Factors influencing the delivery of thrombolysis to patients with acute ischemic stroke.

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Introduction

Stroke is the third leading cause of mortality in the UK after heart diseases and cancer with approximately 150/100,000 stroke patients every year (1). There are two types of strokes as illustrated below. 85% of strokes are ischemic, caused by a clot stopping blood flow to the brain and the other 15% are haemorrhagic strokes, caused by bleeding into the brain.

Haemorrhagic stroke
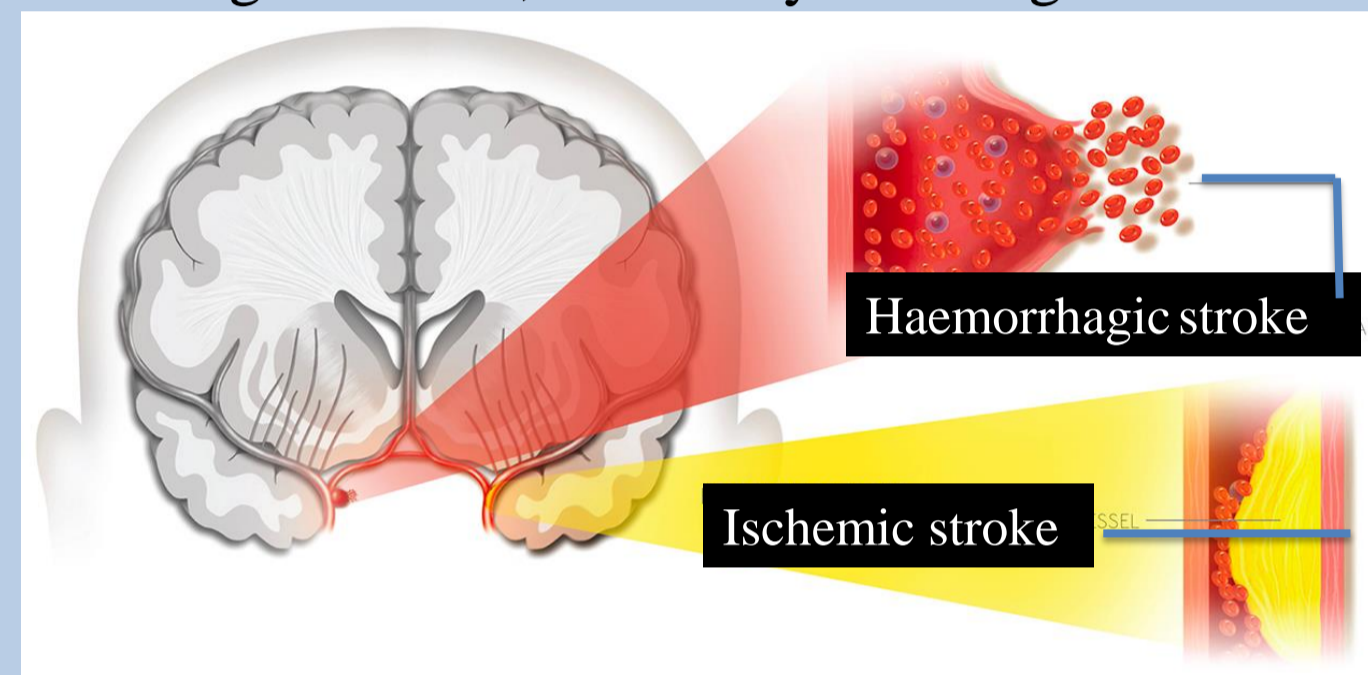
Ischemic stroke

NICE recommendation for stroke therapy is a thrombolytic drug, t-PA which dissolves clots to restore blood flow to the brain. It has to be given within 4.5 hours after the onset of acute ischemic stroke(2). Evidence showed that benefits outweigh the risks of thrombolysis, however thrombolysis rates still vary across all stroke units in the UK. Hence, we seek to study the factors which influence the delivery of thrombolysis in terms of patients' clinical features, health-seeking behaviors and subsequent outcomes in order to reduce unwarranted variation and to inform target areas for service improvement in stroke care.

Aims

1. To compare the clinical features, health-seeking behaviours and outcomes of patients with acute ischemic stroke who do and do not receive thrombolysis.
2. To explore other patient-specific factors influencing thrombolysis delivery to patients with acute ischemic stroke.

Methods

Data of 2371 stroke patients admitted to Northumbria Healthcare NHS Trust between 1.1.2013 till 15.06.2015 were obtained from the Sentinel Stroke Audit Programme (SSNAP). SSNAP is a national clinical audit which collected data from 80,000 stroke patients since January 2013(3). Data was analysed and compared using univariate and multivariate logistic regression.

Results

Total number of patients with ischaemic or haemorrhagic stroke:

Acute ischemic stroke	2083 (88%)
Primary intracranial haemorrhage	288 (12%)

Table below shows the percentages of stroke patients who did and did not receive thrombolysis based on their clinical features.

	Thrombolysed	Non-thrombolysed	P-value
Gender			0.634
Female	158 (48.9%)	1031 (50.3%)	
Male	165 (51.1%)	1017 (49.7%)	
Age (Median; IQR)	75; 66-83	77; 67-87	0.008
Comorbidities n %			
Previous stroke/TIA	84 (26%)	605 (29.5%)	0.193
Congestive Heart Failure	4 (1.2%)	47 (2.3%)	0.224
Hypertension	183 (56.7%)	1139 (55.6%)	0.726
Atrial Fibrillation (Afib)	61 (18.9%)	425 (20.8%)	0.440
Diabetes	53 (16.4%)	365 (17.8%)	0.536
Time of stroke onset to arrival in hospital (median)	3 hours 40 minutes	4 hours 05 minutes	0.157
Modified Rankin score pre-stroke (median; IQR) mRS: 0-2	0; 0-2 280 (86.7%)	1; 0-2 1622 (79.1%)	0.224
:3-5	43 (13.3%)	426 (20.8%)	
NIHSS upon arrival (median;IQR) NIHSS: 0-5	13; 13-19 52 (16.2%)	4; 2-10 1271 (62.1%)	0.001
: 6-10	86 (26.6%)	297 (14.5%)	
: 11-20	117 (36.2%)	267 (13%)	
: 21-25	45 (13.9%)	111 (5.4%)	
: >25	23 (7.1%)	102 (5%)	

{IQR: interquartile range; NIHSS: NIH stroke scale}

In the univariate regression, the independent factors influencing thrombolysis delivery were those with a p-value <0.05. We observed that thrombolysis were more likely to be delivered to younger patients. The upper limit of the age range of patients receiving thrombolysis was 83 years whereas it was 87 years for those who did not receive thrombolysis. NIHSS measures the level of stroke severity ranging from 0-42 in which a higher number indicates higher stroke severity(4). Patients with moderate stroke (NIHSS:13-19) are more likely to receive thrombolysis compared to patients with a mild stroke (NIHSS:2-10). Thrombolysis was also likely to be delivered to patients with a shorter time period between stroke onset to arrival at the hospital. Modified Rankin score indicates an individual's disability in daily activities before stroke on a scale of 0-6, ranging from no symptoms to death(5).

However, pre-stroke disability is not a significant factor for delivery of thrombolysis. Additionally, patients' gender comorbidities were not significant factors for the delivery of thrombolysis.
Below shows the outcomes of patients who received and did not receive thrombolysis:

Patients' outcomes	Thrombolysis	Non-thrombolysis
Death	45 (13.8%)	252 (12.3%)
Institutionalisation	35 (10.8%)	194 (9.5%)
Modified Rankin score at discharge (median;IQR) 1-2 (n=1052) 3-6 (n=1222)	3;2-4 115 (35.6%) 184 (57%)	3;1-4 937 (45.8%) 1038 (50.7%)
Length of stay (median;IQR)	7 days;2-21 days	6 days; 3-20 days

In terms of patients' outcomes, mortality rate among stroke patients who did and did not receive thrombolysis were 13.8% and 12.3% respectively. The number of patients institutionalized who did and did not receive thrombolysis were 10.8% and 9.5% respectively. The length of stay in hospital for patients receiving thrombolysis is 2-21 days (median: 7 days) whereas for patients not receiving thrombolysis was 3-20 days (median: 6 days). A main limitation in this study was the vastly different baseline clinical feature for the outcome of interest in which the severity of stroke is greatly skewed; a relatively large proportion of patients had a mild stroke hence, they tend to not be treated with thrombolysis and will generally have a good outcome.
After a multiple regression analysis was conducted, the NIHSS was the only factor independently associated with the delivery of thrombolysis (OR=1.7; 95% confidence level of 1.3-2.1).

Conclusion

There is a strong association between age and stroke severity with the delivery of thrombolysis. Thrombolysis is more likely to be delivered to younger patients with upper limit of age of 83 years. Patients with moderate stroke were more likely to receive thrombolysis compared to those with a mild stroke. The differential effect of thrombolysis on patients' outcomes could not be compared due a major skew in stroke severity in which a higher proportion of patients had a mild stroke compared to a moderate stroke. Further research is required to examine the barriers and enablers to maximise use of thrombolysis therapy to pursue better guidelines implementation for high-quality stroke care.

References

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5. Rankin J (May 1957) "Cerebrovascular accidents in patients over the age of 60/ II. Prognosis". Scott Med J2(5): 200-15