A Retrospective Cohort Study on the Use of Intravenous Thrombolysis in Stroke Mimics

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Background: The urgency of intravenous thrombolysis in acute ischemic stroke can lead to inadvertent thrombolysis of patients with nonstroke diagnoses (stroke mimics), increasing the risk of adverse events. The objectives of this study were to compare thrombolysed acute ischemic stroke and stroke mimic cases based on demographic factors, physiological parameters, radiological findings, and clinical presentation, and to evaluate the clinical implications of thrombolysing stroke mimics. *Methods:* A retrospective analysis of a single-center database of all thrombolysed strokes and mimics over a period greater than 3 years. Diagnoses were confirmed by expert consensus after a review of clinical factors and imaging. Intercohort variation was assessed using Wilcoxon rank-sum or Pearson's chi-square test. *Results:* The stroke mimic cohort tended to be younger (mean age 59.9 years versus 73.7 years, $P < .001$) and had a lower National Institutes of Health Stroke Score at presentation (mean 5.9 points versus 6.4 points, $P < .01$). However, the time taken from the onset of symptoms to delivery of thrombolytic drugs was longer in the mimic cohort (mean time 170 minutes versus 138 minutes, $P < .01$). Any differences in blood glucose ($P = .07$), time taken from hospital arrival to delivery of intravenous thrombolysis ($P = .57$), and blood pressure on admission (systolic, $P = .09$ and diastolic, $P = .34$) were not statistically significant. No adverse events were reported in the mimic cohort. *Conclusion:* Despite similarities in clinical presentation, thrombolysed stroke mimics are of a different physiological and demographic population, and are associated with fewer adverse events compared with thrombolysed acute ischemic stroke patients. **Key Words:** Thrombolysis—acute ischemic stroke—stroke mimics—t-PA—adverse events.

Introduction

Timely administration of intravenous thrombolysis with tissue plasminogen activator (t-PA) is effective for the management of acute ischemic stroke (AIS).[1,2] Current guidelines allow a window of 4.5 hours from onset to administration reflecting the time-dependent benefit of t-PA.[3] However, this can lead to incorrect thrombolysis of nonvascular conditions, often of various etiology (i.e., a stroke mimic).[4,5]

Common causes of stroke mimics include seizures, hypoglycemia, and migraines.[6,7] Although these conditions are physiologically distinct from AIS, overlap between presenting symptoms makes it difficult to distinguish between the two. Literature reports aphasic disturbances, diplopia, and dysarthria as common presenting

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stroke mimic symptoms.[8] We compared the demographic, physiological, and clinical characteristics of stroke mimics with AIS cases thrombolysed at a London Hyper-acute Stroke Unit (HASU). We also evaluated the safety and clinical implications of thrombolysing stroke mimics based on radiological findings.

Methods

The study was a retrospective analysis of patients admitted to Imperial College Healthcare NHS Trust (ICHNT) HASU between February 14, 2012, and June 15, 2015, inclusive. All patients thrombolysed for presumed AIS were included; thrombectomy cases were excluded.

A diagnosis of stroke mimic was reached following a review of clinical factors and imaging results by expert consensus. Intracerebral hemorrhage was classified following thrombolysis after an independent review of imaging results by two separate investigators.

Demographic, physiological, and clinical factors were compared between the stroke mimic cohort and AIS cohort: patient age and gender; symptom onset to administration of t-PA time; hospital arrival to administration of t-PA time; systolic and diastolic blood pressures, capillary blood glucose, incidence of post-thrombolysis intracerebral hemorrhage; and National Institutes of Health Stroke Score (NIHSS) at admission and pre-event modified Rankin Scale (mRS). Intercohort variation was assessed using Wilcoxon rank-sum or Pearson's chi-square test, depending on the normality of data. All statistical tests were two sided and a P value less than .05 was used to indicate statistical significance. Outcome variables are presented with descriptive statistics where appropriate. All analyses were performed using Stata 14 (StataCorp LP, Texas, USA).

Anonymous data previously acquired for service evaluation purposes were used in this study. The study was reviewed locally and further ethical review was not deemed necessary.

Results

A total of 535 patients were admitted to ICHNT HASU from February 14, 2012, to June 15, 2015, inclusive. After excluding 46 patients who were treated with thrombectomy, 489 underwent thrombolysis for presumed AIS. A statistical summary and baseline clinical characteristic from the data available are offered in Table 1. Missing data were due to lack of documentation, and were completely at random (Table 1).

Stroke Mimic Diagnoses

Following the retrospective review, 50 (11%) of the 489 eligible patients were diagnosed as having a stroke mimic. Of these patients with stroke mimic, 14 (28%) were diagnosed with migraine, 11 (22%) with seizures, and 10 (20%) with functional disorders. Other less common diagnoses included the following: Bell's palsy (2 patients, 4%), chest pain (1 patient, 2%), collapse (2 patients, 4%), lower respiratory tract infection (2 patients, 4%), previous stroke (4 patients, 8%), previous maxillary sinusitis (1 patient, 2%), vasculitis (1 patient, 2%), and vestibular neuritis (2 patients, 4%) (Table 2).

Demographical and Physiological Characteristics

The age range of the stroke mimic cohort was 27–100 years, with an average of 59.5 years (standard deviation [SD] ± 19.2). This group was significantly younger than the AIS group (mean: 73.7 years, SD ± 14.5) (Wilcoxon rank-sum test; $P < .01$). There were no significant differences in patient gender (Pearson's chi-square test; $P = .95$).

Although the mean blood glucose level on admission was lower in the mimic cohort (7.2 mmol/L versus 7.3 mmol/L), this was not statistically significant (Wilcoxon rank-sum test; $P = .07$). The systolic and diastolic blood pressures on average were lower in the mimic cohort (149 mmHg versus 154 mmHg systolic, and 79 mmHg

Table 1. *The patients were divided into stroke mimic cohort and stroke cohort, and the number of patients in each parameter, the median, and the IQR are given. The data were obtained from an anonymized ICHNT dataset*

	Stroke cohort No. of results	Stroke mimic cohort No. of results
Gender (% male)	439 (54)	50 (54)
Age, years (median, IQR)	439 (76, 20)	50 (56, 33)
Door to needle time (median, IQR)—min	432 (37, 22.5)	49 (38, 19)
Onset to needle time (median, IQR)—min	386 (121.5, 74)	48 (148, 112)
Systolic blood pressure (median, IQR)—mmHg	433 (155, 32)	48 (150, 25.5)
Diastolic blood pressure (median, IQR)—mmHg	431 (80, 22)	48 (78.5, 18.5)
Glucose (median, IQR)—mmol/L	420 (6.6, 2.4)	44 (6.1, 1.7)
NIHSS on presentation (median, IQR)	431 (8, 9)	46 (5, 8)
Pre-event mRS (median, IQR)	436 (0, 1)	49 (0, 0)

Abbreviations: ICHNT, Imperial College Healthcare NHS Trust; IQR, interquartile range; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Score.