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Stroke Imaging Selection Modality and Endovascular Therapy Outcomes in the Early and Extended Time Windows

Raul G. Nogueira, MD , Diogo C. Haussen, MD, David Liebeskind, MD , Tudor G. Jovin, MD, Rishi Gupta, MD, Ashutov Jadhav, MD, PhD, Ron F. Budzik, MD, Blaise Baxter, MD, Antonin Krajina, MD, Alain Bonafe, MD, Ali Malek, MD, Ana Paula Narata, MD, Ryan Shields, MsC, Yanchang Zhang, PhD, Patricia Morgan, BSN, RN, Bruno Bartolini, MD, Joey English, MD, PhD, Michael R. Frankel, MD, Erol Veznedaroglu, MD, and for the Trevo Registry and DAWN Trial Investigators

Advanced imaging has been increasingly used for patient selection in endovascular stroke therapy. The impact of imaging selection modality on endovascular stroke therapy clinical outcomes in extended time window remains to be defined. We aimed to study this relationship and compare it to that noted in early-treated patients.

Patients from a prospective multicentric registry (n=2008) with occlusions involving the intracranial internal carotid or the M1- or M2-segments of the middle cerebral arteries, premorbid modified Rankin Scale score 0 to 2 and time to treatment 0 to 24 hours were categorized according to treatment times within the early (0–6 hour) or extended (6–24 hour) window as well as imaging modality with noncontrast computed tomography (NCCT)±CT angiography (CTA) or NCCT±CTA and CT perfusion (CTP). The association between imaging modality and 90-day modified Rankin Scale, analyzed in ordinal (modified Rankin Scale shift) and dichotomized (functional independence, modified Rankin Scale score 0–2) manner, was evaluated and compared within and across the extended and early windows.

In the early window, 332 patients were selected with NCCT±CTA alone while 373 also underwent CTP. After adjusting for identifiable confounders, there were no significant differences in terms of 90-day functional disability (ordinal shift: adjusted odd ratio [aOR], 0.936 [95% CI, 0.709–1.238], *P*=0.644) or independence (aOR, 1.178 [95% CI, 0.833–1.666], *P*=0.355) across the CTP and NCCT±CTA groups. In the extended window, 67 patients were selected with NCCT±CTA alone while 180 also underwent CTP. No significant differences in 90-day functional disability (aOR, 0.983 [95% CI, 0.81–1.662], *P*=0.949) or independence (aOR, 0.640 [95% CI, 0.318–1.289], *P*=0.212) were seen across the CTP and NCCT±CTA groups. There was no interaction between the treatment time window (0–6 versus 6–24 hours) and CT selection modality (CTP versus NCCT±CTA) in terms of functional disability at 90 days (*P*=0.45).

CTP acquisition was not associated with better outcomes in patients treated in the early or extended time windows. While confirmatory data is needed, our data suggests that extended window endovascular stroke therapy may remain beneficial even in the absence of advanced imaging.

Key Words: angiography ▪ internal carotid artery ▪ magnetic resonance imaging ▪ middle cerebral artery ▪ patient selection

Nonstandard Abbreviations and Acronyms

CTA	CT angiography
CTP	CT perfusion
MRI	magnetic resonance imaging
mRS	modified Rankin Scale
MT	mechanical thrombectomy
NCCT	noncontrast computed tomography
NIHSS	National Institutes of Health Stroke Scale
tPA	tissue-type plasminogen activator

The strong benefit of endovascular treatment of large vessel occlusion strokes within the first 6 hours from symptoms onset has now been confirmed in 7 randomized clinical trials.[1–8] In addition, the DAWN (DWI or CTP Assessment With Clinical Mismatch in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention With Trevo) and DEFUSE 3 (Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke) trials have demonstrated a robust benefit of mechanical thrombectomy (MT) in the 6- to 24-hour window.[9,10] However, the DAWN and DEFUSE 3 trials required the use of computed tomography perfusion (CTP) or brain magnetic resonance imaging (MRI) in all patients. Consequently, the current level-1a evidence for MT in the extended window supports the stringent usage of advanced imaging.[11] There is a paucity of prospective data comparing the outcomes of endovascular treatment in patients selected on the basis of noncontrast CT (NCCT)±CT angiography (CTA) alone versus those also undergoing CTP, especially in the extended window. We sought to evaluate the impact of CT imaging selection modality on the clinical outcomes of MT in a large prospective cohort of early and late presenting patients.

METHODS

Anonymized data from the study are available upon reasonable request to the corresponding author.

Trevo Retriever Registry

The Trevo Retriever Registry (URL: https://www.clinicaltrials.gov; Unique identifier: NCT02040259) was a multicenter, prospective, international, open-label, registry of patients undergoing endovascular treatment for large vessel occlusion stroke with the Trevo stent-retriever (Stryker, Fremont, CA) as first-line therapy. A total of 2008 patients were recruited at 76 sites across 12 countries between November 11, 2013 and May 1, 2017. Pretreatment imaging and other entry criteria were based on local institutional protocols. The protocol was amended on March 26, 2015 to incorporate an imaging core lab for central adjudication in 1599 of the 2008 patients. The 90-day

evaluation of the modified Rankin Scale (mRS) was obtained in person or by telephone by a certified assessor at each site. All patients in whom the Trevo Retriever was deployed were included in the intention-to treat analysis. Specifically, there were no inclusion/exclusion criteria other than the utilization of the Trevo device as first-line therapy and the decisions regarding imaging and patient selection protocols were at the discretion of the treatment teams. The study was sponsored by Stryker Neurovascular. A steering committee including academic investigators and representatives of the sponsor designed the study and managed its execution. Other details about the Trevo Registry methodology have been published elsewhere.[12]

Patient Cohort, Baseline and Outcome Variables, and Study Analysis

The study cohort was comprised by all consecutive Trevo Registry patients with occlusions involving the intracranial internal carotid artery or the M1- or M2-segments of the middle cerebral artery, premorbid mRS score of 0 to 2, and time-last-seen-well to arterial puncture 0 to 24 hours. A subgroup of these patients was defined based on the key clinical and demographic features of the DAWN trial (DAWN-like cohort: age ≥18 years, baseline National Institutes of Health Stroke Scale [NIHSS] ≥10, internal carotid artery or M1 occlusion, and premorbid mRS score 0–1) to derive a more homogenous patient population and allow for a closer comparison with the DAWN randomized clinical trial data. Time to treatment was defined as time-last-seen-well to arterial puncture. The study cohorts were categorized according to the pretreatment imaging selection method as (1) NCCT only, (2) NCCT and CTA, (3) NCCT (±CTA) and CTP, (4) brain MRI (±MR angiography), (5) direct to the angiography suite (transfers with the last available image performed beyond 3 hours from the time of arterial puncture), and (6) undefined (if either core lab adjudication or the imaging acquisition times were missing). Patients were also classified according to time to treatment in the early (0–6 hours) versus extended (6–24 hours) window.

Outcome variables encompassed the rates of good outcomes (90-day mRS score 0–2), successful reperfusion defined as a grade 2b or 3 (>50% of the affected territory) on the modified Treatment in Cerebral Infarction scale,[13] symptomatic intracranial hemorrhage defined as per the ECASS 3 Trial (European Cooperative Acute Stroke Study) definition (eg, any apparently extravascular blood in the brain or within the cranium associated with deterioration in NIHSS score of ≥4 points, or that leads to death and is identified as the predominant cause of the neurological deterioration),[14] and 90-day mortality. Univariable analysis was performed to compare the baseline and outcome variables for patients selected based solely on NCCT±CTA versus those selected with NCCT±CTA and CTP in both the early and extended time windows. Adjusted ordinal and binary logistic regression analyses were conducted to assess the effect of CT imaging selection modality within and across the early and extended time windows by the overall mRS distribution (ordinal mRS shift) and by a dichotomized outcome measure of mRS score of 0 to 2 (functional independence) at 90 days.

Statistical Analysis

Patient baseline characteristics and procedural data were analyzed and presented using frequency, mean, SD, median, and interquartile range. In comparing 2 groups, the *t* test or Wilcoxon sum test was applied for continuous variables and Fisher exact test for dichotomous variables. Clopper–Pearson CIs were constructed for inferences of key outcomes. Univariate and multivariate logistic regression was conducted to identify predictors of good outcome. Stepwise selection using score χ^2 statistics was performed using the full Trevo Registry dataset. *P* value for enter is 0.05, and *P* value for stay is 0.05. In patients with missing 90-day mRS, last observation

carried forward was used. All analyses were performed with SAS software (version 9.4; SAS Institute Inc, Cary, NC).

RESULTS

A total of 1826 out of the 2008 Trevo Registry patients had intracranial internal carotid artery, M1, or M2 occlusions, with 1673 of them having a premorbid mRS score of 0 to 2. Out of these, 1603 patients underwent treatment within 24 hours from time-last-seen-well (1173 in the 0–6-hour and 430 in the 6–24-hour window) and constituted the primary study cohort (Figure 1). A total of 109 (6.8%) patients underwent imaging selection on the basis of a non-contrast CT alone while 290 (18.1%) got NCCT and CTA and 553 (34.5%) also underwent CTP. Brain MRI was performed in only 13 (0.9%) patients including MR angiography in 9 (0.6%) of them. A total of 244 (15.2%) patients were direct to the angiography suite transfers who had their last image performed beyond 3 hours from arterial puncture. In 394 (24.6%) patients, either core lab adjudication or the imaging acquisition times were missing (eg, undefined imaging modality).

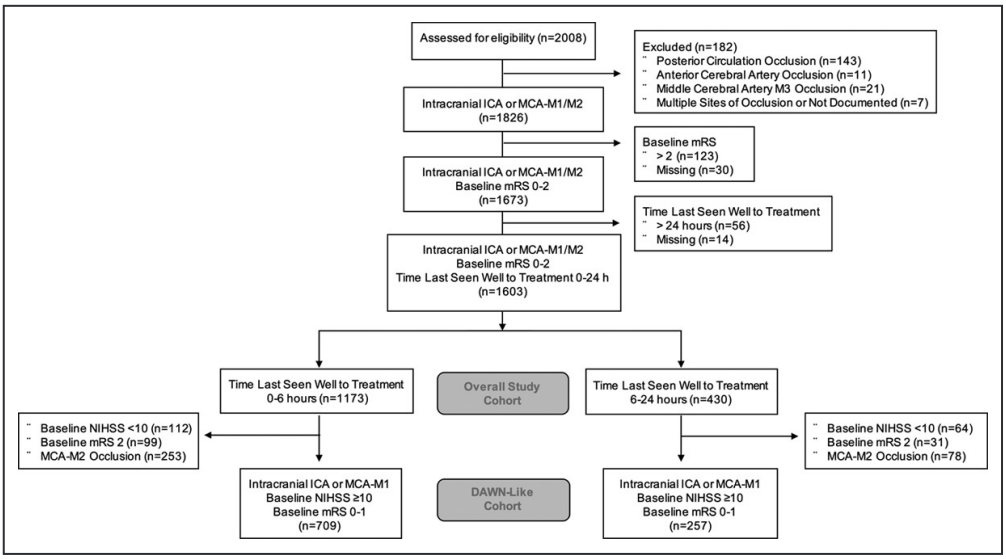

Figure 1. Study flow diagram. ICA indicates internal carotid artery; MCA, middle cerebral artery; mRS, modified Rankin Scale; and NIHSS, National Institutes of Health Stroke Scale.

In the early window, a total of 332 patients were selected with NCCT±CTA alone while 373 also underwent CTP. NCCT±CTA alone patients were slightly older (70.3±13.6 versus 68.5±14.5, *P*=0.093) and had shorter time-last-seen-well to puncture (median, 3.1 [interquartile range, 2.4–4.1] versus 3.4 [2.5–4.5] hours, *P*=0.044). There were no significant differences in the remaining baseline or procedural characteristics across the 2 groups (baseline NIHSS: 16 [12–20] versus 15 [11–20]; Alberta Stroke Program Early CT Score [ASPECTS]: 8 [7–9] versus 8 [7–9]; IV tPA (tissue-type plasminogen activator) use: 69.9% versus 67.6%). Similarly, no significant differences in the rates of good outcomes (55.9% versus 60.6%, *P*=0.202), mortality (13.0% versus 10.5%, *P*=0.302), successful reperfusion (92.8% versus 91.7%, *P*=0.593), or symptomatic intracranial hemorrhage (1.8% versus 2.4%, *P*=0.613) were detected across NCCT±CTA alone versus CTP patients (Table 1). After adjusting for identifiable confounders including age, baseline NIHSS, baseline mRS, ASPECTS, diabetes, time to treatment, there were no significant differences in terms of 90-day functional disability (ordinal mRS shift: adjusted odd ratio [aOR], 0.936 [95% CI, 0.709–1.238], *P*=0.644) or functional independence (mRS score of 0–2: aOR, 1.178 [95% CI, 0.833–1.666], *P*=0.355) across the CTP and NCCT±CTA groups, respectively (Table 2 and Figure 2).

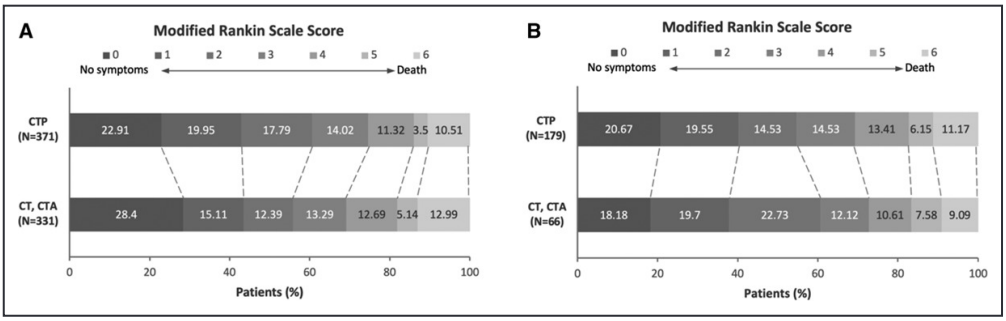

Figure 2. Ninety-d modified Rankin Scale (mRS) distribution in patients with internal carotid artery (ICA), middle cerebral artery (MCA)-M1, MCA-M2 occlusions and PreMorbid mRS score 0–2 in the Early versus Extended Time Windows according to imaging selection modality. A, 0–6-h; (**B**) 6–24-h. Computed tomography perfusion (CTP) vs noncontrast computed tomography (NCCT)±computed tomography angiography (CTA) adjusted odds ratio* for 1-point shift in functional disability at 90 d: 0.936 (95% CI, 0.709–1.238; *P*=0.644) in the 0–6-h and 0.983 (95% CI, 0.581–1.662, *P*=0.949) in the 6–24-h window. No Interaction between treatment time window (0–6 versus 6–24 h) and CT selection modality (CT/CTA versus CTP) in terms of functional disability at 90 d (*P*=0.448). CTP vs NCCT±CTA adjusted odds ratio* for functional independence (mRS score 0–2) at 90 d: 1.178 (95% CI, 0.833–1.666, *P*=0.355) in the 0–6 h and 0.640 (95% CI, 0.318–1.289, *P*=0.212) in the 6–24-h window. *Co-variates: age, baseline National Institutes of Health Stroke Scale (NIHSS), baseline mRS, Alberta Stroke Program Early CT Score (ASPECTS), diabetes, time-last-seen-well (TLSW) to treatment. Exact 90-d mRS score missing in 2 patients in the CTP-early window, one in the CT/CTA-early window, one in the CTP-late-window, and one in the CT/CTA-late-window subgroups.

In the extended window, a total of 67 patients were selected with NCCT±CTA alone while 180 also underwent CTP. NCC±CTA-selected patients were less often females (41.8% versus 58.9%, *P*=0.016) and had a trend towards lower rates of conscious sedation (38.8% versus 52.8%, *P*=0.084). There were no significant differences in the remaining baseline or procedural characteristics across the 2 groups (age, 65.8±15.1 versus 66.7±14.5; baseline NIHSS, 16 [9–20] versus 15 [10–19]; ASPECTS, 8 [7–9] versus 8 [7–9]; and time to treatment, 9.3 [6.8–14.5] versus 10.2 [7.5–14]). Similar to the patients in the early window, there were no significant differences in the rates of 90-day functional independence (60.6% versus 54.7%, *P*=0.412), 90-day mortality (9.0% versus 11.1%, *P*=0.624), successful reperfusion (95.5% versus 93.9%, *P*=0.622), or symptomatic intracranial hemorrhage (1.5% versus 0.6%, *P*=0.470; Table 1). After adjusting for the aforementioned co-variates, there were no significant differences in terms of 90-day functional disability (ordinal mRS shift: aOR, 0.983 [95% CI, 0.581–1.662], *P*=0.949) or functional independence (mRS score of 0–2: aOR, 0.640 [95% CI, 0.318–1.289], *P*=0.212) across the CTP and NCCT±CTA groups, respectively (Table 2 and Figure 2).

Table 1. Baseline Characteristics and Outcomes of Trevo Registry Patients With ICA, MCA-M1, MCA-M2 Occlusions, and PreMorbid mRS Score of 0–2 in the 0–6-Hour and 6–24-Hour Window According to CT Imaging Selection Modality (Univariable Analysis) (Table view)

	0–6-h window			6–24-h window		
	NCCT±CTA (N=332)	CTP (N=373)	*P* value	NCCT±CTA (N=67)	CTP (N=180)	*P* value
Age, mean (SD)	70.3±13.6	68.5±14.5	0.093	65.8±15.1	66.7±14.5	0.656
Female, %	51.5%	50.7%	0.825	41.8%	58.9%	0.016*
Baseline NIHSS, median (IQR)	16 (12–20)	15 (11–20)	0.270	16 (9–20)	15 (10–19)	0.616
Site of occlusion, %			0.540			0.465
ICA	21.1%	20.4%		19.4%	21.1%	
M1	59.0%	56.3%		67.2%	59.4%	

	0–6-h window			6–24-h window		
	NCCT±CTA (N=332)	CTP (N=373)	*P* value	NCCT±CTA (N=67)	CTP (N=180)	*P* value
M2	19.9%	23.3%		13.4%	19.4%	
Baseline ASPECTS, median (IQR)	8 (7–9)	8 (7–9)	0.788	8 (7–9)	8 (7–9)	0.438
TLSW to puncture, h, median (IQR)	3.1 (2.4–4.1)	3.4 (2.5–4.5)	0.044*	9.3 (6.8–14.5)	10.2 (7.5–14)	0.113
IV tPA	69.9%	67.6%†	0.512	23.9%	26.8%‡	0.640
Conscious sedation	48.8%	45.8%	0.167	38.8%	52.8%	0.084
mTICI ≥2b, %	92.8%	91.7%	0.593	95.5%	93.9%	0.622
90-d mRS score 0–2	55.9%§	60.6%§	0.202	60.6%‖	54.7%‖	0.412
sICH within 48 h postprocedure	1.8%	2.4%	0.613	1.5%	0.6%	0.470
90-d mortality	13.0%	10.5%	0.302	9.0%	11.1%	0.624

ASPECTS indicates Alberta Stroke Program Early CT Score; CTA, computed tomography angiography; CTP, computed tomography perfusion; ICA, internal carotid artery; IQR, interquartile range; IV tPA, intravenous tissue-type plasminogen activator; MCA, middle cerebral artery; mRS, modified Rankin Scale; mTICI, modified Treatment in Cerebral Infarction; NCCT, noncontrast computed tomography; NIHSS, National Institutes of Health Stroke Scale; sICH, symptomatic intracranial hemorrhage; and TLSW, time-last-seen-well.

† IV tPA use data missing in 6 CTP patients.

‡ IV tPA use data missing in one CTP patient.

§ Ninety-d mRS score missing in one NCCT±CTA and 2 CTP patients.

‖ Ninety-d mRS score missing in one NCCT±CTA and one CTP patient.

Table 2. Trevo Registry Patients With ICA, MCA-M1, MCA-M2 Occlusions, and PreMorbid mRS Score of 0–2: Association Between Imaging Selection Modality With Good Outcomes (mRS Score 0–2) and Overall Functional Disability at 90 Days in the 0–6-Hours and 6–24-Hour Window (Multivariable Analysis) (Table view)

	0–6 h								6–24 h					
	mRS score 0–2				mRS score 1-point shift				mRS score 0–2				mRS scor	
	OR	95% CI		*P* value	OR	95% CI		*P* value	OR	95% CI		*P* value	OR	95%
Imaging modality (reference: NCCT)									Imaging modality (reference: NCCT)					
CTA	0.60	0.34	1.07	0.103	0.71	0.45	1.12	0.282	1.78	0.48	6.64	0.625	1.54	0.58
CTP	0.82	0.48	1.42	0.858	0.73	0.47	1.13	0.353	1.00	0.33	3.05	0.171	1.38	0.59
Age	0.97	0.96	0.99	<0.0001	0.98	0.97	0.98	<0.001	0.95	0.93	0.97	<0.0001	0.97	0.95
NIHSS	0.92	0.90	0.95	<0.0001	0.91	0.89	0.93	<0.001	0.88	0.84	0.93	<0.0001	0.90	0.87
mRS	0.50	0.39	0.66	<0.0001	0.47	0.38	0.58	<0 0.001	0.66	0.39	1.11	0.113	0.59	0.40
ASPECTS ≥6	1.15	1.04	1.26	0.005	1.18	1.09	1.27	<0.001	1.26	1.05	1.50	0.011	1.19	1.05
Diabetes	0.54	0.37	0.78	0.001	0.56	0.41	0.76	<0.001	0.56	0.30	1.05	0.071	0.74	0.45
TLSW-puncture	0.79	0.69	0.90	0.001	0.80	0.72	0.89	<0.001	0.98	0.92	1.05	0.554	0.96	0.9

ASPECTS indicates Alberta Stroke Program Early CT Score; CTA, computed tomography angiography; CTP, computed tomography perfusion; ICA, internal carotid artery; MCA, middle cerebral artery; mRS, modified Rankin Scale; NCCT, noncontrast computed tomography; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; and TLSW, time-last-seen-well.

Notably, there was no interaction between the treatment time window (0–6 versus 6–24 hours) and CT selection modality (CTP versus NCCT±CTA) in terms of the degree of functional disability at 90 days (P=0.45). Subgroup analysis of the DAWN-like patients yielded similar results with no relationship between imaging selection modality and outcomes in either the early or extended time windows (Table I in the Data Supplement).

DISCUSSION

To our knowledge, no other study based on a large prospective cohort of MT patients has compared the effects of imaging selection modality within and across the early and extended time windows. In this analysis of patients with large vessel occlusion stroke with predominantly favorable imaging profile on presentation, we did not find a relationship between diagnostic CT imaging modality and outcome in either time epoch. While these represent preliminary and exploratory results, they put in question the current consensus guideline recommendations mandating the usage of advanced imaging for extended window thrombectomy patients and suggest that the currently adopted extended window selection criteria may be over stringent. As such, our findings have potentially broad implications to clinical practice as the absence of outcome differences across patients selected with CTP versus NCCT±CTA alone needs to be considered in the background of the additional contrast and radiation exposure, extra costs and potential treatment time delays that are typically associated with use of CTP. More importantly, as advanced imaging is not universally available, the use of non-contrast CT±CTA alone may represent a reasonable option for extended window selection, especially in environments that lack CTP and acute phase MRI capabilities.

DAWN and DEFUSE 3 completely relied on the use of advanced imaging (eg, CT/MR perfusion or diffusion-weighted imaging) for patient selection. Unfortunately, due to technological, logistical, and financial constraints, this has created a significant challenge to the implementation of extended window protocols in many centers across the globe. In addition, as the inclusion and exclusion criteria used in DAWN and DEFUSE-3 were, at least on retrospect, too strict and given their extremely high treatment effect sizes, more inclusive selection paradigms could potentially result in the treatment of a larger proportion of the late presenting patients while still maintaining a significant benefit. As such, the validation of simpler and more inclusive imaging selection, ideally relying solely on NCCT and CTA, has become critical to a more widespread adoption of MT in the extended time window. Concurrently, the utility of perfusion imaging for MT has become increasingly controversial. In the SWIFT PRIME trial (Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment), the use of perfusion imaging did not improve the efficacy of MT but was associated with potential time delays.[15] Likewise, there was no significant interaction between CTP-derived parameters or CTP mismatch and treatment effect in the MR CLEAN trial (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands).[16] A recent analysis of the HERMES cohort (Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials) demonstrated that (1) CTP mismatch volume was not independently associated with functional outcomes and (2) as compared with diffusion-weighted imaging, CTP was independently associated with lower functional independence and less functional improvement.[17] As early window outcomes are highly time-dependent and ≈85% of the patients presenting within 0 to 6 hours have favorable imaging on NCCT (ASPECTS ≥6),[18,19] the trade-offs between treatment speed versus the additional data provided by CTP must be considered. Furthermore, patients may be mistakenly excluded from treatment due to CTP infarct

volume over-estimation.[20] Our study showed similar functional outcomes with the use of NCCT±CTA versus CTP in both the early and extended windows. This remained the case after the adjustment for identifiable confounders. Although counter-intuitive at first glance, the comparable performance of NCCT±CTA versus CTP in the extended window is somewhat expected since the performance of NCCT for the detection of ischemia improves over time.[21] In this setting, imaging selection paradigms based on NCCT Clinical-ASPECTS Mismatch may represent a good option to centers that lack advanced imaging capabilities.[22]

Our study has all the limitations associated with a post hoc retrospective registry analysis including a greater susceptibility to selection bias. This is exacerbated by the fact that, despite its encouragement, consecutive enrollment was not mandated or monitored for. Moreover, given the small sample size of some of the study subgroups, our analysis lacked enough statistical power to properly exclude the possibility of a benefit from CTP and this may have led to a type II error. As our results relate specifically to the defined subpopulation of patients with intracranial internal carotid artery or middle cerebral artery M1- or M2-segment occlusions they cannot be generalized to other populations. Finally, there was no standardization for the imaging protocols across the different sites and many centers did not employ the more sophisticated automated CTP software, which are known to reduce the times for imaging processing/interpretation and to eliminate inter-operator variability. As such, our results should be interpreted with caution and as hypothesis-generating only. Indeed, only well-conducted randomized controlled trials will be able to accurately evaluate the need of CTP for patient selection in endovascular therapy. Fortunately, the MR CLEAN LATE (Endovascular treatment of acute ischemic stroke in the Netherlands for late arrivals; ISRCTN19922220) and the RESILIENT-Extended (Randomization of Endovascular Treatment in Acute Ischemic Stroke in the Extended Time Window; URL: https://www.clinicaltrials.gov; Unique identifier: NCT04256096) trials are currently investigating simpler paradigms for imaging selection in the 6- to 24-hour time window.

CONCLUSIONS

In conclusion, our data add to the increasing body of evidence challenging the utility of CTP in the early window and suggest that extended window patients may be safely treated in the absence of CTP or MRI data. However, as our study was based on a post hoc analysis of a registry, these findings must be properly confirmed in prospective trials.

ARTICLE INFORMATION

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Correspondence

Correspondence to: Raul G. Nogueira, MD, Imaging Selection and Thrombectomy Time Window, Grady Memorial Hospital, 80 Jesse Hill Dr SE, Room 8D108A, Atlanta, GA 30303. Email raul.g.nogueira@emory.edu

Affiliations

Department of Neurology, Emory University School of Medicine, Marcus Stroke & Neuroscience Center, Grady Memorial Hospital, Atlanta, GA (R.G.N., D.C.H., M.R.F.). Department of Neurology, UCLA, Los Angeles, CA (D.L.). Department of Neurology, Cooper University Hospital Neurological Institute, Camden, NJ (T.G.J.). Department of Neurosciences, Wellstar Health System, Atlanta, GA (R.G.). Department of Neurology, Stroke Institute, University of Pittsburgh Medical Center, PA (A.J.). Department of Interventional Neuroradiology, Riverside Methodist Hospital/Ohio Health Research Institute, Columbus (R.F.B.). Department of Radiology, Erlanger Hospital, Chattanooga, TN (B. Baxter). Department of Radiology, University Hospital Hradec Kralove, Czech Republic (A.K.). Department of Neuroradiology, CHU Montpellier, France (A.B.). St. Mary's Medical Center, West Palm Beach, FL (A.M.). Department of Neuroradiology, CHU Tours, France (A.P.N.). Stryker Neurovascular, Fremont, CA (R.S., Y.Z., P.M.). Department of Interventional Radiology, La Pitie Salpetriere, Paris, France (B. Bartolini). Department of Neurology, California Pacific Medical Center, San Francisco (J.E.). Department of Neurosciences, Drexel Neurosciences Institute, Philadelphia, PA (E.V.).

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Disclosures

Dr Bartolini is a consultant and on the advisory board of Stryker. Dr Baxter receives consulting fees and fees for serving on a speakers' bureau from Penumbra and consulting fees from Stryker, Medtronic, Cerenovus, Route 92 Medical, Artio, Marblehead, 880 Medical, Rapid Medical, Vizai and Pulsar and holding US Patent 9526863 on devices and methods for perfusion therapy, licensed to Neuronal Protection System. Dr English is a consultant for and on the advisory board of Penumbra and Medtronic and a consultant for Stryker. Dr Gupta has ownership interest in and receives royalties from UpToDate. He is a consultant/advisory board member of Stryker Neurovascular, Medtronic, Penumbra, Cerenovus, Zoll, and Rapid Medical. He is also serving as an associate editor of the Journal of Neurointerventional Surgery a Journal of Neuroimaging. Dr Krajina is a consultant for and on the advisory board of Stryker. Dr Liebeskind is a consultant for and on the advisory board of Medtronic (Imaging Core Lab) and a consultant for Stryker Neurovascular (Imaging Core Lab). Dr Nogueira has the following disclosures: Stryker (DAWN Trial PI-unpaid; Trevo-2 Trial PI, Trevo Registry Steering Committee), Covidien (SWIFT/SWIFT-PRIME Steering Committee, STAR Trial Core Lab; no compensation >24 months), Penumbra (3D Trial Executive Committee, unpaid), Cerenovus/Neuravi (ENDOLOW Trial and EXCELLENT Registry PI, ARISE-2 trial Steering Committee), Phenox (PROST Trial PI), Imperative Care (Imperative Trial PI), Physician Advisory Board (modest) for Anaconda, Genentech, Biogen, and Prolong Pharmaceuticals, and Physician Advisory Board (stock options) for Brainomix, Viz-AI, Corindus Vascular Robotics, Vesalio, Ceretrieve, and Astrocyte. R. Shields, Dr Zhang, and P. Morgan are employed by Stryker. Dr Veznedaroglu is a co-PI of the Trevo Registry and a consultant for and on the advisory board of Stryker, is a Penumbra patent holder and scientific advisor, is a Trice scientific advisory board consultant, and

holds a Mizuho patent. Dr Jovin has the following disclosures: Consultant: Cerenovus (steering committee/DSMB-modest), Stryker Neurovascular (PI DAWN-unpaid]). Advisor/Stockholder: Anaconda, Methinks, Silk Road, Blockade Medical, Route 92, Corindus, FreeOx Biotech, Vizai, Imperative Care. Dr Haussen is a modest consultant for Stryker, Cerenovus and Vesalio and an investor in Viz-AI. Dr Frankel reports grants from Nico Corporation and consulting fees from expert testimony outside the submitted work. Dr Bonafe receives consultant fees from Stryker, Medtronic, Balt, and Phenox. The other authors report no conflicts.

SUPPLEMENTAL MATERIALS

Table I

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