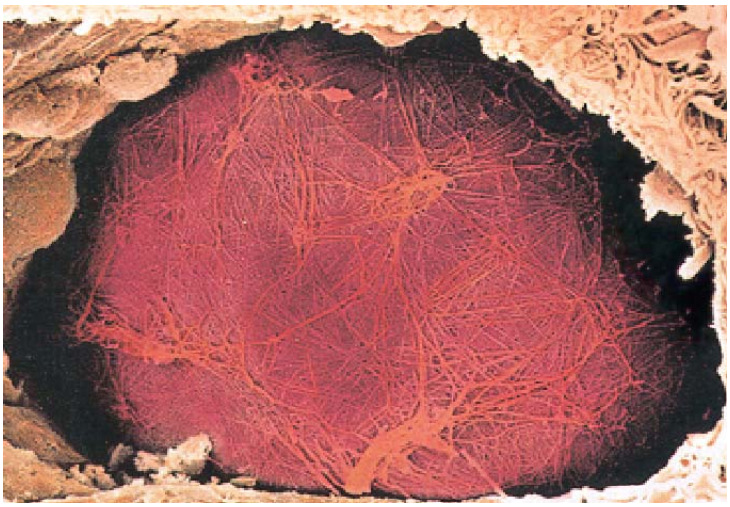
East Midlands Ambulance Service NHS Trust

Pre-Hospital Thrombolysis Pilot

experience gained from the first 14 months



By

Andy Silver – Clinical Governance Manager
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1. Introduction

Under the current Department of Health guidelines on cardiac care, East Midlands Ambulance Service NHS Trust (EMAS) became the first ambulance service in the UK to implement a Pre-Hospital Thrombolysis pilot (November 2000). This process presented us with many hurdles to climb in order to produce a safe, patient centred and staff supported system. Communications were shown to be the key learning point following 14 months of experience, during which time 14 patients have been treated. It is essential that all Ambulance Trusts share good and poor experiences with one another in order to provide the highest standards of care and support for staff and patients.

2. Background

Within the United Kingdom Coronary Heart Disease (CHD) is one of the biggest single causes of death, causing almost 115,000 deaths each year in England. Over the last two years there has been an increasing emphasis towards improving the management and prevention of CHD. A number of published documents; *Saving Lives: Our Healthier Nation [1]; The National Service Framework (NSF) for Coronary Heart Disease (CHD) [2]* and the *NHS Plan [3],* have paved the way towards implementing change through continual improvement in the care of CHD patients. The involvement and recognition of Ambulance Trusts as key components in the process of change has raised the profile, expectations and requirements of Paramedics and Technicians in delivering this agenda. The most significant development to this end is Pre-Hospital Thrombolysis.

NSF for CHD stated that:

'In some places, it may be difficult to reduce 'call-to-needle' times to less than 60 minutes because 'call-to-door' times cannot be reduced below 30 minutes. If, after careful consideration, it is judged that local circumstances make it impossible to reduce 'call-to-door' times to less than 30 minutes, other models of care e.g. out-of-hospital administration of thrombolysis, must be considered.' [2]

This reference to Pre-Hospital Thrombolysis is the first Department of Health documented proposal for the model. This is reinforced within the *NHS Plan* [3]

- *There will be a three year programme to train and equip ambulance paramedics to provide thrombolysis an hour sooner than if they were taken to hospital first, saving up to 3,000 lives a year once fully implemented*

NHS Plan. Section 14.21:117

2.1. 12 Lead ECG Trials

Two 12 Lead ECG Trials involving Derbyshire Ambulance Trust took place in the 1990s. A prospective controlled study published by Millar-Craig et al in 1997, concluded that trained paramedics can reliably diagnose myocardial infarction by 12 lead ECG and reduce 'door-to-needle time' by directly admitting to a Coronary Care Unit (CCU) [4]. The study identified that the diagnostic accuracy by Paramedics was 87.5% in the training phase and 92% in the admission phase. Millar-Craig's findings were reinforced by a second separate study in 1998 by Sandler, which concluded that 88% of paramedic-delivered patients with suspected AMI had the diagnosis confirmed, a better rate of correct diagnosis than other routes of admission. The study also identified that overall time to thrombolysis by paramedics was quicker than other routes of admission, despite the additional time required to perform the 12 lead ECG in the pre-hospital environment [5].

3. Benchmarking

An interface audit was carried out with two CCUs, looking at the post-codes of patients treated for Acute Myocardial Infarction (AMI). The purpose of this was to identify areas with a high occurrence of CHD. From this data, an audit of cardiac cases was performed and call-to-door times were identified using the Medical Priority Dispatch System (MPDS) Code 10 D 03 (chest pains, sweaty and changing colour). This provided the evidence to identify priority areas with a high incidence of patients presenting with cardiac chest pain.

4. Pre-Hospital Thrombolysis Pilot Proposal

Through the NSF-CHD Local Implementation Teams, a proposal was submitted to commence a pilot for Pre-Hospital thrombolysis including implications, costs, training and equipment requirements, proposed CCU involvement and type of drugs to be used. The first site proposed and accepted was for Ashbourne in Derbyshire. This received the full support from the CCU consultants and the local Primary Care Group.

4.1. Consultation

Perhaps the most important aspect is that paramedic PHT has to be a patient-focused, health community initiative, not just an Ambulance Service development. It is therefore essential that the local health community is consulted with in a fully inclusive manner, understands the logistical issues within the pre-hospital environment that make the process different from an in-hospital system, appreciates the additional costs involved and is aware of the potential impact that paramedic PHT can have across the UK.

To set up the first Pre-Hospital thrombolysis (PHT) pilot scheme, a comprehensive national consultation exercise was carried out with the Department of Health, Joint Royal Colleges Ambulance Liaison Committee (JRCALC), Trent Regional Office, local Health Authorities, Regional Pharmacy Advisor, local Consultant Cardiologists, CCU Staff, A&E Departments, Hospital Pharmacy, Thrombolytic Drug Companies, the media and, most importantly, the Ambulance staff responsible for implementing the pilot.

4.2. PHT Model

Paramedic PHT within the United Kingdom is a relatively new concept. With this in mind 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. From the limited evidence, it was decided to use a very cautious approach by beginning with a pilot scheme followed by a gradual roll out, learning with each new experience. In November 2000 an amendment to schedule 5 of the Prescription Only Medicines Act [6] was published, allowing Paramedics to administer Streptokinase as a 60-minute infusion. JRCALC had also produced a 20-question checklist for the administration of Streptokinase. After careful consideration and consultation, EMAS did not believe that this was the drug of choice for Paramedic led PHT and it was decided to use a bolus agent instead of an infusion. It was felt that the simpler the process of administration, the less scope for error. Therefore, after examining the current evidence, it was decided to use a double bolus drug called Reteplase.

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 – this model provides additional support for the paramedic in their decision making process.

4.3. Reteplase / Heparin

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) [7], RAPID 2 (1996) [8] and GUSTO-3 (1997) [9].

Dosage and Administration

Prior to the administration of r-PA, Aspirin (300mg) and an IV Heparin bolus (5,000IU) are administered. Reteplase has a shelf life of 24 months and should be stored below 25°C. It is administered as a slow intravenous injection over 2 minutes at a dose of 10 U bolus, followed by a second 10 U bolus dose 30 minutes later (double bolus). This should then be followed up by an infusion of heparin of 1,000 I.U. per hour, to be commenced 60 minutes following the first heparin bolus [7] and to be administered for at least 24 hours (due to the 1 hour time frame this is carried out in Hospital).

Reteplase and Heparin are not licensed for use by paramedics; therefore a Patient Group Direction (PGD) with a training procedure was implemented along with a PGD Policy.

4.4. Pre-Hospital Thrombolysis Assessment Questions

The JRCALC thrombolysis criteria for the use of Streptokinase were adapted with a few changes for use with Reteplase. 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 and the QRS width was changed to 0.12mm or less from 0.14mm in order to exclude Bundle Branch Block (BBB).

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?
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?

4.5. Patient Drug Information

Staff had some concerns with regard to what information to give the patient regarding thrombolysis and the associated risks. After consulting with the Trusts' solicitors, staff guidelines for patient information regarding thrombolysis were produced as follows:

"You have had a heart attack and the standard treatment for that is a drug called Reteplase. Reteplase carries a small risk of causing internal and external bleeding – the most serious being a stroke. From the answers you have given, the risk appears to be outweighed by the likely benefit of administering Reteplase and the recommendation is that you start treatment for your heart attack as soon as possible.

Do you wish to receive Reteplase?

***If yes** – Indicate patients agreement to the treatment on the patient report form."*

4.6. Procedures

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 is 30-minute time dependent between doses.

4.7. Training

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 program, 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.

4.8. Funding

The NSF-CHD Local Implementation Team provided all the funding to set up the Pilot sites including training and equipment. The finances for the drug came from the CCU budget.

5. PHT Pilot

The Pilot started on the 1st November 2000 at a small rural station in Ashbourne, Derbyshire. The first patient was thrombolysed three weeks later. By beginning with a small pilot, the Trust was able to evaluate the ECG telemetry and build staff confidence. Following every paramedic administration of thrombolysis, one of two senior clinical managers on 24-hour call is notified and the staff performing the PHT are contacted for a de-briefing at the end of the incident. This provides staff support, enables problems to be addressed immediately as required and ensures that the Trust is able to continually learn from each experience. PHT is only carried out on arrival of a patient-moving vehicle due to the potential risks associated with thrombolysis.

5.1. Expanding the Pilot

Over the following nine months, staff from a further three stations (Ripley in Derbyshire and Carlton and West Bridgford in Nottinghamshire) were trained on a gradual roll out program.

5.2 Communications

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

6 Results

At the time of publication, 14 patients have received paramedic thrombolysis. All 14 patients presented with signs and symptoms of an acute myocardial infarction. The diagnoses were confirmed with ST Elevation of greater than 2 mm in two or more consecutive leads on the 12 lead ECG. All 12 lead ECGs were transmitted via GSM through to the CCU for confirmation. When the attending paramedic received ECG confirmation all patients received 5,000 units of IV Heparin and the first bolus dose of 10 units Reteplase. After the first dose of thrombolysis there were no complications (reperfusion arrhythmias, hypotension, bleeding, strokes or cardiac arrests). One patient (49 years old with a Lateral infarction, Patient 11: Appendix A) became hypertensive with a raised diastolic blood pressure after the administration of the first dose of Reteplase. All patients reported an improvement in their symptoms on arrival at hospital and the attending crews noted an improvement in each patient's clinical condition.

- All patients received high concentration Oxygen
- Thirteen patients received 300mg Aspirin and one patient was given 600mg by his GP.
- Three patients also had a GP in attendance, one of which was in a community hospital. Two of these patients also received diamorphine with an anti-emetic.
- Ten patients had two cannulae inserted and four patients had one cannula inserted.
- Nine patients received glyceryl trinitrate (GTN).

- Ten patients received IV Nubain (analgesia), two patients received IV diamorphine (by GP) and two patients received no analgesia.
- Fifteen staff have been involved in performing PHT and five of these on more than one occasion.

An 83-year-old patient was found to be hypotensive with a blood pressure of 80/40mmHg and a bradycardia of 40bpm. The 12 lead ECG demonstrated an antero-lateral infarction (Patient 9: Appendix A). Atropine was administered IV at a dose of 500mcg. The patients BP increased to 130/60mmHg, with a pulse rate of 58bpm. The patient's clinical status was discussed with a CCU Doctor and authorisation was given for thrombolysis. The use of mobile telephones increased the flexibility of the process with added staff support as demonstrated in the case of this patient.

Four patients had a history of previous myocardial infarctions. Patient 5 (Appendix A) had a myocardial infarction seven months earlier. Patient 6 had five previous myocardial infarctions and a triple by-pass operation 10 years ago (symptom free ever since). Patient 10 had two previous myocardial infarctions and Patient 14 had one myocardial infarction four months previously.

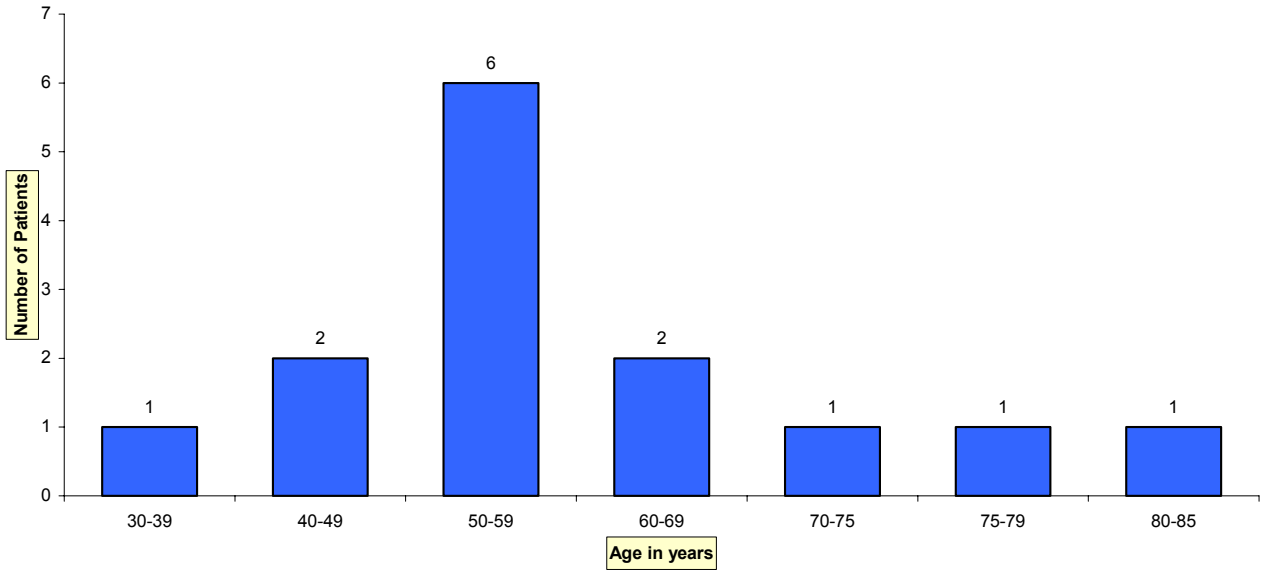
Reteplase has shown itself to be a very simple, user-friendly drug to administer in the pre-hospital environment. All patients received a single dose **only** in the pre-hospital setting. This is due to the ECG being transmitted and thrombolysis being carried out on route to the hospital. Consequently all 14 patients arrived in the CCU within 30 minutes of administration of the first dose (a second dose is carried in the ambulance if this cannot be achieved). No further Heparin is required to be administered until 60 minutes after the initial IV bolus [6] and no weight adjustment of either bolus drug is required. If there are any complications, the second dose can therefore be delayed until an appropriate medical opinion is obtained. This will also hopefully reduce potential risks in the early stages.

As confidence has grown and with lessons learnt from all the staff involved, we have seen an improvement in the times from arrival on scene to time of thrombolysis. It is important to appreciate this aspect of time delay in the first instance of any new system.

6.1 Age Distribution

There is an upper age limit of 75 years within the pilot criteria but there have been two patients thrombolysed outside of this criterion under medical authorisation: a 78 year old (Appendix A - Patient 3) and an 83 year old (Appendix A - Patient 9), both with anterior lateral infarctions. The times from onset of symptoms to thrombolysis were 93 minutes and 65 minutes respectively. No complications were reported from administration of thrombolysis through to hospital discharge. Table 1 demonstrates the age distribution for the 14 patients.

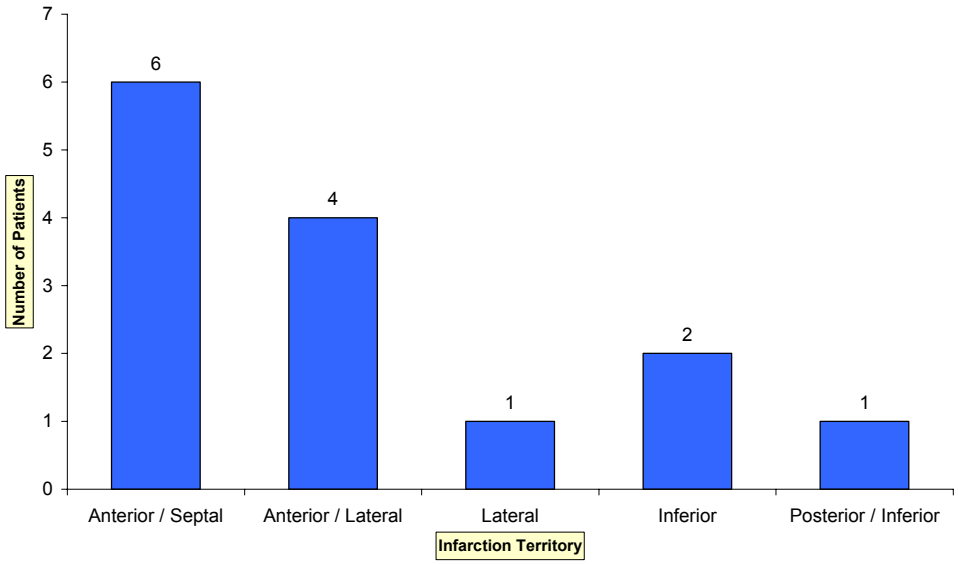
Table 1: Age distribution of thrombolysed patients



6.2 Infarction sites

The distribution of infarction territory for each patient is demonstrated in Table 2.

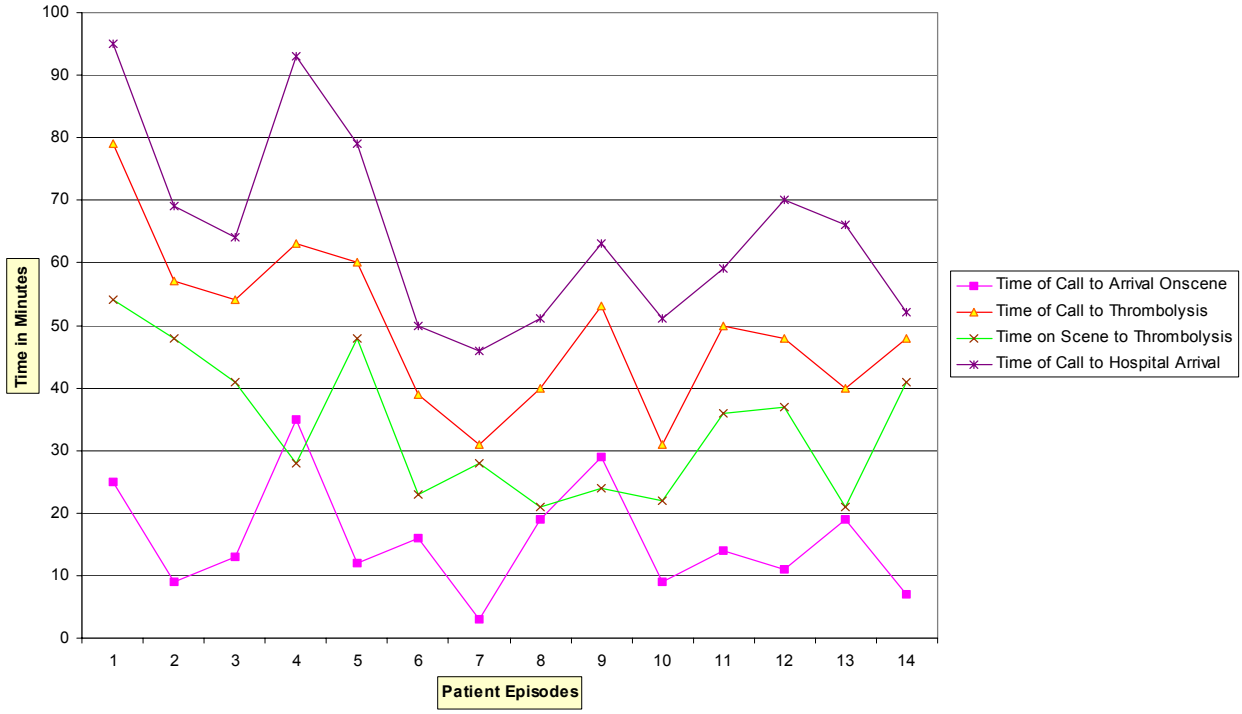
Table 2: Distribution of infarction territory for each patient



6.3 Time Episodes

This pilot was set up following the guidelines as stated within the NSF for CHD: *"If, after careful consideration, it is judged that local circumstances make it impossible to reduce 'call-to-door' times to less than 30 minutes, other models of care e.g. out-of-hospital administration of thrombolysis, must be considered."* [2]
With all these patients it was felt by the attending crew, due to location along with the journey times, that they would not have been in a position to receive thrombolysis within 60 minutes from calling for help if transported to hospital. (The times shown in graph 1 only demonstrate the time taken from the arrival of a patient moving ambulance and do not show the arrival of a fast response paramedic vehicle.) This has stimulated an interesting debate with regard to patients who live in close proximity to a hospital (i.e. less than 30 minutes to hospital from time of call) and may therefore have to wait longer to receive thrombolysis in hospital than patients treated within a more rural location.

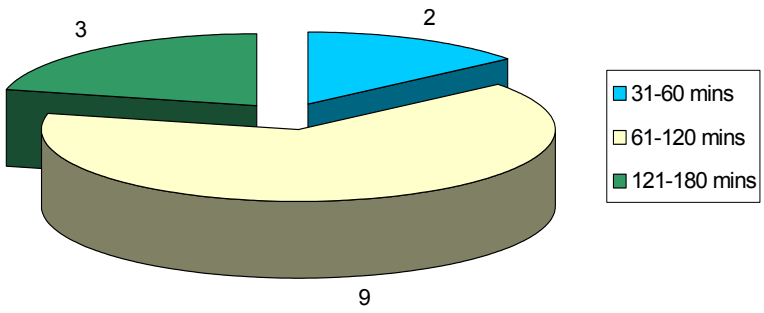
Graph 1: Time episodes for each patient



The timeframes for patients treated within this pilot can be compared to the ER-TIMI 19 trial [10]. The preliminary results from 248 patients in the ER-TIMI trial, demonstrated a median time of 31 minutes from arrival on scene to thrombolysis. The current median time on the 14 patients treated by EMAS is 32 minutes, with an average of 33 minutes.

The most significant improvement is in the time from onset of symptoms to thrombolysis. This is where continuous patient education is required to call for early assistance. The maximum benefit is if the patient receives thrombolysis within the first hour from onset of symptoms. The time from onset of symptoms to thrombolysis for each patient is demonstrated in Chart 1.

Chart 1: Time from onset of symptoms to thrombolysis



6.4 Excluded patients

Data concerning patients excluded from the pilot was also obtained, but with poorer compliance. However, the following data was collected from 17 patients.

- One patient with an Inferior infarction fulfilled the criteria but was not thrombolysed due to a problem in transmitting the ECG. This was due to an upgrade in the ECG software, which was incompatible in certain modes with the receiving station. The Trust was unaware of this incompatibility at the time of transmission. The equipment manufacturers solved the problem within 12 hours.
- One patient had an inferior infarction but was in close proximity to a hospital.
- Four patients had Bundle Branch Block with a QRS duration > 0.12mm.
- Three were patients were excluded due to their age (>75 years), with additional associated risk factors including BBB, taking warfarin and hypertension.
- Two patients had pain > 6 hours.
- Other single complications included, hypertension (190/110mmHg), hypotension (unrecordable), recent surgery, rectal bleeding, ST Elevation <2mm, use of warfarin and peptic ulcer disease excluded thrombolysis.

7. Patient Follow up

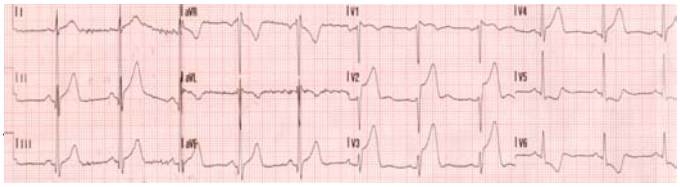
There have been no reported cases of cardiac arrest, reperfusion arrhythmia, stroke, bleeding or cardiogenic shock from any patient to date. Patient 11 (Appendix A) had the second dose of Reteplase delayed by a matter of minutes whilst other medications were administered to reduce a rise in the diastolic blood pressure.

Eleven patients had positive peak creatine kinase or troponin I blood results. One patient had non-resolving anterior ST elevation and went onto receive an angioplasty and a left anterior descending arterial stent (Patient 8).

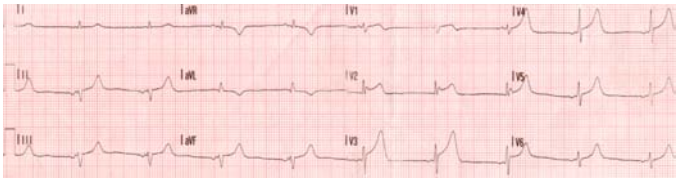
Three patients had negative blood results despite symptomatic signs and symptoms with positive ST elevation. Patient 2 received thrombolysis within 59 minutes from onset of symptoms. Due to unresolved pain, this patient went on to receive an angiogram which showed multiple vessel disease and is being treated through medication. Patient 4 was treated within 90 minutes of onset of symptoms and patient 5 received full treatment, but on comparison of his current ECG to the past discharge ECG, it showed no ECG changes (non-resolved ST segment).

Appendix A

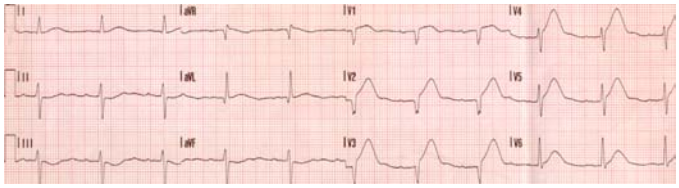
12 Lead ECGs of Patients who have been Thrombolysed on route to Hospital



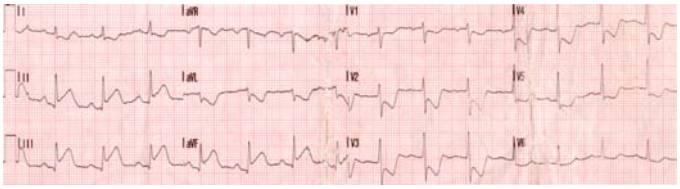
Patient 1



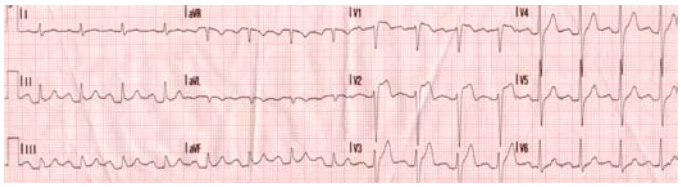
Patient 2



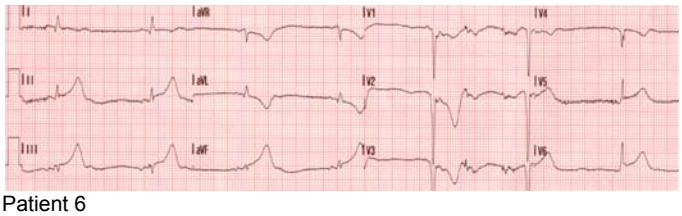
Patient 3



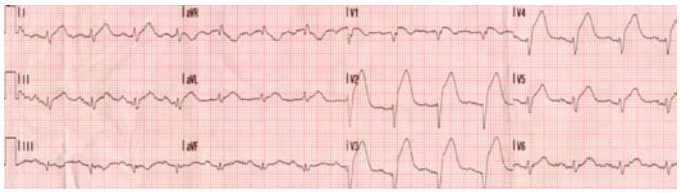
Patient 4



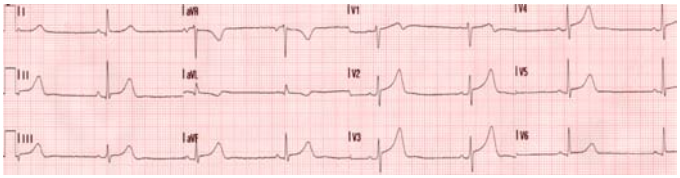
Patient 5



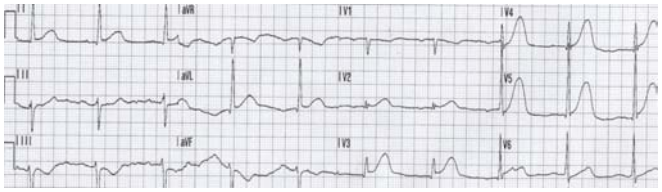
Patient 6



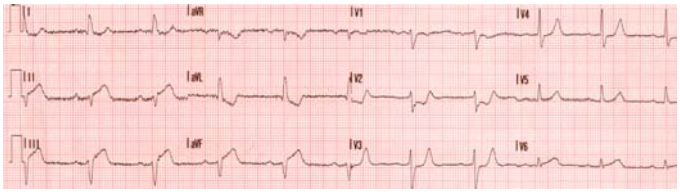
Patient 7



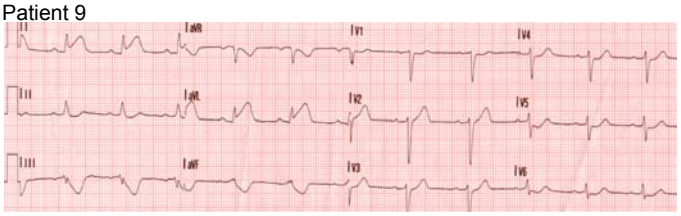
Patient 8



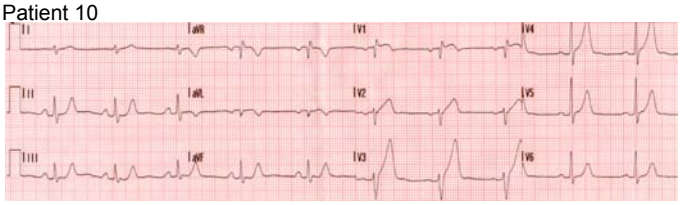
Patient 9



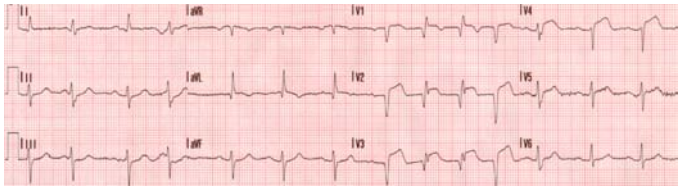
Patient 10



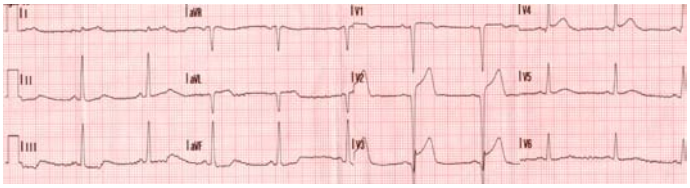
Patient 11



Patient 12



Patient 13



Patient 14

Note: ECG from patient 9 is a copy of a faxed ECG sent to the CCU from an ambulance on route via GSM.

References:

1. Government White Paper – Saving Lives Our Healthier Nation (1999)
2. National Service Framework – Coronary Heart Disease (1998)
3. NHS Plan, Department of Health. (December 2000)
4. Millar-Craig MW, Joy AV, Adamovicz M ,Furber R, Thomas B. Reduction in treatment delay by paramedic diagnosis of myocardial infarction with direct CCU admission. *Heart* 1997;78:456-61
5. Sandler DA. Paramedic direct admission of heart-attack patients to a coronary-care unit. *Lancet* 1998;352:1198
6. Statutory Instrument – 2000 No. 2899. The Prescription Only Medicines (Human Use) Amendment (No. 2) Order 2000 © Crown Copyright 2000
7. 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
8. 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
9. 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
10. 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*