


ORIGINAL RESEARCH

Intravenous Thrombolysis Is Associated With Better Outcomes in Large-Vessel Occlusion Requiring Endovascular Therapy

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BACKGROUND: Intravenous thrombolysis (IVT) and endovascular therapy (EVT) are both important treatments for large-vessel occlusion stroke. However, it is still unclear how the timing of IVT, EVT, and the need for transfer of a patient to an endovascular stroke center for EVT affect outcomes. In this investigation, we study the interaction between IVT, rapidity to EVT, and need for transfer among patients with large-vessel occlusion stroke.

METHODS: This investigation is an analysis of the OPUS-REACH (Optimizing the Use Prehospital Stroke Systems of Care—Reacting to Changing Paradigms) registry of patients with large-vessel occlusion stroke from 9 endovascular centers in the United States. Using the database, we extracted baseline characteristics of patients, whether the patient received IVT, and time intervals in the patients' care. Patient demographics and characteristics were compared between 2 groups using the χ^2 test for categorical variables and 2-sample *t*-tests or Wilcoxon rank-sum tests for continuous variables. Multivariable logistic regression was performed to determine the adjusted associations of the variables with 90-day dichotomized modified Rankin Scale outcome.

RESULTS: A total of 1171 patients were included in the final analysis, and 38.9% had good functional outcome at 90 days. Male sex and lower initial National Institutes of Health Stroke Scale score were nonmodifiable factors associated with good clinical outcomes. We saw no differences in outcome whether a patient underwent primary or secondary transport. On multiple variable analysis, the receipt of IVT was the only modifiable factor associated with good outcomes. We found no overall effect of time from last known well to EVT on 90-day outcomes unless the patient received IVT.

CONCLUSIONS: In this investigation, receipt of IVT was independently associated with improved outcomes at 90 days with an odds ratio of 1.51. Neither shorter time from last known well to EVT nor direct transport to an endovascular stroke center versus transfer to an endovascular stroke center was associated with improved outcomes. We therefore conclude that prehospital algorithms must account for the timely administration of IVT over time to EVT.

The American Heart Association (AHA) gives endovascular treatment (EVT) a class I recommendation for large-vessel occlusion stroke (LVOS) based on multiple clinical trials that show superior outcomes when patients received EVT compared with intravenous thrombolysis (IVT) alone.¹ Most

patients with LVOS arrive at the hospital by emergency medical services (EMS). Patients with LVOS transported by EMS will take 1 of 2 routes to care. First, patients with LVOS could be transported directly to an endovascular stroke center (ESC) by EMS (primary transport), because either the ESC is the closest hospital or a

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protocol is in place to bypass a non-ESC based on suspicion for LVOS. Second, EMS could transport a patient to a non-ESC where the patient could be evaluated, receive IVT, and then be transferred to an ESC for EVT when appropriate (secondary transport).

The optimal route to EVT for patients with LVOS transported by EMS is unclear. In 2018, the AHA gave hospital bypass to an ESC for suspected LVOS a class IIB recommendation.² However, in its later guidelines on stroke systems of care, the AHA suggests that EMS should bypass a non-ESC for an ESC in urban areas if the bypass time is <30 minutes in urban areas, <45 minutes in suburban areas, and <60 minutes in rural areas.³ These recommendations are based on spatial modeling rather than empiric patient-level data.⁴⁻⁹

There is some evidence that the need for transfer of LVOS from a non-ESC to an ESC for EVT results in worse functional outcomes than if patients are transported directly to an ESC. Patients were found to be less likely to ambulate independently and be discharged home if they required transfer from a non-ESC for EVT.¹⁰ However, this research does not account for whether a patient could have been transported directly to an ESC in a reasonable period. Although rapidity of EVT may result in better functional outcomes for patients with LVOS, the magnitude of improvement is greatest in the first few hours after onset.¹¹

Although it may seem a straightforward decision to bypass a non-ESC for an ESC when there is suspicion of an LVOS, there are multiple challenges that limit such decisions. Bypassing a closer hospital in favor of an ESC may delay IVT treatment, which improves outcomes when given before EVT.¹²⁻¹⁶ Because of imperfect LVOS screening tools for EMS, patients may be overtriaged or undertriaged to ESCs.

Several authors have used spatial analysis to model different scenarios for when to bypass non-ESCs in suspected LVOS.^{4,5,17} The recent RACECAT (Transfer to the Closest Local Stroke Center vs Direct Transfer to Endovascular Stroke Center of Acute Stroke Patients With Suspected Large Vessel Occlusion in the Catalan Territory) trial randomized suspected patients with LVOS to transport to either the closest non-ESC or a more distant ESC. These authors found no difference in outcome between the 2 groups.¹⁸

Even with the recent publications, questions remain on how the interaction between IVT, bypass of non-ESCs, and time to EVT affect patient's functional outcomes. In this investigation, we use the OPUS-REACH (Optimizing the Use Prehospital Stroke Systems of Care—Reacting to Changing Paradigms) registry database to investigate the interplay of these factors on LVOS outcomes.

Nonstandard Abbreviations and Acronyms

EMR	electronic medical record
ESC	endovascular stroke center
EVT	endovascular therapy
IVT	intravenous thrombolysis
LKW	last known well
LVOS	large-vessel occlusion stroke
mRS	modified Rankin Scale
OPUS-REACH	Optimizing the Use Prehospital Stroke Systems of Care—Reacting to Changing Paradigms

CLINICAL PERSPECTIVE

What Is New?

- In our investigation, intravenous thrombolysis was the only modifiable factor associated with good functional outcome at 90 days in patients who underwent endovascular therapy for large-vessel occlusion stroke.
- Intravenous thrombolysis was associated with good outcomes in both patients who were transported by emergency medical services directly to an endovascular center and those transferred from a nonendovascular center to an endovascular center.

What Are the Clinical Implications?

- Prehospital stroke transport algorithms must account for the timely administration of intravenous thrombolysis as well as rapid transport to an endovascular stroke center.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request.

The OPUS-REACH registry consortium is a group of 8 health systems in the northeastern United States. The method of the OPUS-REACH registry has previously been described.¹⁹ The consortium consists of 9 ESCs in Pennsylvania, New York, New Jersey, and Delaware. The OPUS-REACH registry contains all LVOSs treated with EVT at 1 of the 9 ESCs between January 1, 2016, and December 31, 2020.

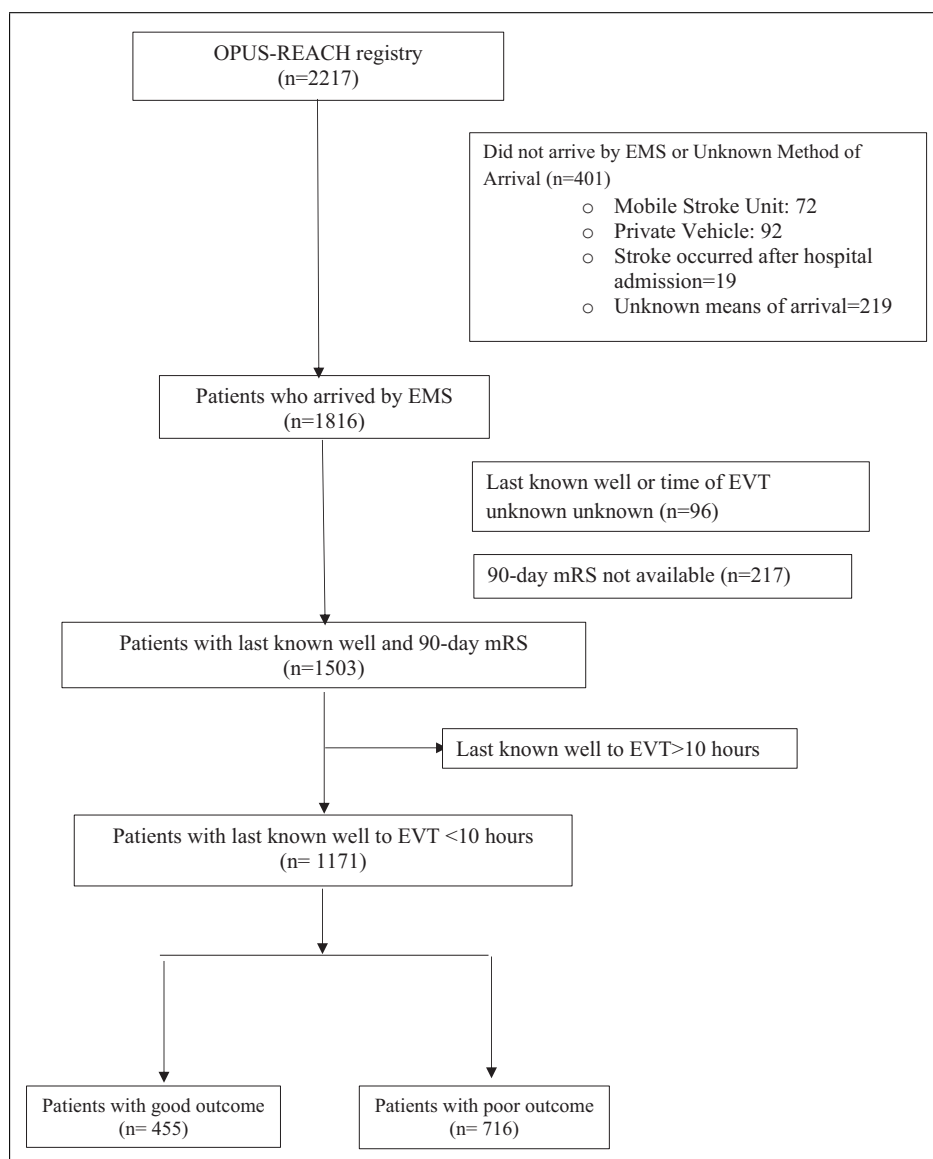


Figure 1. Enrollment diagram. EMS indicates emergency medical services; EVT, endovascular therapy; mRS, modified Rankin Scale; and OPUS-REACH, Optimizing the Use Prehospital Stroke Systems of Care—Reacting to Changing Paradigms.

Each site extracted patient data from its electronic medical record (EMR), stroke databases, and pre-hospital patient care reports. A standardized case report form was completed for each patient using the National Institutes of Health Common Data Elements when possible (<https://cde.nlm.nih.gov/home>). Patient data were deidentified and submitted to a central Research Electronic Data Capture (RedCap) database housed at Temple University.²⁰

The outcome of interest was the modified Rankin Scale (mRS) score at 90 days.^{21,22} The 90-day mRS score was dichotomized into 0 to 2 as a good outcome and 3 to 6 as a poor outcome. If an mRS score was not documented at 90 days as routine patient follow-up or in the EMR, the site investigator estimated the

mRS score from the medical record. Estimating an mRS score from the EMR has been shown to be a reliable method of estimating an mRS score.²³

All patients who underwent EVT at 1 of the 9 ESCs were included in the study. Patients were excluded from analysis if they did not arrive by EMS, did not have a documented last known well (LKW) time, had an LKW time to EVT of > 10 hours, or did not have a 90-day mRS score. Primary transport was defined as EMS transport from the scene to an ESC. Secondary transport was defined as transport to a non-ESC and then later transfer to an ESC for EVT.

Descriptive summary statistics are presented as means (SDs) or medians and interquartile ranges for continuous variables and as frequencies with

Table 1. Demographics and Baseline Characteristics. (n=1171).

Characteristic	Value
Age, median (range), y	71.1 (18–103)
Male sex, n (%)	570 (48.7)
Race, n (%)	
American Indian/Alaska Native	5 (0.5)
Asian/Native Hawaiian/Pacific Islander	8 (0.7)
Black	186 (16.8)
White	896 (80.9)
Other race	13 (1.2)
Unknown	63 (5.4)
Hispanic ethnicity, n (%)	
No	1100 (95.2)
Yes	55 (4.8)
Unknown	16 (1.4)
How did the patient arrive at the ESC?	
Primary transport	814 (69.5)
Secondary transport	357 (30.5)
Initial NIHSS score, mean (SD)	16.5 (7.6)
Last known well to EVT, mean (SD), min	258 (125)
Received intravenous thrombolysis, n (%)	633 (54.1)
Good outcome, n (%)	455 (38.9)

ESC indicates endovascular stroke center; EVT, endovascular therapy; and NIHSS, National Institutes of Health Stroke Scale.

percentages for categorical variables. Patient demographics and characteristics were compared between 2 groups using the χ^2 test for categorical variables and 2-sample *t*-tests or Wilcoxon rank-sum tests for continuous variables. Multivariable logistic regression was performed to determine the adjusted associations of the variables with 90-day dichotomized mRS outcome. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC). $P < 0.05$ was considered statistically significant.

This study was approved by the institutional review board at each of the study sites.

RESULTS

Of the 2284 patients in the OPUS-REACH registry, 1171 were included in our final analysis (Figure 1). A total of 455 patients (38.9%) had good outcomes. Table 1 lists the demographic and baseline characteristics of the patients.

When we dichotomized the entire cohort of patients by good and poor outcomes, we found that 2 nonmodifiable factors, male sex and lower initial National Institutes of Health Stroke Scale score, were significantly associated with good clinical outcome (Table 2). There were no differences in outcomes by race or ethnicity in our study. We saw no difference in outcome if a patient

underwent primary or secondary transport. However, both the receipt of IVT as well as time to IVT were associated with better outcomes in LVOS (mean, 104 versus 119 minutes; $P=0.006$).

We found no difference in the time from LKW to EVT for patients who had good outcomes versus poor outcomes (median, 223 versus 232 minutes; $P=0.21$). When we dichotomized functional outcome by an LKW to EVT interval of <4 , <6 , or <8 hours, we additionally saw no relationship between LKW to EVT and outcomes.

Intravenous Thrombolysis

In our univariable analysis stratified by receipt of IVT, IVT was associated with an absolute improvement in outcomes by $\approx 19\%$ (43.0% versus 25.7%; $P=0.002$) (Table 3). The benefits of IVT plus EVT over EVT alone were demonstrated up to an LKW to EVT interval of about 4 hours (Figure 2). The benefits of IVT plus EVT versus EVT alone were seen in both the direct transport cohort and the cohort of patients who required transfer for their EVT (Figure 3).

Primary Transport Versus Secondary Transport

We found no difference in clinical outcome between patients who underwent primary versus secondary transport in univariable analysis (Table 4). This finding was unexpected despite the direct transport group with an LKW to EVT time of 83 minutes faster (233 versus 316 minutes; $P < 0.0001$).

Multivariable Analysis

A multivariable analysis was performed using the variables that were significant on univariable analysis; each point increase on the National Institutes of Health Stroke Scale was associated with worse outcome (odds ratio [OR], 0.90 [95% CI, 0.89–0.92]) (Table 5). The only modifiable factor that improved outcome was the receipt of IVT (OR, 1.56 [95% CI, 1.19–2.06]). When time was used as a continuous variable, we did not see any differences in outcomes based on stroke onset to EVT. However, we did find a significant interaction effect between stroke onset to EVT in hours when patients received IVT.

Time to EVT

As mentioned above, time from stroke onset to EVT as a continuous variable did not result in better outcomes among our patients. We then compared outcomes by the time interval from LKW to EVT by 2-hour intervals (Table 6). We then further subdivided this cohort into

Table 2. Univariable Analysis for Entire Cohort

Variable	Overall (n=1171)	Good (n=455)	Poor (n=716)	P values
Transport, N (%)				0.46
Primary transport	814 (69.5)	322 (70.8)	492 (68.7)	
Secondary transport	357 (30.5)	133 (29.2)	224 (31.3)	
Sex, N (%)				0.0006
Female	601 (51.3)	205 (45.1)	396 (55.3)	
Male	570 (48.7)	250 (54.9)	320 (44.7)	
Race (n=1108), N (%)				0.12
American Indian	5 (0.5%)	2 (0.4)	3 (0.4)	
Asian/Pacific Islander	8 (0.7)	5 (1.1)	3 (0.4)	
Black	186 (16.8)	69 (16.0)	117 (17.3)	
White	896 (80.9)	345 (80.0)	551 (81.2)	
Other race	13 (1.2)	9 (2.0)	4 (0.6)	
Hispanic ethnicity (n=1155), N (%)				0.91
No	1100 (95.2)	428 (95.3)	672 (95.2)	
Yes	55 (4.78)	21 (4.7)	34 (4.8)	
Initial NIHSS score, N		453	715	<0.0001
Mean (SD)	16.5 (7.6)	13.45 (6.9)	18.49 (7.3)	
Intravenous thrombolysis, N (%)				0.002
No	538 (45.9)	183 (40.2)	355 (49.4)	
Yes	633 (54.1)	272 (59.8)	361 (51.6)	
Stroke onset to EVT, N (%)				
≤4 h	639 (54.6)	258 (56.7)	381 (53.2)	0.24
>4 h	532 (45.4)	197 (43.3)	335 (46.8)	
≤6 h	929 (79.3)	360 (79.1)	569 (79.5)	0.89
>6 h	242 (20.7)	95 (20.9)	147 (20.5)	
≤8 h	1081 (92.3)	416 (91.4)	665 (92.9)	0.36
>8 h	90 (7.7)	39 (8.6)	51 (7.1)	
Last known well to IVT, N	597	257	340	0.006
Median (IQR) minutes	113 (83–159)	104 (80–146)	119 (87–164.5)	
Last known well to EMS dispatch, N	820	330	490	0.33
Mean (SD)	38 (11–118)	38 (9–117)	37.5 (13–119)	
Last known well to EVT, N	1171	455	716	0.21
Median (IQR) minutes	225 (165–330)	223 (154–332)	231.5 (169–330)	

EMS indicates emergency medical services; EVT, endovascular therapy; IQR, interquartile range; IVT, intravenous thrombolysis; and NIHSS, National Institutes of Health Stroke Scale.

patients receiving IVT and those who did not receive IVT. In the adjusted analysis accounting for baseline National Institutes of Health Stroke Scale score, outcomes were better in patients who received EVT within 0 to 2 hours compared with those who received EVT from 2 to 8 hours. No other comparisons resulted in statistically significant differences in outcomes. In the subgroup of patients who received IVT, the analysis revealed that patients who received IVT within 2 hours of stroke onset had better outcomes than those who had times to EVT of 4 to 8 hours. We saw no difference in outcomes comparing any time from onset of stroke to EVT among patients who did not receive IVT.

DISCUSSION

Our study strengthens the findings of recent trials and analyses that suggest IVT plus EVT provides better outcomes than EVT alone. In our patient population, the main driver for good outcomes at 90 days was the receipt of IVT. IVT plus EVT was associated with better outcomes than EVT whether the patient was primarily transported to an ESC or arrived by secondary transport. We were surprised to find no difference in outcomes between patients who arrived by primary transport versus secondary transport to an ESC despite secondary transport adding 80 additional minutes to the interval from LKW to EVT. The no difference in out-

Table 3. Univariable Analysis for IVT Versus No IVT.

Variable	Overall (n=1171)	IVT (n=633)	No IVT (n=538)	P values
Dichotomized outcome, N (%)				0.002
Good	455 (38.9)	272 (43.0)	183 (25.7)	
Poor	716 (61.1)	361 (57.0)	355 (74.3)	
Sex, N (%)				0.993
Female	601 (51.3)	325 (51.3)	276 (51.3)	
Male	570 (48.7)	308 (48.7)	262 (47.7)	
Race (n=1108)				0.12
American Indian	5 (0.5)	2 (0.3)	3 (0.6)	
Asian/Pacific Islander	8 (0.7)	4 (0.7)	4 (0.9)	
Black	186 (16.8)	108 (18.1)	78 (15.2)	
White	896 (80.3)	470 (79.0)	426 (83.0)	
Other	13 (1.8)	11 (1.8)	2 (0.4)	
Hispanic ethnicity (n=1155), N (%)				0.08
No	1100 (95.2)	586 (94.2)	514 (96.2)	
Yes	55 (4.8)	36 (6.8)	19 (3.8)	
Initial NIHSS score (n=1168)		631	537	0.64
Mean (SD)	16.53 (7.6)	16.66 (7.6)	16.39 (7.5)	
Last known well to EVT				
Mean (SD)	258.3 (125.5)	216.5 (92.42)	307.34 (140.6)	<0.0001

EVT indicates endovascular therapy; IVT, intravenous thrombolysis; and NIHSS, National Institutes of Health Stroke Scale.

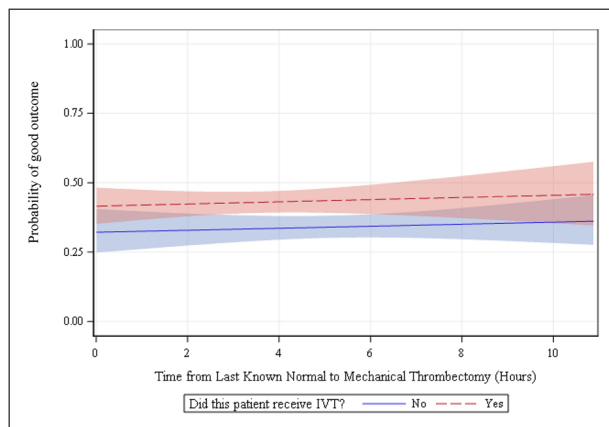


Figure 2. A model of the probability of a good functional outcome (modified Rankin Scale score, 0–2) at 90 days by time from onset of stroke to endovascular therapy. The study cohort is divided into patients who did (red) and did not (blue) receive intravenous thrombolysis (IVT). The shaded areas represent the 95% CIs.

comes may be explained by the fact that all patients were candidates for EVT and therefore had potentially salvageable brain tissue.

In our data, time to EVT was not associated with better outcomes unless the patient received IVT. This finding conflicts with other published studies. Sheth et al found that 81% of patients in the SWIFT-PRIME (Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment) trial had a good outcome (mRS score, 0–2) when EVT was performed within 2 hours of onset, 55% when EVT was performed

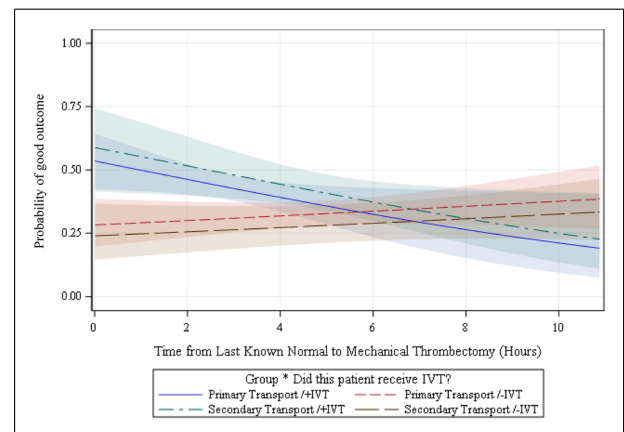


Figure 3. A model of the probability of a good functional outcome (modified Rankin Scale score, 0–2) at 90 days by time from onset of stroke to endovascular therapy. The study cohort is divided into patients who did and did not receive intravenous thrombolysis (IVT) and patients who underwent primary and secondary transport. The shaded areas represent the 95% CIs.

between 2 and 4 hours, and 35% when EVT was performed between 4 and 10 hours.²⁴ In the MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands) trial, every hour from onset to EVT was associated with a 7.7% decrease in good functional outcomes.²⁵ A meta-analysis by Saver et al found similar results.²⁶ However, these studies and the meta-analysis used results from clinical trials that optimized treatment intervals. Jahan et al used the AHA Get With The

Table 4. Univariable Analysis for Primary Transport Versus Secondary Transport

Variable	Overall (n=1171)	Direct (n=814)	Transferred (n=357)	P value
Dichotomized outcome, N (%)				0.46
Good	455 (38.9)	322 (40.3)	133 (37.3)	
Poor	716 (61.1)	492 (59.7)	224 (62.7)	
Sex, N (%)				0.21
Female	601 (51.3)	408 (50.1)	193 (54.1)	
Male	570 (48.7)	406 (49.9)	164 (45.9)	
Race (n=1108), N (%)				0.0002
American Indian	5 (0.5)	4 (0.5)	1 (0.3)	
Asian/Pacific Islander	8 (0.7)	8 (1.0)	0	
Black	186 (16.8)	153 (19.8)	33 (9.2)	
White	896 (80.9)	598 (77.3)	298 (89.0)	
Other	13 (1.2)	10 (1.3)	3 (0.8)	
Hispanic ethnicity (n=1155), N (%)				0.15
No	1100 (95.2)	760 (94.5)	340 (96.6)	
Yes	55 (4.8)	43 (5.5)	12 (3.4)	
Initial NIHSS score (n=1168)		814	354	0.59
Mean (SD)	16.5 (7.6)	16.4 (7.6)	16.8 (7.5)	
Intravenous thrombolysis, N (%)				0.25
No	538 (45.9)	383 (47.0)	155 (43.4)	
Yes	633 (54.1)	431 (53.3)	202 (56.6)	
Last known well to EVT (n=1171)		814	357	<0.0001
Mean (SD)	258.3 (125.45)	232.9 (122.0)	316.0 (113.7)	
Last known well to IVT (n=597)				0.005
Mean (SD)	126.7 (58.45)	122.0 (55.2)	138.8 (64.8)	
Last known well to EMS dispatch (n=820)				0.52
Mean (SD)	88.2 (115.3)	88.5 (112.8)	86.4 (127.6)	

EMS indicates emergency medical services; EVT, endovascular therapy; IVT, intravenous thrombolysis; and NIHSS, National Institutes of Health Stroke Scale.

Guidelines database to analyze the effect of onset to EVT time on functional outcomes.¹¹ Those authors found a large improvement in outcomes (mRS score, 0–2) when EVT was performed in 2 hours of onset and a smaller benefit when EVT was between 2 and 6 hours of onset.

Among our study hospitals, the mean door-to-needle time for ESCs was 41 minutes (SD, 23.8 minutes), whereas the mean time at the non-ESCs was 64.3 minutes (SD, 43.9 minutes). Currently, the AHA guidelines recommend a 60-minute door-to-needle goal, but higher functioning stroke centers can deliver

IVT within ≤ 30 minutes.¹ As door-to-needle times are shorter at ESCs, prehospital transport algorithms should factor in the door-to-needle time at various levels of stroke center certification.

We only included patients with a time from LKW to EVT of < 10 hours. We had few patients who received IVT and had > 10 hours from LKW to EVT. Therefore, we could not make a valid comparison between patients who did and did not receive IVT in the group who underwent EVT at > 10 hours.

The strength of our investigation is in the real-world, pragmatic nature of our data. The patients in

Table 5. Multivariable Logistic Regression Model to Predict Good Outcome

Variable	Odds ratio	95% Confidence limits		P value
NIHSS score	0.904	0.887	0.921	<0.001
Direct transport to ESC	1.097	0.819	1.468	0.53
Receipt of IVT	1.562	1.185	2.060	0.002
Onset to EVT (h)	0.991	0.924	1.063	0.80

ESC indicates endovascular stroke center; EVT, endovascular therapy; IVT, intravenous thrombolysis; and NIHSS, National Institutes of Health Stroke Scale.

Table 6. Functional Outcomes of Patient Treatment With EVT Comparing Different Onset-to-Puncture Time Intervals

a Functional outcomes of patient treatment with EVT (entire cohort)									
Unadjusted No. of patients/total No. (%) by onset-to-puncture interval*		241–360		361–480		481–600		Adjusted OR comparing onset-to-puncture interval (95%CI)†	
Overall	0–120	121–240	241–360	361–480	481–600	0–120 vs 121–240	121–240 vs 241–360	0–120 vs 241–360	0–120 vs 361–480
	455/1171 (38.9)	52/110 (47.3)	206/529 (38.9)	102/290 (35.2)	56/152 (36.8)	39/90 (43.3)	1.73 (1.10–2.69)	2.22 (1.37–3.59)	1.76 (1.02–3.05)
b Functional outcomes of patient treatment with EVT who received intravenous thrombolysis comparing different onset-to-puncture time intervals									
Unadjusted No. of patients/total No. (%) by onset-to-puncture interval		241–360		361–480		481–600		Adjusted OR comparing onset-to-puncture interval (95%CI)‡	
Overall	0–120	121–240	241–360	361–480	481–600	0–120 vs 121–240	121–240 vs 241–360	0–120 vs 241–360	0–120 vs 361–480
	272/633 (43)	40/79 (50.6)	149/339 (54.7)	61/167 (36.5)	16/38 (32.1)	6/10 (60.0)	1.61 (0.96–2.70)	2.29 (1.29–4.08)	2.4 (1.06–5.61)
c Functional outcomes of patient treatment with endovascular therapy who did not receive intravenous thrombolysis comparing different onset-to-puncture intervals									
Unadjusted No. of patients/total No. (%) by onset-to-puncture interval		241–360		361–480		481–600		Adjusted OR comparing onset-to-puncture interval (95%CI)§	
Overall	0–120	121–240	241–360	361–480	481–600	0–120 vs 121–240	121–240 vs 241–360	0–120 vs 241–360	0–120 vs 361–480
	183/538 (34.1)	12/31 (38.7)	57/190 (31.2)	49/114 (35.1)	40/114 (35.1)	33/80 (41.3)	1.61 (0.96–2.70)	2.29 (1.29–4.08)	2.4 (1.06–5.61)

EVT indicates endovascular therapy; and OR, odds ratio.

*No comparisons were statistically significant.

†The differences for 0 to 120 minutes vs 121 to 240, 241 to 360, and 361 to 480 minutes were significant. Remainder of comparisons were nonsignificant.

‡The differences for 1 to 120 minutes vs 241 to 360 and 361 to 480 minutes were statistically significant.

our study reflect actual EMS transport decisions as well as time involved in transferring patients. Unlike the SKIP Trial (Effect of Mechanical Thrombectomy Without vs With Intravenous Thrombolysis on Functional Outcome Among Patients With Acute Ischemic Stroke), DEVT (Effect of Endovascular Treatment Alone vs Intravenous Alteplase Plus Endovascular Treatment on Functional Independence in Patients With Acute Ischemic Stroke), and DIRECT-MT Trail (Endovascular Thrombectomy with or without Intravenous Alteplase in Acute Stroke) studies, we included patients who were transferred from non-ESCs for EVT. This provides a more accurate picture of stroke treatment outside of organized stroke research. Unlike prior studies, we did not estimate transfer time or prehospital time intervals. All times were extracted from prehospital care reports and in-hospital records. In addition, the OPUS-REACH registry consortium has a wide swath of populations and EMS agencies. These include urban areas, rural areas, and suburban areas.

LIMITATIONS

Many patients were excluded on the basis of missing data. For example, 219 patients were excluded because their mode of arrival was unknown, 96 patients were excluded because their time of LKW or EVT was unknown, and 217 patients were excluded because their 90-day mRS score was unknown. Most of the patients who were excluded because of unknown times and unknown arrivals were first seen at non-ESCs. However, it is unclear how this missing data affected our results.

Second, we did not include patients with stroke who were transferred from a non-ESC and did not receive EVT. Patients may be transferred because their needs outstrip the abilities of the transferring hospitals and could be appropriate despite the patient not receiving EVT. We also did not include patients with LVOS who may have stayed at the non-ESC. For example, a patient who had an LVOS but no salvageable tissue on vascular imaging would not be included in this registry.

Third, 208 patients (17.8%) had their mRS score estimated from the EMR. In our prior research, we examined whether the mRS score could be derived from the EMR. In that study, we found that a physician only estimated the absolute mRS score correctly 68% of the time. However, a physician was able to estimate the dichotomized mRS score (good versus poor outcome) 90% of the time. Therefore, we believe this to be a valid, although not optimal, method to determine the mRS score at 90 days. Other studies have shown that various other stroke assessment scales can be accurately derived from the medical record.^{27–29}

CONCLUSIONS

In this large pragmatic registry of 1171 patients with LVOS, receipt of IVT was independently associated with improved outcomes at 90 days with an OR of 1.51. A shorter time from LKW to EVT and direct transport to an ESC versus transfer for ESC were not associated with improved outcomes. We therefore conclude that pre-hospital stroke transport algorithms must account for the timely administration of IVT as well as rapid transport to an ESC.

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