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### ► To cite this version:

A. W. Kraft, R. W. Regenhardt, A. Awad, J. A. Rosenthal, A. A. Dmytriw, et al.. Spoke-administered thrombolysis improves large vessel occlusion early recanalization: the real-world experience of a large academic hub-and-spoke telestroke network.. Stroke: Vascular and Interventional Neurology, 2023, Stroke: Vascular and Interventional Neurology, 3, 10.1161/svin.122.000427 . hal-04873941

**HAL Id: hal-04873941**

**<https://hal.univ-lille.fr/hal-04873941v1>**

Submitted on 8 Jan 2025

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## ORIGINAL RESEARCH

# Spoke-Administered Thrombolysis Improves Large-Vessel Occlusion Early Recanalization: The Real-World Experience of a Large Academic Hub-and-Spoke Telestroke Network

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**BACKGROUND:** Intravenous thrombolysis (IVT) before mechanical thrombectomy (MT) for large-vessel occlusion (LVO) stroke is increasingly controversial. Recent trials suggest MT without IVT is reasonable for patients presenting directly to MT-capable “hub” centers. However, bypassing IVT has not been evaluated for patients presenting to IVT-capable “spoke” hospitals that require hub transfer for MT. A perceived lack of efficacy of IVT to result in LVO early recanalization (ER) is often cited to support bypassing IVT, but data for IVT in patients who require interhospital transfer are limited. Here, we examined LVO ER rates after spoke-administered IVT in our hub-and-spoke stroke network.

**METHODS:** Patients presenting to 25 spokes before hub transfer for MT consideration from 2018 to 2020 were retrospectively identified from a prospectively maintained database. Inclusion criteria were pretransfer computed tomography angiography-defined LVO, Alberta Stroke Program Early Computed Tomography Score  $\geq 6$ , and posttransfer repeat vessel imaging.

**RESULTS:** Of 167 patients, median age was 69, and 51% were women. Seventy-six received spoke IVT, and 91 did not. Alteplase was the only IVT used in this study. Comorbidities and National Institutes of Health Stroke Scale were similar between groups. ER frequency was increased 7.2-fold in patients who received spoke IVT (12/76 [15.8%] versus 2/91 [2.2%];  $P < 0.001$ ). Spoke-administered IVT was independently associated with ER (adjusted odds ratio, =11.5 [95% CI, 2.2–99.6;  $P < 0.05$ ] after adjusting for the timing of last known well, interhospital transfer, and repeat vessel imaging. Interval National Institutes of Health Stroke Scale score was improved in patients with ER (median  $-2$  [interquartile range,  $-6.3$  to  $-0.8$ ] versus  $0$  [ $-2.5$  to  $1$ ];  $P < 0.05$ ).

**CONCLUSION:** Within our network, patients who received spoke IVT had a 7.2-fold increased ER relative likelihood. This real-world analysis supports IVT use in eligible patients with LVO at spoke hospitals before hub transfer for MT.

**Key Words:** stroke ■ thrombectomy ■ thrombolysis

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Stroke: Vascular and Interventional Neurology is available at: [www.ahajournals.org/journal/svin](http://www.ahajournals.org/journal/svin)

**M**echanical thrombectomy (MT) has revolutionized large-vessel occlusion (LVO) stroke care.<sup>1</sup> Before MT, intravenous thrombolysis (IVT) was the mainstay of acute ischemic stroke treatment. However, the efficacy of IVT alone for early recanalization (ER) of LVO is limited, and MT for LVO stroke dramatically improves the likelihood of timely recanalization and functional independence.<sup>2–4</sup> Understandably, there is now a widespread focus on maximizing the benefits of MT, and this has led to controversy regarding the utility of IVT before MT for patients with LVO at centers with MT capability.<sup>5–8</sup> For patients with LVO presenting directly to MT-capable centers, recent trials have demonstrated clinical noninferiority for bridging IVT before MT compared with bypassing IVT and performing MT alone.<sup>9,10</sup> However, there are no randomized trials assessing bridging IVT for patients with LVO in “hub-and-spoke” stroke networks in which patients with LVO first present to “spoke” hospitals that can administer IVT but must be subsequently transferred to MT-capable “hub” centers.

There are several potentially harmful consequences of initiating IVT before MT, including elevated bleeding risk, delays in transport to MT attributable to IVT administration, inadequate dwell time when IVT is started at an MT-capable site, increased MT procedural difficulty, cost, and futility of IVT for recanalization.<sup>5–8</sup> The efficacy of IVT to produce ER in LVO has been studied and ranges from 8% to 41%, and a recent large randomized trial demonstrated ER in 10% of patients with LVO stroke after alteplase administration.<sup>3,11,12</sup> These studies quantifying ER generally included patients presenting directly to MT-capable hub centers. As a result, the efficacy at which spoke-administered IVT can result in LVO recanalization during hub transfer is not well characterized. Studies focusing on bridging IVT for patients with LVO undergoing interhospital transfer are increasingly important, as patients with LVO presenting to spoke versus hub hospitals may be best served by different treatment paradigms. To better understand the influence of spoke-administered IVT on outcomes for patients with LVO, we examined how spoke-administered IVT affects LVO ER frequency for patients within our large academic hub-and-spoke telestroke network.

## METHODS

This study was compliant with the Health Insurance Portability and Accountability Act and was reviewed and approved by the hub site institutional review board. Informed consent was waived on the basis of minimal patient risk and practical inability to perform the study without the waiver. The data that support the findings of

## Nonstandard Abbreviations and Acronyms

<b>ER</b>	early recanalization
<b>ICH</b>	intracerebral hemorrhage
<b>IVT</b>	intravenous thrombolysis
<b>LKW</b>	last known well
<b>LVO</b>	large-vessel occlusion
<b>MT</b>	mechanical thrombectomy
<b>NIHSS</b>	National Institutes of Health Stroke Scale
<b>+spokeIVT</b>	patients who received spoke IVT
<b>–spokeIVT</b>	patients who did not receive spoke IVT
<b>TSCS</b>	telestroke consult

## CLINICAL PERSPECTIVE

- We examined large-vessel occlusion stroke early recanalization rates in patients who first presented to spoke hospitals and were transferred to a hub hospital for mechanical thrombectomy consideration.
- Early recanalization frequency in patients who received spoke-administered intravenous thrombolysis was increased 7.2-fold compared with patients who did not receive intravenous thrombolysis at the spoke (12/76 [15.8%] versus 2/91 [2.2%];  $P < 0.001$ ).
- These real-world data suggest that spoke-administered intravenous thrombolysis dramatically increases large-vessel occlusion early recanalization likelihood and supports continued use of intravenous thrombolytics for mechanical thrombectomy candidates who first present to spoke hospitals and require hub transfer for mechanical thrombectomy.

this study will be made available from the corresponding author upon reasonable request and pending approval of the local institutional review board.

A single hub site was used for this study. Patients with LVO who presented to 25 spoke hospitals from January 1, 2018, to June 30, 2020, were identified from our local Get With the Guidelines–Stroke patient database.<sup>13</sup> The definitions applied are those used in the Get With the Guidelines–Stroke database unless otherwise specified. This database includes demographics, medical history, clinical presentations,

imaging findings, treatments, and functional outcomes for consecutive patients. These data were extracted from the medical record.<sup>14</sup> Inclusion criteria were pretransfer spoke computed tomography angiography (CTA)-defined LVO, Alberta Stroke Program Early Computed Tomography (CT) Score  $\geq 6$ , and repeat vessel imaging upon arrival at the hub hospital. LVO was defined as occlusion of the internal carotid artery terminus, first (M1) and proximal second (M2) segments of the middle cerebral artery, or the basilar artery.<sup>15</sup> Proximal M2 was defined as the horizontal M2 segment within 1 cm from the middle cerebral artery bifurcation.<sup>16</sup> Repeat vessel imaging modalities included CTA, magnetic resonance angiography, or digital subtraction angiography at the time of MT.<sup>17</sup>

ER was defined as LVO recanalization demonstrated by hub site repeat vessel imaging. To be considered ER, repeat imaging could not demonstrate a total occlusion present in the internal carotid artery, M1 or proximal M2 portion of the middle cerebral artery, or basilar artery. Distal migration was defined as an ER event with a new cerebral artery occlusion on repeat imaging that was distal to the original LVO site. Time points used for analysis were last known well (LKW), telestroke consult (TSCS) time, hub arrival time, and repeat vessel imaging time at the hub. TSCS time was defined as when the spoke hospital initiated the TSCS service.

Presenting National Institutes of Health Stroke Scale (NIHSS) score was determined by telestroke and hub neurologists as described, with higher NIHSS numbers reflecting increased clinical stroke severity.<sup>18</sup> All patients underwent head and neck CT and CTA at spoke hospitals prior to transfer.<sup>19,20</sup> Alberta Stroke Program Early CT score and presence of LVO on CTA were determined by a vascular neurologist and confirmed by a neuroradiologist.<sup>21</sup> Alteplase was the only IVT agent used in this analysis. IVT treatment decisions at spokes were guideline based at the discretion of a vascular neurologist through telemedicine.<sup>22</sup> The decision to obtain repeat vessel imaging at the hub was at the discretion of a vascular neurologist and neurointerventionalist. Symptomatic intracerebral hemorrhage (ICH) was defined as any symptomatic intraparenchymal, intraventricular, or subarachnoid hemorrhage during hospitalization.<sup>23,24</sup>

Mean values with SD were reported for continuous variables with normal distributions, and median values with interquartile range (first quartile, third quartile) for those without normal distributions. Percentage and count were reported for categorical variables. Statistical differences were assessed using permutation resampling in which test statistics of interest were compared with null distributions generated from 105 random group permutations.<sup>25</sup> The association of IVT and time intervals between LKW, spoke presentation, hub pre-

sentation, and repeat vessel imaging were assessed using multivariate logistic regression. These covariates were chosen on the basis of baseline characterization analysis showing different time intervals between patients who received spoke IVT (+spokeIVT) and patients who did not receive spoke IVT (–spokeIVT). Unadjusted and adjusted analyses were reported using logistic regression for all covariates analyzed; odds ratios were reported as adjusted odds ratios for all variables listed in each analysis. Two-tailed *P* values  $<0.05$  were interpreted as statistically significant. All statistics were performed with RStudio version 1.4.

## RESULTS

Our database of spoke-to-hub transfers with CTA-defined LVO and Alberta Stroke Program Early CT score  $\geq 6$  contained 258 patients. Of these, 167 patients had records indicating the anatomical LVO location at the spoke and repeat vessel imaging upon hub hospital arrival. Reasons for foregoing repeat vessel imaging included mild symptoms (NIHSS score  $\leq 6$ ), patient goals of care/prestroke baseline, and brain parenchymal imaging with large established infarct. Among patients with repeat vessel imaging at the hub, 76 patients received spoke-administered IVT and 91 did not. No patients who underwent interhospital transfer received IVT at the hub. Repeat vessel imaging modalities included CTA, magnetic resonance angiography, or digital subtraction angiography at the time of MT. There was no significant difference in the percentage of patients who underwent digital subtraction angiography for repeat vessel imaging between the 2 groups (+spokeIVT 58 [76%] versus –spokeIVT 59 [65%];  $P=0.09$ ; Table 1). For 7 patients, ER was discovered by digital subtraction angiography, and MT was aborted (+spokeIVT, 7 [4.2%] versus –spokeIVT, 0 [0%];  $P<0.0001$ ).

“Age, sex, racial, and medical comorbidities were equivalent between the +spokeIVT and –spokeIVT groups (Table 1). NIHSS scores at presentation to the spoke and hub were also similar (median spoke NIHSS +spokeIVT, 16 [10–21], –spokeIVT, 13 [7, 20];  $P=0.13$ ; median hub NIHSS +spokeIVT, 15 [8–20], –spokeIVT, 13 [6–17];  $P=0.36$ ; Table 1). The LKW-to-telestroke time was shorter among +spokeIVT patients (2.2 $\pm$ 2.5 versus 7.6 $\pm$ 5.3 hours;  $P<0.0001$ ; Table 1). Interestingly, TSCS-to-hub arrival was faster among the +spokeIVT patients (2.3 $\pm$ 1.0 versus 2.7 $\pm$ 1.1 hours;  $P<0.05$ ; Table 1). The mean time from hub arrival to repeat vessel imaging was 62.9 (57.2) minutes for all patients in this study (Table 1). The mean interval between hub arrival and vessel imaging was 49.9 (57.0) minutes in +spokeIVT patients versus 73.7

**Table 1. Demographics, Medical History, Presentations, Treatments, and Outcomes**

	+SpokeIVT		-SpokeIVT		Total		P value
	Median/ count/mean	IQR/ %/SD	Median/ count/mean	IQR/ %/SD	Median/ count/mean	IQR/ %/SD	
Age	67	57–81	70	60–81	69	59–81	0.24
Female	40	53	46	51	86	51	0.76
Black	4	5	3	3	7	4	0.46
Hispanic	1	1	4	4	5	3	0.18
Asian	1	1	1	1	2	1	0.50
White	50	66	62	68	112	68	0.74
Hypertension	47	62	61	67	108	65	0.42
Diabetes	17	22	22	24	39	23	0.71
Atrial fibrillation	18	24	31	34	49	29	0.13
Coronary disease	12	16	12	13	24	14	0.51
Prior stroke/TIA	9	12	15	16	24	14	0.38
Dyslipidemia	35	46	42	46	77	46	0.88
Obesity/overweight	24	32	32	35	56	34	0.63
Renal insufficiency	6	8	8	9	14	8	0.78
Smoking	16	21	15	16	31	19	0.43
NIHSS at spoke (N=127, 72, 55)	16	10–21	13	7–20	15	9–20	0.13
NIHSS at hub	15	8–20	13	6–17	13	7–18	0.36
LKW-TSCS (h) (N=166, 76, 90)	2.2	2.5	7.6	5.3	5.1	5.1	<0.0001
TSCS-hub (h)	2.3	1.0	2.7	1.1	2.5	1.1	0.02
Hub-image (min)	50	57	74	55	63	57	0.007
Symptomatic ICH	2	3	4	4	6	4	0.42
<b>Repeat vessel imaging modality</b>							
DSA	58	76	59	65	117	70	0.09
Noninvasive (MRA or CTA)	18	24	32	35	50	30	0.09

M1, first MCA segment; M2, second MCA segment. Unless otherwise specified, total n=167, +spokeIVT n=76, –spokeIVT n=91. DSA indicates digital subtraction angiogram; Hub-image, hub-to-repeat vessel imaging time interval; ICA, internal carotid artery; ICH, intracerebral hemorrhage; IQR, interquartile range; IVT, intravenous thrombolysis; LKW, last known well; LKW-TSCS, LKW-to-TSCS time interval; LVO, large-vessel occlusion; MCA, middle cerebral artery; MRA, magnetic resonance angiography; NIHSS, National Institutes of Health Stroke Scale; +spokeIVT, patients who received spoke IVT; –spokeIVT, patients who did not receive spoke IVT; TIA, transient ischemic attack; TSCS, telestroke consult; and TSCS-hub, TSCS-to-hub arrival time interval.

(55.4) minutes in –spokeIVT patients ( $P<0.01$ ; Table 1). +spokeIVT patients did not have an increased rate of symptomatic ICH (3% in +spokeIVT versus 4% in –spokeIVT;  $P=0.42$ ; Table 1)."

The anatomic distribution of LVO locations identified at the spoke was not different between +spokeIVT and –spokeIVT patients (Table 2). Among all LVO locations, ER occurred in 12 (15.8%) +spokeIVT patients, whereas ER occurred in 2 (2.2%) –spokeIVT patients ( $P<0.001$ ), which amounted to a 7.2-fold increase in the relative likelihood of ER after IVT. In stratifying ER by LVO location, we found statistically significant increases in ER after IVT for LVO located in both the internal carotid artery (1 [7.1%] versus 0 [0%];  $P<0.0001$ ) and middle cerebral artery (11 [18.6%] versus 2 [3.2%];  $P<0.01$ ; Table 2). Distal migration occurred in 6 of 12 ER instances among the +spokeIVT patients and in neither of 2 ER instances among the –spokeIVT patients (Table 3).

We next examined how presentation and transfer latencies influenced ER. Using multivariable logistic regression modeling we found that spoke-administered IVT was associated with ER independent of LKW-to-telestroke time, telestroke-to-hub arrival time, and hub arrival-to-repeat vessel imaging time (odds ratio=8.3 [2.2–54.8];  $P<0.01$ ; adjusted odds ratio=11.5 [2.2–99.6];  $P<0.05$ ; Table 4). TSCS time was used as a surrogate for IVT time because of IVT time not being an available variable for the –spokeIVT patients. There was no difference in time intervals between hub arrival and repeat vessel imaging in patients with ER (80 [70] minutes) compared with patients without ER (61 [56] minutes;  $P=0.23$ ).

We also analyzed how the time interval between LKW and IVT administration influenced ER. The time interval between LKW and IVT administration was not different between individuals with ER (+ER) and those without ER (–ER) (+ER 191.3 [204.9] minutes, n=11;

**Table 2. Spoke Large Vessel Occlusion Location and Early Recanalization Frequency Stratified by Spoke Occ Location**

	Count	%	Count	%	Count	%	P value
<b>Spoke LVO location</b>							
	<b>+SpokeIVT</b>		<b>-SpokeIVT</b>		<b>Total</b>		
ICA	14	18.4	20	22.0	34	20.4	0.11
M1 MCA	49	64.5	45	49.5	94	56.3	
M2 MCA	10	13.2	18	19.8	28	16.8	
Basilar	3	3.9	8	8.8	11	6.6	
<b>ER by spoke LVO location</b>							
	<b>+SpokeIVT</b>		<b>-SpokeIVT</b>		<b>Total</b>		
Any location	12/76	15.8	2/91	2.2	14/167	8.4	<0.001
ICA	1/14	7.1	0/20	0	1/34	2.9	<0.0001
MCA	11/59	18.6	2/63	3.2	13/122	9.8	<0.01
M1	9/49	18.4	1/45	2.2	10/94	10.6	<0.01
M2	2/10	20.0	1/18	5.6	3/28	10.7	0.29
Basilar	0/3	0	0/8	0	0/11	0	1

ER indicates early recanalization; ICA, internal carotid artery; IVT, intravenous thrombolysis; LVO, large vessel occlusion; MCA, middle cerebral artery; +spokeIVT, patients who received spoke IVT; and -spokeIVT, patients who did not receive spoke IVT.

**Table 3. Patients with Early Recanalization and Characterization of Distal Migration Events**

Patient	Spoke occlusion	Hub occlusion
+SpokeIVT ER 1	ICA	None
+SpokeIVT ER 2	M1	None
+SpokeIVT ER 3	M1	None
+SpokeIVT ER 4	M1	None
+SpokeIVT ER 5	M1	M3
+SpokeIVT ER 6	M1	M3
+SpokeIVT ER 7	M1	M4
+SpokeIVT ER 8	M1	M3
+SpokeIVT ER 9	M1	M4
+SpokeIVT ER 10	M1	M3
+SpokeIVT ER 11	Proximal M2	None
+SpokeIVT ER 12	Proximal M2	None
-SpokeIVT ER 1	M1	None
-SpokeIVT ER 2	Proximal M2	None

ER indicates early recanalization; IVT, intravenous thrombolysis; +spokeIVT, patients who received spoke-administered IVT; and -spokeIVT, patients who did not receive spoke administered IVT.

**Table 4. Spoke-Administered Intravenous Thrombolysis Is Associated With Early Recanalization After Correction for Relevant Time Intervals**

Early Recanalization				
	OR (95% CI)	P value	aOR (95% CI)	P value
Spoke IVT	8.3 (2.2–54.8)	0.006	11.5 (2.2–99.6)	0.01
LKW-to-TSCS time	1.00 (1.00–1.00)	0.14	1.0 (1.00–1.00)	0.81
TSCS-to-hub arrival time	1.00 (1.00–1.01)	0.61	1.0 (1.00–1.01)	0.70
Hub-to-repeat imaging time	1.00 (1.00–1.01)	0.25	1.0 (1.00–1.01)	0.16

aOR indicates adjusted odds ratio; IVT, intravenous thrombolysis; LKW, last known well; OR, odds ratio; and TSCS, telestroke consult.

**Table 5. Latency Between Last Known Well and Intravenous Thrombolysis Administration Is Not Associated With Early Recanalization Likelihood**

(A)	+ER n=11		-ER n=60		P value
	Mean	SD	Mean	SD	
LKW-to-IVT time (min)	191.3	204.9	143.7	98.7	0.20
<b>(B) Early recanalization</b>					
	<b>OR (95% CI)</b>				<b>P value</b>
LKW-to-IVT time (min)	1.00 (1.00–1.01)				

(A) There was no difference between the LKW-to-IVT interval in patients with or without ER (IVT time available for 71 patients, +ER n=11, -ER n=60). (B) Linear regression demonstrates no association between LKW-to-IVT time and ER. ER indicates early recanalization; IVT, intravenous thrombolysis; LKW, last known well; and OR, odds ratio.

-ER 143.7 (98.7) minutes, n=60; P=0.20; Table 5). Furthermore, there was no association between the time interval between LKW and IVT administration and ER likelihood (Table 5).

To assess the relationship of early clinical improvement and ER, we compared changes in spoke and hub NIHSS ( $\Delta$ NIHSS) in +ER vs -ER patients. Spoke NIHSS was available for 127 of the 167 patients. In +ER patients (n=12) the median  $\Delta$ NIHSS was -2 (-6.3 to -0.8), whereas in -ER patients (n=115) the median  $\Delta$ NIHSS was 0 (-2.5, 1; P<0.05). Among +ER patients, those with distal migration (n=6) had a median  $\Delta$ NIHSS of -3 (interquartile range=-6.5 to -0.3), whereas in patients without distal migration (n=6) the median  $\Delta$ NIHSS was -2 (interquartile range=-5.0 to -2.0).

## DISCUSSION

In analyzing our real-world experience with spoke-administered IVT, we found that ER occurred in 15.8% of +spokeIVT patients compared with 2.2% of –spokeIVT patients, which amounted to a 7.2-fold relative increase in ER after spoke-administered IVT. All ER events occurred in anterior circulation LVOs. Furthermore, +ER patients, regardless of whether they received spoke-administered IVT, had improved  $\Delta$ NIHSS between the spoke and hub hospital, whereas no  $\Delta$ NIHSS change was found in –ER patients. These results support a continued role for bridging IVT for patients with LVO presenting to spoke hospitals that do not have MT capability.

It is frequently argued that IVT does not effectively result in ER for LVO stroke.<sup>5</sup> However, several studies have demonstrated a >3-fold increase in LVO ER after IVT, with ER rates ranging from 8% to 41%.<sup>3,11,12,26</sup> The reasons ER rates vary widely are likely multifactorial and may include differences in definitions of ER, vessel image sampling timing, patient populations, geography of hospital networks, and rapidly evolving approaches to stroke systems of care. There is a relative paucity of data on LVO ER exclusively after spoke-administered IVT, and our results support improved LVO ER rates when IVT precedes a hub-and-spoke interhospital transfer.

ER likelihood appears to be influenced by LVO location. Our data show that all ER events occurred for anterior circulation LVO. This finding is consistent with previous work showing that basilar artery LVO is less likely to recanalize with IVT alone.<sup>27</sup> Indeed, LVO anatomy may offer useful biomarkers for IVT decisions in the future, and further research is warranted.

Almost half of the observed ER events resulted in distal migration of thrombus. The concern that distal migration following IVT may render patients ineligible for MT has been raised.<sup>8</sup> While distal migration will result in earlier reperfusion of more proximal cerebral territories, it could potentially result in a missed MT opportunity if thrombus migrates from a retrievable to a nonretrievable location. However, there is no evidence that distal migration risks outweigh IVT benefits. To the contrary, distal migration has been associated with improved long-term functional outcomes.<sup>28</sup> In our study, distal migration was not associated with worsened NIHSS among patients with ER, but larger future studies will be needed to establish conclusions on clinical outcomes associated with distal migration after ER.

Importantly, chemical thrombolysis is a time-dependent process. Prior studies showed that 75% of recanalization events occur >30 minutes after IVT bolus, with 25% of recanalization events happening

>1 hour after the IVT bolus.<sup>29</sup> The short IVT dwell times present in trials on bypassing IVT may have been insufficient for IVT to take full effect. In our study, the mean IVT bolus-to-puncture time was 116 (44) minutes (data available for 49 patients). In comparison, the median IVT to puncture time was 29 minutes in the Direct Intra-arterial Thrombectomy in Order to Revascularize AIS Patients With Large Vessel Occlusion Efficiently in Chinese Tertiary Hospitals (DIRECT-MT) trial.<sup>9</sup> Spoke-administered IVT may be especially beneficial given the longer dwell times inherent to interhospital transfers.

Indeed, LVO ER occurs in a minority of patients, and MT for appropriate patients with LVO is the treatment approach most likely to yield functional independence.<sup>1</sup> Some recent trials have demonstrated that IVT bypass is not inferior to bridging IVT for patients with LVO presenting to MT-capable centers.<sup>9,10</sup> These patients, however, are distinct from patients with LVO first presenting to a spoke. For patients with LVO presenting to MT-capable centers, MT eligibility can be rapidly determined, and the procedure can be performed immediately. Patients with LVO presenting to spoke hospitals must undergo interhospital transfer, which can take hours. By the time of hub arrival, they may be ineligible for MT for many reasons.<sup>30–32</sup> For patients with LVO ultimately found to be MT ineligible, bypassing spoke-administered IVT with the hope of expediting MT is a missed opportunity. Furthermore, there is no definitive evidence that spoke-administered IVT delays or worsens MT outcomes. Importantly, it has been demonstrated that spoke-administered IVT is associated with improved 90-day functional outcomes regardless of whether patients undergo MT.<sup>30</sup> In sum, this analysis of our stroke network's experience with spoke-administered IVT suggests IVT is efficacious in yielding ER for patients with LVO stroke. The findings support our commitment to continued use of spoke-administered IVT for eligible patients with LVO who present to a spoke hospital before hub transfer for MT consideration.

This study has implications for a large portion of the LVO stroke population. It is common for patients with acute LVO stroke who ultimately receive MT first to present to spoke hospitals. A large (n=984) national multicenter prospective observational study using the STRATIS (Systematic Evaluation of Patients Treated With Neurothrombectomy Devices for Acute Ischemic Stroke) registry of patients with LVO who received MT demonstrated that 45% of MT-eligible patients with LVO stroke first present to spoke hospitals, whereas 55% present directly to MT-capable hub hospitals. Among MT-eligible patients presenting to spoke hospitals, 67% received IV-tPA.<sup>33</sup> This suggests that in the United States, roughly half of MT-eligible patients with LVO stroke will present to a spoke hospital, with the

majority being IVT candidates. As such, this study potentially has broad implications for LVO systems of care.

Our study has important limitations. The retrospective review and nonrandomized design employed creates the potential for unmeasured confounders. While we controlled for longer delays between LKW and TSCS time in the –spokeIVT group, other biases could have influenced our results. Indeed, –spokeIVT patients may have been in a different stage of LVO progression when MT was being considered.<sup>34</sup> It is possible that ER is less likely several hours after onset. Nonetheless, randomized trials showing increased ER after IVT argue that IVT is driving ER in our population. Furthermore, in the Table 4 analysis, spoke IVT administration time and spoke CT imaging time were not uniformly available for this data set, so TSCS time was used as an approximation. In addition, repeat vessel imaging at the hub was not performed in all cases and the vessel imaging modality was not standardized; there may be unrecognized factors that contributed to selection bias. For example, some patients who had clinical improvement and NIHSS score <6 upon hub arrival might not have had repeat vessel imaging. Importantly, all patients treated with IVT in this study received alteplase. There is increasing usage of tenecteplase, which has been shown to have equivalent outcomes and possibly increased ER rates.<sup>3</sup> Tenecteplase may ultimately be found to result in different rates of ER and ICH for patients with acute LVO stroke transferring from spoke to hub hospitals. Finally, the sample size was relatively small; some analyses, such as those evaluating symptomatic ICH, may have been underpowered.

## CONCLUSIONS

In summary, these results demonstrate that patients with LVO who were treated with IVT at spoke hospitals before hub transfer for MT consideration had a 7.2-fold relative likelihood increase in LVO early recanalization compared with patients who did not receive IVT. Patients with early recanalization patients had improved NIHSS scores and no increase in symptomatic ICH. These results support the continued use of bridging IVT for patients with LVO presenting to MT-incapable spoke hospitals.

## ARTICLE INFORMATION

Received March 17, 2023; Accepted August 11, 2022

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## Acknowledgments

Joyce A. McIntyre and Cynthia Whitney maintained the Massachusetts General Hospital prospective stroke database.

## Sources of Funding

R.W. Regenhardt has research grants from the National Institutes of Health, National Institute of Neurological Disorders and Stroke (R25 NS065743), the Society of Vascular and Interventional Neurology, and the Heitman Foundation.

## Disclosures

There are no relevant competing interests.

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