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IAT-TiMeS: Intra-Arterial Thrombectomy Transfer Metric Study in Texas

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Objective: We aim to report intra-arterial thrombectomy transfer metrics for ischemic stroke patients that were transferred to hub hospitals for possible intra-arterial thrombectomy in multiple geographic regions throughout the state of Texas and to identify potential barriers and delays in the intra-arterial thrombectomy transfer process. *Method:* We prospectively collected data from 8 participating Texas comprehensive stroke/thrombectomy capable centers from 7 major regions in the State of Texas. We collected baseline clinical and imaging data related to the pre-transfer evaluation, transfer metrics, and post-transfer clinical and imaging data. *Results:* A total of 103 acute ischemic stroke patients suspected/confirmed to have large vessel occlusions between December 2016 to May 2019 that were transferred to hubs as possible intra-arterial thrombectomy candidates were enrolled. A total of 56 (54%) patients were sent from the spoke to the hub via ground ambulance with 47 (46%) patients traveling via air ambulance. The median spoke arrival to hub arrival time was 174 min, median spoke arrival to departure from spoke was 131 min, and median travel time was 39 min. The spoke arrival time to transfer initiation was

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68 min. CT-perfusion obtained at the spoke and earlier initiation of transfer were statistically associated with shorter transfer times. *Conclusion:* Transfer of intra-arterial thrombectomy patients in Texas may take over 4 h from spoke arrival to hub arrival. This time may be shortened by earlier transfer initiation and acceptance.

Key Words: Ischemic stroke—Endovascular thrombectomy—Mechanical thrombectomy—Transfer—Large vessel occlusion

Introduction

Treatment with intravenous tissue plasminogen activator (IV t-PA) has been established as an effective treatment for acute ischemic stroke patients treated within the first few hours of symptom onset.[1] Although the treatment window for effectiveness was extended from 3 to 4.5 h, it has been clearly demonstrated that earlier treatment is statistically associated with a higher likelihood of a better outcome.[2,3] In addition, intra-arterial therapy (IAT) has been demonstrated in multiple trials to improve outcomes in acute stroke patients when treated within 6 h and if perfusion imaging is obtained, 6 to 24 h.[4] This had led the American Heart/American Stroke Association to not only release guidelines recommending endovascular procedures for selected patients but also organize stroke systems of care to facilitate the delivery of this treatment.[5]

Unfortunately, not all patients eligible for endovascular therapy present to facilities capable of delivering endovascular treatment and thus, often need to be transferred to comprehensive stroke centers/thrombectomy capable (CSC/TC) centers for the procedure to be performed. Specifically, for Texas, which is a large state with a wide geographic distribution of over 29 million residents, quick access to a center that can deliver this robust treatment is essential. The transfer process is complex and often involves multiple teams of physicians and administrative personnel to coordinate the transfer of the patient. The complexity can often lead to delays in arrival of the patient to the hub and possibly lead to suboptimal outcomes or at times exclude the patient from the procedure due to the limited therapeutic window or progression of ischemic injury.

Currently, there are no standard time metrics recommended for the IAT transfer process. We therefore aim to describe in this study, Intra-arterial Transfer Metrics Study (IAT-TiMeS), the current landscape of IAT transfer time metrics and characteristics at multiple Texas CSC/TC centers to identify potential barriers and/or delays in the transfer process.

Methods

Study Design

We prospectively collected data from 8 participating CSC/TCs from 7 major regions in the State of Texas. All CSCs were designated as such by national accrediting organizations. We allocated enrollment of patients at each site in order to balance the data according to the typical case volume and not be heavily skewed by centers or regions (Fig. 1).

Study population

All patients that were initially evaluated at a spoke site and transferred to a participating Texas CSC/TC (hub) for higher level or care, specifically for evaluation of IAT, were included. Enrollment at each hub was given a prespecified target. We aimed to enroll a total of 100 patients in this observational study.

Data Collection

Baseline clinical and imaging data at the spoke, transfer metrics, and clinical and imaging data at the hub were collected. The study enrollment period began in December 2016 and ended in May 2019; we followed a rolling enrollment approach as sites were initiated. The hub hospital sites included Memorial Hermann − Texas Medical Center in Houston, Texas (20 patients), UTHealth Science Center at San Antonio—University Hospital (5 patients), Texas Tech University Health Science Center in Lubbock, Texas—University Medical Center (9 patients), Texas Tech University Health Science Center in El Paso, Texas—Sierra Medical Center and University Medical Center (9 patients), UTHealth Science Center at Austin, Seton—Seton Medical Center and University Medical Center Brackenridge (20 patients), UT Southwestern Medical Center in Dallas, Texas (10 patients), Baylor Scott and White Medical Center in Dallas, Texas (10 patients) and Valley Baptist Medical Center in Harlingen, Texas (20 patients). Each participating hub site is part of the Lone Star Stroke Clinical Trial Network. IRB approval was obtained at all participating hub sites for this study.

In total, we had 46 spokes sites that transferred patients for IAT evaluation at the hub sites. Thirty-two of the 46 sites were designated as primary stroke centers and the remaining 14 had no stroke center designation and were a mix of community hospitals and free-standing emergency centers.

Statistical analysis

Descriptive statistics (mean, standard deviation, median, quantile, frequency, percentage) were provided for demographic and clinical variables. Wilcoxon rank sum test was used to compare the spoke arrival to hub arrival time

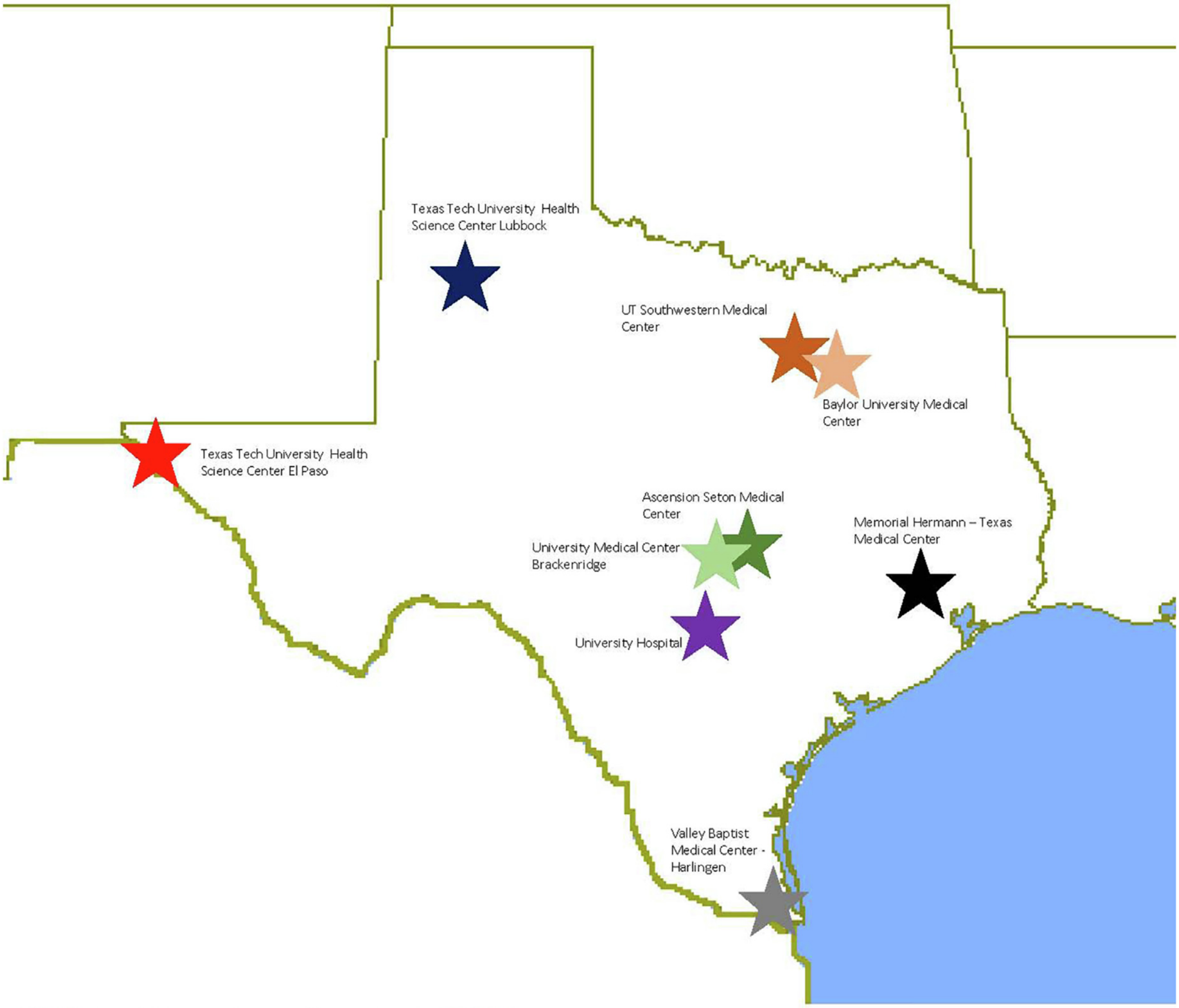

Fig. 1 *Study hub sites.*

between groups such as sex, telemedicine use, IV-tPA use, etc. For groups with more than two levels such as race, Kruskal-Wallis test was used instead. Spearman method was used to evaluate correlation between the spoke arrival to hub arrival time and other continuous variables. All statistical analyses were performed by using the SAS software (version 9.4, the SAS Institute, Cary, NC).

Results

A total of 103 patients were enrolled from 46 spokes at 9 hubs into IAT-TiMeS in the study period and included in the analysis (Table 1a). The mean age of the study group was age 67 years with 49% female. The majority of the patients were white (79%); African and Asian Americans made up approximately 15% of the enrolled patients and about a third of the patient sample were Hispanic. The median NIHSS at the spoke was 14.

Of the 103 patients, 66 (64%) received IV-tPA (Table 1b) at the spoke hospital prior to transfer and 59 (57%) were managed via telemedicine at the spoke hospital prior to transfer to the hub. The median door to needle time was 53 min. Over half of the patients (52%) had CT-angiography of the brain performed at the spoke, but only 12 (11.7%) had CT-perfusion of the brain performed at the spoke.

Upon arrival to the hub, 49 patients (47%) (Table 1c) underwent further imaging with a combination of CT, CT-angiography, and/or CT-perfusion of the brain. Of the 37 patients (69%) that had CT-perfusion performed, 28 (78%) utilized automated CT-perfusion software. Only 11 patients (11%) underwent MRI upon arrival to the hub prior to thrombectomy decision.

In total, 79 of the 103 transferred patients underwent a cerebral angiogram at the hub after arrival and 67 (65%) had subsequent thrombectomy performed. Only 3 (3%) symptomatic intracerebral hemorrhage (ICH) were documented with median length of stay of 5 days (Table 1d).

A total of 56 (54%) patients were sent from the spoke to the hub via ground ambulance with 47 (46%) patients

Table 1a. *Baseline characteristics of transfer cohort (n = 103).*

Baseline Demographics	
Mean Age (SD)	67 (57.0, 78.0)
Female, N (%)	49 (48)
Race, N (%)	
White	81 (79)
African American	13 (13)
Asian	2 (2)
Other/Not Reported	7 (7)
Ethnicity, N (%)	
Hispanic or Latino	33 (32)
Not Hispanic or Latino	65 (63)
Not reported	5 (5)
Past Medical History, N (%)	
Prior Ischemic Stroke	15 (15)
Prior Hemorrhagic Stroke	2 (2)
Prior TIA	8 (8)
Hypertension	73 (71)
Congestive Heart Failure	9 (9)
Atrial Fibrillation	26 (25)
Hypercholesterolemia	28 (27)
Diabetes	34 (33)

Table 1b. *Clinical data.*

IV tPA, Spoke	
Yes	66 (64)
No	37 (36)
Door to Needle time, Median (Q1,3), N = 65	53 (42, 76)
Telemedicine	
Performed at spoke, N (%)	59 (57)
Door to TM Page Time, Median in Minutes (Q1,3)	18 (5, 36)
TM Page Time to Camera Time, Median in Minutes (Q1,3)	9 (6, 12)
NIHSS at Spoke, Median (Q1,3), N = 75	14 (8, 19)
NIHSS at Hub, Median (Q1,3), N = 88	12 (6, 19)
Premorbid mRS, (%) N = 59	
0-No Symptoms	42 (41)
1-No Significant disability	6 (5.8)
2-Slight disability	3 (2.9)
3-Moderate disability	7 (6.8)
4-Moderate disability	1 (1)
Not reported	44 (43)

Table 1c. *Imaging.*

Imaging at Spoke	
ASPECTS, Median (Q1-3), N = 35	10 (8,10)
CTA Performed (%)	
Yes	54 (52)
No	42 (40)
Not Reported	7 (6.8)
CTP Performed (%)	
Yes	12 (11.7)
No	86 (83.5)
Not Reported	5 (5)
Imaging at Hub	
Cerebral angiogram performed at hub, N (%)	
Yes	79 (77)
No	24 (23)
Intra-arterial Thrombectomy performed at hub, N (%)	
Yes	67 (65)
No	36 (35)
Imaging performed at hub prior to cerebral angiogram, N (%)	
Yes	54 (53)
No	49 (47)
CTH performed at hub prior to cerebral angiogram, N (%)	
Yes	50 (91)
No	5 (9)
CTA performed at hub prior to cerebral angiogram, N (%)	
Yes	37 (67)
No	18 (33)
CTP performed at hub prior to cerebral angiogram, N (%)	
Yes	37 (69)
No	17 (32)
Automated CTP software prior to cerebral angiogram	
Yes	28 (78)
No	9 (22)
MRI Brain performed at hub prior to cerebral angiogram, N (%)	
Yes	6 (11)
No	49 (89)
MRA performed at hub prior to cerebral angiogram, N (%)	
Yes	4 (7)
No	50 (93)
MRP performed at hub prior to cerebral angiogram, N (%)	
Yes	3 (5)
No	54 (95)
Automated MRP software prior to cerebral angiogram	
Yes	1 (33)
No	2 (66)
ASPECTS, Median (Q1-3), N = 36	8 (7,9)

traveling via air ambulance (Table 2). The median arrival from spoke to hub time was 174 min, and median travel time was 39 min. The median spoke arrival time to transfer initiation was 68 min. The median spoke arrival time to departure from spoke (door-in to door-out) was 131 min.

The spoke arrival to hub arrival time was not statistically associated with age, sex, race, telemedicine use, IV-tPA use, CT-angiography performed at spoke, or mode of transfer. We did find that patients who underwent CT-perfusion at

Table 1d. *Clinical Outcomes and Complications.*

IV tPA complications—Symptomatic ICH, N (%)	
Yes	2 (2)
No	101 (98)
IAT complications—Symptomatic ICH, N (%)	
Yes	1 (1)
No	102 (99)
Length of Stay, Mean Days (Q1,3), N = 103	5 (3,10)
90 day mRS, (%) N = 59	
0-No Symptoms	10 (9.7)
1-No Significant disability	7(6.8)
2-Slight disability	6 (5.7)
3-Moderate disability	12 (11.7)
4-Moderate disability	9 (8.7)
5- Severe disability	5 (4.9)
6-death	14 (13.6)
Not reported	40 (38.8)
Transfer Time and Outcome	Correlation (p value)
Door to revascularization time	0.18 (0.27)
24 hour NIHSS	0.07 (0.60)
90 day mRS	0.39 (0.005)

the spoke had statistically significant shorter transfer times to the hub (median: 120.5 min vs 185 min, Z statistic = -2.229, $p = 0.028$). Earlier transfer initiation times were also significantly associated with shorter transfer times (Spearman correlation coefficient = 0.79, $p < 0.0001$). Interestingly, we did find a positive correlation between lower transfer times and lower 90-day mRS with Spearman correlation of 0.39 ($p = 0.005$).

We also analyzed transfer times during on vs off hours (on hours: 8a-5p; off hours: 5p-8a) and weekdays vs weekend transfers times. We found no statistical correlation with this analysis.

Table 2. *Transfer Metrics.*

Mode of Transportation, N (%)	
Ground Ambulance	56 (54)
Air Ambulance	47 (46)
Transfer Time Metrics, Median n Minutes (Q1,3)	
Arrival to spoke to arrival at hub, N = 96	174 (120, 255)
Arrival to spoke to departure from spoke, N = 79	131 (93, 187)
Departure from spoke to arrival at hub, N = 81	39 (20, 62)
Arrival to spoke to transfer initiation, N = 84	68 (43, 110)

Discussion

Intra-arterial thrombectomy has been one of most impactful acute ischemic stroke treatments developed in the last decade. However, many patients that are found to have large vessel occlusion (LVO) still need to be transferred to thrombectomy capable centers in order to have the procedure performed. The transfer process can be tedious, and the complex process can be fraught with delays. For example, the patient first needs to be evaluated at the spoke either by the local emergency room team, remote telemedicine team, or local neurologist to determine treatment eligibility that includes IV-tPA. Neuroimaging such as CT brain and when indicated CT-angiography/CT-perfusion needs to be performed if available. Once the patient has been identified as needing transfer, the local team then initiates the transfer by calling a CSC/TC with an accepting physician. Often, this triage can be time consuming, and if the accepting facility is full, the process needs to start over again with another facility. Once the patient is accepted, the patient still needs to be transported, which can also be further opportunity for delays involving availability of air and ground transport, weather, and other factors. Inter-hospital transfers have been shown to delay treatment for patients requiring IAT and impact outcomes.[6]

Currently, there are no practice standards for transfer metrics regarding the IAT transfer process. We aimed to report and describe the IAT transfer times for patients throughout Texas in order to gain a better understanding of the current landscape regarding IAT transfers for the state. We found that in our population, it took nearly 3 h (174 min) for the patients to arrive at the hub before their evaluation for thrombectomy, and transfer times were not impacted by IV-tPA delivery at the spoke or mode of transfer. Patients spent over 2 h (131 min, median, door-in to door-out) at the spoke before departure for the hub, which is an area that needs improvement. This confirms previous findings in retrospective and in single center studies that door-in to door-out time accounts for the bulk of treatment delays. Furthermore, these studies suggest that prolonged door-in to door-out time is associated with worse outcomes.[7]

In IAT-TiMeS, shorter transfer times were noted in patients that underwent CT-perfusion at the spoke and with earlier transfer initiation. We are uncertain why CT-perfusion performed at the spoke was associated with shorter transfer times but postulate that facilities equipped with CT-perfusion may have more resources, higher stroke volumes, and greater experience with stroke transfer processes. They may already have in place protocols, algorithms, and established relationships with thrombectomy centers that have already addressed some transfer barriers. Interestingly, analysis of a late-window (6−24 h) thrombectomy trial suggests that there are patients who are slow progressors, where door-in to door-out times may not negate the benefit of IAT for stroke.[8] These patients may be identified by perfusion imaging. However, our study demonstrates that the majority of patients at spoke centers do not receive perfusion imaging. Furthermore, the late-window slow progressors identifiable on CT-perfusion represent a small segment of patients being transferred for IAT, maintaining the need for optimizing door-in to door-out in general.

We also learned that the practice pattern in our population was quite variable. Not all patients underwent advanced neuroimaging at the spoke or even at arrival of the hub. These variations highlight the complexity when developing stroke systems of care, as it is often dependent on local practice patterns and available resources. We advocate that to shorten IAT transfer times, transfers to the hub must be initiated as early as possible. Often times, transfers are initiated after the patient has been fully triaged with all studies and treatments delivered at the spoke. Ideally, once the patient is suspected at the spoke to have a LVO, possibly with a stroke severity screening assessment, such as the VAN screening tool[9], the transfer process should be initiated.

Many emergency room physician teams at the spoke may be reluctant to begin the transfer process until it is certain that a transfer is required, due to the concern that transfers may need to be cancelled. For example, if the CT-angiography does not reveal an LVO or CT brain shows a hemorrhage, then the transfer for IAT may not be indicated. However, in order to streamline the IAT transfer process, spokes should have a low threshold to contact the accepting hubs early in the emergency triage. Better to cancel a transfer than delay one. Overall, our greatest impact to reduce IAT transfer times in Texas is likely to occur by enhancing door-in door-out protocols at spoke hospitals. In addition to early CSC/TC notification, investing in spoke technology with CTP and automated software may also improve times.[10]

Our study has several limitations. Although our data were gathered prospectively, the analysis was performed retrospectively. The number of patients included in the study is small and results may not be entirely generalizable for all stroke centers throughout the nation or for all patient populations. Also, transfer patterns are often determined by pre-existing relationships between facilities, and not by geographic proximity. Further analysis of transfer patterns and transfer metrics based on proximity may be beneficial to minimize transfer times.

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