

## ORIGINAL RESEARCH

# Thrombolysis for acute ST elevation myocardial infarction: a pilot study comparing results from GP led small rural health emergency departments with results from a physician led sub-regional emergency department

R Krones<sup>1</sup>, P Radford<sup>2</sup>, C Cummingham<sup>1</sup>, D Krones<sup>1</sup>, HM Haines<sup>1</sup>

<sup>1</sup>Rural Health Academic Centre, The University of Melbourne, Victoria, Australia

<sup>2</sup>Benalla Health/Coster St. Medical Practice, Benalla, Victoria, Australia

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Krones R, Radford P, Cummingham C, Krones D, Haines HM

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## ABSTRACT

**Introduction:** Urgent angiogram is best treatment for patients presenting with ST elevation myocardial infarction (STEMI) in the first 90 min after contacting medical help. For Australian residents of inner and outer regional areas and remote or very remote areas, quick access to angiograms is not available. Numerous approaches have been developed to maximize reperfusion but delays due to systematic and patient factors persist. Diminishing confidence of some GPs in small rural health services to administer thrombolytics was one barrier to timely reperfusion identified in northeast Victoria, Australia. The aim of this study was to compare the frequency and outcomes of STEMI patients treated with thrombolysis by GPs in small rural emergency departments (EDs) with the outcomes from thrombolysis for STEMI in the physician-led, sub-regional ED in northeast Victoria.

**Methods:** Data were gathered by a medical file audit. Outcome measures were the frequency of STEMI, symptom to presentation times, mode of transport to hospital, ambulance call to presentation at ED times, door to needle (DTN) times, subsequent percutaneous intervention (PCI) or coronary artery bypass grafts (CABG), physician follow up and death.



**Results:** In total 68 cases were audited. Univariate analysis showed no significant differences between the GP-led or physician-led EDs in time from onset of symptoms to presentation, DTN times, thrombolysis related complications or subsequent access to PCI or CABG. Follow-up care was similar in both groups. Transport to hospital differed between the groups with only half of all cases arriving at the ED by ambulance, almost all of which went to the sub-regional hospital.

**Conclusions:** Thrombolysis for STEMI in the small GP-led EDs had similar results to thrombolysis administered by the physician-led ED. There is substantial time benefit to be gained by encouraging GP-led EDs to provide thrombolysis treatment, thereby improving patient prognosis and survival.

**Key words:** Australia, GPs, rural emergency departments, STEMI, thrombolysis, Victoria.

## Introduction

For the last 20 years thrombolysis has been used in the treatment of acute ST elevation myocardial infarction (STEMI) and has led to major outcome improvement<sup>1,2</sup>. Today an urgent angiogram is accepted as first line treatment for patients presenting with STEMI in the first 90 min after contacting medical help<sup>3,4</sup>. Percutaneous coronary intervention (PCI) is the gold standard in these patients if available and able to be undertaken within 2 hours of symptom onset<sup>5</sup>. This is an achievable treatment for the estimated two-thirds (66.3%) of the Australian population who reside in major cities<sup>6</sup>. For the remaining residents of inner and outer regional areas and remote or very remote areas, quick access to angiograms is not available.

Trials focusing on this situation have shown that the advantage of PCI diminishes when the transport time to an institution with the capacity for PCI is longer than 60 min<sup>5</sup>. Subsequently numerous approaches have been developed including stringed strategies to avoid time delays in hospitals/emergency departments (EDs) and in reducing the time from recognition of symptoms to calling for help and from calling for help to receiving reperfusion<sup>7,8</sup>. Despite improving trends, Barbagelata et al in their 2007 meta-analysis of randomised controlled trials of reperfusion in acute myocardial infarction showed that there are still significant delays in STEMI patients receiving reperfusion in the recommended time window<sup>7</sup>.

In Australia, the National Heart Foundation has stated that if patients cannot reach a hospital for thrombolytic therapy within 90 min of calling the emergency service, out-of-hospital thrombolysis should be considered<sup>9</sup>. Pre-hospital thrombolysis followed by early transfer to a PCI facility as part of a community based system of care is the most effective means to improve outcomes for these non-metropolitan patients<sup>3,7,8</sup>. Further, in order to address the inequities of access to rapid reperfusion in rural areas, Professor Richard Harper Chair of the Cardiac Network of Victoria, has called for all mobile intensive care (MICA) and advanced life support (ALS) ambulances to be equipped with 12 lead ECG capability, and all MICA and ALS ambulance paramedics to be trained to administer thrombolytics with back up from a cardiology advice line. In addition he has promoted the establishment of cardiac catheter laboratories with PCI capability in each region, supported by a major metropolitan cardiac unit<sup>10</sup>.

International and local trials have utilised paramedics to reduce the symptom to needle time for thrombolysis. In Sweden, when compared with regular in-hospital thrombolysis, pre-hospital diagnosis and thrombolysis by trained paramedics in the ambulances was associated with a one hour reduction in time to thrombolysis and reduced adjusted 1 year mortality by 30% in real-life STEMI patients<sup>11</sup>. Pre-hospital thrombolysis is not commonly undertaken in Australia despite its positive outcomes in trials<sup>12</sup>. In-hospital administration of thrombolytics by GPs or physicians remains the mainstay for reperfusion in most rural and remote areas of Australia.



The use of thrombolysis by GPs in rural areas has been intensively examined in Scotland. The GREAT Study<sup>13,14</sup> established that rural GPs are more likely than urban GPs to give pre-hospital thrombolysis<sup>14</sup>. Unfortunately after the completion and publication of the GREAT study, and despite the positive results demonstrated, the utilization rate of thrombolysis by GPs declined significantly<sup>14,15</sup>. Barriers to GPs implementing thrombolysis were identified as training, experience, equipment and organizational factors. Given this, the implications for practice include understanding the incidence and outcomes of utilization of thrombolysis by local GPs, the organisational and transport issues surrounding patients accessing thrombolysis and then further education and training to encourage its use<sup>14</sup>.

Historically, STEMI management in northeast Victoria (250 km from nearest PCI centre) has been characterized by significant delays in performing thrombolysis when patients presented to small GP-led district hospitals and were subsequently transferred on to the physician-led ED at the sub-regional hospital. In 1992 physicians from the sub-regional hospital responded by up-skilling GPs to enable emergency thrombolysis in local hospitals with physician telephone support and fax communication, the premise being that thrombolysis undertaken by trained GPs (even if the GP only has few occasions to practice this skill) is as safe as physician-led thrombolysis. A recent review of this strategy at a clinical meeting in one of the participating GP hospitals found that GPs were not always confident to administer thrombolysis in the case of STEMI and preferred to send the patient on to the physician-led hospital, incurring further delays to reperfusion.

No published studies comparing thrombolysis initiated by rural GPs in small hospitals with thrombolysis initiated by rural physicians in larger regional hospitals could be found, and questions regarding the effectiveness of this approach were raised. In particular the GPs had concerns similar to the barriers identified by Bloie et al<sup>14</sup> where they questioned the safety of them administering thrombolytics when they only treated a few cases per year.

The aim of the current pilot study was to investigate the frequency and outcomes of STEMI treated with thrombolysis performed by GPs in small rural health services and compare it with outcomes from thrombolysis for STEMI in the physician-led, sub-regional hospital (without PCI facilities) in northeast Victoria. It was hypothesized that there would be no difference in patient outcomes between settings.

## Methods

### *Setting*

This multi-site study included patient records from a physician-led, sub-regional hospital without angiography services and five GP-led hospitals which used the physician-led centre as their referral hospital. The sub-regional hospital is 250 kilometers (2 hours 50 min) from the nearest angiography laboratory. The GP hospitals' proximity to the sub-regional hospital ranged from 40 km (35 min) to 103 km (1 hour 20 min). All of the GP-led hospitals have single paramedics with on-call night shift, ambulance services situated in their towns. The sub-regional hospital has multiple crew ALS ambulance services.

All the GP-led hospitals were staffed twenty-four hours by Divisions 1 and 2 registered nurses, with a GP on-call roster system. The physician-led, sub-regional hospital had 24 hour on-site medical ED cover and additional on-call physicians.

### *Retrospective medical file audit*

A medical file audit was undertaken comparing STEMI patients treated with thrombolytics, from five GP-led rural EDs with one physician-led, sub-regional hospital. The outcome measures were:

- frequency of STEMI patients
- symptom to presentation times
- mode of transport to hospital
- ambulance call to presentation at ED times
- door to needle (DTN) times



- subsequent PCI or coronary artery bypass grafting (CABG)
- physician follow up
- death.

Each of the GP-led EDs were referral points for the physician-led facility and each were trained in and utilised the Australian National Heart Foundation *Guidelines for the management of acute coronary syndromes*<sup>9</sup>. The study examined patient histories from 1 July 2005 to 30 June 2008.

### **Ethics approval**

Ethics approval was obtained for this study from Northeast Health Wangaratta Human Research Ethics Committee and the University of Melbourne Human Research Ethics Committee (April 14 2009, #79).

### **Audit identification of records**

All patients thrombolysed at the physician-led centre were identified through the ED thrombolysis log. In one GP-led facility a log was kept, but for the other four a process of identifying admissions to the regional intensive care unit was cross-checked against all rural ED presentations for chest pain/ myocardial infarction/ angina. These files were then reviewed to determine patients who had been thrombolysed. Once identified, the complete hospital medical record for each patient was extracted from the respective medical records department for data collection.

From the medical record, two researchers (DK & RK) recorded a range of details including age, sex, (marital status and home post code was inconsistently recorded and was not included), admission date, ambulance usage, time of arrival and administration of thrombolytic agent, time of first symptoms, type of thrombolytic agent, previous medical history (diabetes mellitus, arterial hypertension, hypercholesterolemia, any smoking history), discharge destination and regular GP of the patient. One researcher (RK) then contacted each patient's GP to determine the patient's outcome including physician follow up; PCI

performed or not; CABG (before and after 30 days post-infarct); and death (before 30 days post-infarct or in the first year) and if death had occurred, the cause of death. The physician researcher (RK) reviewed all ECGs and commented whether ST elevation could be confirmed. In cases where this was not clear, the ECG was also reviewed by a cardiologist.

Univariate statistical analysis of the data at 95% confidence was undertaken using SPSS V17 ([www.spss.com](http://www.spss.com)).

## Results

Seventy-four patients with suspected STEMI presented from 1 July 2005 to 30 June 2008 to the participating hospitals and received thrombolysis. Of the 74, six presented to a GP-led facility but were transferred before thrombolysis. A decision was made to remove these cases from the study. (The study aim was to compare the assessment and subsequent treatment of STEMI with thrombolysis by GPs with physician-led care. These patients were assessed by the GPs but transferred out without being thrombolysed, thus confounding the outcome.) The final number of cases was therefore 68 (43 at the physician-led facility, 25 at the GP-led health services).

### **Patient characteristics**

The median age of all patients at the onset of symptoms was 60 years (IQR 54–72), the youngest was 43 years and the oldest 91 years. Fifty-five (81%) were male and 13 (19%) were female. The median age of males was less than for females (59 vs 74, respectively) but there were only a small number of females in comparison with the male group. There was no significant difference in patients' ages between the physician-led and the GP-led groups (Mann–Whitney *U*,  $Z=0.707$ ,  $p=0.48$ ).

There were four risk factors reported: history of diabetes (either type 1 or type 2), hypercholesterolemia, hypertension or any history of smoking. Four patients (6.7%) had no recorded history of any of the risk factors. Fifteen patients (25%) had at least one risk factor, 28 (46.7%) had at least



two risk factors, seven (11.7%) had at least three and four (10.0%) had all four. Univariate examination of the risk factors between patients attending physician-led hospitals and the other facilities revealed no difference in diabetes history ( $X^2=1.931$ ,  $p=0.165$ ), hypercholesterolemia ( $X^2=0.00$ ,  $p=0.99$ ), hypertension ( $X^2=0.033$ ,  $p=0.856$ ) or smoking ( $X^2=1.471$ ,  $p=0.225$ ).

## ECGs

Review of the ECGs at presentation confirmed 53 (77.9%) with ST elevation. In 10 presentations, ECGs showed changes that could not confirm the decision for thrombolysis (three in physician-led care facility, seven in GP-led hospital) and in five cases the ECG was borderline (one in physician-led and four in GP-led hospital). The audit of ECGs was limited by the presence of multiple ECGs; some without dates and times, complicating the certainty of determining which ECG was the diagnostic trigger for thrombolysis.

## Symptom to presentation time

Overall the median time from reported onset of symptoms to presentation at the first ED was 92.4 min (IQR 53.85–172.05). The shortest time recorded was 21 min (physician-led ED) and the longest 653 min (GP-led ED), there were five patients with no recorded times. There was no significant difference in the time taken from reported onset of symptoms to presentation to the physician-led facility in comparison with the GP-led facilities ( $Z=.942$ ,  $p=0.346$ ).

## Transport to hospital

Method of transport to hospital included: 34 ambulance transports (50%), 26 private vehicle transports (38%) and eight (11.8%) unknown. Of the 34 who used an ambulance, 31 (91%) were taken directly to the physician-led facility and 3 (8.8%) went to a GP-led facility (the nearest hospital to the regional centre). In those patients who used the ambulance service the median time (self-reported) from onset of symptoms to calling the ambulance was 52 min (IQR 24.5–74.75). Of these patients, median time from calling the

ambulance to admission into ED was 59.0 min (IQR 40.25–86.75).

## Door to needle times

The overall median time from admission to the ED and commencement of the administration of thrombolysis (DTN) was 47 min (IQR 30.2–80.75). A Mann–Whitney  $U$  test was undertaken to compare DTN between the groups. The median DTN time at the physician-led facility was 47 min (IQR 27–65) and at the GP facilities was 60 min (IQR 35.5–90.5). This was not a significant difference ( $Z=1.22$ ,  $p=0.222$ ).

## Patient outcomes

Twelve patients did not have the name of their primary GP recorded in their medical history and were lost to follow up. Of the remaining 56 thrombolysis patients, 36 (69.2%) were followed up by a physician, 12 (23.1%) had no specialist follow up and 4 (5.9%) were unknown. Subsequent to thrombolysis, 35 (73%) patients from the physician-led group and 16 (64%) from the GP-led group received PCI. There was no difference between the GP- and physician-led groups ( $X^2 = 0.269$ ,  $p = 0.60$ ) for receiving PCI. Four patients (two physician-led and two GP-led) underwent CABG within 30 days and four patients in the GP group had CABG after 30 days. No patients suffered thrombolysis-related complications.

One patient died in the acute setting at a GP-led hospital and one patient from the GP group died within 30 days of PCI but neither was as a consequence of thrombolysis.

## Discussion

This retrospective audit confirmed the hypothesis that thrombolysis for STEMI when undertaken in GP-led facilities had no difference in outcomes to thrombolysis for STEMI undertaken in physician-led facilities in northeast Victoria.



Of the 68 cases audited only one death was recorded (in the GP setting); however, there was no evidence to suggest that this was related to the administration of the thrombolytic. Follow-up care was similar in both groups indicating that the patients presenting to the GPs are receiving appropriate post-STEMI management. There was no significant difference in the time taken from reported onset of symptoms to presentation, DTN times or thrombolysis related complications.

While there was no statistically significant difference between the groups for post-thrombolysis PCI, it would have been of interest to know the clinical reasons for some patients receiving PCI and others not. Reasons for not receiving this intervention may have included that it was not indicated by a positive angiogram or that they were being managed conservatively. Day to day experience also shows, however, that there is sometimes a lack of available beds in the metropolitan centers – a situation that could be reconciled by the establishment of more regional PCI facilities as recommended by the Cardiac Clinical Network<sup>10</sup>. It must be acknowledged that such facilities could not operate on a 24 hour, 7 days a week basis due to insufficient throughput and availability of sufficiently trained staff. However a system that enables immediate transfer back to rural centers after uncomplicated PCI could alleviate such occasions of ‘bed block’.

Transport to hospital differed between the groups with only half of all the cases arriving at the ED by ambulance – 31 of which went to the sub-regional hospital. The three remaining patients who used an ambulance were thrombolysed in the second largest town. This may indicate that patients in more remote areas do not rely on ambulance services and are probably not aware of the risk that they take when they organize transport themselves. Alternatively, they may have lived very close to the local hospital and made a pragmatic decision for self-transport, or the ambulance service may have made the decision to bypass the smaller GP-led ED. This warrants further research in a prospective study.

While outcomes for GP-led or physician-led thrombolysis are analogous, some important issues have emerged from this study. First, preventable delays to reperfusion persist in the study population. The time to admission combined with admission time to thrombolysis pushes the onset of symptoms to treatment time outside the National Health Foundation guidelines<sup>9</sup>. This is known to have a direct correlation to the subsequent size of the infarct and mortality<sup>1</sup>.

The time taken from symptoms to presentation at either a GP- or physician-led ED ranged from 21 to 653 min with an overall median time of 92 min. While these times are patient self-reported and should be viewed with caution it appears that patients are waiting too long before arranging transport to hospital. In some situations there may be delays in ambulance response times. Another 47 min of delay occurred from arrival at the ED to administration of thrombolysis in the physician-led ED and 60 min in the GP-led ED. A Victorian rural/urban study<sup>16</sup> suggested that a large part of the problem with overall call to needle times for the treatment of STEMI was actually the DTN. While compared with the times reported by Barbagelata<sup>7</sup>, (where for in-hospital thrombolysis, the time-to-admission 149 +/- 45 min and time-to-treatment was in excess of 181 +/- 29 min), the present local results are favourable while there are clear targets for local improvement.

There was a difference between the GP-led settings and the physician-led settings in the accuracy of STEMI diagnosis on ECG. As stated earlier, one of the prompts for undertaking this audit was GPs’ concern as to whether they should thrombolysed or refer on to the sub-regional hospital when being confronted with borderline ECG changes but clinically convincing chest pain. The discrepancies with the accuracy of ECG diagnosis between the two groups bore this out; however, there were no negative clinical outcomes as a result of this. The result of the ECG audit is in no way a criticism of the GPs’ decisions to thrombolysed when confronted with a patient with chest pain and borderline ECG changes. Rather it is a prompt for the ongoing education of GP teams on interpreting ECG and responding quickly.



## Limitations

This pilot study has several limitations which should alert the reader to interpret the findings with some caution. First, this work was a pilot study and the number of cases identified across the regional sites was smaller than what would be required to make broadly generalisable conclusions. Second, the retrospective nature of this work has well known constraints of sometimes poor documentation and missing data. Additionally information regarding onset of symptoms and time of calling the ambulance where documented were from patient self-report, a situation which has changed since the time of this audit. Rural Ambulance Victoria now have an IT-based documentation system which allows exact tracking of call, respond and travel times. This will greatly assist future research efforts. The influence of a variety of other potentially important factors that could affect the time of patient arrival in the ED, such the distance from the hospital at the time the symptoms arose, patients' psycho-social background and the presence of an accompanying person at home, could not be examined.

The results show a low number of women and a relatively large number of lost cases, especially from the group thrombolysed in the rural hospitals. The number of females is difficult to understand but the large number of tourists who visit northeast Victoria in the summer and winter season might explain these losses to follow up. Finally, an accurate audit of the ECGs was hampered in some cases by uncertainty regarding which of the sometimes multiple ECGs was the one which triggered the thrombolysis treatment decision.

A strength of this study has was the involvement of both GP and physician researchers who are actively engaged in rural clinical practice and were expert in interpreting the medical files and ECGs.

## Conclusion

Thrombolysis for STEMI in the small GP-led ED s of northeast Victoria appears to have similar results to

thrombolysis administered by physician-led teams in the sub-regional referral hospital. There is a substantial time benefit to be gained by encouraging GP-led hospitals to provide thrombolysis treatment, thereby improving patient prognosis and survival. Based on these findings the regional GPs in this study should proceed to thrombolysed with confidence. Ongoing education regarding ECG interpretation is recommended. Further work should be done to improve DTN times in both groups, while further research is needed to investigate why many people do not use the ambulance service in the situation of acute chest pain, and whether ambulance services bypass local GP-led EDs in order to bring patients to physician-led care. A prospective study is planned to follow up on the findings of this pilot study.

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