mobile coronary care units.[21, 22] Meta-analyses have shown significant reduction in delay and lower mortality rates associated with pre-hospital compared with in-hospital TT.[9, 23] The National Audit of Myocardial Infarction Project (MINAP) reported that, in its first six months, which was roughly contemporary with this study, 20% of eligible patients were treated within sixty minutes of calling for help.[24] This compares with 32% of patients in this study but only approximately 2% in MINAP received pre-hospital TT. However MINAP showed improvement to 47% achieving target call-to-needle times by the year 2003.

Among patients treated in hospital the NSF recommended door-to-needle time was achieved in only a third of patients compared to 43% of eligible patients in the first six months of MINAP and this figure improved to 78% by 2003.[24] However, in this study, when treatment was administered by accident and emergency staff the target door-to-needle time was achieved in 65% compared with only 32% if intervention by cardiac unit staff was requested. Previous reports have similarly indicated shorter in-hospital delay when TT was provided in accident and emergency departments [18, 25, 26] and the delay was doubled by the need to consult a senior colleague.[18] However, whilst unnecessary delay should be avoided, it is often appropriate to obtain a more senior opinion to ensure accurate selection for this relatively high risk treatment. In addition, the importance of other components of care in acute coronary syndromes, other than TT, must not be underestimated and it is essential that all staff working in this field are appropriately trained. The availability of mainly doctor-led mobile coronary care in Northern Ireland probably contributed greatly to the relatively low overall mortality rate in this study. A task force of the European Society of Cardiology recommended that personnel providing pre-hospital TT should be trained in all aspects of the diagnosis and treatment of myocardial infarction.[27]

About half of all patients with a final diagnosis of acute myocardial infarction had neither diagnostic ST segment elevation nor left bundle branch block on the presenting ECG which is similar to a previous report [28] and a further 12% had contraindications to TT but it was disappointing to find that 15% of patients eligible for TT did not receive it. This compares with previous studies, which have reported 14-33% incidence of administration failure [29-32] while MINAP recently reported only 6% failure rate.[24] It has been demonstrated that increasing the accuracy of ECG analysis by input from consultant staff by means of a fax facility improved decision-making with regard to TT and provided support for junior doctors when the interpretation of the ECG was in doubt.[33] Several mobile coronary care units in Northern Ireland now have the facility to transmit electrocardiograms by modem/fax technology to the central CCU or to a consultant's home for a second opinion.

The recent introduction of serum troponin estimations has led to a dramatic increase in the frequency of diagnosis of myocardial infarction [34, 35] but the number treated by TT has remained relatively unchanged as the increase has been due to inclusion of more patients with non-ST elevation infarction who are not considered suitable for TT resulting in reduction of TT rates for all patients with myocardial infarction from 40% to 26%.[35] This phenomenon explains the apparently low proportion (30%) of myocardial infarction patients who received TT in this study.

It is clear that there are significant shortfalls in achieving NSF targets in Northern Ireland as previously observed in an audit of English hospitals,[36] although MINAP reports marked improvements in performance over recent years.[24] Reasons for delay in this study, which are not realistically amenable to improvement, were identified in at least 30% of patients receiving TT. The target call-to-needle time of ≤ 60 minutes is therefore unrealistic for many of our patients but the most likely method of reducing out-of-hospital delay appears to be increased utilization of pre-hospital TT delivered by adequately staffed mobile units while in-hospital delay could be significantly reduced by improving collaboration between accident and emergency departments and coronary care units. Our findings support the NSF,[16] the NICE guidelines [37] and the European Society of Cardiology task force,[27] all of which have suggested that it is appropriate to provide pre-hospital TT where local call-to-door times are likely to be more than 30 minutes, as pertains throughout the predominantly rural population of Northern Ireland, and that TT should be available in accident and emergency departments.

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Participating Hospitals: Altnagelvin Hospital, Antrim Hospital, Belfast City Hospital, Coleraine Hospital, Craigavon Hospital, Daisy Hill Hospital, Downe Hospital, Erne Hospital, Lagan Valley Hospital, Mater Hospital, Mid-Ulster Hospital, Royal Victoria Hospital, Tyrone County Hospital, Ulster Hospital, Whiteabbey Hospital.

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