Delays in the stroke thrombolysis pathway--identifying areas for improvement.

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Abstract

Despite international consensus on the benefits of thrombolysis for ischaemic stroke (IS), it remains underused. Guidelines now recommend a door-to-needle time of ≤60 minutes. We reviewed the rate and timeliness of thrombolysis for IS at our hospital. 323 stroke patients presented between January 2011 and April 2012.Thirty patients (10.6% of IS) were thrombolysed, mean age was 68.5 years (42 to 88) and 19 patients (63%) were male. Thirty-six patients (12.7% of IS) were not thrombolysed despite arriving within the time-window and symptom resolution was the commonest reason (15 patients; 42%). Despite most thrombolysed patients (42%) presenting to the Emergency Department during daytime working hours, there were delays at each step of the acute care pathway. The mean time for stroke team review was 23 minutes (5-50). The mean door-to-CT and the door-to-needle times were 60 minutes (25-95) and 92 minutes (46-130) respectively. In parallel with national stroke incentives, local audit can highlight barriers to uptake and efficiency within thrombolysis services.

Introduction

It is now almost two decades since the effectiveness of thrombolytic therapy foracute IS was first reported. Results from the NINDS-rtPA trial in 1995,[1] data from large randomized thrombolysis trials[2] along with a Cochrane review,[3] have supported the use of thrombolysis early in the acute IS setting. However, clinical outcomes are time dependent, with those receiving treatment more rapidly having better outcomes in the long and short-term. Pooled analysis of landmark trials reported that although patients benefited from treatment for up to 4.5h, there was a drop in the odds of a favourable outcome by a factor of two with each 90-minute period time delay.[2] Every effort is therefore needed to avoid delays in starting treatment.

Despite benefits, a limited proportion of eligible patients actually receive this treatment, with international reports documenting ongoing suboptimal rates(≤7%) even in well equipped centres.[4-6] Delays in hospital presentation significantly contribute to this, but even when many IS patients are deemed eligible for thrombolysis, the actual rates of treatment can be relatively low.[7,8]Consequently, there is growing interest in highlighting in-hospital obstacles that contribute to low treatment rates and the fragmentation of what should be a well-organized pathway of care from arrival at the hospital door to administration of therapy. Guidelines recommend a door-to-needle target time of≤ 60 minutes,[9,10] clearly requiring efficiency, including the rapid completion of clinical and imaging evaluation before initiating treatment in those without contra-indications. Evidence from the Get with the Guidelines-Stroke national USregistry[11] shows that less than one-third of acute IS patients who receive thrombolysis are actually treated within such guideline-recommended door-to-needle times. Consequently, the American Heart and Stroke Associations have launched 'Target: Stroke Initiative'[12] which includes multiple key best-practice strategies, and aims to achieve a door-to needle-time of ≤ 60minutes for at least 50% of IS patients. The effectiveness of implementing similar strategies has also been explored in Europe.[13]

This study aimed to review the thrombolysis service at Beaumont Hospital (BH) from January 2011 to April 2012 inclusive. We reviewed the rate of thrombolysis and analysed the times taken for medical review, radiological investigation and administration of thrombolysis amongst those eligible to receive such therapy. Reasons for withholding treatment in those who presented within the 4.5 hours treatment-window were also reviewed.

Methods

Beaumont is a 820-bed teaching hospital that provides emergency and acute care services to almost 300,000 people. The thrombolysis service is co-ordinated jointly by the Departments of Geriatric and Stroke Medicine and Neurology. A clear pathway of care outlines the steps that should be promptly undertaken from arrival of the patient with suspected stroke at the hospital, to imaging within the radiology department and administration of thrombolysis, where appropriate. In parallel, an education programme updates rotating medical staff within the ED and stroke service about this care pathway. The hospital stroke registry (for January 2011 to April 2012 inclusive) was reviewed. Two paper-based review proformas were designed for data collection: a 'monthly proforma' collected information on overall numbers of stroke patients that presented each month and a 'thrombolysis' proforma collected information on all thrombolysed patients during the study period. Patients' electronic records and charts were reviewed for any relevant data unavailable within the stroke registry and details of relevant radiological investigations were accessed through the McKesson system.

Results

323 stroke patients presented over a sixteen-month period from January 2011 to April 2012 inclusive (Figure 1). Overall, 10.6% of all IS patients (30patients) received IV thrombolytic therapy during the study timeframe, although rates of thrombolysis varied greatly from month to month (Figure 2).

Table 1 Documented risk factors and medications (at baseline) in thrombolysed patients	
	N (%)
Risk factors	
Hypertension	18 (60)
Hyperlipidaemia	14 (46)
Atrial fibrillation	8 (26)
Cigarette smoking	7 (23)
Ischaemic heart disease	5 (17)
Previous stroke or TIA	8 (26)
Diabetes	4 (13)
Medications	
Anti-platelet therapy	15 (50)
Dual anti-platelet therapy	4 (13)
Anticoagulation	3 (10)
Antihypertensive therapy	11 (38)
Statin	10 (33)

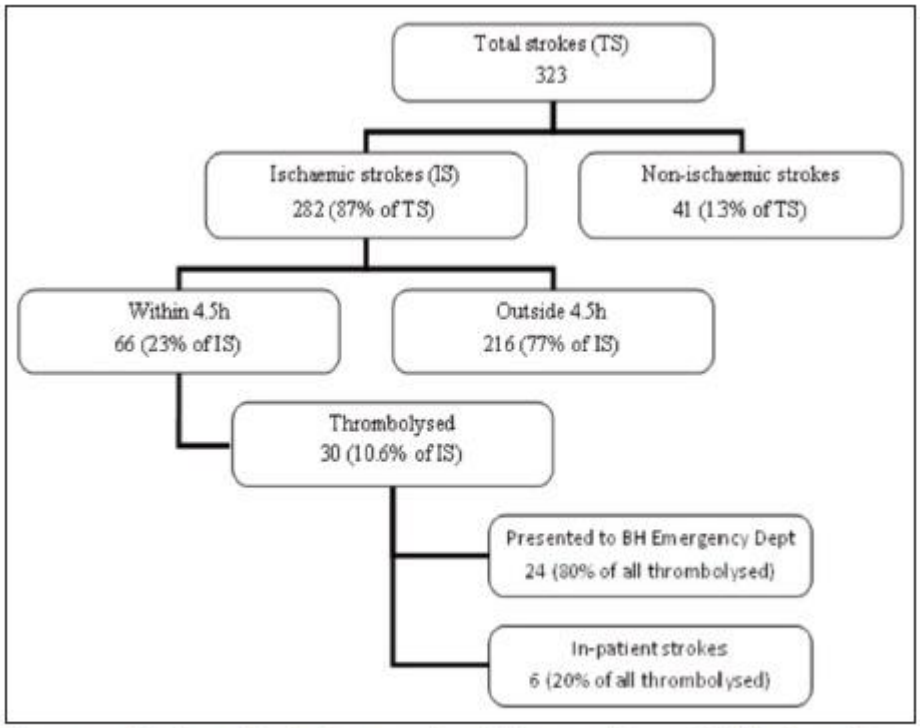

Figure 1 Numbers of patients presenting to Beaumont Hospital (BH) during the 16 month study timeframe (January 2011 to April 2012)

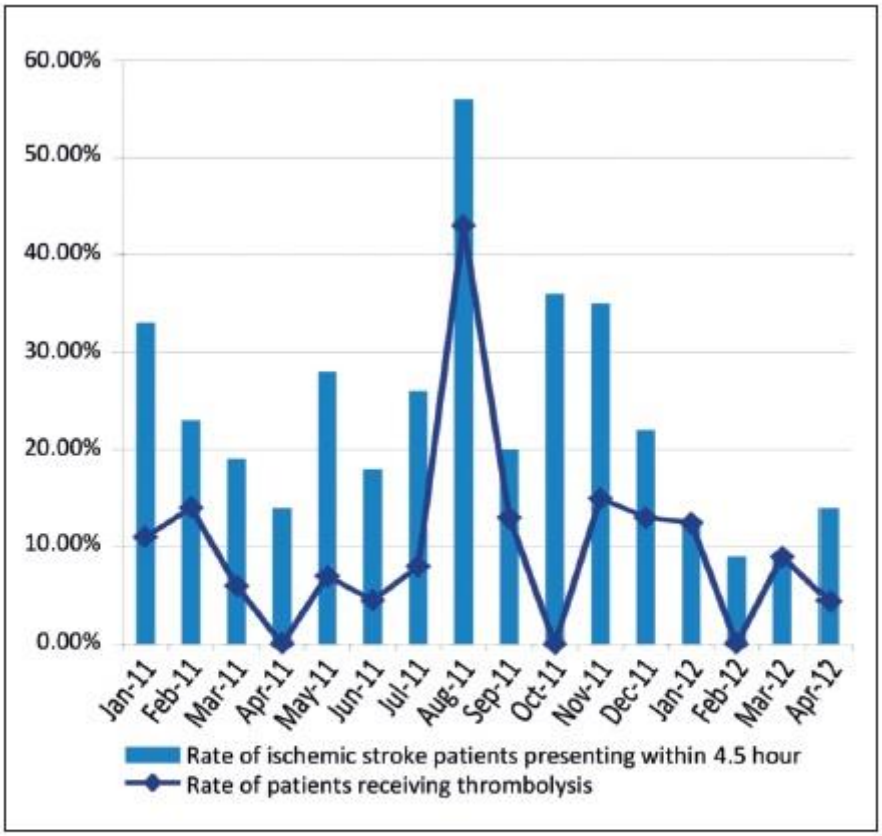

Figure 2 Percentage rates of ischaemic strokes presenting within the 4.5 hours (no. of ischemic strokes within the 4.5 hour window/ total ischemic strokes for that month) and the percentage rate of thrombolysis for each month (no. of patients receiving thrombolysis per month/ total ischemic strokes that month)

Thrombolysed patients
The mean age of this cohort was 68.5 years (range 42 to 88 years) and almost two-thirds (19 patients; 63%) were male. Baseline data are outlined in Table 1. Of the 30 thrombolysed patients, 4 patients had a suboptimal response and were considered for subsequent on-site intra-arterial (IA) thrombolysis and/orthrombectomy. Almost half (10; 42%) of those who presented after their stroke onset arrived between 9am and 5pm, with a further 9 patients (38%) presenting between 5pm and midnight. The remaining patients (20%) presented overnight (midnight to 9 am). Almost all (5/6) of the thrombolysed in-patient strokes received their treatment between 9am and 5pm.

Timelines to administration of thrombolysis
In cases where times were poorly documented within medical notes, nursing notes were reviewed. For patients who presented to the ED after their stroke onset, the mean time (from door) for a review by the stroke service was 23 minutes(5-50). The mean door to CT time was 60 minutes (25-95) and the mean door to needle time was 92 minutes (46-130). For patients who had their stroke onset after admission to hospital, the mean time from symptom onset to review by the stroke service was 9 minutes (5-20). The mean time (from symptom onset) to CT was 42 minutes (15-90) and to needle was 99 minutes (60-150). The proportion of time taken in each step of the treatment pathway is outlined in Figure 3.

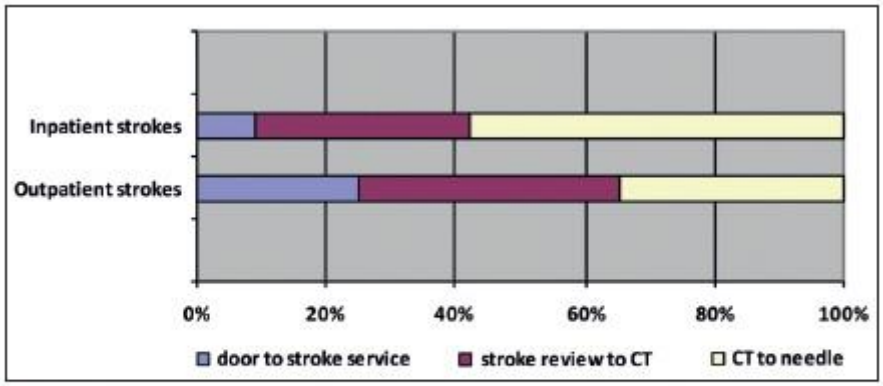

Figure 3 Proportion of time taken from door (or symptom onset) to review by stroke service, CT and needle for patients presenting to ED (outpatient strokes) and patients who have stroke in hospital (inpatient strokes)

Clinical outcomes
Haemorrhagic transformation (defined as any degree of haemorrhage seen radiologically) at 24hours post thrombolysis was noted in 6/30 patients (20%). However this rate decreased to 6.5% (2/30) when the presence of neurological worsening, as defined by the NINDS study,[2] was incorporated into the definition. For thrombolysed patients, the mean number of days spent in the acute stroke unit was 19 (1-63) and the mean length of hospital stay was 44 days (2-164). Most patients were discharged to their own home (26;88%). The proportion of patients with a mRS of ≤2 was 3% at 7 days, 23% at 30 days and 37% at 90 days. The 7-day, 30-day and 90-day mortality was 6%, 13% and 16% respectively.

Patients who presented within the 4.5h time-window and were not thrombolysed
Of the 66 patients who presented within 4.5 hours, 36 patients (12.7% of all IS) were not thrombolysed due to a variety of reasons. The commonest reason was symptom resolution (15 patients; 42%). Other documented reasons for not administering thrombolysis were low NIHSS <4 (14%), patient on anticoagulation (dabigatran (2) or warfarin with INR≥2 (3); 14%) or high NIHSS >24 (8%).

Discussion
Our results show that, although most thrombolysed patients presented during full-service working hours, there was room for improved efficiency at each step in the acute thrombolysis care pathway. Only one-fifth of patients were thrombolysed within the target time-window of one hour and just over one-third were thrombolysed within 90 minutes of arrival at the door (or symptom onset for in-patient strokes). Delivery of thrombolysis took slightly longer amongst in-patients, possibly owing to reduced awareness of the urgency inactivating the stroke care pathway on the wards. In particular we found that there was scope to substantially decrease the proportion of time taken from stroke service review to CT and from CT to needle. During the study timeframe, thrombolysis was not commenced in the radiology department but instead the patient was transferred to another ward for administration of the thrombolysis bolus. Practice has since changed at our centre such that thrombolysis is now commenced in the radiology department.

Although the thrombolysis rate at our hospital compares favourably with international standards, there is room for improvement. One striking finding was that just under one-quarter of patients in our cohort presented within the required time-window for consideration for thrombolytic treatment, similar to that reported in the Get with the Guidelines Stroke Program 2002 to 2009.[14]Heightened public awareness of stroke symptoms, and of the need to present urgently to emergency services can result in more prompt presentation of patients to emergency services.[15,16] However, how campaigns are best delivered and whether they result in sustained improvements in thrombolysis rates remains unclear.[17,18] The upgrading of emergency ambulance services can impact positively on time between symptom-onset to arrival athospital,[19] although the co-ordination of ambulance services at a national level can be challenging. In Ireland the Health Service Executive National Stroke Program is currently working in partnership with national ambulance services to implement ambulance efficient access protocols for patients with ischaemic stroke.

Studies assessing effective, multi-dimensional implementation strategies (education programmes, identification of treatment barriers and service goal-setting) have demonstrated improvements in administration rates and the efficiency of delivery of thrombolysis in IS. The PRACTISE trial[13] implemented strategies to tackle under-utilisation of thrombolysis for IS. They identified obstacles to treatment as inter-organisational, intra-organisational, medical or psychological, against which they targeted intervention strategies. Patients in the intervention centres were more likely to receive thrombolysis (adjusted OR 1.58; 95%CI 1.11-2.27) and a major component of this effect was the more appropriate local application of clear contraindications to treatment. However the intervention did not improve the timeliness of treatment administration. The INSTINCT study assessed whether a similar multilevel intervention could increase alteplase use in community hospitals in Michigan.[20] Although the proportion of thrombolysed patients increased between the pre-intervention and post-intervention periods in intervention hospitals to a greater extent than the control hospitals, the difference was not significant(RR 1.37; 95%CI 0.96-1.93; p=0.08). Authors identified barriers such as inter-departmental communication, familiarity with treatment guidelines and physician motivation as primary issues.

Of those patients who presented to hospital within the 4.5 hour treatment-window, almost one-half (45%) were thrombolysed. The documented reasons for withholding treatment in the remaining patients were clear and in accordance with local and international guidance. The main reason for withholding treatment was symptom resolution, a contra-indication that is clearly outlined in thrombolysis protocols. However, deterioration following spontaneous improvement can occur in up to 30% of certain subgroups.[21] There is emerging evidence that treatment may be unnecessarily withheld in a substantial number of patients due to the application of strict thrombolytic exclusion criteria, many of which are not evidence-based. Studies now suggest that thrombolysis can be used safely in many excluded groups,[22,23] including those with minor, fluctuating or resolving symptoms, advanced age or seizure at onset. Of patients in our study that had thrombolysis

withheld due to symptom resolution, approximately three quarters had an acute infarct on imaging. As further evidence emerges and protocols are revised, perhaps more patients who arrive on time will be eligible for treatment.

In Ireland, significant advances have been made in our stroke services (including thrombolysis rates) since the publication of the National Audit of Stroke Care in 2007. In conjunction with the launch of the National Stroke Program, the Stroke Register was established to collect information on the quality of care administered to stroke patients and this will help to identify areas where prioritised changes are necessary. Multiple guidelines, care bundles and pathways have been disseminated and service development has included the provision of telemedicine to enhance the co-ordination of thrombolysis services over large geographical areas. Stroke governance structures have also been enhanced with the development of local stroke teams and hospital networks and the appointment of clinical leaders. However, in parallel with such collaborative national incentives, local audit and focused initiatives must take place, which can result in significant reductions in time to CT andneedle.[24,25] This would result in more favourable outcomes for many more patients with IS presenting to acute services.

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