East Midlands Ambulance Service NHS Trust

A Comparison Review of Pre-Hospital Thrombolysis Pilot Times In A Rural / Urban Area Of The East Midlands

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1. Introduction

In November 2000, East Midlands Ambulance Service NHS Trust (EMAS) became the first Ambulance Trust in the UK to implement a paramedic Pre-Hospital Thrombolysis (PHT) pilot. The pilot was reviewed in February 2002 [1] and subsequent to the review it was decided to examine the predicted time benefits of PHT. To this end, the 33 patients within the PHT pilot were divided into two groups for comparison: group 1 comprising of the 16 patients who received paramedic thrombolysis in the community and group 2 being the 17 patients with signs and symptoms of acute myocardial infarction (AMI) and treated within the same time frame but excluded from receiving PHT either by the thrombolysis assessment criteria, the ECG criteria, or by being in close proximity to a receiving hospital. For the purpose of this review it was decided not to look at actual in-hospital thrombolysis times, but to use a predicted average door-to-needle time of 15 minutes.

2. Background

Paramedic PHT within the UK is a relatively new concept. In view of this, EMAS was faced with the question of how to introduce paramedic PHT in a safe, controlled manner that supported both patients and staff. There are a number of international studies evaluating the effectiveness of PHT using different models. Based on the limited evidence available, it was decided to use a very cautious approach and begin with a small pilot scheme, to be rolled out gradually as experience and confidence grew. In selecting which thrombolytic drug to use, ease of administration was felt to be one of the most important factors. Therefore, after examining the current evidence, it was decided to use a double bolus drug called Reteplase. All patients who received PHT were administered the second bolus in hospital within the required 30 minute time frame.

Reteplase (r-PA) is a genetically engineered deletion mutant of wild-type t-PA. The structural differences lead to different functional properties, such as a prolonged half-life (approximately 13 minutes). It is not weight adjusted and is administered as a double bolus 30 minutes apart. Clinical trials to support this drug are: INJECT (1995) [2], RAPID 2 (1996) [3] and GUSTO-3 (1997) [4].

2.1 The Pilot

A set of operating procedures for the Paramedic, Control and Hospital were produced. The attending Paramedic would assess the patient and, on suspicion of a myocardial infarction, perform a 12 lead ECG. If this demonstrated an infarction and the travelling time to hospital was more than 30 minutes from the *'call for help'*, the patient would then be assessed against the PHT assessment sheet. If all the criteria were fulfilled, then the ECG would be transmitted to the receiving unit. The paramedic would carry out this procedure on route to hospital, cutting down the on-scene time. Ambulance control would then be informed as to the destination unit that the ECG had been sent to. Ambulance control would contact the unit to ensure that they were aware that an ECG had been transmitted to them. The Hospital would confirm that the 12 lead ECG complied with the ECG diagnostic criteria and this would be relayed back to the attending paramedic prior to the administration of the thrombolysis. If the journey time was greater than 30 minutes, or on arrival at CCU no doctor was available to authorise the nursing staff to administer the second dose, it would then be administered by the paramedic. This is because Reteplase has a 30-minute time dependency between doses.

To help provide a seamless pathway of care, the paramedic transmits the ECG from a 'Medtronic Physio Control Lifepak 12' ECG machine to the Receiving Unit where a nominated senior cardiac nurse or medical practitioner **confirms** the ECG criteria to thrombolyse. The legal decision to thrombolyse is made by the paramedic under a patient group direction (PGD). This model provides additional support for the paramedic in their decision making process.

Initially all communications were established to pass through the ambulance control centre. This caused some concerns and confusion leading to an increase in time delays to thrombolysis with the first three patients. To rectify this, mobile telephones were introduced onto all ambulances carrying out PHT, in order to facilitate direct contact with the CCU. Dedicated receiving telephones within the CCU are utilised for this purpose. This improved many aspects of the system such as staff support, transfer of relevant patient information, thrombolysis times, team working with the crew and CCU staff and the assistance of medical authorisation for any patient that falls outside

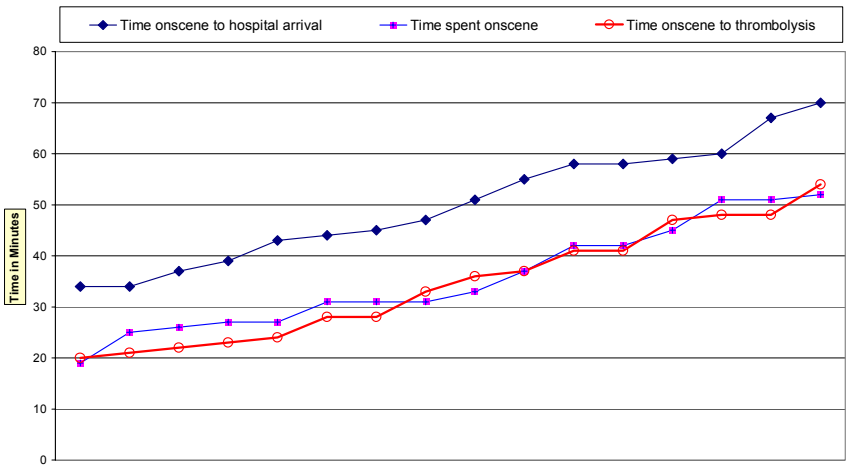
the pilot criteria. Medical authorisation for such patients has occurred on two occasions, each patient presenting as being previously fit but falling outside the age criteria.

The Joint Royal College Ambulance Liaison Committee (JRCALC) thrombolysis question criteria for the use of Streptokinase was adapted for use with Reteplase. The following amendments were made: a diastolic blood pressure of <95 mmHg was added to the question covering blood pressures; the time frame was increased from 3 hours to 6 hours from onset of symptoms to thrombolysis; the minimum heart rate was lowered from 50 to 40 beats per minute; the QRS width was changed to 0.12mm or less from 0.14mm in order to exclude Bundle Branch Block (BBB) (Appendix 1).

In total 41 paramedics underwent training over a 9-month period. All staff had been previously fully trained in performing and diagnosing 12 Lead ECGs for a minimum of 12 months. A one-day training programme, to reinforce existing knowledge and introduce thrombolysis, was produced with support from Roche (the manufacturers of Reteplase) who also provided training videos, drug packs and training slides covering thrombolysis. Staff were given a 12-lead ECG pass/fail examination prior to commencing the training programme.

3. Review

From the data obtained from the 16 patients in the PHT group, the following time frames were reviewed: total time spent on scene, time from arrival on scene to administration of thrombolysis and time from arrival on scene to arrival at hospital (graph 1). The PHT group was compared against the group of 17 patients who were excluded from receiving PHT by the assessment criteria (appendix 1). The reasons for the exclusion of these patients are shown in Table 1. This second group had the following times reviewed: total time spent on scene, time from arrival on scene to arrival at hospital and time from arrival on scene to predicted time of administration of in-hospital thrombolysis (graph 2). The time of in-hospital thrombolysis was estimated by using a 15 minute door to needle time, which should be achievable with appropriate pre-arrival information in most prepared A&E / CCU departments within the UK.



Graph 1: PHT Group

Graph 2: Comparison Group

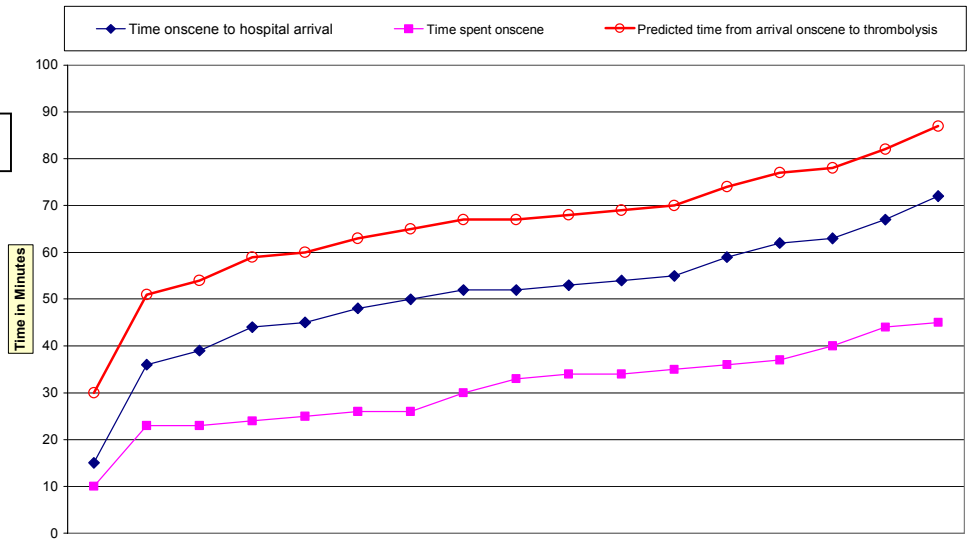


Table 1: Reason for Exclusion from PHT

No of Patients	Reason for Exclusion		No of Patients	Reason for Exclusion
1	Close proximity to hospital		1	Liver Failure
3	Bundle Branch Block		1	Peptic Ulcer
3	Onset of symptoms >6 hours		2	High / Low Blood Pressure
2	Less than 2 mm ST Elevation		1	Taking Warfarin
1	Unable to send ECG		1	Recent Operation
1	Confusion over recent Thrombolysis			

4. Results

The data was collated and mean and median times were calculated (table 2).
From this data, it would appear that **by spending an extra 4.5 minutes on scene, patients can receive thrombolysis with Reteplase an average of 34 minutes earlier than if taken directly to hospital.**

This data although limited in patient numbers is shown to be of relevance when compared with the data from the preliminary results of the ER TIMI 19 trial (209 patients) which showed a median time from arrival on scene to administration of thrombolysis (Reteplase) as 31 minutes in the pre-hospital group compared against a control group of 504 patients treated in-hospital at 64 minutes. This demonstrated a 33 minute median time saving to thrombolysis [5].

Table 2: Comparison Times

Total time spent on scene (minutes)				
	Mean	*Median*	*Lower Range*	*Upper Range*
PHT Group	35.5	32	19	52
Excluded Group	31	33	10	45
Arrival on scene to hospital arrival (minutes)				
PHT Group	50	49.5	34	70
Excluded Group	51	52	15	72
Arrival on scene to administration of thrombolysis (minutes) *(estimated 15 minutes door to needle time is used in the excluded group)*				
PHT Group	32	34.5	20	54
Excluded Group	66	67	30	87

Appendix 1

Primary Assessment

1. Is the patient conscious, coherent, and able to understand that clot-dissolving drugs will be used?
2. Has the patient had symptoms characteristic of a coronary heart attack and did the worst pain build up over several minutes, rather than starting totally abruptly over several seconds, with a typical distribution of pain for 30 minutes duration or more?
3. Is the patient aged between 14 and 75 years of age
4. Did the continuous symptoms start less than 6 hours ago?
5. Can you confirm that breathing does not influence the severity of the pain?
6. Can you confirm that the heart rate is between 40 –140 BPM?
7. Can you confirm that the systolic blood pressure is more than 80mmHg and less than 160 mmHg and that the diastolic pressure is below 95mmHg?
8. Does the electrocardiogram show abnormal ST segment elevation of 2 mm or more (0.08 seconds after the J point) in at least standard leads or at least 2 adjacent precordial leads, not including V1 ? (ST elevation can sometimes be normal in V1 and V2).
9. Is the QRS width 0.12 mm or less, and is bundle branch block absent from the tracing?
10. Can you confirm that there is NO atrioventricular block greater than 1st degree? (If necessary after treatment with IV atropine).

Secondary Assessment (Contraindications)

11. Can you confirm that the patient is not likely to be pregnant, nor has delivered within the last two weeks?
12. Can you confirm that the patient has not had a peptic ulcer within the last 6 months?
13. Can you confirm that the patient has not had a stroke of any sort within the last 12 months and no permanent disability from a previous stroke?
14. Can you confirm that the patient has not been treated for any other serious brain condition? (This is intended to exclude patients with cerebral tumours)
15. Can you confirm the patient has no diagnosed bleeding tendency, has had no blood loss within the last 8 weeks (except for normal menstruation), and is not on ANY anticoagulant therapy i.e. (Heparin, Warfarin) except Aspirin?
16. Can you confirm the patient has not had any surgical operation, tooth extractions, significant trauma, or head injury within the last 3 months?
17. Can you confirm that the patient has not had chest compression for resuscitation for a period of longer than 5 minutes within the last 10 days?
18. Can you confirm that the patient is not being treated for liver failure, renal failure, or any other severe systemic illness?

References:

1. East Midlands Ambulance Service NHS Trust PHT Audit Report (Feb 2002)
2. International Joint Efficacy Comparison of Thrombolytics (INJECT). Randomised, double-blind comparison of reteplase double bolus administration with streptokinase in acute myocardial infarction. *Lancet*.1995;346;8971:329-336
3. Bode C, Smalling RW, Berg G et al. Randomised comparison of coronary thrombolysis achieved with double bolus reteplase (recombinant plasminogen activator) and front- loaded, accelerated alteplase (recombinant tissue plasminogen activator) in patients with acute myocardial infarction (RAPID II). *Circulation*.1996;94:891-898
4. A comparison of reteplase with alteplase for acute myocardial infarction. The Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO-III). *N Engl J Med*.1997;337:1118-1123
5. Morrow DA, Antman EM, Sayeh A et al. Pre-hospital administration of reteplase for ST-segment elevation MI: preliminary results of the ER-TIMI 19 trial. *ESC 2001*