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ORIGINAL ARTICLE

Understanding Delays in MRI-based Selection of Large Vessel Occlusion Stroke Patients for Endovascular Thrombectomy

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Abstract

Purpose Given the efficacy of endovascular thrombectomy (EVT), optimizing systems of delivery is crucial. Magnetic resonance imaging (MRI) is the gold standard for evaluating tissue viability but may require more time to obtain and interpret. We sought to identify determinants of arrival-to-puncture time for patients who underwent MRI-based EVT selection in a real-world setting.

Methods Patients were identified from a prospectively maintained database from 2011–2019 that included demographics, presentations, treatments, and outcomes. Process times were obtained from the medical charts. MRI times were obtained from time stamps on the first sequence. Linear and logistic regressions were used to infer explanatory variables of arrival-to-puncture times and effects of arrival-to-puncture time on functional outcomes.

Results In this study 192 patients (median age 70 years, 57% women, 12% non-white) underwent MRI-based EVT selection. 66% also underwent computed tomography (CT) at the hub before EVT. General anesthesia was used for 33%. Among the entire cohort, the median arrival-to-puncture was 102 min; however, among those without CT it was 77 min. Longer arrival-to-puncture times independently reduced the odds of 90-day good outcome (ΔmRS $\leq$ 2 from pre-stroke, aOR = 0.990, 95%CI = 0.981–0.999, p = 0.040) when controlling for age, NIHSS, and good reperfusion (TICI 2b–3). Independent determinants of longer arrival-to-puncture were CT plus MRI (β = 0.205, p = 0.003), non-white race/ethnicity (β = 0.162, p = 0.012), coronary disease (β = 0.205, p = 0.001), and general anesthesia (β = 0.364, p < 0.0001).

Conclusion Minimizing arrival-to-puncture time is important for outcomes. Real-world challenges exist in an MRI-based EVT selection protocol; avoiding double imaging is key to saving time. Racial/ethnic disparities require further study. Understanding variables associated with delay will inform protocol changes.

Keywords Ischemic stroke · Systems of care · Process improvement · Magnetic resonance imaging

The authors Robert W. Regenhardt and Neal M. Nolan contributed equally to the manuscript.

Availability of Data and Material The data that support the findings of this study are available from the corresponding author upon reasonable request and pending approval of our local institutional review board.

Code Availability None relevant.

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Introduction

Given the dramatic efficacy of endovascular thrombectomy (EVT), optimizing systems of its delivery is crucial to maximize the number of eligible large vessel occlusion (LVO) stroke patients who can access therapy [1, 2]. While outcomes after stroke vary, imaging criteria can help select patients who stand to benefit [3, 4]. Noncontrast computed tomography (CT) and CT angiography (CTA) typically suffice for patients who present within 6 h from onset of ictus, but advanced imaging is recommended for extended window patients or those with unknown onset [5]. Estimating the benefit of EVT above medical therapy for LVO involves assessing irreversibly infarcted core versus ischemic penumbra, or the region of threatened brain tissue that is salvageable but will ultimately infarct without reperfusion [6]. Several imaging approaches have been established to quantify the volume of infarcted core versus penumbra. Although there is no definitive recommendation on the choice of imaging modality for EVT selection, magnetic resonance (MRI) diffusion-weighted imaging (DWI) is the gold standard for infarct core assessment, defining it with more precision than CT-based approaches [5].

However, time delay is a key variable in penumbral sustenance, and increased delay is associated with a reduced likelihood of EVT [7]. Recent guidelines recommend arrival-to-puncture (ATP) times for EVT of less than 90 min [4]. Indeed, this is the primary reason to consider CT-based EVT selection in some centers since it can be more readily available in a timely manner. Several years before EVT was established as standard of care, we reported median ATP times of 143 min, which improved to 107 min after a parallel workflow protocol was implemented at our institution in 2011 [8]. ATP times utilizing MRI for EVT selection in the context of a randomized trial demonstrated median times of 68 min [9]. Understanding delay associated with MRI has several implications for acute stroke management. Therefore, we sought to identify determinants of ATP time for LVO stroke patients who underwent MRI-based selection for EVT from 2011–2019 in a contemporary real-world setting to understand and improve time metrics.

Methods

This study was approved by our local institutional review board. Informed consent was waived based on minimal patient risk. The data that support the findings of this study are available from the corresponding author upon reasonable request and pending approval of our local institutional review board.

We retrospectively identified consecutive acute anterior circulation LVO stroke patients who underwent MRI-based selection for EVT from a prospectively maintained database at a single referral center from January 2011 to September 2019 [10]. For anterior circulation LVO, our center established local guidelines for EVT in January 2011, ensuring all included patients would have undergone emergent imaging. We purposely included a wide breadth of patients over this time frame to identify determinants of MRI-related delay. We control for a protocol change in 2015 related to changes in EVT evidence by including this in our multivariable models. While the decision to obtain MRI was at the discretion of treating clinicians, our local guidelines after the 2015 change allowed EVT selection by CT/A for patients presenting within the 6 h window and emphasized MRI/A for those presenting after 6 h [11]. MRI was typically limited to DWI, FLAIR, and SWI. MRA was obtained if vessel imaging was not already available. Furthermore, before the change most patients with a focal neurologic deficit were first screened with CT to rule out hemorrhage, resulting in some that were double-imaged with both CT and MRI.

Our database includes demographic information, past medical history, clinical presentations, treatments, and outcomes for consecutive patients treated with EVT. Presenting NIH Stroke Scale (NIHSS) score was determined as described [4, 12] with higher numbers reflecting increased clinical stroke severity. Alteplase treatment decisions were guideline-based at the discretion of a vascular neurologist [4]. EVT treatment decisions were based on protocolled selection criteria, including NIHSS, last known well (LKW), and infarct volume, with consensus between a vascular neurologist and neurointerventionalist [13]. LVO was defined as occlusion of the internal carotid artery terminus, first segment of the middle cerebral artery, or proximal second segment of the middle cerebral artery. Cervical internal carotid artery disease was defined as severe stenosis (>70%) or occlusion related to atherosclerosis or dissection [14].

Thrombolysis in cerebral infarction (TICI) scores were determined by a neurointerventionalist using the modified scale: 2a partial filling <50%, 2b partial filling ≥50%, 3 complete perfusion [15]. Adequate reperfusion was considered TICI 2b–3 [16]. Intracerebral hemorrhage was defined as any symptomatic or asymptomatic PH1 or PH2 by ECASS criteria during the hospitalization [17]. The 90-day modified Rankin Scale (mRS) score was obtained by telephone call and available for 87% of patients [18]. Good outcome was defined as 90-day changed ΔmRS ≤ 2 from pre-stroke, which allows the inclusion of patients with pre-stroke disability [19, 20].

Patients who underwent MRI during EVT treatment selection were identified retrospectively. While infarct volumes for acute treatment decisions were calculated using the ABC/2 method, more precise infarct volumes for research purposes were determined retrospectively [21]. Infarcts were traced from pre-EVT MRIs by a vascular neurologist using Slicer version 4.8.1 (Brigham and Women's Hospital), blinded to clinical data. RegLSM (University of Calgary) was used to register these to MNI-152 space, and FSL (FMRIB Analysis Group) was used to calculate volumes [22]. Some patients underwent CT ± CTA imaging at an outside hospital prior to transfer [23, 24]. Arrival time, or consult time for in-house stroke, was obtained from the medical chart. CT time was obtained from the imaging time stamp. MRI time was obtained from the time stamp on the first sequence obtained. Arterial puncture time was obtained from the medical chart.

Median values with interquartile range (IQR) were reported for continuous variables. Percent and count were reported for categorical variables. Logistic regression analyses were performed to assess associations with dichotomous outcomes, and linear regression analyses were performed to assess for associations with continuous outcomes. Variables were determined a priori and those with prespecified significance of $p < 0.10$ in univariable analysis were subsequently included in multivariable models; all included variables are presented in the results. Two-tailed P values <0.05 were interpreted as statistically significant. Analyses were performed with SPSS version 23.0 (IBM Corp, Armonk, NY, USA).

Results

A total of 381 consecutive patients underwent EVT for anterior circulation LVO during the study period, and 192 underwent hyperacute MRI at the hub hospital during EVT treatment selection. Of these 192, the median age was 70 years (IQR 57–80 years) with 9% having baseline mRS ≥ 2. Women comprised 57%, and non-white race/ethnic groups comprised 12%. Risk factors included atrial fibrillation (35%), diabetes (23%), hypertension (72%), coronary disease (18%), and prior stroke or transient ischemic attack (15%) (Table 1).

A slight majority (56%) were spoke transfers from within the hub-and-spoke Telestroke network. 66% underwent CT imaging in addition to MRI at the hub before EVT. The median NIHSS was 16, and median MRI-calculated pre-EVT infarct volume was 22cc. Intravenous alteplase was administered to 54% of patients; 22% received it at the hub before EVT. The median LKW-to-puncture time was 5.5 h, and 33% were treated with the patient under general anesthesia. Adequate reperfusion was achieved in 71%, while intracerebral hemorrhage was observed in 8%. 47% achieved a good 90-day outcome (Table 1).

Regarding time metrics among the entire cohort of patients undergoing MRI-based EVT selection from 2011–2019, the median ATP time was 102 min, with a median arrival-to-MRI time of 42 min and a median MRI-to-puncture time of 52 min. Interestingly, these time metrics among several subgroups were substantially faster. Among those undergoing conscious sedation (N = 129), the median ATP time was 89 min, with an arrival-to-MRI of 39 min and an MRI-to-puncture of 46 min. Furthermore, among those who did not undergo CT in addition to MRI (i.e., not double-imaged), the median ATP time was 77 min, with

Table 1 Demographics, medical history, clinical presentations, treatments, and outcomes for patients undergoing acute MRI during EVT treatment selection

	Count/median	Percent/IQR
Age, years, median (IQR)	70	(57–80)
Female	110	57%
Black	5	3%
Hispanic	8	5%
Asian	6	3%
White	156	88%
Baseline mRS ≥ 2	17	9%
Atrial fibrillation	68	35%
Diabetes	44	23%
Hypertension	138	72%
Coronary disease	35	18%
Stroke or TIA history	28	15%
Smoking	37	19%
Spoke transfer	108	56%
In-house stroke	18	9%
Nighttime (1800-0600h)	89	46%
NIHSS, median (IQR)	16	(13–20)
Hub CT before MRI	126	66%
Infarct volume, mL, median (IQR)	22	(12–43)
Cervical ICA atherosclerosis	33	17%
Cervical ICA dissection	9	5%
ICA terminus occlusion	34	18%
M1 occlusion	141	73%
M2 occlusion	17	9%
Left sided occlusion	99	52%
IV alteplase, anywhere	104	54%
IV alteplase, hub	42	22%
LKW-to-alteplase, h, median (IQR)	2.02	(1.50–2.76)
LKW-to-puncture, h, median (IQR)	5.53	(4.12–7.33)
General anesthesia	63	33%
TICI 2b–3	137	71%
ICH	15	8%
90-day ΔmRS ≤ 2, N = 173	82	47%

IQR interquartile range, *mRS* modified Rankin Scale, *TIA* transient ischemic attack, *NIHSS* National Institutes of Health stroke scale, *CT* computed tomography, *MRI* magnetic resonance imaging, *mL* milliliters, *ICA* internal carotid artery, *M1* first middle cerebral artery segment, *M2* middle cerebral artery segment, *IV* intravenous, *LKW* last known well, *h* hour, *TICI* thrombolysis in cerebral infarction, *ICH* intracerebral hemorrhage

Table 2 Time metrics at the hub for patients undergoing acute MRI during EVT treatment selection

All Cases 2011–2019, Count (%)	*192*	*100%*
Hub arrival-to-puncture, min, median (IQR)	102	(77–130)
Hub arrival-to-MRI, min, median (IQR)	42	(31–57)
Hub MRI-to-puncture, min, median (IQR)	52	(38–76)
No hub CT before MRI, count (%)	*66*	*34%*
Hub arrival-to-puncture, min, median (IQR)	77	(57–112)
Hub arrival-to-MRI, min, median (IQR)	25	(20–39)
Hub MRI-to-puncture, min, median (IQR)	46	(33–70)
Conscious sedation, count (%)	*129*	*67%*
Hub arrival-to-puncture, min, median (IQR)	89	(67–116)
Hub arrival-to-MRI, min, median (IQR)	39	(25–54)
Hub MRI-to-puncture, min, median (IQR)	46	(33–63)

IQR interquartile range, *MRI* magnetic resonance imaging, *CT* computed tomography

an arrival-to-MRI of 25 min and an MRI-to-puncture of 46 min (Table 2).

Importantly, ATP time independently reduced the odds of 90-day good outcome when analyzing the entire cohort (aOR = 0.990, 95%CI = 0.981–0.999, $p = 0.040$), even when controlling for the most common determinants of long term outcomes including age (aOR = 0.976, 95%CI = 0.953–0.999, $p = 0.047$), NIHSS (aOR = 0.880, 95%CI = 0.809–0.957, $p = 0.003$), and TICI 2b–3 reperfusion (aOR = 15.50, 95% CI = 4.775–34.78, $p < 0.0001$) (Table 3).

To understand determinants of ATP time, several a priori-determined variables were examined. In univariable analyses, longer ATP time was associated with pre-2015 protocol patients, non-white race/ethnic groups, coronary disease, not being a spoke transfer, in-house stroke, receiving alteplase at the hub, general anesthesia, and undergoing CT in addition to MRI at the hub. These were included in a multivariable model, which showed independent determinants were non-white race/ethnic groups ($\beta = 0.162$, $p = 0.012$), coronary disease ($\beta = 0.205$, $p = 0.001$), general anesthesia ($\beta = 0.364$, $p < 0.0001$), and undergoing CT in addition to MRI at the hub ($\beta = 0.205$, $p = 0.003$). Furthermore, a sensitivity analysis was performed of only patients undergoing conscious sedation; this revealed similar findings (Table 4).

Discussion

In this cohort of 192 patients who underwent MRI-based EVT selection from 2011–2019, longer ATP time independently reduced the odds of good 90-day outcome. Among patients who did not undergo CT in addition to MRI at the hub (i.e., not double-imaged), the median ATP time was 77 min. Independent determinants of longer ATP time were double-imaging with CT in addition to MRI, non-white race/ethnicity, coronary disease, and general anesthesia.

Noncontrast CT and CTA suffice to select patients for EVT who present within 6 h from stroke onset, but advanced imaging is often required for extended window patients or those with unknown onset [5]. MRI or CT perfusion (CTP) are commonly used in this setting to evaluate infarct core size. There has been some prior work quantifying delays associated with MRI. Even in the hyperacute setting, times have varied widely based on the center. Indeed, we observed differing times within our own center based on several factors, including year in relation to triage protocol changes, anesthesia type, and double imaging with both CT and MRI. In the context of the randomized GOLIATH trial, the median ATP time utilizing MRI for EVT selection was an impressive 68 min; most of this time was spent from MRI-to-puncture with median 54 min for conscious sedation and 61 min for general anesthesia [9]; however, other reports have described MRI-related delays of 30 min [5] and up to 90 min at one Korean center [25].

There is ongoing debate about the risks and benefits of utilizing MRI for EVT triage. MRI is regarded as the gold standard for infarct core assessment, with higher sensitivity and specificity [5]. Other imaging modalities, most notably CTP, can overestimate core size and exclude patients who may stand to benefit from treatment [26]. Furthermore, the utilization of MRI to assess precise infarct volume and topography can significantly improve our understanding of LVO stroke and enhance patient outcomes through research endeavors [10, 16]. Despite these advantages, MRI utilization has not always translated to improved patient outcomes in clinical practice. In one series of 72 EVT-treated patients presenting within 8 h of LKW, there was no significant difference in 90-day functional outcomes when MRI was uti-

Table 3 Arrival-to-puncture time independently reduces the odds of 90-day ΔmRS ≤ 2 when controlling for the most common determinants of long-term outcomes, age, NIHSS, TICI 2b–3

	Univariable			Multivariable		
	OR	95% CI	*P*	aOR	95% CI	*P*
Arrival-to-puncture, min	0.991	(0.984–0.999)	0.032	0.990	(0.981–0.999)	0.040
Age	0.974	(0.955–0.995)	0.013	0.976	(0.953–0.999)	0.047
NIHSS	0.888	(0.828–0.953)	0.001	0.880	(0.809–0.957)	0.003
TICI 2b–3	9.598	(3.993–23.07)	<0.0001	15.50	(4.775–34.78)	<0.0001

OR odds ratio, *CI* confidence interval, *Min* minutes, *NIHSS* NIH stroke scale, *TICI* thrombolysis in cerebral infarction

Table 4 Determinants of arrival-to-puncture time among patients undergoing acute MRI during EVT treatment selection

	Univariable		Multivariable		Multivariable, CS Only	
	Beta	*p*	Beta	*p*	Beta	*p*
After 2015 protocol	–0.267	< 0.0001	–0.089	0.202	–0.137	0.103
Age, years	0.103	0.160	–	–	–	–
Female	0.068	0.354	–	–	–	–
Non-white race/ethnicity	0.152	0.044	0.162	0.012	0.213	0.012
Baseline mRS ≥ 2	0.032	0.664	–	–	–	–
Atrial fibrillation	0.112	0.126	–	–	–	–
Diabetes	0.103	0.157	–	–	–	–
Hypertension	0.055	0.452	–	–	–	–
Coronary disease	0.248	0.001	0.205	0.001	0.179	0.030
Stroke or TIA history	0.054	0.463	–	–	–	–
Smoking	–0.086	0.242	–	–	–	–
Spoke transfer	–0.296	< 0.0001	–0.065	0.431	–0.212	0.053
In house stroke	0.164	0.024	0.101	0.119	0.063	0.450
Nighttime (1800-0600 Hours)	–0.043	0.553	–	–	–	–
NIHSS	–0.004	0.954	–	–	–	–
IV Alteplase, anywhere	0.021	0.771	–	–	–	–
IV Alteplase, hub	0.178	0.014	0.050	0.525	–0.070	0.487
LKW-to-puncture, Hr	–0.043	0.557	–	–	–	–
General anesthesia	0.454	< 0.0001	0.364	< 0.0001	–	–
Hub CT before MRI	0.345	< 0.0001	0.205	0.003	0.273	0.003

Non-white race/ethnicity, coronary disease, general anesthesia, and obtaining a hub CT before hub MRI (i.e., double imaging) were independently associated with longer arrival-to-puncture times. Final column shows sensitivity analysis of only patients undergoing conscious sedation.
CS conscious sedation, *mRS* modified Rankin Scale, *TIA* transient ischemic attack, *NIHSS* National Institutes of Health stroke scale, *IV* intravenous, *LKW* last known well, *CT* computed tomography, *MRI* magnetic resonance imaging

lized in addition to CTA [5]. Another series also found no difference in favorable functional outcomes for patients who underwent MRA vs. CTA within 4.5 h from LKW [25]. One study showed that patients who underwent MRI-based triage were actually less likely to achieve functional independence than those selected using CTP-based triage, but there may have been selection bias based on patient characteristics (e.g., time since LKW) [27]. While MRI can be expediently used [9, 28], there are real-world delays that may account for worse outcomes in some cases. Our present data support this hypothesis.

Understanding these delays is key to minimizing them if MRI is to be used. Our present analysis identified four independent determinants of longer ATP time: double imaging with CT in addition to MRI, non-white race/ethnicity, coronary disease, and general anesthesia. Whether patients present in the early or late window, double imaging is likely to add delay without benefit [5, 25, 27, 29]. Ours and others' data support that for patients presenting in the extended window, it is reasonable to forego CT/CTA and proceed directly to advanced imaging with MRI/MRA in settings where these resources are available. Our own protocol changed in 2015 as data evolved to emphasize prioritizing MRI/MRA for patients presenting after 6 h and CT/CTA for those presenting before. Before that time, we screened all patients with CT first to rule out hemorrhage resulting in patients who were double imaged. Another common scenario prompting imaging triage protocol consideration occurs when patients who first present to spoke centers are then transferred to the EVT-capable hub. When CT/CTA is obtained at the spoke, there may be no need for additional imaging if the patient arrives to the hub within the early window. MRI or CTP may be reserved for those patients arriving in the extended window with the goal to minimize repeat imaging when possible.

Other determinants of longer ATP times in our cohort were non-white race/ethnicity, coronary artery disease, and general anesthesia. With respect to race, our findings align with several previous descriptions of disparities in EVT access and utilization by race [30–32]. This disparity in our series, comprised of 12% non-white patients, is surprising given the protocolized nature of our triage. Among other EVT series, several dimensions of broader health inequality have been suggested, including system factors, such as delayed or limited access to care, but also patient-provider relationship factors, including disparate levels of inclusion within healthcare networks and delays or inaccuracies in communication across language or cultural barriers [30].

These all represent targets for system improvements to minimize delay, in addition to implicit bias training for healthcare providers. Others have found delays associated with cardiac disease history, among other comorbidities like diabetes and advanced age [33]. The reasons for delay associated with coronary disease are speculative but could include the prevalence of stents or cardioelectronic implants (e.g., pacemakers) among CAD patients, which have been associated with MRI compatibility and safety clearance delays [34]. Options to minimize delay include implementing protocols for rapid device clearance, ideally before hub arrival in the case of spoke transfers or considering CT-based triage for these patients [35]. Data regarding delays related to the use of general anesthesia are mixed [36, 37]. Delay may relate to additional time for intubation, more complicated transport, and imaging acquisition challenges with these patients, especially if they are intubated in the emergency department at the time of presentation [37].

Importantly, the use of MRI for acute stroke is not restricted to EVT selection alone. Administration of intravenous thrombolysis to patients waking up with stroke symptoms can be guided by MRI. MRI allows greater treatment access for the thrombolytic population than CT-based selection does, but this approach faces similar system process challenges as the EVT population [38]. A better understanding of the causes of MRI delays may positively impact access to thrombolysis for stroke patients, too.

Limitations of our analyses include those related to its single-site retrospective design. There is risk of selection bias given our inclusion of only patients who underwent pre-EVT MRI (50%); however, all pre-EVT MRI were obtained in the acute setting for EVT triage so there should be little impact on interpretation of time metric analyses. Furthermore, our site is a tertiary care center in a mid-sized city with a largely white population, which may limit generalizability. Further study of non-white racial/ethnic groups is warranted. While we have controlled for changes in local imaging triage protocols in our multivariable model, we cannot fully exclude that they may have influenced the results over this 9-year period. Importantly, the criteria for patient selection to determine patient eligibility for EVT also evolved over time.

In conclusion, minimizing ATP time may be important for 90-day outcomes. Despite the manifold benefits of MRI-based stroke treatment selection, there exist real-world challenges; avoidance of double imaging is essential to accelerate treatment access. Racial/ethnic disparities were identified that require further study. A deeper understanding of the variables associated with delay in MRI-based triage protocols is a key step to inform protocol changes and improve outcomes after stroke.

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Declarations

Conflict of interest R.W. Regenhardt, N.M. Nolan, J.A. Rosenthal, J.A. McIntyre, M. Bretzner, A.K. Bonkhoff, S.B. Snider,A.S. Das, N.M. Alotaibi, J.E. Vranic, A.A. Dmytriw, C.J. Stapleton, A.B. Patel, N.S. Rost and T.M. Leslie-Mazwi declare that they have no competing interests.

Ethical standards This study was approved by the local institutional review board. Consent to participate: informed consent was waived based on minimal patient risk. Consent for publication: informed consent was waived based on minimal patient risk.

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