

# Auditing thrombolysis service for stroke at Mater Dei Hospital

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## Abstract

**Objectives:** Thrombolysis for acute ischaemic stroke was introduced locally in October 2010. In 2012, the practice was audited to analyse the prevalence of inclusion and exclusion criteria for thrombolysis. Data about the local incidence of stroke, demographics and outcome was also obtained.

**Methods:** All patients admitted to Mater Dei Hospital with a diagnosis of stroke over an 8 month period were recruited. Standard data collection sheets were used to obtain data.

**Results:** 251 patients were admitted with a confirmed stroke over the 8-month period. The time of onset was recorded in only 37.4% of cases. All patients had CT scanning of the brain within 24 hours of presentation, of which 70% were performed within 3 hours. The commonest 5 reasons for which thrombolysis was withheld were: presentation beyond 3 hours of symptom onset (73.7%), age over 80 years (29.9%), hypertension (13.9%), haemorrhagic stroke (13.1%) and minor deficit or rapid improvement (8.4%). Overall, only 4 patients (1.59%) were eligible for thrombolysis in our cohort, all of whom received the treatment.

**Conclusion:** The study identified late presentation to A&E as the commonest exclusion criterion for thrombolysis. This prompted the launch of a stroke awareness 'Act FAST' campaign and increasing efforts to educate general practitioners to refer patients with acute stroke immediately. In addition, stroke pathway booklets were reviewed and simplified to increase their use. Since July 2013, the time window has been widened to 4.5 hours in accordance with international guidelines. Ongoing audit of thrombolysis is being carried out.

## Keywords

Thrombolysis, cerebrovascular accident, stroke

## Introduction

### *Background*

Most strokes occur secondary to arterial occlusion in the circulation to the brain. Thrombolysis in such circumstances was first studied in the late 1960s and the 1970s but these studies had to be abandoned in view of a high risk of intracranial haemorrhage. Since then, new thrombolytic agents such as recombinant tissue plasminogen activator (rtPA) have been developed. Studies carried out in late 1980s and early 1990s reported positive outcomes with respect to recanalisation and safety of the new drugs.<sup>1</sup> The positive results prompted further studies, including a larger randomised, placebo-controlled trial by the National Institute of Neurological Diseases and Stroke, the results of which were published in 1995. This study ensured that patients were treated within 3 hours of symptom onset and found that there was significant benefit in patients who received thrombolysis, compared to those treated with placebo. This benefit was evident at three months from stroke onset, with no increase in mortality.<sup>2</sup> The first National Clinical Guidelines for Stroke were published by the Royal College of Physicians (RCP) in the year 2000. At the time, the use of rtPA was limited to specialist centres under strict criteria. The drug was not yet licensed in the UK.<sup>3</sup> In contrast, latest RCP guidelines published in 2012 recommend that thrombolysis is considered within 3 hours of symptom onset "regardless of age or stroke severity" provided there are no contraindications. Patients under the age of 80 should be considered for treatment between 3 and 4.5 hours of symptom onset.<sup>4</sup>

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*Aims of the audit*

In 2008, after the publication of the third edition of the National Clinical Guidelines for Stroke by the Royal College of Physicians of London, a local audit was carried out to compare the practice with the standards set by the guideline.<sup>5</sup>

Based on the results of the audit, stroke guidelines were formulated at Mater Dei Hospital. These have been readily available as booklets at the Accident and Emergency department. The pathways were introduced in October 2010 together with a thrombolysis service, aiming to ensure that patients eligible for thrombolysis are identified at triage and are fast-tracked through the necessary investigations. The documents also cover the management of patients who do not receive thrombolysis based on international recommendations.

In 2012 a second study was carried out. The main aim was to audit the practice of thrombolysis in acute ischaemic stroke with an analysis of the prevalence of the inclusion and exclusion criteria. Secondary aims included obtaining data about the incidence of stroke, demographics and outcome.

The results were then analysed to identify any outstanding inclusion or exclusion criteria that could be addressed in order to increase the number of patients who could benefit from this treatment.

**Methodology**

*Patient Population*

The audit covered the 8-month period between the 1st March and the 31st October 2012. Patients who were discharged with an alternative diagnosis including that of a transient ischaemic attack, were excluded. In-patient strokes were not included due to the absence of an effective mechanism to identify these patients.

*Data collection Sheet Design*

Standard data collection sheets were designed. Data collected in the audit was based on the content of local stroke guideline booklets. The audit focused on the inclusion/exclusion criteria for thrombolysis.

*Data Collection*

Ethical approval was obtained from the University of Malta Research Ethics Committee. Data was collected prospectively, recording documentation of assessment, results and management. Sources of data collection included access to patient files, nursing notes, PACS (Picture Archiving and Communications System), iSOFT (Healthcare Software) and ECS (Electronic Case Summary).

**Results**

*Recruitment*

Over the 8-month period of the audit, a total of 321 patients were admitted to hospital with a clinical

diagnosis of stroke, of which 70 were excluded due to a different discharge diagnosis.

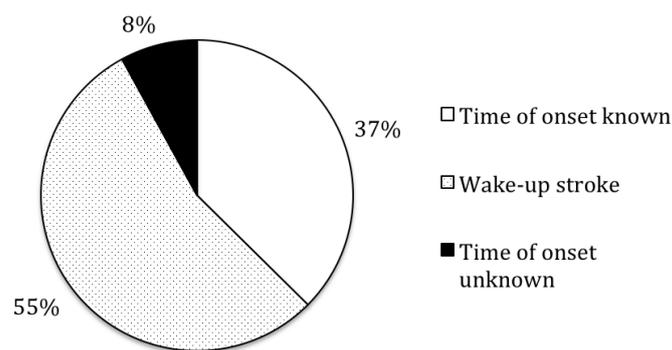
*Demographics*

The total number of patients included was 251; of whom 137 were male and 114 female. The mean age was 73 years (range 21 – 95), with a median age of 75 years.

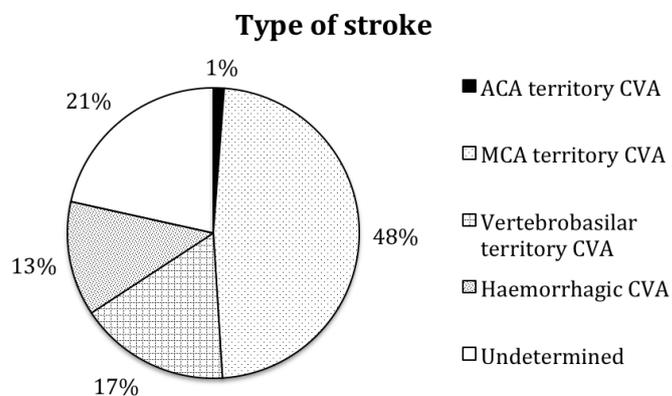
*Time of onset, presentation and discharge outcome*

The time of onset of symptoms was known in 37.4% of patients (n=94). Of those with unknown onset, 7.9% (n=20) were wake up strokes. 72.6% (n=182) presented to the emergency department between 8.00 a.m. and 8.00 p.m (Figure 1). Figure 2 displays the type of stroke classified by the arterial territory involved, if it was possible to determine it clinically or by imaging. 26.2% (n=66) presented within 3 hours of initial symptoms (Figure 3).

**Figure 1: Percentage of strokes classified by time of symptom onset**

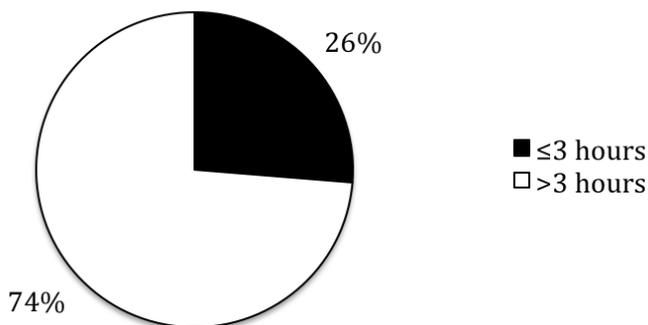


**Figure 2: Type of stroke as determined by symptomatology and/or imaging**



**Figure 3:** Time frame between symptom onset and presentation to the Accident and Emergency Department

**Time of presentation**

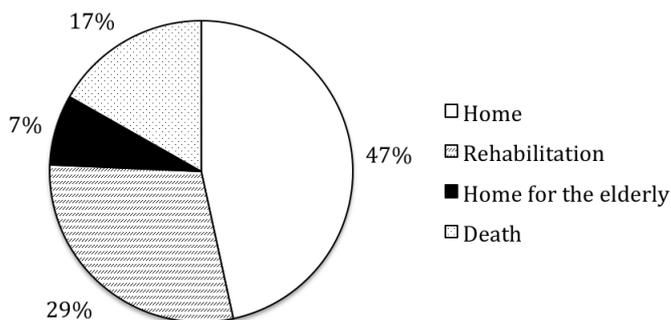


*Brain imaging*

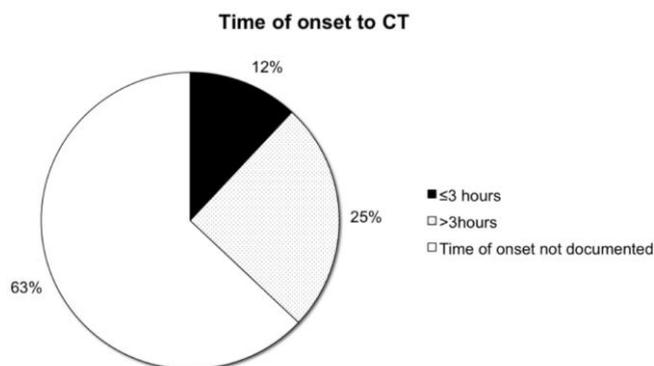
All patients presenting with a presumed stroke underwent CT scanning of the brain within 24 hours of presentation. 70% of scans were performed within 3 hours of presentation. Data regarding the timeframe between symptom onset and CT scanning is limited because the time of onset was only documented in a minority of cases. The time delay from symptom onset and from presentation to CT imaging is illustrated in figure 5.

**Figure 4:** Pie chart showing the discharge destination of patients admitted with stroke

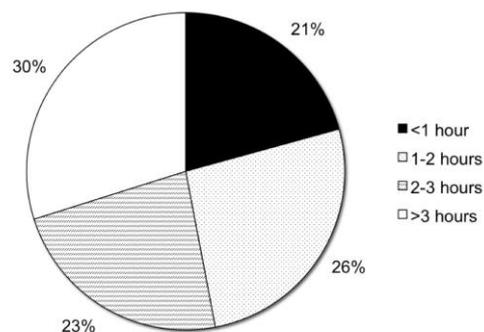
**Discharge destination**



**Figure 5:** Pie charts showing the time frame between (a) symptom onset and (b) time of presentation to cross-sectional brain imaging



**Time of presentation to CT**



The scans showed features of early ischaemic change in 51 patients (20.3%), extensive ischaemic change (more than a third of MCA territory) in 10 patients (4.0%), and haemorrhage in 33 patients (13.1%). No significant abnormality was reported in the remaining cases. Results of CT scans are presented in figure 6.

**Figure 6:** Findings on cross-sectional brain imaging of patients admitted with a diagnosis of stroke

**CT scan findings**

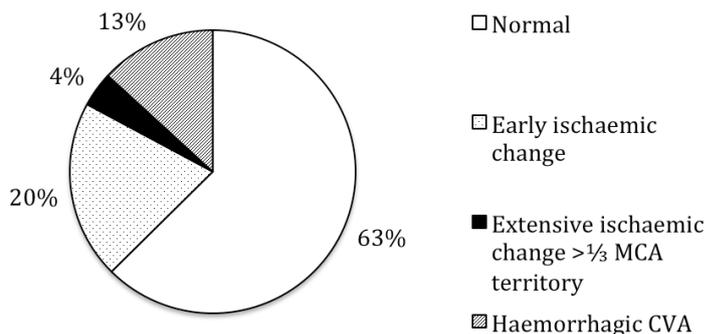
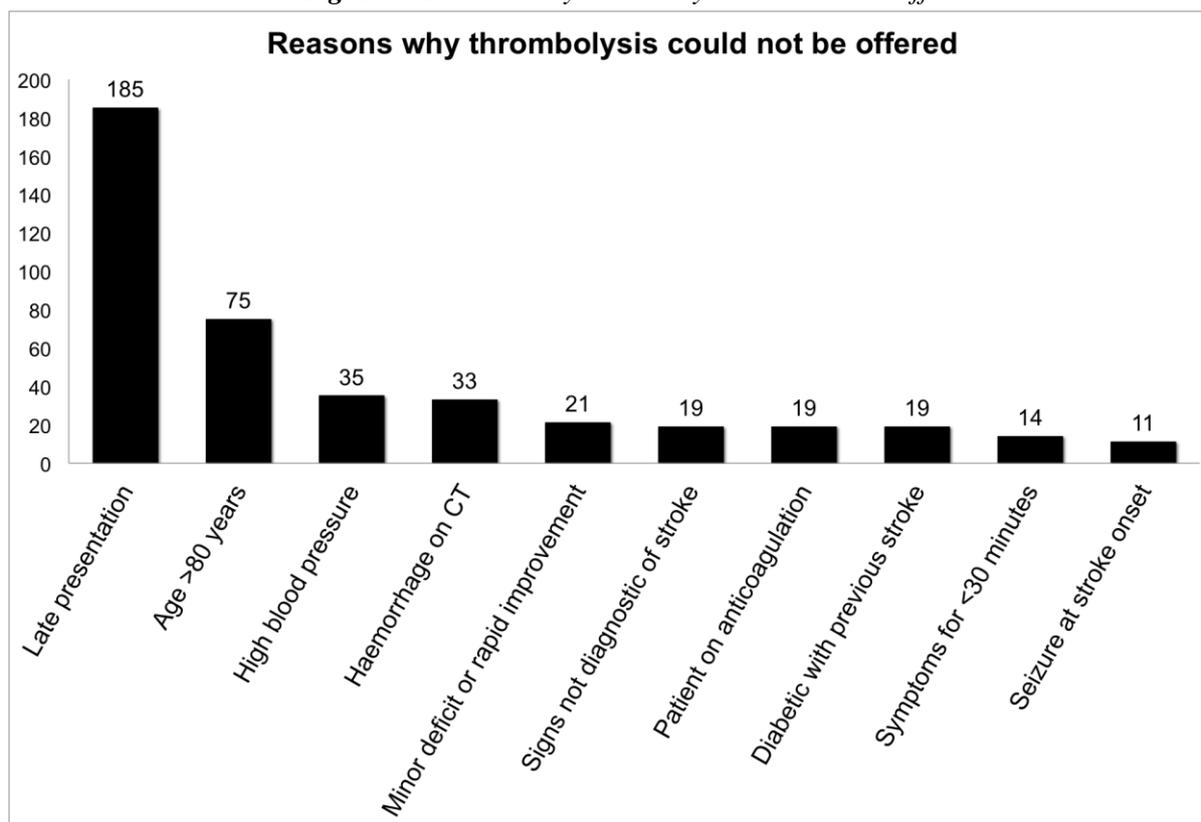


Figure 7: Reasons why thrombolysis could not be offered



*Thrombolysis*

4 patients (1.59%) were eligible for thrombolysis after evaluation of all the inclusion and exclusion criteria, all of whom accepted to receive this treatment modality. The commonest ten reasons why thrombolysis could not be offered to the patients are listed below and shown in figure 7:

1. presentation after 3 hours of onset of symptoms: 185 patients (73.7%)
2. age >80 years: 75 patients (29.9%)
3. blood pressure above 185/110 mmHg: 35 patients (13.9 %)
4. haemorrhagic stroke: 33 patients (13.1%)
5. minor deficit or improving symptoms: 21 patients (8.4%)
6. signs and symptoms not diagnostic of stroke: 19 patients (7.6%)
7. prior anticoagulation: 19 patients (7.6%)
8. diabetes with previous stroke: 19 patients (7.6%)
9. symptoms lasting less than 30 minutes: 14 patients (5.6%)
10. seizures: 11 patients (4.4%)

The characteristics of the thrombolysed patients are presented in the table below:

Table 1: Characteristics of the thrombolysed patients

Patient	Age	Sex	NIHSS	CT min	Complications of rTPA	24h NIHSS	Outcome
1	57	M	9	11	No	4	Rehabilitation
2	57	F	11	9	No	13	Rehabilitation
3	59	M	14	28	No	15	Died after 4 days
4	65	M	11	41	No	15	Home

*Documentation*

Documentation was found to be poor in the audit, even after introduction of the stroke pathway booklets. The ROSIER scale used at triage of patients at the Accident and Emergency Department was completely and appropriately filled in most cases. However the stroke booklet was filled only in a minority of cases, and the data was scattered. National Institute of Health Stroke Scale (NIHSS) was documented for only 55 patients (22%). Documentation of the presence of inclusion or exclusion criteria was often absent or unclear. For example, for 9 patients for whom thrombolysis was withheld, the reason was only evident after going through the patients’ case notes thoroughly.

**Discussion**

Thrombolytic therapy is of proven and substantial

benefit for select patients with acute cerebral ischaemia. The evidence for thrombolysis in stroke to date includes 21 completed randomized controlled clinical trials enrolling 7152 patients, using various agents, doses, time windows, and intravenous or intra-arterial modes of administration.<sup>6</sup>

Despite being the most effective therapy if instituted within the first 4.5 hours, thrombolysis is still underused worldwide.<sup>7</sup> A study published from the Intercollegiate Working Party for Stroke showed that thrombolysis rates are currently low in the UK. 28% of patients presented within 3 hours of admission. Of these only 14% met all four National Institute of Neurological Disorders and Stroke study inclusion criteria. By increasing the time window to 4.5 hours only another 2% became eligible. Overall only 1.4% of patients were thrombolysed<sup>8</sup>, which is in fact comparable to our 1.59%. Locally, the time window has been widened from 3 to 4.5 hours of symptom onset since July 2013, in accordance with international guidelines based on ECASS-3 trial results.<sup>9</sup>

The local guidelines introduced in October 2010 were geared at recognising patients who will be eligible for thrombolysis from triage. Despite short distances and relatively easy access to medical services in Malta, we note that delayed presentation to A&E was the commonest reason for non-suitability for thrombolysis. Prompt presentation relies on the patients' or witnesses' ability to identify physical changes and recognize the need for urgent medical assistance. Hence the call for nationwide promotion of stroke awareness, by simple achievable means, such as advertising on public media the 'Act FAST' campaign – i.e. "Facial weakness, Arm weakness or Speech problems? Time to call emergency services". Stroke awareness leaflets have been developed in collaboration with the Health Promotion Department and launched in October 2013. Likewise, since 2008, there have been efforts to educate general practitioners to refer immediately and appropriately for medical treatment. The results of a public education campaign will probably take time to become evident but efforts at continuing to raise the awareness should intensify.

Poor compliance with the use of local guideline booklets raised the necessity to review the stroke pathway booklets and simplify them to make them more user-friendly. Review of these booklets was accompanied by refresher courses for the medical doctors in the department of A&E and department of Medicine. The local guidelines are continuously being updated, based on the recent changes in international guidelines<sup>4</sup>.

These efforts seek to increase the number of patients who benefit from thrombolysis. To date, 37 patients have received this treatment for ischaemic stroke. Ongoing audit of thrombolysis is being carried

out. We hope to publish results after five years of service.

## References

1. Adams HP, Brott TG, Furlan AJ, Gomez CR, Grotta J, Helgason CM et al. Guidelines for Thrombolytic Therapy for Acute Stroke: A Supplement to the Guidelines for the Management of Patients With Acute Ischemic Stroke A Statement for Healthcare Professionals From a Special Writing Group of the Stroke Council, American Heart Association. *Circulation*. 1996; 94: 1167-1174.
2. The National Institute of Neurological Disorders and Stroke rt-PA Study Group. Tissue Plasminogen Activator for Acute Ischaemic Stroke. *N Engl J Med* 1995; 333: 1581-1588.
3. Wise J. New clinical guidelines for stroke published. *BMJ*. 2000 Mar 25; 320(7238): 823.
4. Intercollegiate Stroke Working Party. National clinical guideline for stroke, 4th edition. London: Royal College of Physicians, 2012.
5. Mallia M, Dingli P, Micallef D, et al. Stroke audit at Mater Dei Hospital; Benchmarking Local Practice. *Malta Medical Journal* (in press).
6. Saver JL. Thrombolytic Therapy in Stroke [Internet]. *eMedicine*. [updated 2012 Sep 18; cited 2014 Jan 14]. Available from: <http://emedicine.medscape.com/article/1160840>
7. Lahr MMH, van der Zee D-J, Vroomen PCAJ, Luijckx G-J, Buskens E. Thrombolysis in Acute Ischaemic Stroke: A Simulations Study to Improve Pre- and in-Hospital Delays in Community Hospitals. *PloS ONE* 8(11): e79049.
8. Rudd AG, Hoffman A, Grant R, Campbell JT, Lowe D; Intercollegiate Working Party for Stroke. Stroke thrombolysis in England, Wales and Northern Ireland: how much do we do and how much do we need? *J Neurol, Neurosurg Psychiatry* January 2011 82(1): 14-19
9. Hacke W, Kaste M, Bluhmki E, Brozman M, Dávalos A, Guidetti D, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. (ECASS III) *N Engl J Med* 2008 Sep 25; 359(13):1317-29.