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Authors
Shah, Shreyansh
Xian, Ying
Sheng, Shubin
et al.

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Use, Temporal Trends, and Outcomes of Endovascular Therapy after Interhospital Transfer in the United States

Shreyansh Shah, MD[1,2], **Ying Xian, MD, PhD**[1,2], **Shubin Sheng, PhD**[2], **Kori S. Zachrison, MD, MSc**[3], **Jeffrey L. Saver, MD**[4], **Kevin N. Sheth, MD**[5], **Gregg C. Fonarow, MD**[6], **Lee H. Schwamm, MD**[7], **Eric E. Smith, MD, MPH**[8]

[1.]Department of Neurology, Duke University Hospital, Durham, NC

[2.]Duke Clinical Research Institute, Durham, NC

[3.]Department of Emergency Medicine, Massachusetts General Hospital, Boston, MA

[4.]Department of Neurology, UCLA Medical Center, Los Angeles, CA

[5.]Department of Neurology, Yale School of Medicine, New Haven, CT

[6.]Division of Cardiology, UCLA Medical Center, Los Angeles, CA

[7.]Department of Neurology, Massachusetts General Hospital, Boston, MA

[8.]Department of Clinical Neurosciences, Hotchkiss Brain Institute, University of Calgary, Calgary, AB, Canada

Abstract

BACKGROUND: The use of endovascular therapy (EVT) in acute ischemic stroke patients with large vessel occlusion (LVO) has rapidly increased in the US following pivotal trials demonstrating its benefit. Information about the contribution of interhospital transfer in improving access to EVT will help organize regional systems of stroke care.

METHODS: We analyzed trends of transfer-in EVT from a cohort of 1,863,693 ischemic stroke patients admitted to 2,143 Get With The Guidelines-Stroke participating hospitals between January 2012 and December 2017. We further examined the association between arrival mode and in-hospital outcomes using multivariable logistic regression models.

RESULTS: Of the 37,260 patients who received EVT at 639 hospitals during the study period, 42.9% (15,975) arrived to the EVT providing hospital after interhospital transfer. Transfer-in EVT cases increased from 256 in Q1 2012 to 1,422 in Q4 2017, with sharply accelerated increases following Q4 2014 ($p<0.001$ for change in linear trend). Transfer-in patients were younger, more likely to be of white race, arrive during off-hours and treated at comprehensive stroke centers. Transfer-in patients had significantly longer last known well to EVT initiation time (median 289 min vs 213 min, absolute standardized difference 67.33) but were more likely to have door to EVT initiation time of ≤ 90 minutes (65.6% vs 23.6%, absolute standardized difference 93.18). In-hospital outcomes were worse for transfer-in EVT patients in unadjusted and in risk-adjusted

Corresponding author: Shreyansh Shah, MD, Duke University Medical Center, Box 3824, Durham, NC 27710. Phone: 919-684-1965, Fax: 919-613-3606, Shreyansh.Shah@duke.edu.

models. While the difference in in-hospital mortality disappeared after adjusting for delay in EVT initiation (14.7% vs 13.4%, adjusted odds ratio (aOR) 1.01, 95% confidence interval (CI) 0.92-1.11), transfer-in patients were still more likely to develop symptomatic intracranial hemorrhage (sICH) (7.0% vs 5.7%, aOR 1.15, 95% CI 1.02-1.29) and less likely to have either independent ambulation at discharge (33.1% vs 37.1%, aOR 0.87, 95% CI 0.80-0.95) or to be discharged to home (24.3% vs 29.1%, aOR 0.82 95% CI 0.76-0.88).

CONCLUSIONS: Interhospital transfer for EVT is increasingly common and is associated with a significant delay in EVT initiation highlighting the need to develop more efficient stroke systems of care. Further evaluation to identify factors impacting EVT outcomes for transfer-in patients is warranted.

Keywords

Ischemic Stroke; Endovascular Treatment; Interhospital Transfer; Outcome

INTRODUCTION

Endovascular therapy (EVT) using stent retrievers is an effective treatment for acute ischemic stroke caused by large vessel occlusion (LVO).[1–7] There has been significant increase in the use of EVT in the United States over the past few years following publication of landmark studies illustrating the benefits of this therapy.[8] In spite of increasing numbers of hospitals being able to provide EVT in recent years,[8] interhospital transfer presumably also plays an important role in driving this increase. However, there are currently scarce data on the extent to which interhospital transfer is improving access to EVT in clinical practice. Furthermore, it is unknown whether hospitals with EVT capabilities are seeing increasing numbers of acute ischemic stroke patients arriving by interhospital transfer. This information may be helpful for organizing regional stroke systems of care and for designing quality improvement initiatives.

Previous studies have shown that EVT following interhospital transfer is associated with a reduced likelihood of good clinical outcome due to delayed treatment;[9–11] however, the generalizability of this finding has not been confirmed. Investigation of outcomes using a nationwide contemporary clinical practice-derived data set will confirm these findings and help identify opportunities for improvement and to guide the discussion on creation of systems of care for stroke.

The aim of this study was to describe the frequency and temporal trend of interhospital transfer for EVT in clinical practice using Get With The Guidelines-Stroke (GWTG-Stroke), a large nationwide registry representative of the U.S. stroke population.[12] We hypothesize that following publications of pivotal trials demonstrating the benefit of EVT, there would be a substantial increase in the frequency of EVT occurring after interhospital transfer, further, that this transfer-in group would increasingly contribute to patients receiving EVT in the United States. We also aim to compare outcomes of EVT between patients who received the therapy after interhospital transfer and those who presented directly to the EVT providing hospital.

METHODS

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results. Data used for this study is confidential and not sharable according to the terms of the contracts between the American Heart Association and hospitals participating in GWTG-Stroke.

Study Population

The GWTG-Stroke program is an initiative developed by the American Heart Association/ American Stroke Association for quality and performance improvement. Details of the program, including case ascertainment and data collection methodologies, have been described previously.[13, 14] Hospital participation is voluntary, and participating hospitals use a web-based Patient Management Tool (PMT, Quintiles Cambridge, MA) to collect de-identified clinical data and outcomes, access decision support, and provide real-time online reporting of performance on quality of care measures. Consecutive patients admitted with stroke or transient ischemic attack are identified either prospectively by clinical diagnosis or retrospectively using administrative billing codes and confirmed by chart review by trained study personnel to confirm eligibility and to abstract study variables. Participating sites receive either human research approval to enroll cases in GWTG-Stroke without requiring individual patient consent under the common rule or a waiver of authorization and exemption from subsequent review by their Institutional Review Board. Patient-level data available for analysis include age, sex, race, medical history, last known well time, arrival time at the EVT providing hospital, time of arterial puncture, discharge disposition and destination. The initial National Institutes of Health Stroke Scale (NIHSS) score used for risk adjustment was measured on admission to the EVT providing hospital. Patients were defined as receiving EVT if its use was documented on either the standard or comprehensive stroke center case report forms. Hospital-level characteristics collected as part of the GWTG-Stroke include bed size, geographic region, academic status, ischemic stroke volume, and stroke center certification by the Joint Commission. The Duke Clinical Research Institute serves as the statistical coordinating center for the GWTG-Stroke program and provides analysis of de-identified data for research. The Institutional Review Board at Duke University Health approved this study.

Outcomes of Interest

Trends of transfer-in EVT were described by the overall frequency of transfer-in EVT, trends in absolute frequency of transfer-in EVT over time, and frequency of transfer-in EVT normalized by number of hospitals providing EVT over time. In-hospital outcomes among patients treated with EVT were compared among transfer-in and direct arrival groups. Primary patient-level outcomes of interest included in-hospital mortality, symptomatic intracerebral hemorrhage (sICH) within 36 hours, independent ambulation at discharge, discharge to home, and length of stay.

Statistical Analysis

Inclusion and exclusion criteria for study populations are shown in Figure 1. Transfer-in EVT case frequency over time was analyzed as the absolute number of transfer-in EVT cases for each study quarter and also by the number of transfer-in EVT cases normalized for the number of GWTG-Stroke hospitals providing EVT for each study quarter. Transfer-in EVT trends were also analyzed as the percentage of all patients who received EVT. To analyze the changes in patient arrival mode at EVT providing hospitals over time, we restricted the study population to the subset of hospitals with at least one EVT/quarter for the last four study quarters. To test changes in trends after publication of pivotal RCTs began in Q4 2014, we used weighted linear regression with two linear splines with a knot at Q4 2014 to compare the slope of the changes from Q1 of 2012 to Q4 2014 and Q1 2015 to the most recent data harvested at the time of analysis in Q4 2017.

Univariate analyses were performed to compare transfer-in patients with direct arrivals across variables of interest. Categorical variables are presented as either percentages or frequencies, whereas continuous variables are reported as medians with 25th and 75th percentiles. To avoid influence from the large sample size, standardized differences were calculated for baseline characteristics, and values greater than 10% were considered significantly different. Differences between outcomes were assessed with multivariable logistic regression models using generalized estimating equations to account for in-hospital clustering of patients. Adjusted odds ratio for in-hospital outcomes were provided before and after adjusting for delay in EVT initiation. Models were adjusted for pre-specified patient characteristics, including age, race, sex, NIHSS, IV t-PA yes/no, arrival time off hours (5 pm to 7 am from Monday to Friday, Saturdays, and Sundays), and medical history (atrial fibrillation, prosthetic heart valve, previous stroke/transient ischemic attack, coronary heart disease or previous myocardial infarction, carotid stenosis, peripheral vascular disease, hypertension, dyslipidemia, diabetes mellitus, and current smoking). In addition, we collected the following hospital characteristics: region, teaching status, number of beds, average annual volume of ischemic stroke, t-PA and EVT, Joint Commission primary and comprehensive stroke center certification, and rural location. These covariates were either complete or had small missing values (<3%), except for NIHSS (4.76% missing) and last known well to EVT initiation time (27.67% missing). Missing values for patient characteristics were imputed to the most frequent category for categorical variables, with the exception of medical history. All medical history variables were imputed to none. Missing values for continuous variables were imputed to the median with the exception of excluding missing values for last known well to EVT initiation time in the outcome models adjusting for last known well to EVT initiation time. If missing, hospital characteristics were not imputed, and thus, these missing values were excluded from the models. Odds ratios and 95% confidence intervals were computed for all unadjusted and adjusted analyses.

SAS version 9.4 (SAS Institute, Cary, NC) was used for statistical analyses. A p-value < 0.05 was considered significant.

RESULTS:

The initial study cohort included 1,863,693 ischemic stroke patients admitted to 2,143 hospitals participating in the GWTG-Stroke between January 2012 and December 2017. After applying exclusion criteria, as shown in Figure 1, we analyzed data from 37,260 patients who received EVT at 639 hospitals. Of these, 15,975 (42.9%) patients had received EVT after transfer from another hospital (transfer-in) during the study period.

The number of patients receiving EVT after interhospital transfer increased from 256 cases per quarter in Q1 2012 to 1,422 cases per quarter in Q4 2017. Analysis of the trend for transfer-in EVT case volume over time showed that prior to the announcement of results from the first pivotal RCT in Q4 2014,[15] the frequency of transfer-in EVT was slowly increasing by an additional 90.14 cases per year. Following that, the rate of increase for transfer-in EVT went from 90.14 additional cases per year to 336.83 additional cases per year ($p<0.001$ for difference in slopes) (Figure 2A). This trend of increasing transfer-in EVT remained after normalizing for the number of hospitals providing EVT, indicating that it was not only due to the increasing number of EVT providing hospitals (Figure 2B). Prior to publication of pivotal trial RCTs, the proportion of transfer-in patients amongst all patients treated with EVT was stable. Following the RCTs, it steadily increased by 1.66% per year ($p<0.001$ for difference in slope) (Figure 2C).

In contrast, during the study period, the proportion of ischemic stroke patients arriving after interhospital transfer among all ischemic stroke patients admitted to EVT-providing hospitals increased linearly (from 25.2% in Q1 2012 to 31.2% % in Q4 2017) and did not exhibit an inflection at the time in Q4 2014 when pivotal EVT trials were published (Figure 2D).

There were important differences in patient level characteristics between transfer-in and direct arrival patients (Table 1). Compared with direct arrival patients, transfer-in patients were younger, more often white, and more likely to arrive during off hours. Transfer-in EVT patients were more likely to receive EVT at hospitals with teaching hospital status, higher annual volume of IV t-PA administration, and EVT therapy and Joint Commission certified Comprehensive Stroke Centers. As a proportion, patients treated with EVT after interhospital transfer were more common in the Midwest and less common in the South (Table 2).

Comparison of available time metrics from GWTG-Stroke showed that median last-known-well-to-EVT initiation time was 289.0 minutes (IQR, 230-356) in the transfer-in group compared with 213.0 minutes (IQR, 159-280) in the direct arrival group ($P<0.0001$, absolute standardized difference 70.97). In contrast, door-to-EVT initiation time was significantly shorter for the transfer-in group, suggesting that longer delays in initiation of EVT for the transfer-in group were the result of longer transit times to reach the EVT providing hospitals (Figure 3). Median door-to-EVT initiation time was 68.0 minutes (IQR, 40-110) for the transfer-in group compared with 128.0 minutes (IQR, 92.0-176.0) for the direct arrival group ($P<0.0001$, absolute standardized difference 67.33). Door-to-EVT initiation time ≤ 90 minutes was achieved for 65.6% of transfer-in patients in comparison to 23.6% of direct arrival patients ($P<0.0001$, absolute standardized difference 93.18).

Overall, the rate of in-hospital mortality was 14.0% in patients who had EVT, and sICH was observed in 6.2%. Approximately 27% of patients were discharged to home, and 35.4% of patients were able to ambulate independently by discharge. Comparison of in-hospital clinical outcomes between transfer-in and direct arrival patients who received EVT is presented in Table 3. In unadjusted analysis, transfer-in EVT patients exhibited poorer in-hospital outcomes, including increased rates of in-hospital mortality and sICH, along with decreased likelihood of independent ambulatory status at discharge and discharged to home. Outcomes for the transfer-in group continued to be inferior after adjustment for patient and hospital factors. Additional risk adjustment for the time delay in receiving EVT nullified the difference in in-hospitality mortality rate between the transfer-in and direct arrival patients, but all remaining endpoints continued to be worse for the transfer-in group (Table 3).

DISCUSSION:

In this study of >37,000 acute ischemic stroke patients treated with EVT at GWTG-Stroke participating hospitals, we found that interhospital transfer is an increasingly important contributor to improving access to this crucial therapy in the United States but is associated with delayed treatment and worse functional outcomes compared to direct presentation. The number of patients receiving EVT after interhospital transfer increased by 456% during the study period, with marked acceleration after publication of pivotal RCTs. In Q4 of 2017, 44.6% of EVTs were performed on patients arriving after interhospital transfer. Increasing use of EVT is paralleled by increasing frequency of interhospital transfer as a mode of arrival for ischemic stroke patients at the hospitals providing EVT. As interhospital transfer of acute ischemic stroke patients is expected to continue to rise further with expansion of the time window for mechanical thrombectomy using advanced imaging,[16, 17] this study using a large, national registry provides much needed contemporary quantitative observations for organizing stroke systems of care.

Although EVT is a highly effective treatment for a subset of stroke patients with LVO, providing access to this lifesaving therapy in a timely manner is emerging as the major challenge for stroke systems of care.[18] Patients who are potential candidates but who are not brought directly to the centers capable of providing EVT must be transferred to an EVT providing hospital for further assessment and treatment. In a meta-analysis of pooled individual patient data from five RCTs demonstrating the beneficial effect of EVT, 30.2% of patients who received EVT had arrived after interhospital transfer.[19] With increasing regionalization of stroke care in the US, interhospital transfers for stroke patients have significantly increased over the last decade,[20] but only a few studies have examined the role of interhospital transfer in improving access to EVT in a real world setting. A recent study that examined real-world time metrics of EVT delivery for 984 patients treated at 55 large academic centers observed an interhospital transfer rate of 45.2% among patients receiving EVT.[10] Another study comparing EVT outcomes between direct arrival and transfer-in patients reported that 36.1% of patients were treated with EVT after interhospital transfer.[9] These studies were conducted to compare outcomes of EVT between transfer-in and direct arrival groups but were not designed to examine either the trends in interhospital transfer for EVT or the downstream effects of interhospital transfer on EVT providing hospitals. Ours is the largest study to address the trend, frequency and outcomes of interhospital transfer for EVT.

Our study shows that interhospital transfer is associated with delayed initiation of EVT therapy. There was a mean delay of 63.7 minutes for EVT initiation in patients arriving by interhospital transfer. Our data suggests that the primary reason for this delay was the additional time required for patients to arrive at the EVT providing hospital. Once patients arrived at the EVT providing hospital, arrival to EVT initiation time was actually shorter by 56.4 minutes for the transfer group, and they were three times more likely to have door-to-EVT initiation time of ≤ 90 minutes compared to direct arrivals. This may reflect the benefit of pre-notification at the EVT center, enabling teams to prepare prior to the patient's arrival.

The worse outcomes for the transfer-in group observed in our study validate similar observations from previous smaller studies by leveraging a large contemporary database representative of the nationwide stroke population in the US.[9, 10, 12, 21] A previous US study examining outcomes of transfer-in EVT reported higher in-hospital mortality (18.6% versus 14.9%) but similar rates of ICH (17.2% versus 18.7%) and discharge to home (16.7% versus 17.7%) between transferred and directly admitted patients, respectively.[9] However, this analysis was performed using billing diagnosis codes, and outcomes were presented without any adjustment. Another more comprehensive analysis included 984 patients from 55 sites to assess 90-day functional outcomes after adjusting for an extended set of covariates, including baseline NIHSS and imaging characteristics.[10] This study concluded that transfer-in patients exhibited worse functional outcomes, but after accounting for treatment delay, this difference disappeared. In contrast, after adjusting for the time delay in receiving EVT, all observed outcomes, with the exception of in-hospital mortality, were worse for the transfer-in group in our study. A separate analysis from the GWTG-Stroke dataset shows that last known well to EVT initiation time is independently associated with EVT outcomes,[22] but the fact that worse outcomes persisted for the transfer-in group even after adjusting for the treatment delay suggests a role for other factors. These potential factors include bias in patient selection for transfer and contribution from a number of other unmeasured confounding factors that were not available for adjustment in our dataset, including worse pre-EVT CT scan, inappropriate hemodynamic management during the transfer, and need for intubation prior to transfer, amongst others.

Worse outcomes associated with transfer-in EVT revealed here highlight the need for enhancing stroke systems of care for treatment of strokes caused by acute LVO. Expanding EVT capability to more centers can improve access but will have to be balanced with the need for maintaining sufficient case volume and competence of EVT providers at these new centers.[23] Transport of mobile neurointerventional teams to sites that have on-site angiographic suites for EVT delivery is another creative solution to the traditional spoke-and-hub model.[24, 25] Direct transport of patients suspected to have LVO by emergency medical service (EMS) to EVT providing centers can be advantageous compared to taking patients to the closest hospital but would need careful consideration of a number of factors to create an optimized bypass algorithm for a given stroke system.[26–32] Development of prehospital screening tools with high accuracy for field diagnosis of LVO would facilitate efficient triaging.[33] Prehospital evaluation using mobile stroke units, smartphone based applications and telemedicine have the potential to help identify potential thrombectomy patients and bypass interhospital transfers.[34–36] However, it would not be feasible to eliminate interhospital transfer entirely, as current prehospital assessment tools suffer from low accuracy, and a number of centers are not capable of providing EVT.[37] Our findings emphasize the need to improve the process of interhospital transfer by minimizing delays at the originating hospitals, transport services, and receiving hospitals. Increasing transfer time reduces of odds of patients receiving EVT.[38] Quality improvement programs focused on time-based metrics, such as door-in to door-out time, should be used to provide feedback on performance and improve workflow at centers that receive stroke patients but are not EVT capable. Early mobilization of transport crew and stronger linkage between spoke-hubs is also associated with faster treatment times.[39, 40] Implementation of vascular imaging at the initial hospital and development of image sharing tools would reduce futile transfer and obviate the need for repeat imaging at the receiving facility.[41, 42] Efforts at the EVT providing centers focused on improving transfer acceptance processes and innovative approaches, like interhospital transfer directly to the neuroangiography suite, have been shown to shorten reperfusion times for patients arriving by interhospital transfer.[43] The significant scope for improving efficiency in interhospital transfer was highlighted by the fact that implementation of a standardized protocol with some of the elements discussed above resulted in a 38% reduction of door-in to door-out time and doubled the likelihood of a favorable outcome for patients with suspected LVO who presented to hospitals without endovascular capability.[40]

Further research to understand the barriers and facilitators to interhospital transfer will be useful to eliminate disparities in access to EVT. While sex and insurance status was not different between direct arrival and transfer cohorts, there were differences in age and race between the two groups. It is unclear whether this disparity was introduced at the originating hospital for the transfer-in patients or at the receiving hospitals providing EVT. A recent study using the GWTG-Stroke registry showed that although the frequency of EVT has significantly increased in the US following publication of pivotal RCTs, there remains significant geographic disparities across the US in the manner in which this increase has spread.[8] It will be useful to identify whether regions with lower rates of increase in EVT uptake have less established interhospital transfer networks.

Finally, there are several limitations to this study. Hospital participation in GWTG-Stroke is voluntary, and therefore, trends in interhospital transfer for EVT and comparison of outcomes found in this study may not be generalizable to non-participating US hospitals or stroke systems in other countries. Although this is the largest study to date providing comparison of EVT outcomes between patients arriving directly to the EVT-providing hospitals and patients arriving after interhospital transfer, it is not a randomized study, and differences in outcomes between these two groups may reflect unmeasured confounding variables or selection bias. Risk adjustment for baseline stroke severity was performed using NIHSS data available upon patient arrival to the GWTG-Stroke hospital where EVT was provided. For the transfer group, this may have underestimated baseline stroke severity, as 56.6% of patients in the transfer group had received IV t-PA prior to transfer, which can result in clinical improvement en route. Furthermore, we did not have the ability to compare baseline stroke severity using imaging parameters, such as ASPECTS scores or arterial occlusion location, as this information is not available in the database. We have provided adjusted model for last known well to EVT initiation time, but we had to exclude 27.67% of patients for this model for whom this information was missing. Another limitation of our study is that for patients who survived hospitalization, the only functional outcome measure analyzed was ability to ambulate independently at discharge, which was determined by trained data abstractors at each participating GWTG-Stroke hospital after a careful review of patient medical records. We did not have a post-discharge functional outcome that was ascertained using a standardized methodology available for comparison. Also, as the latest data in our study is from December 2017, it does not take into account the further increase in interhospital transfer for EVT that is anticipated after recent publications showing the benefit of mechanical thrombectomy up to 16 to 24 hours after stroke onset.[16, 17]

CONCLUSIONS:

This large, clinical practice-based study shows that interhospital transfer for providing EVT is becoming increasingly frequent. Interhospital transfer is associated with significant delays in EVT initiation. Functional outcomes for patients receiving EVT after interhospital transfer are worse even after adjusting for the delay in EVT initiation. Expansion of EVT capability, development of tools for efficient triaging, and quality improvement initiatives focused on increasing efficiency of the interhospital transfer process are needed to optimize outcomes for patients receiving EVT. Identifying barriers to using interhospital transfer and factors affecting outcomes for transfer-in patients will help improve access to EVT in geographical regions where access to EVT is currently lacking.

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Clinical Perspective

What is new?

- A significant number of acute ischemic stroke patients receiving endovascular therapy (EVT) in the US are receiving this therapy after interhospital transfer.
- Interhospital transfer for the purpose of EVT has significantly increased following the publication of pivotal randomized controlled trials demonstrating the beneficial effects of EVT.
- EVT after interhospital transfer is associated with a delay in receiving the treatment.
- Outcomes of EVT after interhospital transfer are inferior compared to EVT after direct arrival and this relationship persists even after adjusting for the delay in EVT initiation.

What are the clinical implications?

- Hospitals providing EVT are providing care for increasing numbers of acute ischemic stroke patients arriving to them via interhospital transfer.
- Patient outcomes may be improved by making EVT more widely available, efficiently triaging patients to EVT centers, reducing interhospital transfer times and identifying additional factors adversely affecting outcomes for this group of patients.

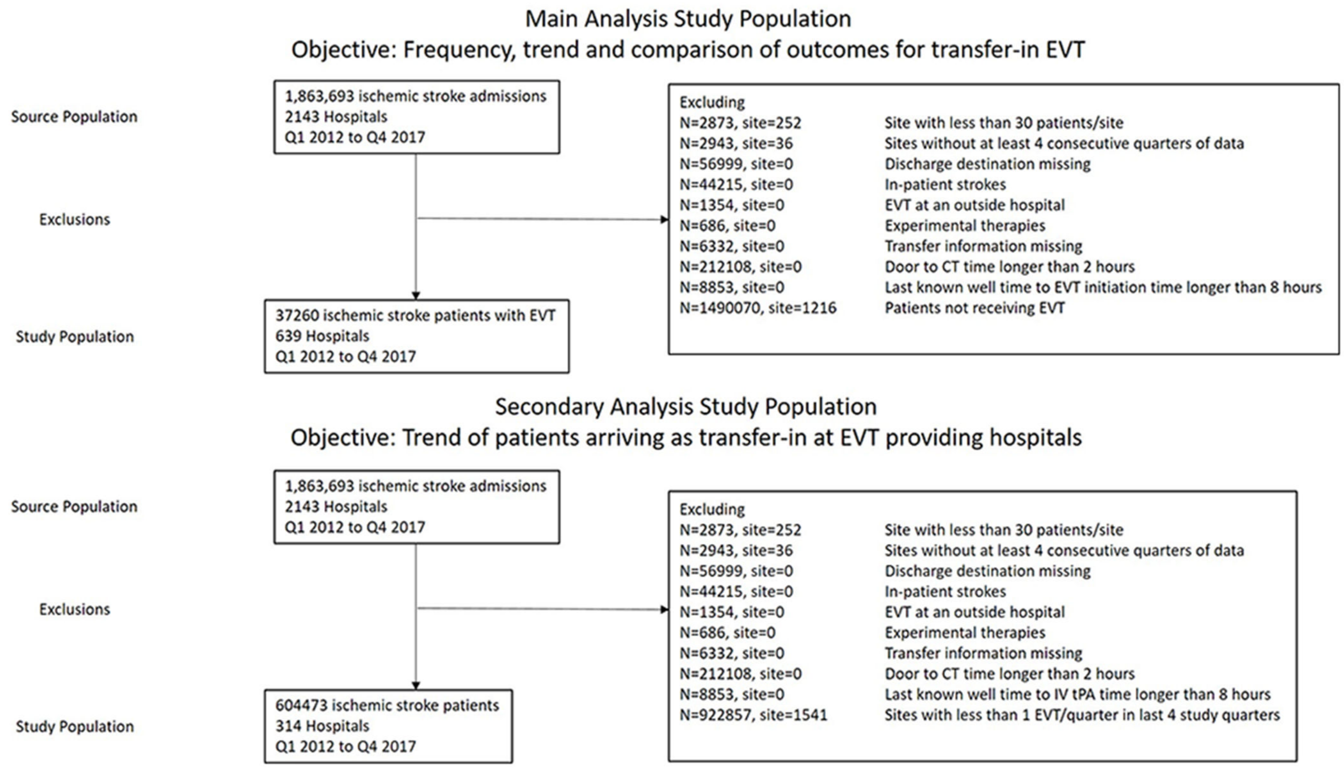

Figure 1:

Study flow diagram. EVT: Endovascular therapy; Q1: first quarter; Q4: fourth quarter.

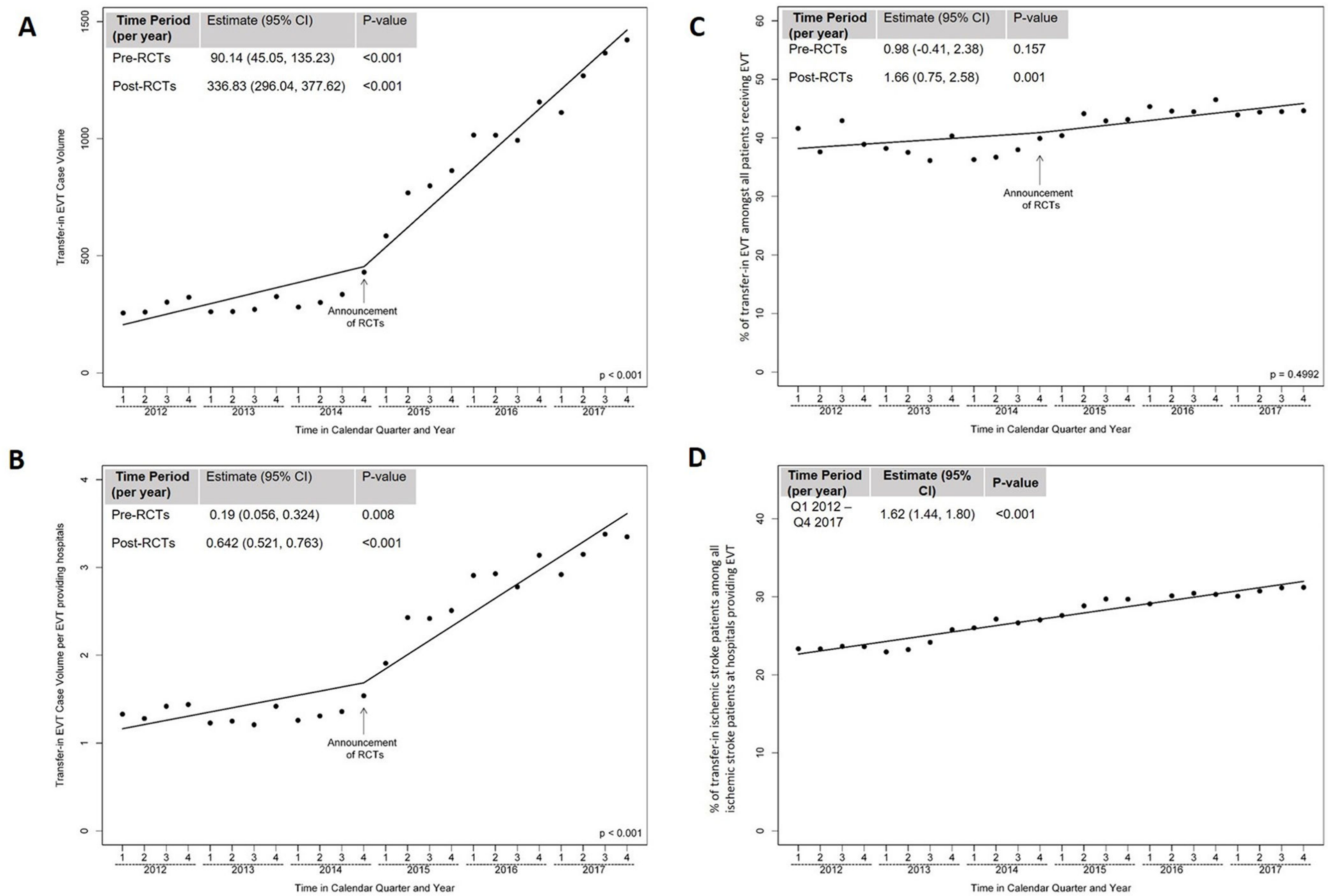

Figure 2:

Trends and frequency of transfer-in EVT. Frequency over time of patients receiving EVT after interhospital transfer. (A) Frequency over time of patients receiving EVT after interhospital transfer normalized for hospitals providing EVT. (B) Trends over time in the percentage of transfer-in EVT among all patients receiving EVT. (C) Trends over time in the percentage of transfer-in ischemic stroke patients among all ischemic stroke patients at hospitals providing EVT. (D) CI indicates confidence interval; EVT, endovascular therapy; and RCT, randomized controlled trial.

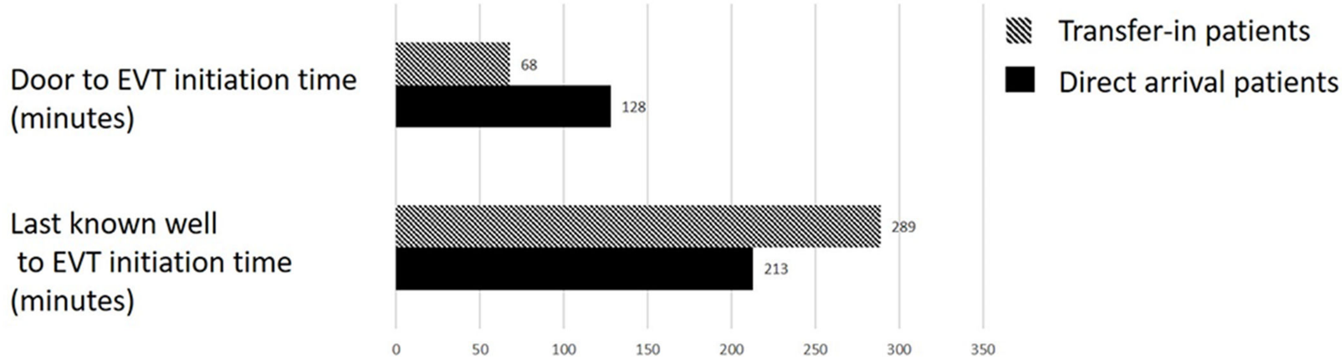

Figure 3:
Median times for EVT for transfer-in versus direct arrival patients.

Table 1.

Characteristics of patients treated with EVT

	Transfer-in (N=15975)	Direct arrival (N=21285)	Standardized Difference (%)
Age, years (Mean±SD)	**69±14.7**	**71.0±14.8**	**10.3**
Women (%)	48.7	50.7	4.0
Race/ethnicity (%)			
White	**73.2**	**68.4**	**10.5**
Black	**11.8**	**15.8**	**11.6**
Asian	2.4	3.5	3.5
Hispanic	5.3	7.6	9.2
Medical history			
Atrial fibrillation (%)	33.0	32.9	0.2
Prior Stroke/TIA (%)	19.5	22.8	8.2
Myocardial Infarction (%)	23.7	22.9	2.0
CHF (%)	11.9	11.6	0.8
Carotid Stenosis (%)	2.9	2.9	0.2
Diabetes (%)	25.0	24.7	0.7
PVD (%)	3.6	3.5	0.5
Hypertension (%)	69.1	69.3	0.5
Smoker (%)	18.4	16.4	5.4
Dyslipidemia (%)	40.7	40.6	0.3
NIHSS on arrival to EVT providing hospital (Median, IQR)	17 (11,22)	16 (11,21)	5.6
Arrival during off Hours (%)	**53.9**	**46.1**	**15.5**
IV t-PA prior to EVT	56.6	57.6	2.0

Abbreviations: SD: Standard Deviation. TIA: Transient Ischemic Attack. CHF: Congestive Heart Failure. PVD: Peripheral Vascular Disease. NIHSS: National Institute of Health Stroke Scale. EVT: Endovascular Therapy. IQR: Interquartile Range. IV t-PA: Intravenous tissue plasminogen activator. Standardized Differences greater than 10% are considered imbalanced.

Table 2.

Hospital Characteristics at Patient Level

	Transfer-in	Direct arrival	Standardized Difference (%)
Total Number of Beds (Mean±SD)	610.0±387.4	539.0±427.6	9.4
Annual Stroke Volume (Mean±SD)	401.0±169.4	362.3±180.7	8.5
Annual IV t-PA Volume (Mean±SD)	**34.6±20.0**	**35.7±21.4**	**14.2**
Annual EVT volume (Mean±SD)	**37.3±37.4**	**31.1±31.1**	**24.8**
Teaching Hospital (%)	**95.2**	**89.6**	**21.4**
Primary Stroke Center (%)	23.5	29.6	13.8
Comprehensive Stroke Center (%)	27.0	18.6	20.0
Regional Distribution (%)			
West	18.8	19.9	3.6
South	**32.8**	**40.0**	**16.4**
Midwest	**25.5**	**18.7**	**14.9**
Northeast	22.8	21.3	2.8
Rural (%)	0.2	0.4	3.8

Abbreviations: SD: Standard Deviation. IV t-PA: Intravenous tissue plasminogen activator. EVT: Endovascular Therapy. Standardized Differences greater than 10% are considered imbalanced.

Table 3:

Association of outcomes by arrival group (transfer-in group vs direct arrival group)

Outcomes	Transfer-in	Direct arrival	Unadjusted Odds Ratio (95% Confidence Interval)	Adjusted Odds Ratio* (95% Confidence Interval)	P Value	Adjusted Odds Ratio† (95% Confidence Interval)	P Value
In-hospital mortality (%)	14.67	13.42	1.17 (1.10, 1.24)	1.14 (1.06, 1.24)	0.0008	1.01 (0.92, 1.11)	0.8258
Symptomatic Intracranial Hemorrhage (%)	7.02	5.65	1.28(1.17, 1.39)	1.25 (1.14, 1.38)	<0.0001	1.15 (1.02, 1.29)	0.025
Independent ambulation at discharge‡ (%)	33.12	37.16	0.80 (0.76, 0.85)	0.78 (0.72, 0.84)	<0.0001	0.87 (0.80, 0.95)	0.002
Discharge destination home‡(%)	24.32	29.15	0.77 (0.72, 0.81)	0.71 (0.66, 0.76)	<0.0001	0.82 (0.76, 0.88)	<0.0001
Length of stay‡ (median, interquartile range)	6 (4,10)	6 (4.10)	1.12 (1.06, 1.18)§	1.19 (1.11, 1.26)§	<0.0001	1.08 (1.00, 1.16)§	0.0395

*Adjusted for baseline covariates, including age, sex, race, NIHSS, IV t-PA yes/no, arrival during off hrs. vs on hrs., comorbid conditions, and hospital characteristics, including annual stroke, IV t-PA and EVT volume, stroke center certification, size and academic hospital yes/no

†Adjusted for baseline covariates as above and last known well to EVT initiation time

‡In-hospital death excluded

§Odds Ratio for > 6 days vs ≤ 6 days as 6 days is the median among survivors