# The Impact of Inter-Hospital Transfer on Clinical Outcomes following Endovascular Treatment for Acute Ischemic Stroke

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## ABSTRACT

### PURPOSE

Hospitals designated as primary stroke centers offer noninvasive treatment for acute ischemic stroke, but only comprehensive stroke centers are equipped to provide endovascular treatment. When stroke patients needing endovascular treatment present to the emergency department at a primary stroke center, they then require inter-hospital transfer to a comprehensive center for definitive treatment. Recent studies have found significant treatment delays and poor clinical outcomes in patients requiring inter-hospital transfer[1,2]. The primary aim of this study is to determine if inter-hospital transfer impacts clinical outcomes after endovascular treatment for acute ischemic stroke. A secondary aim is to determine whether inter-hospital transfer coincides with any significant treatment delay.

### METHODS

This study involves retrospective chart review for 107 patients undergoing endovascular treatment for acute ischemic stroke at one of three hospitals in Austin, Texas from October 2016 to September 2018. 26 patients required inter-hospital transfer, while 81 (the control group) presented directly to a hospital offering endovascular treatment. Two-tailed T- and U-tests were used for analysis of parametric and non-parametric variables pertaining to time intervals and baseline characteristics. Odds ratios were calculated to compare dichotomized outcomes between groups, with significance determined by chi-square.

### RESULTS

Inter-hospital transfer significantly prolonged onset to groin (mean difference = 37.2 min, $p=.02$). The transfer group was more likely to experience intracranial hemorrhage (53.9% > 22.2%, $p<.01$). Clinical outcomes did not significantly differ between groups.

### CONCLUSIONS

Although observed trends in these data suggest poor outcomes for transfer patients, small sample size limits the significance of these findings. However, the significant treatment delay seen in the transfer group warrants a discussion on city protocol changes regarding patient transport via emergency services. Protocol changes favoring direct delivery of patients to comprehensive stroke centers may reduce treatment delay and yield improved clinical outcomes.



### KEYWORDS

Acute ischemic stroke, intraarterial thrombolysis, endovascular, thrombectomy, transfer, reperfusion time

**INTRODUCTION**

Acute ischemic stroke (AIS) is a time-sensitive emergency. Longer stroke duration means longer periods of cerebral ischemia, which yield larger infarct sizes[3]. Therefore, it is of utmost importance to provide patients with access to treatment as quickly as possible in order to promote optimal recovery rates and functional outcomes. There are two approved options for treatment of AIS. First, recombinant tissue plasminogen activator (rt-PA) may be administered intravenously to dissolve the clot. However, rt-PA is only approved in the U.S. within a three-hour time window from stroke onset, and contraindications sometimes prevent its administration.

The second treatment option, endovascular treatment (EVT), has been shown to be significantly beneficial for a specific subset of patients with large vessel occlusions which tend to cause more severe stroke symptoms[4,5,6,7,8]. Compared to rt-PA, EVT is a more invasive treatment option for definitive clot removal and cerebral reperfusion. It involves intraarterial insertion of specialized equipment into the cerebral vasculature for direct aspiration, stent retrieval, or other mechanical disruption of the clot, sometimes in conjunction with angioplasty, in order to restore cerebral perfusion back for baseline. For both rt-PA and EVT, post-treatment outcomes improve when the treatment is provided more quickly[9,10]. Therefore, when treatment is delayed, the treatment becomes less effective and post-treatment outcomes worsen. A three-phase trial published in Neurology in 2009 sought to quantify the impact of this delay; this study concluded that a 45-minute delay to reperfusion (restoration of cerebral blood flow) resulted in a 10.6% decrease in the likelihood of a good clinical outcome[11].

In order to maximize the efficiency of stroke systems of care, attention must be paid both to out-of-hospital as well as in-hospital protocols. By analyzing the effectiveness of these protocols, it is possible to identify and minimize avoidable treatment delays and expedite treatment. When considering out-of-hospital protocols, the primary concern involves transporting the patient as quickly as possible to the proper destination where treatment can be administered.

Only certain hospitals possess the resources and personnel required to offer EVT. Hospitals designated as primary stroke centers are able to offer rt-PA to these patients, but only comprehensive stroke centers are equipped to provide both rt-PA as well as EVT. When stroke patients needing EVT present to the emergency department at a primary stroke center, they then require inter-hospital transfer to a comprehensive center for definitive treatment. Recent studies have demonstrated significant EVT delays and poor clinical outcomes in patients requiring inter-hospital transfer compared to patients who were transported directly to a treatment facility[1,2]. Due to this delay and the associated functional outcomes, inter-hospital transfer should be reserved only for cases in which the transfer will be beneficial to the patient. Otherwise, strides should be taken to ensure that unnecessary transfers are avoided in order to minimize delay to EVT.

The primary aim of this study is to determine if inter-hospital transfer impacts clinical outcomes after EVT for acute ischemic stroke. The primary clinical outcome is lack of disability at discharge, defined by an NIH stroke scale score of 0 or 1. Other clinical outcomes will also be assessed to supplement this analysis. The secondary aim is to determine whether there is any association between inter-hospital transfer and delayed EVT. The time interval between stroke onset and groin puncture in the operating room (signifying initiation of the EVT procedure) will be used to assess this delay.

## METHODS

### *Selection Criteria*

This retrospective study includes 107 patients receiving EVT for acute ischemic stroke at one of three treatment facilities in Austin, TX from October 2016 to September 2018. According to hospital stroke protocols, each patient underwent specialized computed tomography or magnetic resonance imaging which confirmed the presence of a large vessel occlusion with a significant perfusion mismatch, indicating the patient's need for EVT.

### *Patient Groups*

Patient groups were determined by the need for inter-hospital transfer. 26 patients first presented to a primary stroke center for workup, imaging, and rt-PA administration (if indicated). They then underwent inter-hospital transfer to a treatment facility where EVT was available. The remaining 81 patients included in this study serve as the control group, having avoided the need for inter-hospital transfer by presenting directly to a treatment facility.

### *Notable Exception: Classification of Inpatient Stroke Onset*

Three patients experienced stroke onset as an inpatient in a primary stroke center where EVT is not available. Patients fitting this description were included in the control group, despite their need for inter-hospital transfer. This grouping is justified because these patients did not present with stroke symptoms to the Emergency Department of a primary stroke center, and the only transport time they experienced was the actual transfer between hospitals. Patients included in the transfer group should have experienced two transport times (transport to primary stroke center, then transport to treatment facility).

### *Study Design*

The study design involved retrospective chart review to collect data for comparisons between transfer patients and the control group. Chart review was performed via manual data extraction, and the resulting database was complete with no missing data for any variable utilized in this analysis. An expanded discussion of the standardized methodology required to extract this data is included in Appendix A.

The two research questions that prompted this study involve a comparison of clinical outcomes and treatment delays. The primary clinical outcomes to be measured included (1) an NIH stroke scale score of zero or one (indicating no residual disability) at the time of discharge, and (2) discharge home (as opposed to discharge to a rehabilitation facility, to a nursing facility for hospice care, or death prior to discharge). Secondary clinical outcomes to be assessed include (1) any intracranial hemorrhage during inpatient recovery (regardless of the amount or severity of the hemorrhage) and (2) independence at discharge (as measured by a score of 0-2 on the modified Rankin scale, or mRS).

The second research question involves the association of inter-hospital transfer with any significant treatment delays. The focus of this question lies in the actionable time interval, meaning the time that may be affected by ensuing protocol changes to enhance the efficiency of stroke systems of care. With this focus in mind, the most relevant time interval for study begins with the moment the stroke symptoms were first witnessed and care was initiated for the patient, often referred to as "first abnormal." The interval ends with the moment at which the endovascular procedure is initiated, marked by groin puncture for insertion of the microcatheter. This specific time interval, referred to here as "onset to groin", was to be determined for each patient to allow for group comparison.

***Statistical Analysis***

To facilitate effective comparisons between the transfer and non-transfer groups, different statistical methods were used depending on the characteristics of the data. For comparison of any continuous variables that reasonably approximate a normal distribution, two-tailed t-test assuming equal variance was utilized; variables assessed in this way include onset to groin, endovascular procedure duration, and age. For other quantitative variables that were determined to convey a non-normal distribution (small range, ordinal variables), the non-parametric variant of the t-test was applied, called the Wilcoxon rank sum test (u-test). Relevant non-parametric variables included NIH stroke scale scores, mRS scores, Thrombolysis in Cerebral Infarction (TICI) scale scores, and number of procedural passes during EVT.

Qualitative comparisons were essential to compare demographics and baseline characteristics between groups, as well as to compare the incidence of a variety of good and bad outcomes following EVT. For these dichotomized data, unadjusted odds ratios were calculated and chi-square test of independence was used to determine the significance of group differences. In addition to various demographics and baseline characteristics, relevant qualitative outcomes included disposition at discharge (home, inpatient rehabilitation, hospice, or death), lack of disability at discharge (NIHSS score of zero or one), and independence at discharge (mRS score 0-2).

| Group Comparison - Demographics and Baseline Characteristics | | | |
|---|---|---|---|
| Variable | Transfer n=26 | Control n=81 | p |
| *Demographics & Risk Factors* | | | |
| Age (Mean ± SD) | **67.7 ± 14.2** | 65.4 ± 15.7 | .49 |
| Age under 60 | 34.6% | **35.8%** | .91 |
| Age 60-74 | 34.6% | 34.6% | 1.00 |
| Age 75+ | **30.8%** | 29.6% | .91 |
| Women | **57.7%** | 51.9% | .60 |
| White | **80.8%** | 64.2% | .11 |
| Witnessed stroke onset | **57.7%** | 50.6% | .53 |
| Stroke onset while sleeping | **23.1%** | 19.8% | .72 |
| Taking aspirin | 23.1% | **32.1%** | .38 |
| Taking any antiplatelet medication | 34.6% | **37.0%** | .82 |
| Taking any anticoagulation medication | 7.7% | **16.0%** | .29 |
| Hyperlipidemia | 46.2% | **55.6%** | .40 |
| Taking a statin medication | 34.6% | **37.0%** | .82 |
| Hypertension | 65.4% | **69.1%** | .72 |
| Atrial fibrillation | 30.8% | **39.5%** | .42 |
| Coronary artery disease | 15.4% | **29.6%** | .15 |
| Congestive heart failure | 15.4% | **21.0%** | .53 |
| Diabetes mellitus | **34.6%** | 21.0% | .16 |
| Past stroke or transient ischemic attack | 19.2% | **22.2%** | .75 |
| Current cigarrette smoker | 23.1% | **27.2%** | .68 |
| Any cigarette smoking history | 42.3% | **46.9%** | .68 |
| *Stroke Severity & Treatment Factors* | | | |
| Initial NIHSS (Mean ± SD)* | 19 ± 4.9 | **19.6 ± 7.3** | .84 |
| rt-PA (tissue plasminogen activator) given | 53.8% | **54.3%** | .97 |
| # of Passes During EVT (Mean ± SD)† | **2.5 ± 1.6** | 2.2 ± 1.7 | .21 |
| EVT Procedure Time, min (Mean ± SD)† | **53.7 ± 35.4** | 38.1 ± 31.1 | .052 |
| Reperfusion Rate (TICI 2b or 3)‡ | 73.1% | **92.6%** | **<.01** |

**NIHSS = NIH Stroke Scale; †EVT = Endoascular Treatment; ‡TICI = Thrombolysis in Cerebral Infarction scale*
*SD = standard deviation*

**Table 1. Demographics and Baseline Characteristics.** *Comparing the transfer group characteristics with control, as well as a determination of statistical significance of these group differences.*

## RESULTS

### *Patient Group Comparison*

107 patients undergoing EVT for ischemic stroke from October 2016 to September 2018 were included in this study. 81 patients presented directly to one of three treatment facilities (the control group) and 26 initially presented to one of seven outside emergency rooms, thereafter requiring inter-hospital transfer to one of these three treatment facilities. The mean transfer time, or the time interval from arrival at the primary stroke center to arrival at the treatment facility, for these 26 transfer

patients was 131.5 minutes (range 38 - 409). Table 1 presents a comparison of demographic data and baseline characteristics between the transfer group and the control. The only statistically significant difference between these two groups is the reperfusion rate, or the percentage of patients achieving a post-EVT TICI score of 2b or 3 (Transfers: 73.1%, Control: 92.6%, p<.01). Of note, mean duration of the EVT procedure also appeared to be different, although this difference did not reach statistical significance [mean (min) ± standard deviation; transfers: 53.7 ± 35.4, control: 38.1 ± 31.1, p=.052].

***Onset to Groin***

The time interval utilized for comparison of EVT delays between groups is the interval from "onset to groin", defined as the interval from the first confirmed time of symptom onset to the initiation of the endovascular procedure, as marked by the moment of groin puncture. As shown in Figure 1, this time interval significantly differed between the groups (p = 0.02), with a 37.23-minute difference in means.

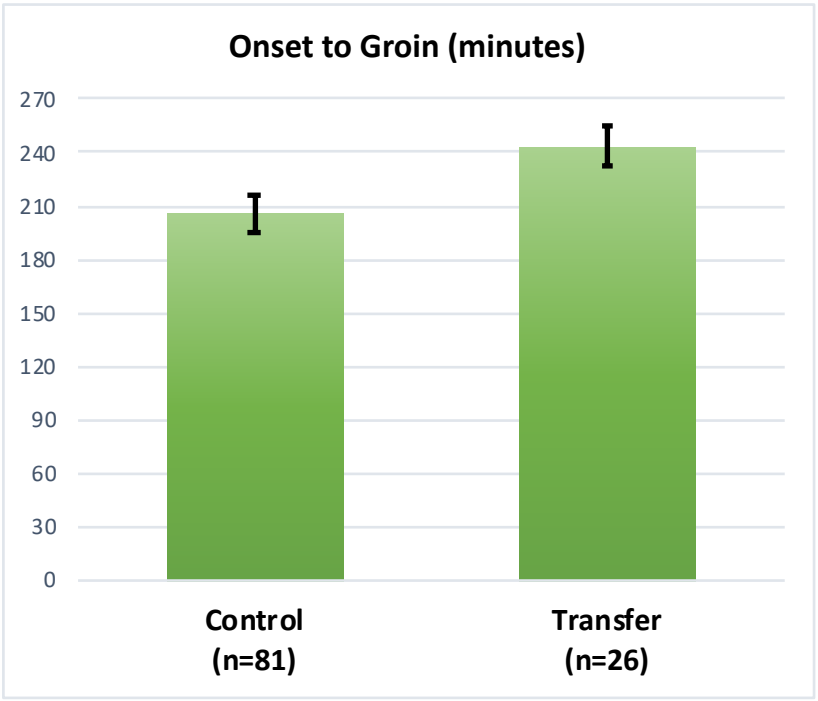


**Figure 1. Endovascular Treatment Delay.** *Shown is the time between "onset" (initial recognition of stroke symptoms) and groin puncture, marking the start of the endovascular procedure. Mean onset to groin time for the control group was 206.04 min (standard deviation = 95.33) and for the transfer group was 243.27 min (standard deviation = 57.21). Standard error bars are shown (SEM control group = 10.59; SEM transfer group = 11.22). Difference in means is 37.23 minutes, significant at p=0.02.*

***Clinical Outcomes***

Clinical outcome measures are presented in Table 2. The only statistically significant outcome was the percentage of patients experiencing any intracranial hemorrhage after EVT: the transfer group was significantly more likely to experience intracranial hemorrhage (transfers: 53.9%, control: 22.2%, p<.01), although retrospective chart review did not allow for a determination of whether these hemorrhages became symptomatic. Although other outcomes did not reach a level of statistical

significance, a trend was demonstrated in rates of disability at discharge, independence at discharge, and rates of returning home after discharge (versus inpatient rehabilitation, hospice care or death). Analysis of these three variables demonstrates that patients in the control group were approximately twice as likely to achieve these good clinical outcomes. The combined rate of in-hospital death or initiation of hospice care was found to be higher for the control group, countering the previously described trend, although this finding was also not statistically significant.

| Likelihood of a Bad Outcome after Inter-hospital Transfer | | | | | |
|---|---|---|---|---|---|
| Variable | % Transfer (n=26) | % Control (n=81) | OR | $\chi 2$ | p |
| Intracranial Hemorrhage After EVT | **53.9** | 22.2 | **4.08** | 9.39 | <.01 |
| Death or Hospice | 19.2 | **30.9** | 0.53 | 1.32 | .25 |
| No Disability at Discharge (NIHSS 0-1)* | 15.4 | **30.9** | **2.46** | 2.39 | .12 |
| Independent at Discharge (mRS 0-2)** | 15.4 | **34.6** | **2.91** | 3.46 | .06 |
| Discharged Home | 15.4 | **29.6** | **2.32** | 2.07 | .15 |

*OR (Odds Ratio): Odds of a Bad Outcome in the Transfer Group relative to the control group*
**NIHSS: NIH stroke scale; **mRS: modified Rankin scale*

**Table 2. Procedural and Clinical Outcomes.** *Odds Ratios comparing transfer patients to the control group, with significance determined by $\chi 2$ test of independence.*

***Sources of Error***

Due to the group differences (illustrated in Table 1), we extended our analysis to explore the relevance of factors that were potentially contributing to the observed clinical outcomes. Table 3 describes the likelihood that any of the listed variables are associated with achieving a level of no disability (the primary clinical outcome of this study) by the time of discharge.

Given that post-EVT reperfusion success was the only statistically significant group, and also considering that reperfusion success seemed to be associated with achieving no disability by time of discharge (although this outcome was not statistically significant), we determined that further exploration of this variable was warranted. Therefore, we continued this exploration of confounding variables by investigating whether reperfusion success was associated with any of the five procedural/clinical outcomes of this study, the same five outcomes which were analyzed and reported in Table 2. Instead of splitting into the transfer group and control group, this second analysis instead compared successful versus unsuccessful EVT reperfusion, independent of transfer status. The results of these analyses, along with the significance levels, are reported in Table 4. As is evident from the table, EVT reperfusion success actually demonstrated a generally more significant association with these outcomes than did inter-hospital transfer, suggesting that this variable was a significant confounder of the results reported in Table 2.

| Sources of Error | | | | | |
|---|---|---|---|---|---|
| | % NIHSS 0-1 (n=107) | | | | |
| Variable | True | False | OR | χ2 | p |
| *Demographics & Risk Factors* | | | | | |
| Age under 60 | **34.2** | 23.2 | 1.72 | 1.51 | .22 |
| Age 60-74 | 21.6 | **30.0** | 0.64 | 0.86 | .35 |
| Age 75+ | 25.0 | **28.0** | 0.86 | 0.10 | .75 |
| Woman | **35.1** | 18.0 | 0.41 | 3.94 | **.047*** |
| White | **27.4** | 26.5 | 1.05 | 0.01 | .92 |
| Witnessed stroke onset | **33.9** | 19.6 | 2.11 | 2.77 | .10 |
| Stroke onset while sleeping | 18.2 | **29.4** | 0.53 | 1.12 | .29 |
| Taking aspirin | **31.3** | 25.3 | 1.34 | 0.40 | .53 |
| Taking any antiplatelet medication | **28.2** | 26.5 | 1.09 | 0.04 | .85 |
| Taking any anticoagulation medication | **33.3** | 26.1 | 1.42 | 0.34 | .56 |
| Hyperlipidemia | **29.8** | 24.0 | 1.35 | 0.46 | .50 |
| Taking a statin medication | 25.6 | **27.9** | 0.89 | 0.07 | .80 |
| Hypertension | 21.9 | **38.2** | 0.45 | 3.13 | .08 |
| Atrial fibrillation | **27.5** | 26.9 | 1.03 | 0.01 | .94 |
| Coronary artery disease | **39.3** | 22.8 | 2.19 | 2.85 | .09 |
| Congestive heart failure | **28.6** | 26.7 | 1.10 | 0.03 | .87 |
| Diabetes mellitus | 23.1 | **28.4** | 0.76 | 0.28 | .60 |
| Past stroke or transient ischemic attack | 17.4 | **29.8** | 0.50 | 1.40 | .24 |
| Current cigarette smoker | 25.0 | **27.8** | 0.86 | 0.08 | .77 |
| Any cigarette smoking history | 24.5 | **29.3** | 0.78 | 0.31 | .58 |
| *Stroke Severity & Treatment Factors* | | | | | |
| rt-PA (tissue plasminogen activator) given | **32.8** | 20.4 | 1.90 | 2.05 | .15 |
| Successful reperfusion (TICI 2b or 3)‡ | **29.8** | 7.7 | 5.09 | 2.82 | .09 |

*OR (Odds Ratio): Odds of a Good Outcome when exposed to the specified variable.*

**p<.05; ‡TICI = Thrombolysis in Cerebral Infarction scale, SD = Standard Deviation*

**Table 3. Sources of Error.** *Describes the likelihood that various demographics, baseline characteristics and other treatment factors are associated with the primary clinical outcome: achieving a level of no disability (NIHSS score 0 or 1) at the time of hospital discharge.*

| Confounding Variable: Post-EVT Reperfusion Success | | | | | |
|---|---|---|---|---|---|
| | Reperfused? | | | | |
| | Yes (n=94) | No (n=13) | | | |
| Variable | % affected | | OR | $\chi^2$ | p |
| Intracranial Hemorrhage After EVT | 26.6 | **53.8** | 3.22 | 4.04 | .04 |
| Death or Hospice | 25.5 | **46.2** | 2.50 | 2.41 | .12 |
| No Disability at Discharge (NIHSS 0-1)* | **29.8** | 7.7 | 5.09 | 2.82 | .09 |
| Independent at Discharge (mRS 0-2)** | **34.0** | 0.0 | n/a | 6.31 | .01 |
| Discharged Home | **29.8** | 0.0 | n/a | 5.24 | .02 |

*OR (Odds Ratio): Odds of a Bad Outcome after failed reperfusion relative to successful reperfusion*
**NIHSS: NIH stroke scale; **mRS: modified Rankin scale*

**Table 4. Post-EVT Reperfusion Success as a Confounding Variable.** *Describes the likelihood that post-EVT reperfusion success rate impacts procedural and clinical outcomes, independent of inter-hospital transfer.*

**DISCUSSION**

When designing this project, we hypothesized that inter-hospital transfer would not only be associated with increased delay to EVT, but that it would also yield poor clinical outcomes relative to controls. This hypothesis was adapted from the literature search, which seemed to consistently replicate these results. This analysis of acute ischemic stroke patients in Austin does illustrate a significant delay to EVT, but does not demonstrate any significant impact of inter-hospital transfer on clinical outcomes.

Although inter-hospital transfer did not significantly impact clinical outcomes, our results demonstrate a trend suggesting that transfer patients may have worse clinical outcomes (see Table 2). Pertaining to clinical outcomes, transfer patients were approximately twice as likely to achieve no disability (NIHSS score 0 or 1) and functional independence (mRS score 0 to 2) at the time of discharge, and were similarly twice as likely to be discharged directly home (instead of requiring inpatient rehabilitation, hospice care, or experiencing death in-hospital). The only outcome that was inconsistent with this trend was whether the patient required hospice care or experienced death in-hospital. This poor outcome was more likely in the control group; the reason for this is unclear, although several patients in this dataset sufficiently recovered from the stroke but then died due to other chronic health conditions, so the association between stroke recovery and incidence of death/hospice may be less useful than the other outcomes.

Study limitations, including the retrospective study design and small sample size, likely limit the statistical significance of these clinical outcome comparisons. Since there were only 26 transfer patients, the likelihood is high that the patients selected for this group may not effectively represent the general population of stroke patients requiring inter-hospital transfer. In addition, this study was retrospective, so we were unable to match patient selection into the experimental and control groups. Although our group comparison (given in Table 1) demonstrates fairly similar characteristics of both groups, we did notice a significant difference in reperfusion rate between groups, with patients in the transfer group being much less likely to achieve successful reperfusion compared to controls. It is unclear why these procedures appeared to be more difficult in the transfer group, despite almost identical average age and pre-procedural NIHSS scores. Since this analysis is not able control for the multitude of variables that

may influence clinical outcomes after stroke, we recognize that the clinical outcomes seen in this analysis may be significantly affected by these confounders and should be interpreted accordingly.

Since the patient groups were not matched according to demographics and baseline characteristics, we performed supplementary statistical analyses in order to explore significant differences between groups and also to determine the effect of relevant variables on clinical outcomes. Since our primary clinical outcome was lack of disability (NIHSS score 0 or 1) at discharge, we chose to explore any association between this clinical outcome and various demographics, baseline characteristics, and treatment factors (represented in Table 3). In fact, the only significant predictor of residual disability at discharge was the male gender. Other variables approached statistical significance, but when contemplating how these factors affect stroke recovery, most of these variables did not appear to favor poor outcomes in transfer patients and thus were not considered potential confounders.

The only variable that seemed to contribute to the transfer group's poor clinical outcomes was the post-EVT reperfusion success rate. Since transfers were significantly less likely to experience successful cerebral reperfusion (as shown in Table 1), we decided to take this analysis a step further by determining the direct impact of post-EVT reperfusion success on all five outcome measures from Table 2. The results of these analyses (represented in Table 4) demonstrate that successful reperfusion after EVT significantly impacted the following two clinical outcomes: independence at discharge (mRS score 0 to 2) and ability to be discharged home. Given that the impact of inter-hospital transfer on clinical outcomes was not statistically significant, and also considering the significance of post-EVT reperfusion success as a confounding variable, we are clearly unable to conclude that there is any relationship between inter-hospital transfer and clinical outcomes in this population of patients with acute ischemic stroke in Austin.

In contrast to the clinical outcome data, our analysis of EVT delay times provided significant results for discussion and interpretation. The results of this analysis are illustrated in Figure 1. The average time from onset to groin for the transfer group was 37.2 minutes longer than the control group of patients transported directly to a treatment facility. Although this finding was in fact significant, there are still extraneous variables contributing to this outcome other than inter-hospital transfer. For example, patients who live long distances away from the city will have longer transport times to any hospital. Due to these long distances, these patients will be automatically transported by EMS to primary stroke centers, thus contributing to the observed EVT delay seen in our analysis. Further study is needed in order isolate actionable delay related to inter-hospital transfer from inevitable delays associated with long distances. In order to better isolate inter-hospital transfer as the sole variable, it may be necessary to exclude patients outside of a certain mile radius from central Austin. This analysis has not yet been completed, but is certainly a future direction for this database.

In addition, it is enlightening to interpret this EVT delay in the context of transfer times. For transfer patients, it took an average of 131.5 minutes from arrival at the primary stroke center to arrival at the treatment facility. Despite this 131.5-minute delay to arrival at the hospital offering EVT, the actual time delay to EVT procedure initiation was only 37.2 minutes. The remaining 94 minutes of delay were eliminated by expedited triage and processing of transfer patients. These patients often were delivered immediately to the operating room for EVT. These various in-hospital compensatory measures are shown to be highly effective at reducing treatment delays, but the remaining 37.2-minute delay still warrants further exploration into the efficacy of inter-hospital transfer, as well as other potential sources of unnecessary delay to EVT.

**CONCLUSIONS**

Since the analysis of clinical outcomes failed to produce statistically significant results, this study concludes that clinical outcomes were not significantly affected by inter-hospital transfer. However, we can conclude that inter-hospital transfer is associated with delayed initiation of EVT. Although this study did not account for confounding variables that may be contributing to this finding, EVT delay after inter-hospital transfer has been repeatedly demonstrated in the literature. Our findings, in conjunction with this evidence, suggest that protocol changes favoring direct transport to a treatment facility may reduce delays to treatment and improve clinical outcomes.

**FUTURE DIRECTIONS**

The primary goal of this and similar studies is to improve stroke systems of care in order to expedite access to appropriate treatment measures for patients with acute ischemic stroke. More specifically, the top priority moving forward from this study is to isolate the source of delay to EVT. This necessitates exploration of various confounding variables that may be contributing to delayed EVT in patients requiring inter-hospital transfer. Specific to the Austin region, future studies in this population should focus on variables affecting transportation times. These variables may include measured distances between patients and various hospitals, as well as consideration of traffic flow at various times throughout the week and weekend. These analyses will exclude inevitable delays and highlight areas of potential improvement in the current system.

Once actionable treatment delays have been identified, discussions should ensue regarding how protocol changes might reduce delays for specific populations in the Austin area. These discussions should consider estimated transportation times to primary and comprehensive stroke centers, integrating both travel distance and traffic flow. According to current protocols in Austin, stroke patients may only be delivered by EMS to an EVT facility if this facility is within 15 minutes by ambulance; otherwise, the patient must be transported to the nearest primary stroke center for assessment and rt-PA administration. It may be patient beneficial to extend this rule in Austin from 15 to 20 or possibly 30 minutes.

When considering these city protocol changes, we must always be mindful of the balance between EVT and rt-PA administration. An extension of this 15-minute rule effectively favors EVT, while possibly delaying the patient's access to rt-PA. Since clinical outcomes following rt-PA administration are also time sensitive, this protocol change may be harmful to the patient, especially if it is discovered upon arrival at the treatment facility that EVT is not indicated. Therefore, prior to implementation of any protocol changes, strides should be made to identify which patients may benefit from the suggested changes and which patients may potentially be harmed.

Ideally, discussions on protocol changes should integrate patient screening to determine the likelihood of needing EVT. If EMS can be trained to utilize a highly specific screening tool to identify these high-risk patients, then EMS will be empowered to prioritize direct transportation to a treatment facility for this subset of patients. In fact, EMS protocol in Austin currently utilizes the Cincinnati Pre-hospital Stroke Severity Scale (CPSS) in order to describe the stroke symptoms with a score from 0 to 4. The current protocol utilizes this score solely for identification of patients with acute ischemic stroke. However, original studies of this scale defined its efficacy for predicting large vessel occlusion, which specifically increases the likelihood that EVT will be indicated[12,13]. At CPSS scores of 2 or above, the specificity of this scale in predicting large vessel occlusion is 90.2%. Therefore, if EMS protocol can be adapted to favor direct transportation to a treatment facility for these high-risk patients with a CPSS score of 2 or above, EVT delay may be reduced and post-procedural outcomes may be improved.

Following any alteration to current city stroke management protocols, ongoing study will be necessary to determine the impact of these changes and ascertain the specific effect of the changes on treatment delays as well as clinical outcomes. Delays to both rt-PA administration as well as to EVT initiation should jointly be explored and correlated with the corresponding clinical outcomes in order to illustrate the full picture of how the changes are affecting patients. Once further analyses are completed, collaboration with the Capital Area Trauma Regional Advisory Council (CATRAC) will be necessary to begin the discussion on the feasibility and implementation of various protocol changes. The focus of all future studies and protocol changes should be centered on maximizing the efficiency of stroke systems of care in Austin. By maintaining this focus, we will promote better clinical outcomes and superior quality of life after stroke.

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**APPENDIX: Expanded Methodology - A Description of Systematic Methodology for Data Acquisition, and a Discussion of the Data's Relevance to Stroke Research**

**Project Design**

When I first began working on this project, Dr. Miley presented me with a list of all the patients who underwent endovascular treatment for ischemic stroke at any of Seton's comprehensive stroke centers in Austin between October 2016 and September 2018. The list included 109 names, along with diagnostic and procedural codes, birthdates, and estimated times of hospital admission and discharge. He also provided me with a template spreadsheet which had been used previously to build a similar database of thrombectomy patients in a different city. The template suggested over 100 data points to be collected for each patient with regard to the details of their present stroke, medical history, stroke treatment, and outcomes. With these resources, I began the work of adapting this spreadsheet for use in our local Seton hospital system to create a database of patients receiving thrombectomy treatment at Seton hospitals between October 2016 and September 2018.

**Project Development**

I perceived that my most important task was to develop a systematic, consistent method of data collection that would maximize the accuracy and consistency of data included in this database. For each data point included in this database, I completed several cycles of trial and error in order to locate the most reliable information concealed inside each patient chart. I had to explore the entirety of the electronic health record to find consistencies and, more importantly, variability in where the data was housed and how it was represented. Further, I was faced with the imperfect task of retrospectively validating data points when inconsistencies arose in reporting data. By exploring the charts and gradually learning the background behind how each observation was made and how data was reported, I began to dig further into the chart to unearth the backbone of the reported data. I began to more accurately perceive which data was thorough and reliable, and locate problem areas where inaccuracies may be introduced. As you might imagine, these discoveries were often inconvenient, as they required me to revisit previous patient charts to revise data which I had already entered into the database. These months of data collection were filled with data exploration, discovery that led to new insight, and thorough revision to ensure data consistency. In the sections below, I describe my finalized methods of data acquisition within the Seton Ascension Compass Electronic Health Record, as well as from the Austin Radiological Association (ARA) image database.

**Determination of Time Intervals & Treatment Delay**

*Stroke Onset*

Defining the precise time of symptom onset and discovery is critical for determining appropriate treatment and analyzing treatment outcomes. The first relevant time is the time designated **"last known well" (LKW)**, which refers to the last confirmed moment in time that the patient was symptom free, prior to the onset of stroke symptoms. After LKW, it is important to define the **"time of first abnormal" (TFA)**. This refers to the first moment in time when we can reasonably confirm that the patient was experiencing a stroke. When a stroke is witnessed, LKW is equal to first abnormal time, both of which reflect the true moment of stroke onset. However, unwitnessed onset (including instances when patients first discover their symptoms upon waking up from sleep) introduces uncertainty into the true

duration of the stroke. Due to the importance of a witnessed onset, our database includes (in addition to all of the relevant time checkpoints) a designation of whether the onset was witnessed, and whether the patient first noticed symptoms upon waking.

Understandably, there is often discrepancy in the chart regarding these times. Usually, the best place to locate these times was in the initial encounter note by the neurology stroke consult team, in their consultation or history & physical (H&P) note. However, since stroke patients are often aphasic at arrival, this history may be difficult to obtain prior to rt-PA administration and/or endovascular treatment. In these instances, LKW and first abnormal times may not be found in this initial note, but may be included in the note addendums, or may be clarified in later progress notes by the neurology team. Occasionally, these times were not reported in any notes by the neurology team; in these instances, it was sometimes helpful to explore nurse and physician documentation from the ED, including both encounter notes and triage assessments to look for information regarding the patient history and timing of symptom onset.

Variability in reported times may occur if the patient provides different accounts to different team members, or if the patient's report conflicts with reports given by family members or other witnesses. This variability is understandable, since patients often lack insight into the true timing of symptom onset.

Some patients were already admitted at a hospital prior to stroke onset. The "first abnormal" for these patients was the time that hospital staff (usually floor nurses) identified the symptoms and initiate a code stroke.

*Initiating the Treatment Cascade*

For the purpose of analyzing the time intervals in the treatment cascade, it was important to identify the **"discovery time" (DT)**, referring specifically to the time that care was initiated for this patient. Sometimes, the patient was able to call 9-1-1 on their own behalf, or indicate to a family member that the call should be made on their behalf. Other times, the patient is incapacitated but witnesses immediately contact emergency medical services (EMS). Thus, it is appropriate to assume that the "first abnormal" time is usually equivalent to the "discovery time." However, some patients did not have the luxury of being discovered or receiving assistance immediately after stroke onset. For example, some patients may be alone at home when they become aware of symptom onset; however, the symptoms are debilitating and prevent the patient from contacting anyone for assistance. These patients may report a known LKW/first abnormal time, but were unable to initiate the treatment cascade until they were discovered hours or days later.

Time of discovery is useful in telling us when the treatment cascade was initiated, but does not necessarily have any bearing on the true timing of stroke onset. This data point is essential for calculating systematic time intervals related to patient care, and is especially relevant to a discussion on the extent of treatment delay introduced by inter-hospital transfers.

When stroke onset was witnessed, no additional work was needed to determine the discovery time. However, in cases where discovery time differed from first abnormal time, my task was to determine precisely when care was initiated for this patient. This process proved to be tedious, for it required thorough exploration of the patient's chart. Again, the initial encounter note by the neurology team was a good starting point, for it often provided a concise timeline to help frame the patient's story. However, these notes often failed to provide a concise time when the patient was discovered or when EMS was first contacted. After reviewing these initial notes, I explored EMS documentation (specifically the EMS run sheet when provided) to identify the time the 9-1-1 call was received. This was often the first and most relevant "discovery time" that could be confirmed by the chart. When the EMS run sheet

was not available in the chart, I reviewed other ED documentation to search for the earliest confirmed checkpoint that estimates the initiation of the process of stroke management.

One notable exception in the dataset is a patient who was delivered by EMS to the hospital for possible stroke symptoms but was regarded as having a low stroke risk due to recreational drug use and other seemingly confounding variables. The patient was not initially treated as a code stroke, but eventually neurology was consulted to rule out this possibility. Results of CT stroke protocol at this time highlighted a large vessel occlusion, which prompted initiation of emergent stroke treatment. In this case, I considered the discovery time to be the time the neurology team became aware of the occlusion, because prior to this moment there was no discussion of administering rt-PA or performing thrombectomy for this patient.

*Initial Hospital Arrival Times*

Hospital arrival times were primarily obtained from the ED Patient Summary, which provided a time that consistently reflected the patient's arrival to the ED. Sometimes this form was not available in the patient chart due to various circumstances. For example, some patients were taken directly to the imaging suite upon arrival and thus were never formally admitted to the ED. In these cases, I referred to the EMS run sheet if available to access the time at which EMS documented that they had arrived at the destination. In cases where a patient presented to an outside hospital (a primary stroke center) prior to inter-hospital transfer, ED and EMS documentation were often unavailable. In these cases, I found the Transfer Memorandum document to be helpful in providing time of arrival at the outside hospital. If none of these forms were available in the chart, I then examined outside records that had been scanned into the EHR in search of any documented arrival time. These steps allowed me to identify each patient's initial arrival time.

*Inter-Hospital Transfer Locations and Transfer Initiation*

For transfer patients, the transferring hospital (the primary stroke center where the patient was initially examined) was usually explicitly indicated in the initial note by the neurology team, or in ED nurse or physician notes. If not explicitly indicated, then I reviewed the EMS run sheet, the Transfer Memorandum form, or scanned outside records to identify the primary stroke center. Once the location was identified, I then searched for the precise time at which the transfer was initiated. Transfer Memorandum forms usually provided this information; if the time was not available, then I referred back to the EMS run sheet to identify the time at which EMS was called requesting emergency transfer to a comprehensive stroke center.

*Comprehensive Stroke Center Arrival Times*

For transfer patients, I needed to determine the time at which each patient arrived at the comprehensive stroke center (their final destination for definitive stroke treatment), referred to as the "time to destination". As previously mentioned, ED Patient Summary forms were the primary source of these times. If unavailable, I would search EMS and ED documentation as previously described for a documented arrival time. For non-transfer patients, this step was unnecessary, since they were delivered directly to a comprehensive stroke center and thus did not require inter-hospital transfer for EVT.

*Classification of Inpatient Strokes*

A few of the patients included in this dataset were already admitted to a hospital for other health reasons prior to the onset of stroke symptoms. Being already located at a hospital, these patients often benefitted from an expedited path to treatment. If the patient was already admitted to a comprehensive stroke center, no inter-hospital transfer was needed for EVT, thus their time to

destination was also equivalent to zero. However, if the patient was admitted to a primary stroke center, inter-hospital transfer was quickly initiated upon symptom discovery. This description applies to only three of the 109 patients in the database. This unique group of patients requiring transfer after an inpatient stroke prompted a discussion on the proper definition of a transfer in this dataset. In all other transfer patients, there were to transit times (home to primary facility, and primary to comprehensive facility) as well as two hospital arrival times. However, this group of inpatient strokes experienced only one transit time (primary to comprehensive facility) and one arrival time (at the comprehensive facility, i.e. the "destination" for EVT). Because of the expedited nature of management for inpatient strokes, we felt they most accurately represented the non-transfer group, and were defined as such in all of our statistical analyses.

**NIH Stroke Scale**

*Initial/Admission*

The National Institutes of Health (NIH) has created a stroke scale designed to determine stroke severity based on a specific clinical assessment. The NIH stroke scale (NIHss) is used on initial assessment to generally determine stroke severity to help predict whether a patient will eventually need EVT for a large-vessel occlusion. Higher NIH scores are often indicative of this type of severe occlusion that will require EVT. NIHss scores are documented in various locations in the patient chart. Fortunately, Compass includes "chart search" functionality that enabled me to search for all NIHss scores that were formally documented as a "result" in the chart. These scores were recorded by nursing staff trained to score patients on this stroke scale. These documented "results" served as the primary source of NIHss scores for this database. NIHss scores may often be found elsewhere in the chart. The initial NIHss score could often be found in the initial encounter note by the neurology team. Other locations for this initial NIHss score at admission included full or brief operative notes by the neurointerventionalist, ED nurse/physician documentation, or occasionally scanned outside records from the outside hospital prior to transfer.

*24-Hour NIH Score*

After the admission NIHss score was determined, I looked for the first documented NIHss score at least 24 hours after restoration of cerebral blood flow. If this was not documented in the patient chart as a "result," then I looked through neurology progress notes for a documented NIH score by any physician from the neurology team. Again, the "chart search" function was very helpful: by searching for "NIH" or "NIHss" I was able to locate any mention of an NIHss score in the notes, and thus determine which score most closely represented 24 hours after reperfusion.

*Final/Discharge NIH Score*

A patient's final NIHss score at discharge is a relevant outcome measure that helps us understand how close a patient is to a full recovery from their stroke symptoms. These scores were located by the same method as the 24-Hour scores, with the only distinction being that I was looking for the final documented score in any of these locations in the chart prior to discharge.

**Glasgow Coma Scale**

Glasgow Coma Scale (GCS) provides a measure of the patient's level of alertness and responsiveness. This score supplements the NIHss score in depicting stroke severity and thus was included in this database. The primary source of documented GCS scores was the EMS Run Sheet, which

documented the patient's score immediately prior to arrival. If this report was unavailable, I referred to ED documentation; often the triage assessment included the first observed GCS score after admission to the ED. Occasionally, neither of these locations were available to provide a GCS score. In these instances, I searched Outside Records and examined successive evaluations by hospital care teams to locate a GCS score that was documented prior to the patient receiving EVT.

**IV rt-PA time and amount**

IV rt-PA is administered in two phases: patients first receive an initial bolus with 10% of their prescribed dose of rt-PA, after which the remaining 90% of the medication is administered slowly via an IV "drip". When the bolus is administered and the drip initiated prior to inter-hospital transfer, this procedure may informally be referred to as "Drip and ship." For each patient, I recorded whether the time and amount of medication administered, whether they were considered a "drip and ship" patient, and also listed any contraindications to rt-PA for patients who were not prescribed this treatment. The medication administration record (MAR) was essential for identifying the time and amount of IV rt-PA administered to each patient, although the time was often also specified in the initial neurology note. MAR sometimes was unavailable for transfer patients, but I was always able to find documentation of medication administration in scanned outside records or neurology team notes. Contraindications to rt-PA administration were found either in the first encounter note from the neurology team or from successive addendums by neurology attending physicians or future neurology progress notes.

**Neuroimaging Protocol**

*"Decision-Making" Neuroimaging*

When a patient presents for suspected stroke, neuroimaging protocol is initiated to confirm or rule out acute ischemic stroke. This image is referred to as the "decision-making" image because of its role in determining the need for EVT when a large-vessel occlusion is revealed. In addition to looking for an occlusion, these images also provided a depiction of "perfusion mismatch," which refers to the proportion of salvageable brain tissue (known as the penumbra) in the area of ischemia. A large mismatch indicates that there is a significant amount of tissue that has not yet infarcted, and thus EVT has potential to salvage a large amount of brain tissue if EVT is promptly initiated.

*Imaging Options: Computed Tomography and Magnetic Resonance Imaging*

A specific type of computed tomography (CT) imaging, called CT Angiography, has been traditionally preferred as an effective method to visualize large vessel occlusion. However, magnetic resonance imaging (MRI) also offers an effective method of visualizing these vessels, and is gaining favor among physicians relative to CT-Angiography despite the greater time requirement of an MRI. Due to the ongoing debate in the scientific community between MRI and CT for in-hospital stroke screening protocols, we recorded the specific types of imaging undergone by each patient, as well as specific times that imaging occurred in order to provide another time point for evaluation of potential treatment delays.

*Image Acquisition*

For all information regarding neuroimaging data, I accessed the ARA imaging database. Since each image in an image set includes a unique time printed directly on the image, I examined the image set for each patient to determine the earliest time printed on any image in the set, thus indicating the exact time imaging began. This data was available for all patients with two exceptions; these patients

were imaged at the Cedar Park Regional Medical Center prior to transfer, and their images were not available in the ARA system.

**Identifying the Occluded Vessel**

Common locations of large-vessel occlusions include proximal segments of the anterior, middle and posterior cerebral arteries. Other involved vessels may include the basilar or vertebral arteries that feed the posterior circulation, or the internal carotid artery that provides blood flow to both the middle and anterior cerebral arteries.

Decision-making imaging provides the first opportunity to locate the occlusion and identify the brain region with deficient blood flow. The image report (written by the radiologist who read the images) often specified the specific location of the occlusion. However, this image often referred to a region of decreased perfusion without specifically identifying the location of the clot. Cerebral angiogram, an image performed intraoperatively to visualize cerebral vessels, is a much more specific test for identifying vessel occlusions and stenosis. Each operative report describes what was seen via this intraoperative imaging method, so I was able to defer to this note to learn of the specific location of the occlusion. Of note, some patients receive rt-PA prior to EVT, so the clot seen on pre-operative CT/MRI imaging had sometimes dissolved or relocated due to this treatment or from natural causes. Therefore, the specific locus of occlusion that became the target of the thrombectomy procedure was most reliably obtained from the cerebral angiogram image descriptions found in the operative note.

**Endovascular Treatment: Procedure Details and Time Intervals**

*Learning About EVT Procedures and Terminology*

In order to properly define the intricate details of each endovascular procedure, I first needed to invest a significant amount of time studying the procedure itself and learning the function of various tools and equipment that are used for various purposes. There was a steep learning curve pertaining to the procedure-specific vocabulary that was used to procedure details, techniques and outcomes. I studied the terminology used to classify and describe vessel characteristics, location and quality of occlusions and blood flow, success of various interventions, and the reasoning behind decisions to proceed and terminate procedures. I observed variabilities in terminology between physicians. The process of data acquisition continued this learning process as I continued to encounter variabilities that required additional study and contemplation to better understand the decision-making process imbedded in each procedure.

*TICI Scale*

The Thrombolysis in Cerebral Infarction (TICI) scale is a standardized scale that defines the extent of cerebral perfusion, and can be used to define improvements in cerebral blood flow achieved by EVT or rt-PA administration. The TICI score before and after each procedure was recorded in order to evaluate the immediate success of the procedure, measured by the extent to which blood flow was restored.

*Procedure Methods and Equipment*

For each procedure, I determined first if the procedure could be defined as a mechanical thrombectomy, meaning that either aspiration, stent retrieval, or wire methods were used to remove the clot. Aspiration refers to the positioning of microcatheters at the predetermined clot location in an

attempt to directly aspirate the clot out of the vessel. “Stent retrieval” refers to a multi-step method involving (1) deployment of a temporary stent at the clot location, (2) positioning of a microcatheter at this location, and (3) removal of the stent during simultaneous microcatheter aspiration in an attempt to capture and remove clot within the stent. Wire thrombectomy, as it sounds, refers simply to the use of a wire to mechanically manipulate and disrupt the clot without the use of any microcatheter or stent. Different vessel and clot characteristics (such as vessel diameter, tortuosity and clot size) dictate the need for different procedures and approaches. This variable clot environment determines clot accessibility with various types of wires and microcatheters; sometimes unique challenges require a new access route in order to successfully reach the clot without introducing excessive risk of vessel wall rupture.

An additional procedure, called angioplasty, refers to intraarterial inflation of a specialized balloon in order to forcibly expand the vessel walls in an attempt to restore blood flow. This procedure attempts to restore blood flow through stenotic vessels, and is particularly useful in stenosis of the common and internal carotid arteries. These vessels, although not completely occluded, may be significantly stenosed, thus predisposing the affected brain regions to under-perfusion. Angioplasty, therefore, is a secondary measure that can be used to increase blood flow in vessels adjacent to the occluded vessel. Angioplasty was often followed by insertion of a permanent stent in the carotid arteries in an attempt to maintain vessel patency after the procedure.

Combined use of operative notes and the invasive procedure report was essential to determine which methods were utilized and how many attempts were made with each method in various vessel locations. Using this information, I calculated the number of attempts, or “passes,” that each patient underwent. Knowledge of total number of passes is informative for any comparison of procedure duration and associated risk between patient groups. In addition to number of passes, I also recorded the specific names and specifications of various equipment used, including the types and measurements of microcatheters, stents, and angioplasty balloons.

For each procedure, I also utilized these same notes and reports to determine if any intra-operative medication was administered, particularly vasodilators, thrombolytics, and any other medication administered intra-arterially. On occasion, the Medication Administration Record (MAR) was useful in identifying these medications administered intra-operatively.

*Procedure Time Intervals*

Each procedure has a specific start and end time. Our analysis of time intervals and delays to treatment highlight the importance of recording the specific procedure start times and other relevant checkpoints. Particularly helpful metrics pertaining to start time include the patient’s arrival time into the angiography suite, and the exact time of microcatheter insertion. Microcatheter insertion time thus defines the exact point in time when all preliminary workup and procedure preparation has been completed and the neurointerventional procedure has officially begun. Other relevant checkpoints include the time the clot is reached by the microcatheter, and the “reperfusion time,” which refers to the time at which cerebral blood flow is maximally restored after partial or complete clot removal. By recording all of these checkpoints, we can perform an analysis that goes beyond a simple calculation of the delay to the procedure start time. It also allows for an analysis of variations in procedure time that may correlate with procedure success, complications, and long-term outcomes.

To locate documented procedure times, the primary sources were the brief or full operative notes written by the physician, which often included several if not all of these aforementioned procedure checkpoints. For any times not specifically documented in the operative reports, the next place to check was the invasive procedure report. This report provides a detailed list of the sequence of

events during the procedure along with the corresponding times at which each step occurred. However, the specific time of each checkpoint was not always explicitly stated in this report. In these instances, I looked for the first time in the procedure note at which I could confirm that a particular checkpoint had been reached. For example, if the patient's time of arrival to the room was not explicitly stated, I recorded the first reported time the patient was being prepped by staff members, indirectly confirming the patient had arrived by this time. If the "clot-reaching time" was not explicitly stated, I recorded the earliest time at which thrombectomy was attempted, since thrombectomy cannot commence until the clot has been reached by the microcatheter system. If the exact time of reperfusion was not explicitly stated, then I recorded the time at which the confirmatory cerebral angiogram was performed, because this confirmed that all thrombectomy attempts had been completed prior to the creation of these final images. By using these reasonable estimates, reliable microcatheter insertion times and reperfusion times were able to be recorded for all 109 patients in the dataset.

**Neuroimaging Follow-Up**

It is not uncommon for patients to experience complications following EVT and rt-PA administration. Follow-up images (either MRI or CT with or without contrast) are utilized to screen for any appearance of hemorrhage. Hemorrhagic transformation refers to when cerebral blood vessel walls are compromised and leak blood into interstitial space in the brain as a result of ischemic damage to brain tissue incurred by stroke. Small amounts of hemorrhage usually do not require any additional intervention, but more severe hemorrhage may necessitate neurosurgical intervention to remove the hematoma and limit the mass effect on the brain that may result in irreversible neurological damage. Mass effect refers to an increase in pressure put on brain tissue due to a developing hematoma, or due to swelling of brain tissue (edema) which is a physiologic effect of ischemic damage to brain tissue. A primary indicator of mass effect is the degree of midline shift (observable shift of midline brain structures to the right or left, measured in millimeters) or any brain herniation indicating an overall increase in intracranial pressure. Certain clinical symptoms raise suspicion for worsening brain hemorrhage and mass effect, such as fluctuating neurological exam findings including level of consciousness. For research purposes, a clinically symptomatic brain hemorrhage following EVT is defined as a confirmed hemorrhage that clinically results in an increase in the patient's NIH stroke score by four or more points. Serial image reports written by the radiologist were helpful in determining if any amount of hemorrhage or mass effect was visualized in the image. If any significant hemorrhage or mass effect was present, then we reviewed documented NIH scores to determine if a four-point NIH score increase was consistent with the timing of the hemorrhage.

**Functional Outcomes: the modified Rankin Scale**

The modified Rankin score is a scaled score from 0-6 reflecting the patient's level of disability. A score of 0 suggests that there are no residual symptoms from the stroke, and 6 indicates the patient has died in the hospital before discharge. In the literature, scores of 0-2 are often referred to as "independent" because scores, despite varying severity of residual symptoms, are able to remain completely independent following the stroke (although their disability may prevent them from doing certain activities they performed previously). Scores of 3 or above suggest dependence for some or all essential daily tasks. A score of 4 is given if the patient requires assistance with mobility and cannot walk on their own.

These Rankin scores are important to be included in our database because they are essential for describing functional outcomes in patients at the time of discharge. However, these scores were not

documented during the patient's admission, so these patients had to be carefully retroactively scored based on notes in the patient chart. The most helpful information was acquired from the physical therapy discharge note, as well as previous physical therapy notes. These notes usually provided descriptive information regarding a patient's physical capabilities, limitations, and prognosis for recovery. To supplement this information, we also looked at neurology progress notes at and around the time of discharge in order to more specifically assess the presence and severity of residual symptoms. With this information, Dr. Miley and I worked independently to score each patient and thoroughly reviewed these notes to determine the proper Rankin score for each patient. Particular attention was paid to patients who were at first glance borderline between a score of 2, classifying them as "independent" versus a score of 3, classifying them as "dependent." These scores were all secondarily reviewed to confirm the accuracy of these scores.

**Destination after Discharge**

Prior to discharge, the requisite level of care was determined for each patient dictating whether the patient be sent home directly, or first require inpatient rehabilitation prior to a return home. If the patient had no reasonable chance at recovery or the patient or power of attorney decided to withdraw care, then comfort care was initiated and hospice was pursued unless patient died in the hospital prior to discharge.

In our database, we identified three categories of destination at discharge: home, IPR, or death/hospice. Combined utilization of the discharge summary, the final progress note from the primary care team (usually neurology), the discharge note from physical therapy, and case management notes allowed us to effectively determine the patient's immediate destination following discharge from the hospital.

**Medication History**

For the database, it was of interest to record whether each patient was taking medications for stroke prevention. These may be helpful in future investigations into the relationship between stroke severity or recovery and specific medications, particularly statins, antiplatelets or anticoagulants. This information may also be relevant for predicting incidence and severity of hemorrhagic conversion of ischemic stroke.

Locating medication history in the patient chart was often tricky for various reasons. Patients were commonly aphasic at admission, and therefore could not report their recent medication history. Therefore, various locations often needed to be searched for this information. Often home medications were listed in the first encounter neurology note. If medications were unknown at this time, they may be described in the addendum or future progress notes once a family member could be contacted to learn this information (or once the patient recovered sufficiently from stroke symptoms so that they could personally divulge this information. Unfortunately, the information provided in these notes was occasionally incomplete. I consistently referred to ED triage notes for affirmation that there were no other relevant home medications. For this affirmation process, it became very helpful in many patient charts to use the "chart search" function to search the phrase "home med" which often brought up the triage note or radiologic notes where home meds had been completely documented. This became a great way to verify the medication history and ensure that this documentation was complete.

**Past Medical History & Stroke Risk Factors**

The stroke database includes documented past medical history, providing the opportunity to analyze outcomes of stroke and neurointervention dependent on various stroke risk factors. I included any documented history of hypertension, atrial fibrillation, coronary artery disease, congestive heart failure, hyperlipidemia, diabetes mellitus, history of ischemic stroke or transient ischemic attack (TIA), tobacco smoking history, and cancer/metastasis. We also record the LDL and Hemoglobin A1c lab values at admission, in case the patient deserves a new diagnosis of diabetes or hyperlipidemia that was previously missed. These conditions have all been shown to increase the risk of ischemic stroke. Therefore, it is relevant to study if these risk factors also have any bearing on outcomes related to stroke treatment and intervention.

To locate documentation of these risk factors, I first looked through the neurology first encounter note (H&P or consultation note) if available. I then looked through preceding H&P notes to search for any relevant history that had been left out. In addition to looking through specific notes, I also utilized the chart search function in order to ensure that the database completely reflected the patient's various risk factors. Through experience with this project, I became aware of several acronyms used in various notes by physicians to describe medical history terms, including the following (hypertension-HTN, diabetes mellitus-DM, coronary artery disease-CAD, congestive heart failure-CHF, transient ischemic attack-TIA, and various acronyms for hyperlipidemia including HLD, HLP, and DLD. I found the chart search function to be extraordinarily helpful in looking through physician notes patient-reported history in various other locations.