

**Use of the Prime ECG™ to aid in the early detection of acute myocardial infarction in an Emergency Department setting.**

**A collaborative project between the Dept of Emergency Medicine and the Academic Department of Cardiology at the Leeds General Infirmary.**

**Project leads:**

Dr A.A. Khan  
Specialist Registrar in Emergency Medicine

Dr J. Greenwood  
Lecturer in Cardiology

Dr Tajek B. Hassan  
Consultant in Emergency Medicine

Professor Stephen Ball  
Professor of Cardiology

Other contributors: Dr J. Gomez, Dr J Humphries, Ms H. McLelland, and Mr M. Naim.

Correspondence to:  
Dr Taj Hassan  
Dept of Emergency Medicine  
Leeds General Infirmary  
Leeds, UK.  
Tel: (0113) 392 6470  
Email: [Taj.Hassan@leedsth.nhs.uk](mailto:Taj.Hassan@leedsth.nhs.uk)

## **1.0 Project Summary.**

In the UK approximately 300,000 patients suffer with acute myocardial infarction (AMI) per year. Early recognition and treatment of AMI is vitally important with thrombolysis being a critical time sensitive intervention.

Previous work (1) has shown that there is a delay in thrombolysing patients with initially non diagnostic electrocardiographic changes – patients with ‘evolving myocardial infarction’, and those with conduction abnormalities such as left bundle branch block (LBBB).

Currently patients presenting with chest pain are triaged by a nurse and a 12 lead electrocardiogram (ECG) is performed. The ECG is used as the diagnostic test and patients with diagnostic changes of AMI are given thrombolysis according to locally agreed protocols. Patients with initial non-diagnostic ECG changes are reviewed with subsequent ECGs being performed at regular intervals and thrombolysis being administered dependant on these ECGs.

The PRIME ECG <sup>TM</sup> is a novel system, which allows a more complete body surface electrical map of the heart. It has been shown in studies to be more specific and sensitive for the diagnosis of AMI.

We aim to determine through a pilot study and then a formal trial to assess the impact of using the PRIME ECG <sup>TM</sup> in patients presenting with chest pain and other symptoms, which are suggestive of an acute coronary event. We hypothesise that the PRIME system will be significantly more accurate in the early detection of AMI in an Emergency department setting as compared to a standard ECG.

## **2.0 Introduction**

### **2.1 Background**

Currently diagnosis of AMI is dependant on the 12 lead ECG and the use of cardiac enzymes. The 12 lead ECG has been shown to be only 50% sensitive for the detection of AMI (3). The role of enzyme markers also leads to delays in diagnosis of AMI. Myoglobin levels do rise acutely post AMI however have poor specificity for AMI. Elevated levels of creatinine kinase (CK)-MB mass and cardiac troponin –T or troponin-I have high specificity for AMI. These markers take 4-6 hours to begin to rise and do not reliably exclude AMI until after at least 12 hours following symptom onset.

The utilization of the PRIME ECG <sup>TM</sup> aims to overcome these shortcomings. Initial studies suggest that the system can reveal information about the severity and extent of the ischaemic process with greater sensitivity and specificity than conventional 12 lead ECG (4).

By using the PRIME ECG <sup>TM</sup> in patients who present to the Emergency department with symptoms and signs suggestive of AMI, we hope to demonstrate that a reduction in the time to making an accurate diagnosis can occur.

## 2.2 Research evidence

Patients with symptoms suggestive of AMI who go onto be thrombolysed in the Emergency department can be divided into three groups (1). A significant proportion will have diagnostic ECG changes indicative of AMI. Approximately 27.7% will have evolving changes of AMI and be thrombolysed once clear changes have been identified on the ECG. The last group, approximately 5.5% will have a LBBB pattern and require thrombolysis on clinical grounds. This group also have delayed thrombolysis due to difficulties in decision making.

The PRIME ECG is a recent diagnostic innovation and research has been carried out on its possible applications in more accurate and early detection of AMI. Menown et al (4) looked at the role of body surface mapping (BSM) in the early diagnosis of acute myocardial infarction. Patients were recruited consecutively as they presented to a cardiac ambulance or the accident and emergency department, or medical wards. This study recruited 760 subjects, 635 with chest pain and 125 controls. The 760 subjects were randomly allocated into a training set and a validation set. Multiple logistic regressions were used in the training set to identify which variables gave best discrimination between the groups. A model of these variables was then tested prospectively in the validation set.

It was found that the PRIME ECG achieved a sensitivity of 96% and specificity of 77% in distinguishing AMI's from normal ECGs. When asked to discriminate AMIs from abnormal ECGs, PRIME achieved 77% sensitivity and 85% specificity. Not all patients with AMI present with ST elevation, 40-50% patients with AMI present without ST elevation, these patients are a higher risk group. Another study by Menown et al (5) looking at 54 patients with chest pain less than 24 hours duration and ST depression were recruited. A 12-lead ECG and 80-lead body surface map were recorded at presentation from which univariate and multivariate prediction models of acute myocardial infarction were developed. Multivariate analysis was highly effective in demonstrating high sensitivity of 88% (compared to 38% with 12 lead method) and good specificity of 75%.

Similar work has identified a role of the PRIME system in diagnosis of right ventricular or posterior wall acute myocardial infarction (6). The role of PRIME as a non-invasive assessment of reperfusion post thrombolysis has also been suggested (7).

## **2.2 Target group**

At present, the Emergency department of the Leeds General Infirmary assesses approximately 5000 patients with chest pain to exclude cardiac disease of which 5% go on to be thrombolysed.

Patients attending the department with chest pain are stratified into a number of groups according to their symptoms, signs and ECG findings. Patients with acute changes of AMI are managed along standardised protocols. A second group of patients have LBBB on their ECG and are thrombolysed on clinical grounds alone. A third high-risk group have symptoms, signs and changes on the ECG strongly suggestive of an acute coronary syndrome ('evolving changes') or are labelled as 'unstable angina'.

The pilot study will recruit patients from these 3 groups in the Emergency department setting.

- The pattern of changes using PRIME will be confirmed after a standard 12 lead ECG has identified AMI and treatment has been instituted.
- The PRIME system will record changes after LBBB has been diagnosed using a standard 12 lead ECG and appropriate treatment has been instituted.
- The PRIME system will be used to record changes after a standard 12 lead ECG has stratified patients into the third 'high risk' category with either evolving changes of AMI or changes consistent with 'unstable angina'.

## **5.0 Aims**

The PRIME ECG study will be a pilot study in collaboration with the Academic Department of Cardiology. It will have two main aims:

- a) To evaluate the potential role of PRIME in patients with continuing cardiac sounding chest pain (at least 30 minutes) suggestive of acute myocardial infarction and an initial non-diagnostic 12 lead ECG.
- b) To confirm the pattern of changes in a cohort of patients with confirmed AMI on the 12 lead ECG and evaluate the perfusion pattern within the first hour after thrombolysis using the PRIME system.

### **5.1 Specific hypotheses**

- a) The PRIME ECG is significantly better in diagnosing AMI as compared to the standard 12 lead ECG interpretation in patients with an initial 'non diagnostic' 12 lead ECG.

b) The PRIME ECG can accurately identify patients in the Resuscitation Room in whom there is a failure to achieve adequate reperfusion following thrombolytic therapy.

## **6.0 Plan of investigation**

### **6.1 Trial design**

The pilot study will be a prospective non-interventional observational study.

#### **Group A (see appendix 1)**

This group of patients will be those that are having an AMI. This will be diagnosed on the 12 lead ECG. These patients will then proceed to have thrombolysis as per current trust policy. The performance of the PRIME ECG will in no way compromise the administration of the thrombolytic agent. A PRIME ECG will be carried out as soon as thrombolysis has been commenced.

After completion of thrombolysis a 12 lead ECG and a further PRIME ECG will be carried out. This component of the study will enable further development in pattern recognition of acute myocardial infarction using the PRIME system. It will also help in identifying patterns of reperfusion in patients who have been thrombolysed in Accident & Emergency and indicate which patients will need further therapy.

#### **Group B**

This group of patients are those which present to A&E with cardiac sounding chest pain which has lasted more than 30 minutes in duration in which the first 12 lead ECG is normal or non diagnostic.

Current practice dictates that these patients have a further ECG 20 minutes later, as a proportion of these patients will progress to have an AMI. In this group of patients a PRIME ECG will be carried out after the initial 12 lead ECG to identify the presence of any acute ischaemia on the PRIME system. Should the patient proceed to having an AMI then thrombolysis will only be administered on the evidence provided by the 12 lead ECG.

After thrombolysis has been administered then a 12 lead ECG and PRIME ECG will be repeated post thrombolysis.

Algorithms for both groups of patients are shown (Appendix 1).

### **6.2 Patient selection**

#### **ENTRY CRITERIA**

Patients recruited into the study will fall into two groups:

- Patients with a definite AMI, as diagnosed by history and changes on a 15 lead ECG.

- Patients who give a history of cardiac type pain lasting at least 30 minutes, but have a non-diagnostic 12 lead ECG for AMI. This will include patients with left bundle branch block (LBBB) and those with possible posterior myocardial infarction

#### EXCLUSION CRITERIA

- Any patient who is neurologically compromised will not be entered into the PRIME study.
- Patients who have non-specific, vague and short periods of chest pain will also be excluded from the study.

#### 6.3 Diagnostic endpoints

- a) Final clinical diagnosis on discharge as confirmed by cardiac markers and ECG changes.
- b) Mortality at 30 days

#### 6.5 Trial observations

##### Group A

Trial observations in this group will include

- a) Identification of AMI patterns using both PRIME ECG and the 12 lead ECG.
- b) Assessment of the PRIME system in diagnosing reperfusion patterns post thrombolysis.
- c) Mean and median door to needle times and proportion of patients meeting the NSF-CHD standards.

##### Group B

Trial observations in this group will include

- a) Door to diagnostic ECG time comparing PRIME with the 12 lead ECG.
- b) Sensitivity and specificity of diagnosis of AMI with the PRIME ECG.
- c) Mean and median door to needle times for the PRIME system and serial 12 lead ECGs

A power calculation has shown that 197 patients have to be enrolled (assuming a 10% drop out rate), to detect if there is a significant difference between the 12 lead ECG and the PRIME ECG, this was using the sensitivity and specificity provided in section 2.1- research evidence.

#### 7.0 Data collection and review

Data will be collected on standardised data sheets (appendix 2).

**The following information will be collected for each patient enrolled into the study:**

- a) Completed study data collection sheet
- b) Copy of the A&E card
- c) Copies of the patients 15 lead ECG
- d) PRIME ECG this will be stored on the software provided in electronic format.

- e) An electronic Microsoft ACCESS database will also be set up to record the relevant data.

The data will be initially reviewed on a fortnightly basis in view of the amount of information that will be generated.

## 8.0 Project milestones

Month	Milestone
1	Application to LREC, education and training programme
2-4	Study period
4-5	Data analysis and write-up
6	Application for larger prospective study.

## 9.0 Potential applications and dissemination of results

### 9.1 Potential applications

The PRIME system provides a new innovative approach to the diagnosis of acute coronary syndromes in the Emergency department setting. Studies in the Coronary Care setting suggest that the PRIME system provides an important advantage in the earlier diagnosis of patients presenting with 'evolving myocardial infarctions'. We hope that its introduction and validation in the Emergency department will lead to a reduction in the time taken to thrombolyse this important subgroup of patients. The PRIME system may also be helpful in identifying the subgroup of patients who would need further procedures to establish coronary perfusion post thrombolysis.

### 9.2 Dissemination of results

The results of this initial study will be available as a report to the Leeds Emergency Medicine Research Group and to the Academic Department of Cardiology at the Leeds Teaching Hospital Trust. In addition we anticipate that the results will be presented at national and international meetings and be submitted to a leading peer-reviewed journal

## References

1 Khan AA, Taylor A, Kirke C, Hassan TB, Hamer DW. Eliminating barriers to rapid thrombolysis in accident and emergency. Are the targets appropriate and achievable? *JAEM* 2000; **17:447**

2 [www.doh.gov.uk/nsf/coronary/htm](http://www.doh.gov.uk/nsf/coronary/htm)

3 Ketley D, Woods KL . For the European Secondary prevention STUDY group. Selection factors for the use of thrombolytic treatment in acute myocardial infarction. A population based study of current practices in the UK. *Br Heart Journal*; 1995 74: 224

4 Menown I B A, Allen J McC.Anderson J. Body Surface map Models for the Early Diagnosis of Acute Myocardial Infarction. *Journal of Electrocardiography* 1998; **31:180-88**

5 Menown IBA, Allen J, McC.Anderson J. St depression only on the initial 12-lead ECG: early diagnosis of acute myocardial infarction. *European Heart Journal* (2001); **22,218-227**

6 Menown IBA, Allen J,McC.Anderson. Early Diagnosis of Right Ventricular or Posterior Infarction associated with Inferior wall left Ventricular Acute Myocardial Infarction. *American Journal of Cardiology*.2000; **85:934-938**

7 Menown IBA, Allen J, McC.Anderson J Adgey A.A.J. Early Diagnosis of Right Ventricular or Posterior Infarction Associated with Inferior Wall Left Ventricular Acute Myocardial Infarction. *American Journal of Cardiology* (April 2000) **85**, 934-938