Bigger, Faster?: Associations Between Hospital Thrombolysis Volume and Speed of Thrombolysis Administration in Acute Ischemic Stroke

Benjamin D. Bray, James Campbell, Geoffrey C. Cloud, Alex Hoffman, Pippa J. Tyrrell, Charles D.A. Wolfe and Anthony G. Rudd
on behalf of the Intercollegiate Stroke Working Party Group

Stroke. 2013;44:3129-3135; originally published online September 19, 2013;
doi: 10.1161/STROKEAHA.113.001981
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0039-2499. Online ISSN: 1524-4628

Bigger, Faster?

Associations Between Hospital Thrombolysis Volume and Speed of Thrombolysis Administration in Acute Ischemic Stroke

Benjamin D. Bray, MRCP; James Campbell, LLB; Geoffrey C. Cloud, FRCP; Alex Hoffman, MSc; Pippa J. Tyrrell, FRCP; Charles D.A. Wolfe, FFPHM; Anthony G. Rudd, FRCP; on behalf of the Intercollegiate Stroke Working Party Group

Background and Purpose—There is evidence that high-volume hospitals may produce better patient outcomes. We aimed to identify whether there were any associations between hospital thrombolysis volume and speed of thrombolysis (tissue-type plasminogen activator [tPA]) administration in patients with ischemic stroke.

Methods—Data were drawn from 2 national clinical audits in England: the Stroke Improvement National Audit Program and the 2012 Sentinel Stroke Audit. Hospitals were categorized into 3 groups based on the annualized volume of thrombolysis: 0 to 24, 25 to 49, and ≥50 cases per annum. Arrival-brain scan, onset-tPA, and arrival-tPA times were compared across groups and stratified by onset-arrival time. Multilevel logistic models were used to estimate the odds of receiving tPA within 60 minutes of arrival.

Results—Of the 42 024 patients with acute ischemic stroke admitted to 80 hospitals, 4347 received tPA (10.3%). Patients admitted to hospitals with an annual thrombolysis volume of ≥50 cases per annum had median arrival-tPA times that were 28 and 22 minutes shorter than patients admitted to hospitals with volumes of 0 to 24 and 25 to 49, respectively. Onset-tPA times were shorter by 24 to 32 minutes across strata of onset-arrival times. In multivariable analysis, patients admitted to hospitals with a volume of ≥50 cases per annum had 4.33 (2.21–8.50; $P<0.0001$) the odds of receiving tPA within 60 minutes of arrival. No differences in safety outcomes were observed, with similar 30-day mortality and complication rates across the groups.

Conclusions—Hospitals with higher volumes of thrombolysis activity achieve statistically and clinically significant shorter delays in administering tPA to patients after arrival in hospital. **(*Stroke*. 2013;44:3129-3135.)**

Key Words: hospitals, high-volume ■ stroke ■ thrombolytic therapy

Thrombolysis with tissue-type plasminogen activator (tPA) has been demonstrated in randomized controlled trials (RCTs) to improve functional outcomes after acute ischemic stroke.[1] Evidence from individual RCTs[2] and systematic review[1] showed that tPA is most effective when administered soon after the onset of stroke symptoms, with minimal benefits seen 4.5 hours after stroke onset. Improving the rapidity of tPA administration has, therefore, been an important goal for stroke quality improvement strategies in many countries.[3,4]

In addition to prehospital delays, the rapidity of tPA treatment is also determined by the speed with which the admitting hospital identifies, investigates, and initiates treatment in patients with suspected stroke. The hospital characteristics that determine this response have not been well studied,[5] although this is an important question for the configuration and certification of stroke services. In particular, there have been few studies describing the association between the volume of thrombolysis performed by a hospital and the rapidity of tPA administration. Studies in some settings, such as subarachnoid hemorrhage[6] and acute myocardial infarction,[7] have found that high-volume hospitals achieve better outcomes, although in other settings there seems to be no relationship between volume and outcomes.[8] We, therefore, set out to identify whether there was an association between the volume of thrombolysis performed by hospitals and the time between stroke onset, arrival at hospital, brain scanning, and tPA administration for patients with acute ischemic stroke.

Methods

Data were collected through the Stroke Improvement National Audit Program (SINAP), which is a prospective national audit of the first 72 hours of stroke care after admission in England.[9] Participation in the

Received April 29, 2013; final revision received July 22, 2013; accepted August 9, 2013.

From the Division of Health and Social Care Research, King's College London, London, United Kingdom (B.D.B., C.D.A.W., A.G.R.); Royal College of Physicians, London, United Kingdom (J.C., A.H.); St George's Hospital, London, United Kingdom (C.C.G.); University of Manchester, MAHSC, Salford Royal NHS Foundation Trust, Salford, United Kingdom (P.J.T.); and National Institute for Health Research Comprehensive Biomedical Research Centre, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom (C.D.A.W., A.G.R.).

Correspondence to Benjamin D. Bray, MRCP, Department of Primary Care and Public Health Sciences, Floor 7, Capital House, 42 Weston St, London SE13QD, United Kingdom. E-mail benjamin.bray@kcl.ac.uk

***Stroke* is available at http://stroke.ahajournals.org** **DOI: 10.1161/STROKEAHA.113.001981**

audit is voluntary, and hospitals are not reimbursed for participation. Currently, 106 (66%) hospitals in England admitting patients with acute stroke submit data to SINAP. Data of consecutive patients admitted to participating hospitals were abstracted from local care records and prospectively submitted for the audit via a secure web-based tool. The web tool includes real-time data validation checks, and records of individual episodes of care cannot be submitted for the audit until all data fields are filled. Data were linked at the patient level using a unique patient National Health Service (NHS) number to Hospital Episode Statistics (the national administrative data set of admission diagnoses and hospital activity) and the national register of death notifications. Data linkage was performed by a secure third party (the NHS Information Center for Health and Social Care), and no patient-identifiable information was made available to the investigators.

Adult (≥18 years of age) patients admitted with acute ischemic stroke to an SINAP participating hospital in England between January 1, 2011, and August 31, 2012, were included. Patients who were diagnosed with a stroke while already a hospital inpatient for another condition were excluded. To ensure that an unbiased estimate of thrombolysis volume was obtained, only patients admitted to a hospital with ≥40 records included in SINAP and >80% case ascertainment compared with Hospital Episode Statistics were included (case ascertainment is likely to be higher in Hospital Episode Statistics because the data are submitted by hospitals for the purposes of financial reimbursement). Nine hospitals were excluded on the basis of total stroke admissions of <40, and 17 hospitals were excluded on the basis of <80% estimated ascertainment. The hospital thrombolysis volume per annum was categorized into 3 groups: 0 to 24 (low), 25 to 49 (medium), and ≥50 (high) per annum. Because there are no accepted definitions of thrombolysis volume, we defined the categories so as to try to achieve a balance between the numbers of patients and hospitals included in each group. A further subanalysis was performed in hospitals with high volume, defined as a volume of ≥100 per annum. Because of potential confounding between symptom onset-arrival time and arrival-tPA time, analyses were stratified by onset-arrival time into the following categories: <60 minutes, 60 to 119 minutes, 120 to 179 minutes, and ≥180 minutes.

Stroke subtype was classified according to the Oxford Community Stroke Project classification.[10] Post-thrombolysis complications were defined pragmatically; symptomatic intracranial hemorrhage was defined as evidence of intracerebral hemorrhage on brain imaging in association with a clinically significant decline in neurological function. The duration of each of the stages of the thrombolysis pathway was calculated for each patient receiving tPA: time between onset of stroke symptoms and arrival at hospital (onset-arrival), time between arrival and computed tomography or MRI brain imaging (arrival-scan), and time between arrival and receipt of tPA (arrival-tPA).

Prehospital travel distances were estimated using patient and hospital postcodes. For reasons of patient confidentiality, the data set only included the district segments of the patient postcode. Distances were, therefore, estimated from the center of each district. Postcode district latitude and longitude data were sourced from the Ordnance Survey.[11] Great circle distances (the distance between 2 points on a globe) between patient's postcode district and the admitting hospital were calculated using the GEODIST add-on for Stata.

The characteristics (stroke unit size and type of thrombolysis provision) of the admitting hospital were obtained from the Sentinel Stroke Audit 2012.[12] This is a 2-year cross-sectional survey of stroke service provision and characteristics completed by all hospitals admitting patients with acute stroke in England. The data used in this analysis are those obtained in June 2012 and represent a snapshot of stroke service organization at that time.

Analysis

The distribution of arrival-scan and arrival-tPA times across hospitals was illustrated by plotting scatter plots of median times. The distributions of times between groups were compared with violin plots using the kernel density estimator to represent the distribution of times in each group.[13] Thrombolysis rate (as a percentage of all patients admitted with ischemic stroke) and median arrival-tPA times were plotted against onset-arrival time, grouped by 15-minute intervals. Onset-arrival, arrival-scan, and arrival-tPA times were compared across groups using Kruskal–Wallis tests. Categorical variables were compared using the Pearson χ^2 test. Adjusted odds ratios of patients having an arrival-tPA time of ≤60 minutes were estimated by fitting multilevel multivariable logistic regression models. Random intercepts for each hospital were included to account for clustering of patients at this level. The other covariates included in the model were age (as a continuous variable), sex, OCSP type, and out-of-hours admission. Out-of-hours admission was defined as admission on a weekday between 6 PM and 8 AM or any time on weekends or public holidays. Models were also fitted with onset-arrival time, prehospital distance, and total annual stroke admissions per hospital. To reduce possible bias from errors in recording times, patients were dropped from the analysis if the arrival-tPA time was ≤0 minutes or >1440 minutes (n=12 patients). A complete case sensitivity analysis was performed using data from all hospitals in SINAP, irrespective of the ascertainment rate estimated from administrative data. Hypothesis tests were 2-tailed, α=0.01. All analyses were performed using Stata MP 12.

Results

Of the 42 024 patients admitted with acute ischemic stroke to 80 hospitals, 4347 (10.3%) received tPA. Using the total number of patients with ischemic stroke as the denominator, the thrombolysis rate was highest for hospitals with volume ≥50 per annum (15.3% versus 9.1% and 4.7% for medium and low volumes, respectively) There were significant differences in patient characteristics between the groups of hospitals: patients admitted to hospitals with a volume of ≥50 per annum were older (P=0.004), had longer onset-arrival times (P=0.0001), shorter prehospital travel distances (P=0.0001), and were more likely to have been admitted out of regular hours (P=0.0001; Table 1). There were also differences in stroke type, with a higher proportion of patients with posterior circulation syndromes receiving tPA at the high-volume hospitals (P=0.0001). High-volume hospitals administered tPA to a greater proportion of patients presenting at all thrombolysis-eligible time periods after the onset of stroke symptoms (Figure 1), including patients arriving at hospital >3 hours after the onset of symptoms.

Hospital-level characteristics are summarized in Table 1. Hospitals with a volume of ≥50 per annum were larger (absolute difference, 10 beds), admitted a greater number of patients overall, and had on-site 24/7 thrombolysis provision. Thrombolysis volume and total admission volume were strongly positively correlated (Pearson R, 0.81). Hospitals with medium and low volumes had a mixture of thrombolysis provision, although even in the lowest-volume category, 87% offered 24/7 thrombolysis provision either on-site or with local arrangements with other hospitals.

High-volume hospitals (volume ≥50 per annum) achieved the quickest median arrival-scan and arrival-tPA times, with the fastest times achieved by hospitals with a volume ≥100 per annum (Figures 2 and 3). Median arrival-tPA times were 28 and 22 minutes shorter in high-volume hospitals compared with low- and medium-volume hospitals, respectively (P<0.0001; Table 2). Onset-tPA times were 20 to 30 minutes shorter for patients with onset-arrival times ≤180 minutes (Table 2).The fastest times were observed for the 8 hospitals with volumes ≥100 per year, which had a median arrival-tPA time of 41 minutes (interquartile range, 30–60 minutes). More than double

Table 1. Characteristics of Thrombolysed Patients and Participating Hospitals

	Thrombolysis Volume per Annum			
	0–24	25–49	≥50	*P* Value
Hospitals, n	31	31	18	
Patients with ischemic stroke, n	10881	14816	16237	
tPA recipients, n (%)	514 (4.7)	1355 (9.1)	2479 (15.3)	
Characteristics of tPA recipients				
Male, %	57.5	55.7	53.8	0.21
Median age (IQR)	73 (64–79)	73 (63–80)	74 (64–81)	0.004
Onset-arrival time, min	68 (50–96)	75 (55–105)	80 (58–125)	0.0001
Median prehospital travel, km (IQR)	5.4 (1.6–11.0)	7.0 (2.5–14.7)	4.1 (1.7–7.9)	0.0001
Out-of-hours admission,* %	42.4	50.0	52.6	<0.0001
OCSP subtype,† %				<0.0001
TACI	27.6	28.8	27.7	
LACI	15.8	12.0	9.8	
POCI	2.1	6.2	7.2	
PACI	53.9	52.7	55.0	
Other	0.6	0.4	0.2	
Hospital characteristics				
Ischemic stroke admissions per annum	247 (152–302)	379 (279–440)	745 (556–959)	<0.0001
Number of stroke unit beds	26 (19–28)	25 (20–35)	36 (28–50)	
Thrombolysis provision, %				
24/7 on-site	66	89	100	
<24/7 on-site, 24/7 through local arrangements	13	11	0	
None on-site, 24/7 through local arrangements	6	0	0	
<24/7 on-site, no local arrangements	13	0	0	

Continuous variables are medians and interquartile ranges. IQR indicates interquartile range; LACI, lacunar infarct; PACI, partial anterior circulation infarct; POCI, posterior circulation infarct; TACI, total anterior circulation infarct; and tPA, tissue-type plasminogen activator.

*Out-of-hours admissions defined as admission on Saturday or Sunday, public holiday, or from 6 PM to 8 AM on a weekday.

†Oxford Community Stroke Project classification.

the proportion (63% versus 30%) of patients received tPA within 1 hour of arrival in high- versus low-volume hospitals. In both univariate analysis (odds ratio, 3.75; 95% confidence interval, 1.92–7.27) and multivariate analyses adjusted for case mix (adjusted odds ratio, 4.33; 95% confidence interval, 2.21–8.50), patients admitted to high-volume hospitals were significantly more likely to receive tPA within 1 hour of arrival (Table 3). Similar results were observed after adjusting for onset-arrival time and prehospital distance, but thrombolysis volume was not independently associated with arrival-tPA time when adjusting for total number of admissions. No significant differences were observed between medium- and low-volume hospitals in the odds of receiving tPA within 1 hour of hospital admission. There were no observed differences in any of the specified post-thrombolysis outcomes, with similar rates of 7- and 30-day mortality, symptomatic intracranial hemorrhage, and any tPA complications between the hospital groups (Table 2). Arrival-scan, arrival-tPA times, mortality, and complication rates were not materially different in the complete case sensitivity analysis (results not shown).

Conclusions

This analysis demonstrates that hospitals with high volumes of thrombolysis activity achieve clinically and significantly faster arrival-tPA and onset-tPA administration times for patients admitted with acute ischemic stroke. No differences in arrival-tPA times were observed between low- and medium-volume hospitals, suggesting that there may be a threshold effect for thrombolysis volume. The most rapid treatment times were achieved by the highest-volume hospitals, with thrombolysis volumes of ≥100 per annum. There was no evidence that faster times were achieved at the expense of patient safety, with similar mortality and complication rates across all groups. Given the importance of timely treatment with tPA in improving outcomes after stroke, these findings may have implications for the configuration, regionalization, and certification of stroke services.

Evidence from RCTs is consistent in showing that the earlier the tPA is administered after the onset of stroke, the better the outcomes. In 1 pooled analysis of 3 landmark RCTs, the odds ratio for a favorable outcome was 2.8 for tPA administration in 0 to 90 minutes and 1.4 if tPA was administered after 180 to 270 minutes had elapsed after stroke onset.[14] In this context, the differences in arrival-tPA times seen in our study are likely to be clinically significant. Arrival-tPA times were 28 and 22 minutes faster in the high-volume versus low- and medium-volume groups, respectively (relative reductions of 36% and 31%). Onset-tPA times were 23 to 32 minutes shorter for patients

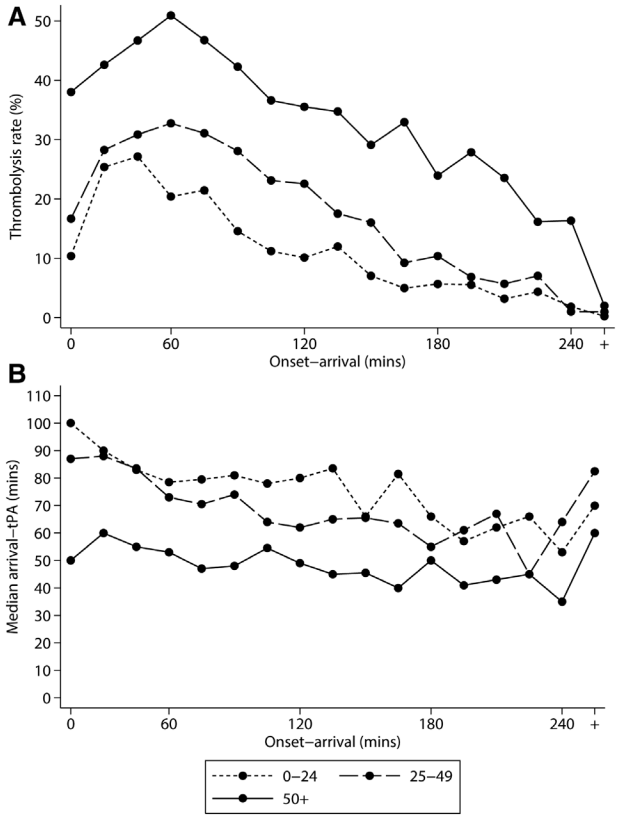

Figure 1. Thrombolysis rate (**A**) and median arrival-tissue-type plasminogen activator (tPA) time (**B**) by onset-arrival time for each of the 3 groups of thrombolysis volume.

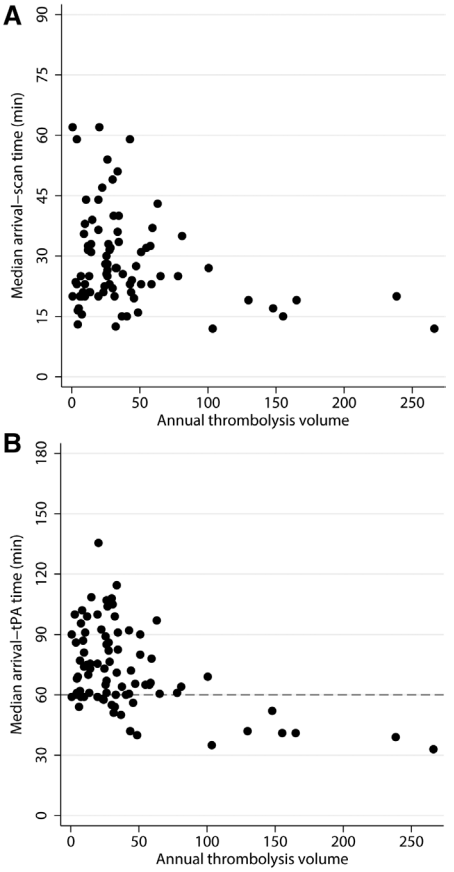

Figure 2. Median arrival-scan (**A**) and arrival-tissue-type plasminogen activator times (**B**) by hospital annual thrombolysis volume.

admitted ≤3 hours from onset. These differences would be expected to lead to improved functional outcomes for patients, although these were not directly measured in this study. Overall arrival-tPA times are consistent with those reported in the large international Safe Implementation of Treatments in Stroke (SITS) register,[15] and the times achieved by the high-volume centers are equivalent to those reported from some single centers.[16] At least 1 reason for the faster arrival-tPA times in high-volume hospitals was fewer delays between arrival and brain scanning. More detailed information about the thrombolysis pathway was not available in the data set, and so it is not possible to characterize how the high-volume hospitals achieved faster times. Other studies have reported several methods for reducing thrombolysis times, such as prehospital notification[17] and stroke pathway redesign,[18] and further studies to identify the means by which the high-volume hospitals achieved lower in-hospital delays would be useful.

This study identified significant differences in the patient population being treated with tPA between the volume groups, with high-volume hospitals administering tPA to a greater proportion of patients presenting out of regular hours, with posterior circulation syndromes and longer onset-arrival times. These differences seem to be because of the high-volume hospitals achieving their high volumes not just by having a greater total number of stroke admissions but also by administering tPA to a greater proportion of the potentially eligible stroke population. It is possible that this relates to greater experience or confidence in administering tPA in high-risk or more marginal patients or that the high-volume hospitals have better processes in place for the investigation and decision making required for tPA administration. Studies from other countries have demonstrated that high-volume hospitals achieve higher thrombolysis rates,[19] and although this may be, to some extent, tautological, these data suggest that high volumes are not just the result of high numbers of

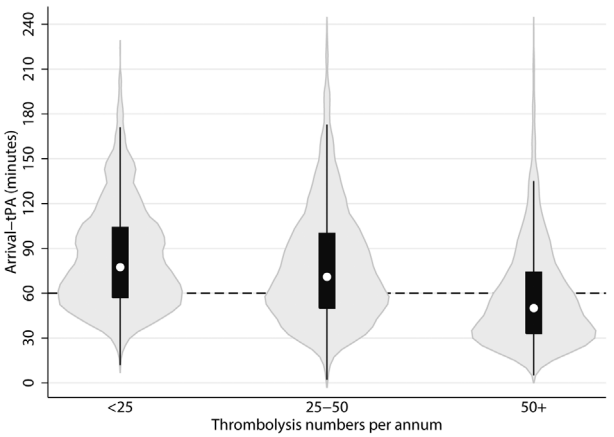

Figure 3. Violin plot of arrival-tissue-type plasminogen activator (tPA) times by thrombolysis volume. The black bars are the interquartile range, the white marks the median, the whiskers delineate the upper and lower adjacent values, and the shaded area is the kernel density.

Table 2. Thrombolysis Times and Outcomes by Hospital Thrombolysis Volume

	Thrombolysis Volume per Annum			
	0–24	25–49	≥50	*P* Value
All patients				
Median onset-arrival time, min	497 (111–1078)	447 (101–1007)	505 (110–1150)	<0.0001
tPA recipients				
Median arrival-scan time, min	30 (18–49)	27 (16–45)	20 (13–31)	<0.0001
Median arrival-tPA time, min				
All	78 (57–105)	72 (50–101)	50 (33–75)	<0.0001
Onset-arrival time <60 min	84 (58–106)	80 (57–106)	54 (35–80)	<0.0001
Onset-arrival time 60–119 min	80 (58–107)	68 (48–99)	49 (33–74)	<0.0001
Onset-arrival time 120–179 min	72 (58–102)	64 (50–91)	44 (31–66)	<0.0001
Onset-arrival time ≥180 min	65 (50–76)	74 (51–122)	51 (32–74)	<0.0001
Median onset-tPA time, min				
All	158 (125–195)	150 (120–195)	142 (109–194)	<0.0001
Onset-arrival time <60 min	123 (100–150)	120 (100–150)	99 (81–125)	<0.0001
Onset-arrival time 60–119 min	165 (135–190)	153 (130–180)	135 (110–160)	<0.0001
Onset-arrival time 120–179 min	225 (194–244)	206 (185–230)	193 (173–215)	<0.0001
Onset-arrival time ≥180 min	290 (260–270)	44 2 (259–945)	292 (250–720)	0.10
Arrival to tPA within 1 h, %	30.4	38.4	63.3	<0.0001
7-day mortality, %	6.8	6.6	5.2	0.13
30-day mortality, %	10.0	10.6	10.1	0.88
sICH rate, %	5.5	4.2	4.3	0.46
Any tPA complications, %	11.3	10.3	9.7	0.50

Times (in min) are shown as medians and interquartile ranges. sICH indicates symptomatic intracranial hemorrhage; and tPA, tissue-type plasminogen activator.

overall stroke admissions but also of greater propensity to administer tPA.

Although there have been studies in many healthcare settings of the relationship between hospital volume and patient outcomes,[20] there have been few that have specifically addressed stoke thrombolysis. Data from the Get with The Guidelines-Stroke Program in the United States identified a similar relationship between hospital volume and the probability of arrival-tPA times of ≤60 minutes.[21] However, the volumes reported were much lower than those in our study (the highest-volume category in the cohort was 20+ per annum and so would have categorized hospitals as high volume that would have been classified as low volume in our study), and overall thrombolysis rates were significantly lower in the US cohort (4.3% versus 10.3% of patients with acute ischemic stroke). In contrast, data from the SITS East register

Table 3. Odds Ratios of Arrival to tPA Time of ≤60 min Using an Annual Volume of <25 as the Reference Category

	ORs of Arrival-tPA Time ≤60 min			
	Volume	OR	95% CI	*P* Value
Univariable	25–49	1.57	0.97–2.84	0.14
	≥50	3.75	1.92–7.27	0.0001
Multivariable—patient variables*	25–49	1.73	0.95–3.15	0.075
	≥50	4.33	2.21–8.50	<0.0001
Multivariable—patient variables* and onset-arrival time	25–49	1.73	0.94–3.15	0.075
	≥50	4.33	2.21–8.49	<0.0001
Multivariable—patient variables,* onset-arrival time, and prehospital distance	25–49	1.64	0.89–3.01	0.11
	≥50	4.14	2.10–8.17	<0.0001
Multivariable—patient variables* and total annual admissions	25–49	1.32	0.71–2.46	0.38
	≥50	1.99	0.79–5.02	0.14

CI indicates confidence interval; OR, odds ratio; and tPA, tissue-type plasminogen activator.
*All multivariable models include patient-level variables: age, sex, OCSP type, and out-of-hours admission.

of 9 central and Eastern European countries found no relationship between hospital volume and arrival-tPA times of ≤60 minutes.[22] Although there are also methodological differences in these studies (such as registry inclusion criteria), the lack of consistency in the findings suggests that volume effects may be specific to particular health systems.

These findings have important implications for the configuration and certification of stroke services. In particular, they suggest that concentrating stroke thrombolysis services into a smaller number of high-volume centers, where geography and demographics permit, may lead to improved thrombolysis rates and treatment times. However, it is important to note that there was considerable variation in arrival-tPA times, with some low-volume hospitals achieving median arrival-tPA times of ≤60 minutes. In addition, all the high-volume centers were in urban areas, and low volumes of thrombolysis will be partly the result of low population density in the hospital catchment area, geography, and the quality of local transport infrastructure. Service reconfigurations also need to consider the risk of increasing prehospital times, and there was some evidence that high-volume hospitals have longer prehospital times, although the difference between high- and low-volume hospitals was small (8 minutes) and may be confounded by differences in the denominator populations. Some areas of England (such as Greater London) have already gone through planned reorganizations to concentrate stroke services into high-volume centers, and these are likely to have influenced the results of this study.[23]

Strengths and Limitations

This study includes data from a large national cohort of stroke patients and describes the real-world outcomes of contemporary stroke care. We also used clinical data to adjust for potential confounders and statistical techniques to allow for clustering of patients at the hospital level, noting criticisms of previous studies over these issues.[20]

One of the main critiques of previous studies of hospital volume has been the potential for selection bias. This is likely to be less of a concern for an emergency condition such as stroke compared with elective procedures and surgical conditions and for process measures such as treatment times rather than outcome measures such as mortality. However, although we excluded hospitals with low estimated case ascertainment, we cannot rule out variation in stroke ascertainment and reporting rates between hospitals. It is also important to note that these data are observational in nature, and although the analysis controlled for several patient-level confounders, the results may be attributable to unmeasured hospital characteristics. Finally, the outcome measured in this study was treatment time and not a direct measure of patient outcome such as disability, although RCTs of tPA suggest that reduced treatment times are associated with better outcomes.

Summary

Data from a large national cohort suggest that there is a volume effect for stroke thrombolysis in England, with a volume threshold for hospitals achieving clinically and statistically significant quicker thrombolysis for patients with acute ischemic stroke. This is despite high-volume hospitals performing thrombolysis administration to a wider, and more diverse, population of patients. These findings suggest that concentrating thrombolysis services into high-volume sites may reduce thrombolysis delays but also show that volumes could be increased if low-volume centers administered tPA to a greater proportion of stroke admissions.

Acknowledgments

We thank the many hundreds of individuals who have contributed to the Stroke Improvement National Audit Program and Sentinel Stroke Audits. The audits would not have been possible without their hard work and dedication. We also thank the Intercollegiate Stroke Working Party for their guidance and work to support the audits.

Sources of Funding

The Stroke Improvement National Audit Program audit is commissioned by the Healthcare Quality Improvement Partnership on behalf of the Department of Health in England. The National Sentinel Stroke Audit 2010 was commissioned by the Healthcare Quality Improvement Partnership on behalf of the Department of Health in England. No specific funding from any source was sought for this study. The research was supported by the National Institute for Health Research (NIHR) Biomedical Research Center based at Guy's and St Thomas' NHS Foundation Trust and King's College London. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, or the Department of Health.

Disclosures

A.G. Rudd is National Clinical Director of Stroke, NHS England. The other authors report no conflicts.

References

1. Wardlaw JM, Murray V, Berge E, del Zoppo G, Sandercock P, Lindley RL, et al. Recombinant tissue plasminogen activator for acute ischaemic stroke: an updated systematic review and meta-analysis. *Lancet*. 2012;379:2364–2372.
2. Marler JR, Tilley BC, Lu M, Brott TG, Lyden PC, Grotta JC, et al. Early stroke treatment associated with better outcome: the NINDS rt-PA stroke study. *Neurology*. 2000;55:1649–1655.
3. Jauch EC, Saver JL, Adams HP, Bruno A, Connors JJ, Demaerschalk BM et al. Guidelines for the early management of adults with acute ischaemic stroke (AHA/ASA Guideline). *Stroke*. 2013;44:870–947.
4. Intercollegiate Stroke Working Party. *National Clinical Guideline for Stroke*. 4th ed. London, UK: Royal College of Physicians; 2012.
5. Evenson KR, Foraker RE, Morris DL, Rosamond WD. A comprehensive review of prehospital and in-hospital delay times in acute stroke care. *Int J Stroke*. 2009;4:187–199.
6. McNeill L, English SW, Borg N, Matta BF, Menon DK. Effects of institutional caseload of subarachnoid hemorrhage on mortality: a secondary analysis of administrative data. *Stroke*. 2013;44:647–652.
7. Ross JS, Normand SL, Wang Y, Ko DT, Chen J, Drye EE, et al. Hospital volume and 30-day mortality for three common medical conditions. *N Engl J Med*. 2010;362:1110–1118.
8. Shahin J, Harrison DA, Rowan KM. Relation between volume and outcome for patients with severe sepsis in United Kingdom: retrospective cohort study. *BMJ*. 2012;344:e3394.
9. Royal College of Physicians. Stroke Improvement National Audit Programme. http://www.rcplondon.ac.uk/projects/stroke-improvement-national-audit-programme-sinap. Accessed April 25, 2013.
10. Bamford J, Sandercock P, Dennis M, Burn J, Warlow C. Classification and natural history of clinically identifiable subtypes of cerebral infarction. *Lancet*. 1991;337:1521–1526.

11. Ordnance Survey OpenData. http://www.ordnancesurvey.co.uk/oswebsite/products/os-opendata.html. Accessed April 25, 2013.
12. Royal College of Physicians. Sentinel Stroke Audit Programme. http://www.rcplondon.ac.uk/resources/national-sentinel-stroke-audit. Accessed April 25, 2013.
13. Hintze JL, Nelson RD. Violin plots: a box plot-density trace synergism. *Am Stat*. 1998;52:181–184.
14. Hacke W, Donnan G, Fieschi C, Kaste M, von Kummer R, Broderick JP, et al. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS and NINDS rt-PA stroke trials. *Lancet*. 2004;363:768–774.
15. Ahmed N, Wahlgren N, Grond M, Hennerici M, Lees KR, Mikulik R et al. Implementation and outcome of thrombolysis with alteplase 3–4.5 h after an acute stroke: an updated analysis from SITS0-ISTR. *Lancet Neurol*. 2010;9:866–874.
16. Sobesky J, Frackowiak M, Zaro Weber O, Hahn M, Möller-Hartmann W, Rudolf J, et al. The Cologne stroke experience: safety and outcome in 450 patients treated with intravenous thrombolysis. *Cerebrovasc Dis*. 2007;24:56–65.
17. Kim SK, Lee SY, Bae HJ, Lee YS, Kim SY, Kang MJ, et al. Pre-hospital notification reduced the door-to-needle time for iv t-PA in acute ischaemic stroke. *Eur J Neurol*. 2009;16:1331–1335.
18. Lindsberg PJ, Häppölä O, Kallela M, Valanne L, Kuisma M, Kaste M. Door to thrombolysis: ER reorganization and reduced delays to acute stroke treatment. *Neurology*. 2006;67:334–336.
19. Heuschmann PU, Berger K, Misselwitz B, Hermanek P, Leffman C, Adelmann M. Frequency of thrombolytic therapy in patients with acute ischaemic stroke and the risk of in-hopsital mortality: the German Stroke Registers Study Group. *Stroke*. 2003;34:1106–1112.
20. Halm EA, Lee C, Chassin MR. Is volume related to outcome in health care? A systematic review and methodologic critique of the literature. *Ann Intern Med*. 2002;137:511–520.
21. Fonarow GC, Smith EE, Saver JL, Reeves MJ, Bhatt DL, Grau-Sepulveda MV, et al. Timeliness of tissue-type plasminogen activator therapy in acute ischemic stroke: patient characteristics, hospital factors, and outcomes associated with door-to-needle times within 60 minutes. *Circulation*. 2011;123:750–758.
22. Mikulik R, Kadlecova P, Czlonkowska A, Kobayashi A, Brozman M, Svigelj V. Factors influencing in-hospital delays in treatment with intravenous thrombolysis. *Stroke*. 2012;43:1578–1583.
23. Hunter RM, Davie C, Rudd A, Thompson A, Walker H, Thomson N, et al. Impact on clinical and cost outcomes of a centralized approach to acute stroke care in London: a comparative effectiveness before and after model. *PLoS One*. 2013;8:e70420.

Correction

The version of the article “Bigger, Faster? Associations Between Hospital Thrombolysis Volume and Speed of Thrombolysis Administration in Acute Ischemic Stroke” by Bray et al that published ahead-of-print on September 19, 2013 contained an error in the author byline. Dr Geoffrey C. Cloud, FRCP appeared as Cloud C. Geoffrey, FRCP. This will be corrected in the online and print versions as Geoffrey C. Cloud, FRCP.