

Trends in Interhospital Transfers and Mechanical Thrombectomy for United States Acute Ischemic Stroke Inpatients

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Objective: Stroke care in the US is increasingly regionalized. Many patients undergo interhospital transfer to access specialized, time-sensitive interventions such as mechanical thrombectomy. *Methods:* Using a stratified survey design of the US Nationwide Inpatient Sample (2009-2014) we examined trends in interhospital transfers for ischemic stroke resulting in mechanical thrombectomy. *International Classification of Disease—Ninth Revision (ICD-9)* codes were used to identify stroke admissions and inpatient procedures within endovascular-capable hospitals. Regression analysis was used to identify factors associated with patient outcomes. *Results:* From 2009-2014, 772,437 ischemic stroke admissions were identified. Stroke admissions that arrived via interhospital transfer increased from 12.5% to 16.8%, 2009-2014 (P -trend < .001). Transfers receiving thrombectomy increased from 4.0% to 5.2%, 2009-2014 (P -trend = .016), while those receiving tissue plasminogen activator increased from 16.0% to 20.0%, 2009-2014 (P -trend < .001). One in 4 patients receiving thrombectomy were transferred from another acute care facility ($n = 6,014$ of 24,861). Compared to patients arriving via the hospital “front door” receiving mechanical thrombectomy, those arriving via transfer were more often from rural areas and received by teaching hospitals with greater frequency of thrombectomy. Those arriving via interhospital transfer undergoing thrombectomy had greater odds of symptomatic intracranial hemorrhage (adjusted odds ratio [AOR] 1.19, 95% CI: 1.01-1.42) versus “front door” arrivals. There were no differences in inpatient mortality (AOR 1.11, 95% CI: .93-1.33). *Conclusions:* From 2009 to 2014, interhospital stroke transfers to endovascular-capable hospitals increased by one-third. For every ~15 additional transfers over the time period one additional patient received thrombectomy. Optimization of transfers presents an opportunity to increase access to thrombectomy.

Key Words: Ischemic stroke—thrombectomy—endovascular—interventional—thrombolysis—transfer—interfacility transfer—interhospital transfer—transport
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Introduction

Following an acute ischemic stroke, time to brain reperfusion is the most critical aspect in preventing disability.¹ The availability of thrombolysis up to 4.5 hours from stroke onset, and the need for specialty and subspecialty care following thrombolytic therapy has led to an extensive network of primary and comprehensive stroke centers in the US.² However, studies have identified poor recanalization with thrombolytics alone for large vessel occlusions.¹ Mechanical thrombectomy or clot retrieval for large vessel occlusions may be performed with good efficacy and may be offered in longer timeframes compared to that for thrombolysis³⁻⁷—usually within large, comprehensive stroke centers. The validation of mechanical thrombectomy as a proven treatment for acute ischemic stroke has further underscored the importance of prompt transfer of stroke patients to centers with available neurosurgical and/or angiographic capabilities.³⁻⁸ The American Heart Association/American Stroke Association recommends emergent evaluation and triage of stroke patients in primary stroke centers with consideration of tissue plasminogen activator (tPA) administration and urgent transfer to a comprehensive stroke center with angiographic capabilities for further evaluation, intervention, and monitoring.⁹ However, under optimal conditions a large proportion of the US population will be unable to access comprehensive stroke centers in a timely manner.¹⁰ More expeditious or efficient transfer mechanisms may be available in some areas, including helicopter transport^{11,12} or mobile stroke units,¹³ with the goal of decreasing time to intervention of stroke. Despite the expanding sophistication in the care and networks serving stroke patients, there is little known about the frequency and outcomes of mechanical thrombectomy for stroke patients undergoing interhospital transfer.

Methods

Database

We conducted a retrospective observational study of the Nationwide Inpatient Sample (NIS) from the Agency for Healthcare Research and Quality, Healthcare Cost and Utilization Project (HCUP)¹⁴ from January 1, 2009 to December 31, 2014 to examine nationwide trends in interhospital transfers for acute ischemic stroke and the relationship between transfers and thrombectomy. For this type of study, formal consent is not required. All HCUP data have been deidentified, and therefore, the analysis is exempt from federal regulations for the protection of human research participants, and institutional review board approval was not necessary. The analysis is in compliance with the HCUP data use agreement.

Hospitalization Selection

We included adult patients (age ≥ 18 years) with a primary diagnosis of acute ischemic stroke (Fig 1). The analysis was restricted to hospitals with the capabilities to

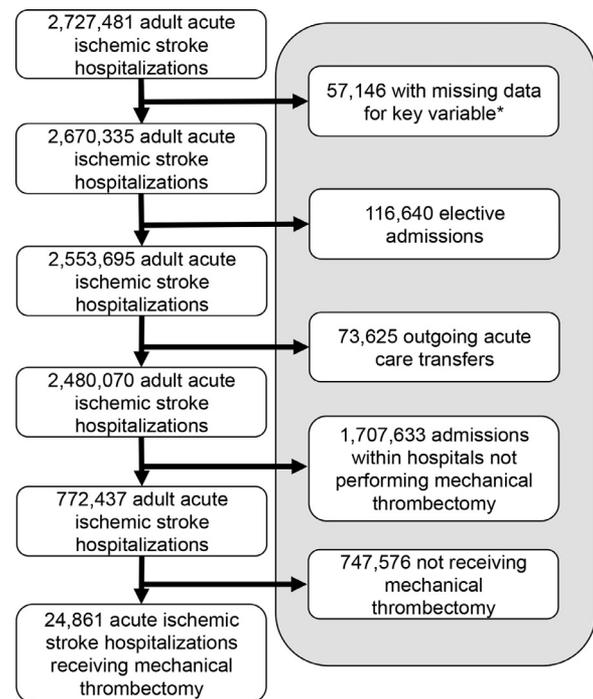


Figure 1. Patient selection method

*Key variables include patient urban/rural origin, age, sex, payer, length of stay, death, and hospital teaching status.

†Hospitals performing mechanical thrombectomy were identified as those centers performing at least one thrombectomy annually.

perform mechanical thrombectomy which was defined as performing at least one annually. *International Classification of Disease—Ninth Revision* (ICD-9) primary diagnosis codes were used to identify acute stroke admissions (ICD-9 diagnosis code 433.x1, 434.x1, 436). ICD-9 codes were used to identify tPA administration (ICD-9 procedure code 99.10 for “front door” patients or ICD-9 diagnosis code V45.88 for interhospital transfers)¹⁵ and mechanical thrombectomy (ICD-9 procedure code 39.74).¹⁶ Elective admissions and transfers out of hospital were excluded. Those admissions with missing data regarding urban/rural origin, age, sex, payer, length of stay, death, and hospital teaching status were excluded (Fig 1).

Outcome Measures

Patients transferred into hospitals were explicitly identified using available NIS variables for transferred-in patients. Transfers were defined as interhospital transfers whereby a patient is seen within the emergency department of one acute care facility and subsequently transferred to another acute care hospital. “Front door” arrival was defined as patient arrival directly to the hospital from the scene.

We identified patient outcomes including length of stay, discharge disposition, inpatient mortality, and hospital charges directly from the dataset. Hospital charges were converted to costs using hospital cost-to-charge

ratios and adjusted to 2014 US dollars using the medical consumer price index for all urban consumers.¹⁷ Gastrostomy and tracheostomy were identified from any of 15 procedural fields (ICD-9 procedure codes 43.1, 43.11, 43.19, 43.2, 44.32 and 31.1, 31.21, 31.29, respectively). Symptomatic intracranial hemorrhage was identified from available secondary diagnoses (ICD-9 diagnosis code 431).

Statistical Analysis

The stratified survey design of the NIS was used to obtain nationwide estimates. Due to changes in data collection methods for 2012 and beyond, adjusted discharge weights were used per HCUP guidelines to better estimate trends.¹⁸ We compared categorical variables using chi-squared tests and continuous variables with Student *t* test or Wilcoxon rank-sum tests as indicated. Trends were assessed using a Cochran–Armitage test of trends. Multi-variable logistic regression analysis was used to identify factors associated with interhospital transfer versus “front door” arrival mechanical thrombectomy. Regression analysis was additionally used to determine the association with interhospital transfer mechanical thrombectomy and

various patient outcomes. For the analysis of outcomes logistic regression was used for binary variables and negative binomial regression was used for continuous variables. Statistical significance was set a priori at *P* < .05. Analyses were performed using Stata version 14.1 (Stata, College Station, TX).

Results

We identified 772,437 acute ischemic stroke admissions from 2009 to 2014 within hospitals performing mechanical thrombectomy. The proportion of stroke admissions that arrived via interhospital transfer increased from 12.5% in 2009 to 16.8% in 2014 (*P*-trend < .001) (Fig 2A). Among all transferred stroke patients, 16.0% received tPA or “drip and ship” transfer in 2009 compared to 20.0% in 2014 (*P*-trend < .001). Among all transferred stroke patients, 4.0% received mechanical thrombectomy in 2009 compared to 5.2% in 2014 (*P*-trend = .016) (Fig 3). The absolute increase in interhospital stroke transfers increased by 12,960 patients and the absolute increase in interhospital transfers undergoing thrombectomy increased by 833 patients from 2009 to 2014, or one additional

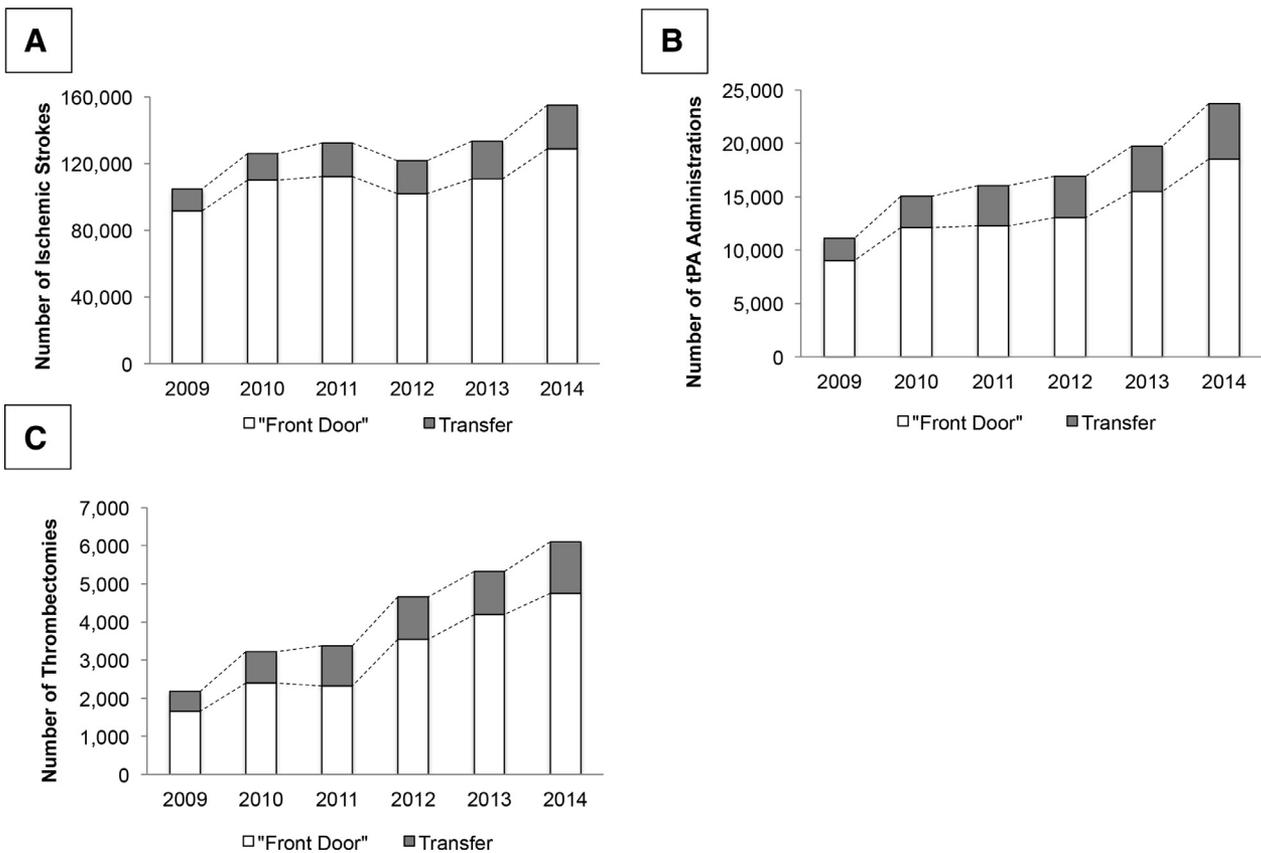


Figure 2. Trends in interhospital transfer versus “front door” arrival for (A) total ischemic stroke (B) tPA administration and (C) mechanical thrombectomy, 2009-2014*

* “Front door” patients are defined as those arriving directly to the admitting hospital via EMS or other means. Transfer patients are those who were seen at an acute care facility hospital or emergency department and subsequently transferred to another acute care hospital.

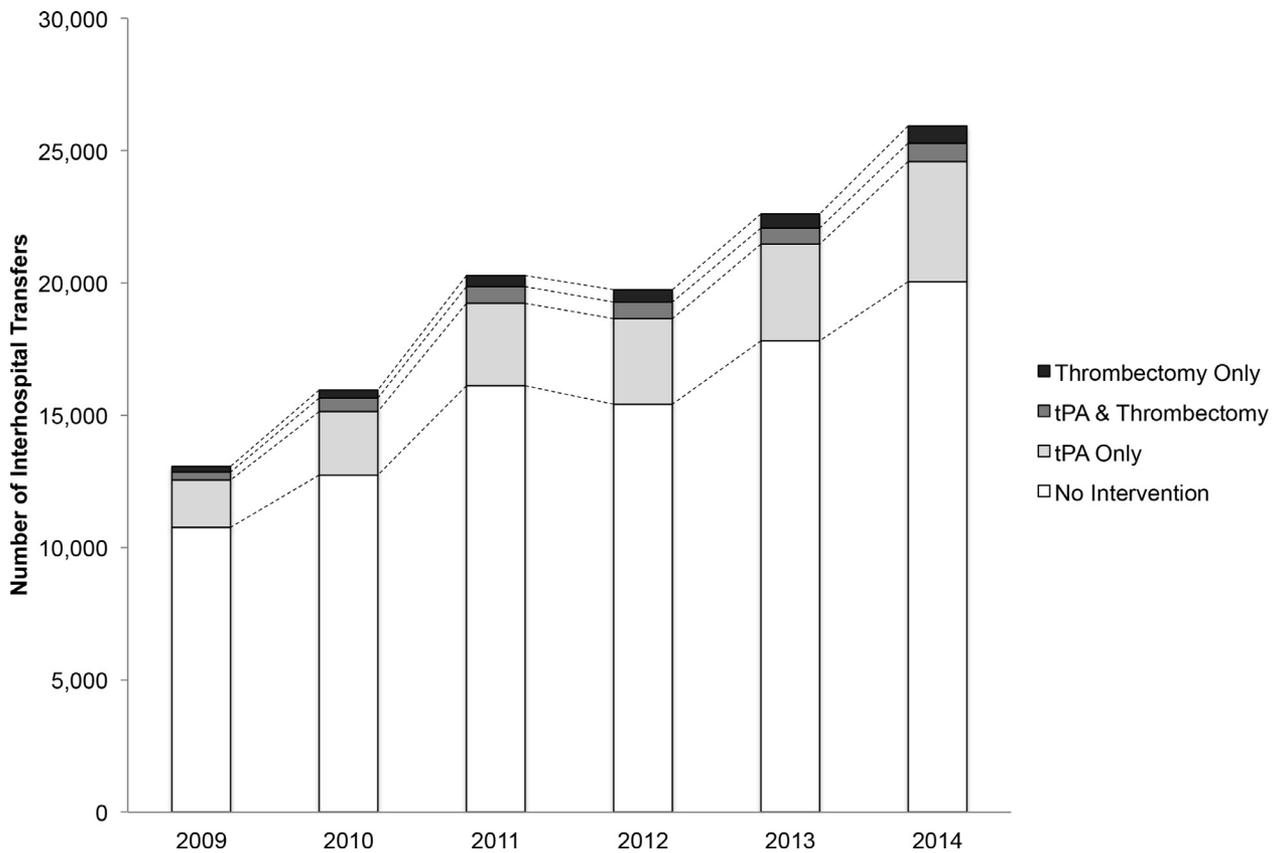


Figure 3. Distribution of interventions among ischemic stroke patients undergoing interhospital transfer, 2009-2014*

Abbreviation: tPA=tissue plasminogen activator

*Interventions were divided into those receiving thrombectomy, tPA only, or both, as well as those receiving neither procedure or no acute intervention.

thrombectomy for every 15 additional transfers (**Table I** and **Table II** in the Supplementary Appendix).

There were 102,538 (13.3%) stroke admissions identified as receiving tPA from 2009 to 2014. The proportion of admissions receiving tPA that arrived via interhospital transfer (i.e., “drip and ship”) increased from 18.8% in 2009 to 22.0% in 2014 (P -trend = .002) (**Fig 2B**). There were 24,861 (3.2%) stroke admissions that received mechanical thrombectomy from 2009 to 2014 within hospitals performing mechanical thrombectomy. Among those who received mechanical thrombectomy, nearly 1 in 4 (24.2%; $n = 6,014$) arrived via interhospital transfer (**Fig 2C**) – and while the number of transferred patients receiving thrombectomy increased over time the proportion relative to “front door” arrivals receiving thrombectomy remained unchanged (P -trend = .49).

Compared to “front door” patients who received mechanical thrombectomy, those arriving via interhospital transfer were more often from rural areas (**Table 1**). Additionally, interhospital transfers were more often privately insured, less likely to have received tPA (in addition to thrombectomy), and more likely to be admitted to teaching hospitals and facilities with greater frequency of

thrombectomy procedures among stroke inpatients (**Table 1**).

Those arriving via interhospital transfer who received mechanical thrombectomy had greater odds of symptomatic intracranial hemorrhage and lower odds of discharge home compared to those arriving via “front door”. The unadjusted absolute difference between interhospital transfers and “front door” patients receiving mechanical thrombectomy in subsequent symptomatic intracranial hemorrhage was 3% ($P = .02$) and discharge home (for survivors) was 7% ($P < .001$). However, there were no differences between interhospital transfer versus “front door” thrombectomy in length of stay, hospital costs, gastrostomy and tracheostomy placement, and inpatient mortality (**Table 2**).

Discussion

We found that from 2009 to 2014, approximately 1 in 5 transferred stroke patients received tPA and 1 in 20 transferred stroke patients received mechanical thrombectomy within endovascular-capable, or hospitals performing endovascular revascularization. For every ~15 additional

Table 1. Patient and hospital characteristics associated with interhospital transfer mechanical thrombectomy

Patient and hospital characteristics	Transfer, No. (%)	“Front door”, No. (%)	Unadjusted odds ratio (95% CI)*	Adjusted odds ratio (95% CI)*
Total mechanical thrombectomies	6014 (100)	18,847 (100)	NA	NA
Sex				
Male	3173 (53)	9396 (50)	Reference	Reference
Female	2841 (47)	9451 (50)	.89 (.78-1.01)	.96 (.83-1.10)
Age, mean years (SD)	65 (15)	68 (15)	NA	NA
Age Categories, years				
18-59	2009 (33)	5397 (29)	Reference	Reference
60-69	1394 (23)	4057 (22)	.92 (.77-1.10)	.93 (.76-1.13)
70-79	1643 (27)	4844 (26)	.91 (.77-1.08)	1.02 (.81-1.28)
≥80	968 (16)	4549 (24)	.57 (.47-.69)	.64 (.50-.82)
Patient location				
Urban	4561 (76)	16,571 (88)	Reference	Reference
Rural	1453 (24)	2276 (12)	2.43 (2.05-2.87)	2.45 (2.06-2.92)
Charlson index [†]				
Score: 0	2148 (36)	6346 (34)	Reference	Reference
Score: 1-2	2972 (49)	9356 (50)	.94 (.81-1.08)	.94 (.81-1.09)
Score: ≥3	894 (15)	3145 (17)	.84 (.69-1.02)	.86 (.70-1.07)
Payer				
Medicare	3130 (52)	11,021 (58)	Reference	Reference
Private	1898 (32)	4905 (26)	1.36 (1.18-1.58)	1.33 (1.09-1.61)
Medicaid	456 (8)	1620 (9)	.99 (.77-1.27)	1.00 (.74-1.34)
Other [‡]	530 (9)	1301 (7)	1.43 (1.13-1.83)	1.33 (1.00-1.78)
tPA administration				
No	2637 (44)	6886 (37)	Reference	Reference
Yes	3377 (56)	11,961 (63)	.74 (.65-.84)	.80 (.70-.92)
Hospital teaching status				
Nonteaching	508 (8)	3401 (18)	Reference	Reference
Teaching	5506 (92)	15,446 (82)	2.39 (1.92-2.97)	2.07 (1.65-2.59)
Hospital thrombectomy rates [§]				
1st quartile	376 (6)	2207 (12)	Reference	Reference
2nd quartile	844 (14)	3798 (20)	1.31 (.97-1.76)	1.28 (.95-1.74)
3rd quartile	1278 (21)	4609 (24)	1.62 (1.23-2.16)	1.72 (1.29-2.29)
4th quartile	3516 (58)	8233 (44)	2.52 (1.94-3.27)	2.59 (1.98-3.39)

Abbreviations: CI, confidence intervals; SD, standard deviation; tPA, tissue plasminogen activator.

*Logistic regression analysis was used to calculate the odds of a thrombectomy resulting from interhospital transfer compared to “front door” arrival. Adjustments were made for patient and hospital characteristics.

[†]Charlson comorbidity index is that tailored for stroke outcomes studies.

[‡]Other payments include self-pay, no charge, and other payment.

[§]Hospital thrombectomy rates (or the proportion of stroke patients receiving thrombectomy within individual hospitals) were divided into quartiles: 1st quartile <1.6%; 2nd quartile 1.7%-3.0%; 3rd quartile 3.1%-5.1%; 4th quartile ≥5.2%.

stroke transfers from 2009 to 2014, one additional transferred patient received mechanical thrombectomy. Although the increasing number of interhospital transfers for stroke has made a positive epidemiological impact on increasing access to revascularization via thrombectomy, our data show that the promise of timely and effective endovascular therapy has not been fulfilled for the majority of interhospital stroke transfers. Additionally, we found that approximately one-fourth of all mechanical thrombectomies were performed on patients arriving via interhospital transfer over the time period examined. This study demonstrates trends prior to the positive results of several trials supporting mechanical thrombectomy for proximal large vessel occlusions, and the extension of the

window for this therapy out to 24 hours from stroke onset, and therefore may underestimate more recent trends. However, these results highlight interhospital transfers as a major source for case-volume among hospitals performing thrombectomy. As a result, there is a critical need to optimize the decision-making and logistics of interhospital stroke transfers to increase access to meaningful interventions such as thrombectomy.

Our study finds that interhospital stroke transfers that received mechanical thrombectomy were more likely to be from rural or smaller metropolitan areas compared to “front door” arrivals, yet this group was additionally less likely to receive tPA (i.e., “drip and ship”). This may represent an opportunity to improve the rates of

Table 2. Association of interhospital transfer mechanical thrombectomy versus “front door” arrival with patient outcomes

Outcomes	Transfer	“Front door”	Unadjusted odds ratio (95% CI)*	Adjusted odds ratio (95% CI)*, †
Length of stay, mean days (SD)	9.2 (10.3)	9.5 (9.4)	.98 (.91-1.05)	.99 (.92-1.05)
Hospital costs, ‡ mean \$US (SD)	49,352 (31,723)	50,243 (36,854)	.98 (.94-1.03)	1.00 (.95-1.04)
Gastrostomy, No. (%)	959 (16)	2,914 (15)	1.04 (.87-1.24)	1.08 (.90-1.31)
Tracheostomy, No. (%)	332 (6)	1,069 (6)	.97 (.73-1.29)	.85 (.63-1.15)
Symptomatic ICH, No. (%)	1,139 (19)	3,076 (16)	1.20 (1.01-1.42)	1.19 (1.01-1.42)
Non-home discharge among survivors, § No. (%)	3,838 (78)	11,125 (71)	1.42 (1.19-1.68)	1.60 (1.34-1.92)
Home discharge among survivors, No. (%)	1,085 (22)	4,454 (29)	.71 (.60-.84)	.62 (.52-.75)
Inpatient mortality, No. (%)	1,091 (18)	3,268 (17)	1.06 (.89-1.25)	1.11 (.93-1.33)

Abbreviations: CI, confidence interval; ICH, intracranial hemorrhage; SD, standard deviation.

*Logistic regression analysis was used, and odds ratios were reported except for length of stay and hospital costs, where negative binomial regression analysis was used and an incident rate ratio was reported.

†The association of thrombectomy resulting from interhospital transfer compared to “front door” arrival was studied on various outcomes using the outcome as the dependent variable in a multivariable regression analysis adjusting for patient and hospital characteristics listed in Table 1.

‡Hospital costs were derived from hospital charges using hospital cost-to-charge ratios and were adjusted to 2014 US dollars using the medical consumer price index for all urban consumers.

§Non-home discharge includes that to skilled nursing facility, long term care, acute rehabilitation, or hospice facilities.

thrombolytic delivery to stroke patients prior to transfer for evaluation of endovascular therapy, with focus on rural and smaller population regions. Increasing access to neurological expertise to rural areas, potentially by expansion of stroke or emergency neurology telemedicine networks,¹⁹ may be one means to improve tPA delivery rates in rural areas. Nonetheless, 15% of thrombectomies over the time period were performed on patients from rural areas where approximately 20% of the US population lives²⁰ – signifying a major success of the interhospital transfer system.¹¹

We find that interhospital stroke transfers are more likely to arrive at teaching centers and high-volume thrombectomy performing centers, likely as a result of the highly centralized “hub-and-spoke” network for stroke care. Additionally, stroke transfers appear to be continually rising with many undergoing interhospital transfer even in the absence of significant interventions such as tPA administration or mechanical thrombectomy (Fig 3). This may be due to the need for specialized post-stroke care, neurological intensive care services, or the need for targeted stroke prevention for these patients. This could also partially reflect a lack of understanding and identification of stroke or stroke mimics, or what constitutes a need for higher level of neurologic care.²¹ Large comprehensive stroke centers at the middle of stroke networks will either need to accommodate greater patient volumes or find a means to achieve greater efficiency in the transfer process. Avoiding transfers of small strokes at low risk for complications or stroke mimics that otherwise do not require higher level of neurological care may provide one means to off-load the increasing transfer volumes seen by these already large-volume centers. This could be accomplished by triage via telemedicine networks,²² expanding cross-discipline or remote healthcare

provider stroke education, or implementing screening tools that can reliably identify large vessel occlusion strokes that may benefit from thrombectomy.^{23,24}

While our study finds that interhospital transfers receiving mechanical thrombectomy had no difference in hospital costs, length of stay, inpatient mortality, or gastrostomy and tracheostomy placement compared to “front door” arrivals, we did find that transfers were more likely to have symptomatic intracranial hemorrhage and more likely to be discharged to a support facility (e. g., skilled nursing facility, acute rehab) versus home. This suggests there is a greater risk of subsequent hemorrhage following delayed thrombectomy, however, the absolute difference in hemorrhage rates between the transfer and “front door” patients was small (3%). Second, transferred patients may rely on greater support and rehabilitation following discharge, possibly indicating greater disability following the procedure compared to “front door” arrivals. These findings may be a result of greater time to revascularization for those requiring transfer, which may be due to distance barriers or symptom misidentification. However, interpretation of these differences is significantly limited by the absence of better adjustment for disease severity within NIS data such as the National Institute of Health stroke scale, or measures of disability such as modified Rankin scale. These results highlight the need to better understand differences that may improve mechanisms that accelerate time to endovascular revascularization for interhospital transfers, such as helicopter transport or mobile stroke units.

Our study has several limitations. As an administrative claims database, the NIS collects information retrospectively for the purpose of billing and relies on ICD-9 codes, which limits the granularity of these data. For instance, the database does not contain information on stroke

severity (e.g., National Institutes of Health stroke scale), infarct volume or lateralization, arterial distribution, or timing from symptom onset to interventions such as tPA and thrombectomy, which could provide better adjustments for differences in outcomes between interhospital transfers and “front door” arrivals. In addition, in the absence of modified Rankin scores or long-term follow-up it is difficult to measure differences in disability though we have attempted to extrapolate using discharge information. We also are unable to identify which hospitals have certification for comprehensive stroke center designation versus endovascular-capable primary stroke center designation, however, given that our study focused on thrombectomy-performing centers we likely isolate mostly comprehensive stroke centers. Finally, our study provides an examination of data prior to the release of major trials examining mechanical thrombectomy in large vessel occlusions demonstrating positive results,^{3–7} and therefore, these results may underestimate more recent trends. In addition, this study does not reflect interhospital transfers in the wake of the recently expanded window to 24 hours with perfusion imaging, which is likely to expand eligibility for thrombectomy significantly, further underscoring the reason our data will underestimate current transfer practices.²⁵

In summary, our analysis provides a well-powered and generalizable examination of the relationship between interhospital stroke transfers and mechanical thrombectomy using the most up-to-date data available. Our findings represent a paradigm shift in acute stroke treatment from intravenous tPA alone to the use of endovascular intervention with or without tPA, and in parallel, society's development of rapid priority patient transport to comprehensive or endovascular-capable stroke centers. The observed increase in interhospital transfers for acute ischemic stroke for the purpose of thrombectomy marks an important movement and positive change toward more aggressive treatment for stroke. Future studies will need to determine the changing trends in interhospital transfer for mechanical thrombectomy given more recent developments in clinical trials for mechanical thrombectomy,^{3–7} which can now be offered as late as 24 hours from symptom onset.²⁵

Author Contributions

BG and TB conceived the study.

BG was responsible for data acquisition.

BG, TP, CZ, AK, AS and TB were responsible for analysis/interpretation of the data as well as critical revision for intellectual content.

Statistical analysis was performed by BG.

Study supervision was by TB.

Acknowledgment: Dr. George takes full responsibility for the data, the analyses and interpretation, and the conduct of the research.

Supplementary Material

Supplementary data to this article can be found online at doi:10.1016/j.jstrokecerebrovasdis.2018.12.018.

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