

PERSONAL VIEW

The case for urban prehospital thrombolysis

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Emerg Med J 2002;19:441-443

This is the first part in a debate on the benefits and disadvantages of urban prehospital thrombolysis. I put the case for prehospital thrombolysis in the urban environment and argue that it is a rational development that will save lives and reduce long term morbidity.

Ten years ago thrombolysis was carried out almost exclusively in hospital coronary care units. Since then much has changed: in my present appointment around 75% of patients who receive in-hospital thrombolysis do so from emergency physicians, and local audit shows that we are rather better at it than our inpatient colleagues (EM Gilby, *et al*, Bournemouth, annual conference of the British Association for Accident and Emergency Medicine, 2001). What is now more common is to hear arguments that were once used by cardiologists to block emergency department thrombolysis being turned against thrombolysis in the urban community. We are told that paramedics aren't properly trained, that it isn't safe to transport a patient who is being thrombolysed, and that it hardly takes any time for the patient to get to hospital anyway. In a particularly ironic twist it is suggested that paramedics can send in an electrocardiogram (ECG) or radio ahead when they have a patient with possible acute myocardial infarction (AMI), permitting a "fast track" system to be set up. Such a system is all too reminiscent of the "fast track" that cardiologists sought to establish between emergency departments and coronary care units, but which was subsequently shown to be inferior to immediate thrombolysis in the emergency department.¹

The National Service Framework for coronary heart disease sets a challenging new standard: "People thought to be suffering from a heart attack should be assessed professionally and . . . thrombolysis should be given within 60 minutes of calling for professional help".² This supersedes the 90 minute standard set by the British Heart Foundation and has caused understandable concerns.³ Current "door to needle" times in the UK are at best 20-40 minutes, and often more.¹ Furthermore, it seems unlikely that the "door to needle" time can be reduced much below 20 minutes without compromising patient assessment. The effect of this is to leave local ambulance services attempting to deliver a "call to door" time of less than 30-40 minutes. The evidence shows that this is not currently achieved, even in urban areas.⁴ Indeed, in Aberdeen only 48% of patients in urban and suburban areas achieved a "call to needle" time of less than 60 minutes when a "scoop and run" policy was used followed by immediate in-hospital thrombolysis,² and other

studies have consistently shown that the median call to needle time exceeds 60, and often 90, minutes when patients are thrombolysed in hospital.⁵ Even when a prehospital ECG was performed and transmitted to the coronary care unit in Derby, UK, the average call to needle time was reported as 93 minutes, with an average door to needle time of 37 minutes.⁶

The solution to this problem may well be prehospital thrombolysis, which in the Aberdeen audit increased the number of urban and suburban patients achieving a call to needle time of less than 60 minutes to 74%.³ A recent meta-analysis of six randomised trials of prehospital thrombolysis (n=6434) demonstrated a significantly decreased all cause hospital mortality among patients treated with prehospital thrombolysis compared with in-hospital thrombolysis (odds ratio 0.83; 95% confidence intervals 0.70 to 0.98),⁷ and no trial has ever reported a negative outcome from this practice. One study, the Grampian Region Early Anistreplase Trial (GREAT), demonstrated a statistically significant mortality difference in rural patients receiving prehospital thrombolysis,⁸ but no urban study to date has been sufficiently powered to demonstrate a similar mortality benefit.⁹

Having demonstrated, then, that prehospital thrombolysis is both achievable and capable of reducing all cause mortality, what is standing in its way? There seem to be four main arguments against this innovative practice, and I will therefore address each in turn.

1 PARAMEDICS CANNOT GIVE PREHOSPITAL THROMBOLYSIS SAFELY

Presaging the National Service Framework, a task force of the European Society of Cardiology and the European Resuscitation Council recommended in 1998 that: "the time taken before definitive treatment is given should generally not exceed 60 minutes from the time the ambulance is alerted. If this time is expected to be exceeded, pre-hospital thrombolysis should be considered".¹⁰ They also recommended "consideration of pre-hospital initiation of thrombolytic therapy by medically trained and certified non physician personnel . . ." or "the first qualified person to see the patient . . ." because this avoids time-consuming handovers and reassessments. Although thrombolysis by general practitioners has been shown to be effective in rural areas,⁸ such an approach is unlikely to prove practical for

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Abbreviations: ECG, electrocardiogram; AMI, acute myocardial infarction

the vast majority of patients in urban and suburban regions, who will instead be reliant on paramedics, working under medical direction, for the administration of prehospital thrombolysis.

Inevitably, education and close supervision of paramedics will be required, and emergency physicians, rather than cardiologists, should undertake this as emergency medicine already has close links with the ambulance service. In the USA and Netherlands computerised ECG interpretation has been used to guide paramedics with good success in the more obvious infarcts,^{11,12} but a preferable approach is likely to be the electronic transmission of ECGs to the receiving hospital where a senior physician can interpret the trace and provide direct advice and authorisation for thrombolysis via a two way communication link. With clear protocols and checklists for the paramedic to follow this has already been shown to be successful in Scandinavia,¹³ and is now being adopted in some regions of the UK. A further incentive has recently been provided by the introduction of single bolus thrombolytics. These are considerably easier to administer than the infusions or double boluses used in the past and, although more expensive, remove a further barrier to effective paramedic administered prehospital thrombolysis. It is to be hoped that the increased cost of such novel agents will be more than offset by the health gains of earlier treatment. Ultimately it may be possible for paramedics, with the appropriate training, experience, and certification, to administer thrombolysis to patients with a straightforward AMI without recourse to a physician. This may seem a long way off at present, but it is worth remembering that in the early days of resuscitation from prehospital cardiac arrest, paramedics in the USA were not permitted to defibrillate a patient in ventricular fibrillation until they had first used telemetry to transmit the ECG trace to hospital for confirmation by a physician.¹⁴ Indeed, there were considerable doubts as to whether paramedics would be able to safely operate a defibrillator without medical supervision. This may seem incredible today, but provides a useful lesson for the introduction of prehospital thrombolysis, which may also herald a new era of improved communication between the prehospital and in-hospital environments.

One argument that is sometimes used against prehospital thrombolysis is that AMI is infrequent enough to cause problems with skill retention by paramedics.¹⁵ In fact, while 15 000 patients suffer major trauma in the UK each year,¹⁶ 300 000 suffer AMI.⁵ Assuming that half of these die in the community and two thirds are not eligible for thrombolysis then the incidence of AMI that could benefit from prehospital thrombolysis is still three to four times that of major trauma. Furthermore, the need to retain appropriate skills is an argument in favour of urban, rather than rural, prehospital thrombolysis as the vast majority of AMIs will occur in areas of high population density.

2 PREHOSPITAL COMPLICATIONS ARE UNACCEPTABLY HIGH

Several studies have shown that the risks of transporting patients during, or immediately after, thrombolysis are low and indistinguishable from the risks of transporting patients who have sustained an AMI and not been thrombolysed.^{17,18} In particular, there are no reports of early haemorrhagic problems during transport despite the growing experience of transfer for urgent angioplasty after unsuccessful thrombolysis.¹⁹ The main complication of concern is ventricular fibrillation or tachycardia, but this occurs in AMI with or without thrombolysis, and is a condition that paramedics are already very capable of dealing with.

3 THE TIME SAVINGS ARE SMALL AND INSIGNIFICANT IN URBAN AREAS

No study has so far quantified the "critical transport time", below which prehospital thrombolysis may no longer be clinically

worthwhile. Nevertheless, the myth of short city journey times is now being exploded, and urban areas should consider auditing their local ambulance transport times: in the centre of Bristol less than 30% of patients with AMI have a call to door time under 30 minutes (EM Gilby, *et al*, Bournemouth, annual conference of the British Association for Accident and Emergency Medicine, 2001). As city roads become increasingly congested it is hardly surprising that a recent study comparing the costs of conventional and tele-dermatology in urban and rural areas found that transport costs were higher for an urban population, in part because urban patients took over twice as long to negotiate traffic as their rural counterparts (3.5 min/km versus 1.4 min/km).²⁰

The precise benefits of earlier thrombolysis are, however, easier to quantify. It has been demonstrated that for patients presenting two hours after the start of symptoms each hour's delay in receiving thrombolysis leads to the loss of 21 lives per 1000 treated (measured at 30 days).⁸ This suggests that seven lives can be saved for every 1000 patients treated just 20 minutes earlier, but there is also strong evidence that the earlier thrombolysis is given the greater the benefit, particularly when the "pain to needle" time is less than two hours.²¹ Within the first hour of symptoms a reduction of 20 minutes in the "pain to needle" time may save as many as 20 lives per 1000 treated, to say nothing of the functioning myocardium preserved and morbidity prevented. These benefits of very early treatment are most likely to be observed in an urban environment, and may even exceed the reported benefits of primary angioplasty over thrombolysis.²²

4 THE MONEY WOULD BE BETTER SPENT IN OTHER WAYS

The task force of the European Society of Cardiology and the European Resuscitation Council summarises the case against further expenditure on acute hospital therapies very well: "A greater investment in hospital treatments (for example, primary PTCA or newer, more expensive and marginally more effective thrombolytic agents) is therefore unlikely to result in any appreciable fall in total mortality . . . epidemiological data suggest that greater deployment of resources for pre-hospital care has more potential for reducing the case fatality rate of AMI than has the intensification of treatment in hospital".¹⁰ It is difficult to add to this compelling argument.

The other main area of alternative expenditure is public education to reduce the "pain to call" or "decision" time. This is frequently observed to be the longest component of the total pain to thrombolysis time, and is therefore an obvious target for intervention. Education of those patients already known to have ischaemic heart disease is currently undertaken in hospitals and primary care, but it has also been observed that the "pain to needle" time can be reduced by a media campaign.²³ In the short-term this can be an effective use of resources, but has to be traded off against the substantial increase in emergency department workload that occurs as a result of increased presentations with chest pain attributable to other causes,²⁴ a prospect that few clinicians would relish in the UK at present. The effects of such a campaign also wear off quickly after the first week of intervention,²⁵ so that the overall benefit remains doubtful.

CONCLUSION

As soon as a patient with AMI is unloaded from an ambulance another delay of at least 20 minutes is guaranteed. Prehospital administration permits thrombolysis to be given at the time when there is greatest potential for long term benefit, and when the largest amount of myocardium can be saved by even modest decreases in the "pain to needle" time.

"Fast track" systems will not overcome this delay, and if we have learnt anything from the movement of thrombolysis

from coronary care to the emergency department it is that thrombolysis should be given as soon as it is indicated, and by the first professional qualified to do so.¹

With training and support, advice on which is already available,²⁶ paramedics will be able to provide effective urban thrombolysis that saves lives and reduces long term morbidity. Certainly errors will be made, and complications will occur, but these will be no different to those already occurring in hospitals every day. There remains a need for high quality research, to compare prehospital and in hospital thrombolysis and determine their relative roles, but all the indications are that this new development will be both clinically and cost effective.

It seems that we have been given an opportunity to foster the natural development of thrombolysis. From its early growth on coronary care we have seen it through to adulthood. Now it is time for thrombolysis to go out into the wider world: to facilitate the research necessary to confirm this will be difficult, but also a demonstration of our own maturity.

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Funding: none.

Conflicts of interest: the author has previously received a small research grant from Ortivus, the manufacturers of "Mobimed" ECG and clinical data transmission equipment, but has no ongoing involvement with, or financial interest in, this company.

REFERENCES

- 1 **Edhouse JA**, Sakr M, Wardrope J, *et al*. Thrombolysis in acute myocardial infarction: the safety and efficiency of treatment in the accident and emergency department. *Emerg Med J* 1999;**16**:325–30.
- 2 **Department of Health**. National Service Framework For Coronary Heart Disease. London: HMSO, 2000. Also available at: <http://www.doh.gov.uk/nsc/coronary.htm#chdnsc>
- 3 **Rawles J**. New standard of 60 minutes has been proposed but may be too rigorous. *BMJ* 1999;**318**:1554.
- 4 **Anonymous**. *The role of telemedicine in the acute myocardial infarction workshop*. Warwick: Institute of Healthcare Management, 2000.
- 5 **Rawles J**, Sinclair C, Jennings K, *et al*. Call to needle times after acute myocardial infarction in urban and rural areas in northeast Scotland: prospective observational study. *BMJ* 1998;**317**:576–8.
- 6 **Millar-Craig MW**, Joy AV, Adamowicz M, *et al*. Reduction in treatment delay by paramedic ECG diagnosis of myocardial infarction with direct CCU admission. *Heart* 1997;**78**:456–61.
- 7 **Morrison LJ**, Verbeek PR, McDonald AC, *et al*. Mortality and prehospital thrombolysis for acute myocardial infarction: a meta-analysis. *JAMA* 2000;**283**:2686–92.
- 8 **Rawles J**. Magnitude of benefit from earlier thrombolytic treatment in acute myocardial infarction: new evidence from Grampian region early anistreplase trial (GREAT). *BMJ* 1996;**312**:212–16.
- 9 **Myers RBH**. Prehospital management of acute myocardial infarction: electrocardiogram acquisition and interpretation, and thrombolysis by prehospital care providers. *Can J Cardiol* 1998;**14**:1231–40.
- 10 **Anonymous**. The pre-hospital management of acute heart attacks: recommendations of a task force of the European Society of Cardiology and the European Resuscitation Council. *Eur Heart J* 1998;**19**:1140–64.
- 11 **Kudenchuk PJ**, Ho MT, Weaver WD, *et al*. Accuracy of computer-interpreted electrocardiography in selecting patients for thrombolytic therapy. *J Am Coll Cardiol* 1991;**17**:1486–91.
- 12 **Grijseels EWM**, Bouten MJM, Lendrink T, *et al*. Pre-hospital thrombolytic therapy with either alteplase or streptokinase. *Eur Heart J* 1995;**16**:1833–8.
- 13 **Weydahl PG**, Ljosland M, Stumberg S, *et al*. Prehospital ECG reduces the treatment delay in AML and facilitates prehospital thrombolysis. [In Norwegian]. *Tidsskr Nor Laegeforen* 2000;**120**:2247–9.
- 14 **Eisenberg MS**. *Life in the balance: emergency medicine and the quest to reverse sudden death*. Oxford: Oxford University Press, 1997:224–32.
- 15 **Gibler WB**, Kereiakes DJ, Dean EN *et al*. Prehospital diagnosis and treatment of acute myocardial infarction: a north-south perspective. *Am Heart J* 1991;**121**:1–11.
- 16 **Burdett-Smith P**. Estimating trauma centre workload. *J R Coll Surg Edinb* 1992;**37**:128–30.
- 17 **Coccolini S**, Berti G, Bosi S, *et al*. Prehospital thrombolysis in rural emergency room and subsequent transfer to a coronary care unit: Ravenna myocardial infarction (RaMI) trial. *Int J Cardiol* 1995;**49** (suppl):S47–58.
- 18 **Bermejo GJ**, Casero LA, Duran HJM, *et al*. The safety of the treatment of an acute myocardial infarction by immediate intravenous fibrinolysis in the regional hospital environment. [In Spanish]. *Rev Esp Cardiol* 1994;**47**:666–671.
- 19 **Widimsky P**, Groch L, Zelizko M, *et al*. Multicentre randomised trial comparing transport to primary angioplasty vs immediate thrombolysis vs combined strategy for patients with acute myocardial infarction presenting to a community hospital without a catheterisation laboratory. The PRAGUE study. *Eur Heart J* 2000;**21**:823–31.
- 20 **Loane MA**, Bloomer SE, Corbett R, *et al*. A randomised controlled trial assessing the health economics of realtime tele-dermatology compared with conventional care: an urban versus rural perspective. *Journal of Telemedicine and Telecare* 2001;**7**:108–18.
- 21 **Boersma E**, Maas ACP, Deckers JW, *et al*. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. *Lancet* 1996;**348**:771–5.
- 22 **Boersma E**. Acute myocardial infarction: bring the treatment to the patient. *Heart* 1999;**82**:404.
- 23 **Herlitz J**, Hartford M, Blohm M, *et al*. Effect of a media campaign on delay times and ambulance use in suspected acute myocardial infarction. *Am J Cardiol* 1989;**64**:90–3.
- 24 **Mitic WR**, Perkins J. The effect of a media campaign on heart attack delay and decision times. *Can J Public Health* 1984;**75**:414–18.
- 25 **Blohm M**, Herlitz J, Hartford M, *et al*. Consequences of a media campaign focussing on delay in acute myocardial infarction. *Am J Cardiol* 1992;**69**:411–13.
- 26 **Aufderheide TP**, Kereiakes DJ, Weaver WD, *et al*. Planning, implementation, and process monitoring for prehospital 12-lead ECG diagnostic programs. *Prehospital and Disaster Medicine* 1996;**11**:162–171.