Imaging as a Selection Tool for Thrombectomy in Acute Ischemic Stroke

Pathophysiologic Considerations

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Abstract

Large vessel occlusion (LVO) stroke represents a stroke subset associated with the highest morbidity and mortality. Multiple prospective randomized trials have shown that thrombectomy, alone or in conjunction with IV thrombolysis, is highly effective in reestablishing cerebral perfusion and improving clinical outcomes. In unselected patients and especially in patients with poor collaterals, the benefit of reperfusion therapy is exquisitely time sensitive; the earlier thrombectomy is started, the lower the likelihood of disability or death. Understanding both the pathophysiologic underpinnings and the modifying factors of this strong time-to-treatment effect demonstrated in numerous randomized clinical trials is important for implementation of intrahospital workflow measures to maximize time efficiency of thrombectomy. Reducing delays in reperfusion therapy initiation has become a priority in acute stroke care, and therefore a thorough understanding of the main systems-based factors responsible for these delays is critical. Because the time spent evaluating the patient in the emergency department, which typically includes neuroimaging studies performed in scanners remote from the angiography suite, represents the main source of delays in thrombectomy initiation, the direct to angiography (DTA) model has emerged as a means to substantially reduce treatment times and is being instituted at an increasing number of thrombectomy centers across the world. The aim of this report is to introduce DTA as an emerging stroke care paradigm for patients with suspicion of LVO stroke, review results from studies evaluating its feasibility and impact on outcomes, describe current barriers to its more widespread adoption, and propose potential solutions to overcoming these barriers.
Large vessel occlusion (LVO),\(^1\) defined as internal carotid artery (ICA), middle cerebral artery (MCA) M1 and M2 segments, and basilar artery (BA) occlusion, causes approximately one-third of acute ischemic strokes (AIS) but accounts for more than 60% of morbidity and 90% of mortality due to AIS.\(^2\) Thus, LVO stroke constitutes prognostically the most severe form of AIS, with outcomes that to date have only been shown to be improved by timely reperfusion of the ischemic brain. This can be accomplished with IV therapy (using lytic drugs such as tissue plasminogen activator [tPA] or tenecteplase) or with endovascular therapy (EVT), typically in the form of mechanical thrombectomy.

Because intracerebral hemorrhage may be clinically indistinguishable from ischemic stroke, it must be ruled out as a prerequisite to reperfusion therapy. A noncontrast CT, the simplest neuroimaging modality capable of reliably detecting intracranial blood, is widely considered sufficient for the purposes of time-based (0–4.5 hours) IV thrombolytic administration. The minimum necessary imaging requirements for performance of EVT vary widely across thrombectomy centers but usually involve at least an additional CT angiogram (CTA) to confirm large vessel occlusion (LVO). In addition, many centers routinely perform additional “advanced imaging” in the form of CT perfusion (CTP) or MRI to assess the extent of mismatch, that is, the volume of already infarcted brain (core) in relation to the volume of the entire “at risk” tissue. These advanced imaging modalities provide pathophysiologic information that is unique to each patient with LVO stroke and thus allow the institution of individualized patient treatment strategies, which theoretically is an appealing concept.

A major downside of these imaging studies is the additional time required for their completion that translates into delays in reperfusion. Furthermore, emerging data suggest that in the early time window, the vast majority of patients have a pathophysiologic constellation that is predictive of a favorable response to EVT. Therefore, reduction of neuroimaging studies to the minimum possible is emerging as a viable alternative to the more established selection paradigms. Identification of factors that are predictive of highest clinical benefit when the simplest imaging selection modalities are used remains an area of active research. However, it is increasingly being recognized that time window and stroke severity at presentation may distinguish between those patients in whom delays caused by additional imaging may be harmful and those patients in whom delays caused by imaging are unlikely to result in measurable harm. Direct to angiography (DTA) is a recently coined term used to describe a time-efficient method of delivery of patients with LVO stroke directly to the neuro-angiography suite without time spent on additional evaluations, including neuroimaging studies in the emergency department. This approach has been associated with substantial gains in time to reperfusion, but it requires significant additional resources compared to the traditional intrahospital workflow paradigms. To better understand the rationale for this emerging approach and its determinants of maximal benefit, we review the importance of time, the role of imaging, and existing models of triage and transfer of LVO stroke.

**Why Is Time Important?**

**Time and Outcomes**

The time-dependent benefit demonstrated by the National Institute of Neurologic Disorders and Stroke (NINDS) IV tissue plasminogen activator (tPA) trial brought about a paradigm shift in the treatment of acute ischemic stroke.\(^3\) Time became a fundamental patient selection criterion for reperfusion therapy, and early reperfusion is now recognized as a vital factor in achieving favorable outcomes, as captured by the aphorism “time is brain.” In 2015, five landmark randomized controlled trials demonstrated the superiority of EVT over medical therapy alone for patients with LVO stroke, the vast majority of whom were treated in the 0–6 hours time window.\(^4-8\) A meta-analysis of these studies showed that the benefit of thrombectomy in nonselected patients is exquisitely time-dependent.\(^9\) The magnitude of the treatment effect is strongly correlated to the time from stroke onset to reperfusion, and treatment benefit can no longer be demonstrated with a high degree of certainty after 7.3 hours after stroke onset.\(^10\) There are abundant data confirming the effect of time on outcomes postthrombectomy.\(^10-13\) The HERMES collaborators reported that for every 100 patients treated, every 15 minutes of earlier reperfusion results in a 2.5% higher chance of achieving independence in activities of daily living.\(^10\) Retrospective data suggest that every minute of delay to recanalization leads to the reduction of 4.2 days of disability-free survival.\(^14\)

**Heterogeneity in Stroke Pathophysiology**

Two years after the publication of the early time window trials, the DAWN and DEFUSE-3 trials led to a dramatic expansion
of the therapeutic time window for thrombectomy, with benefit demonstrated up to 24 hours from stroke onset.\textsuperscript{15,16} These trials, however, were highly selective with regard to inclusion criteria, and only enrolled patients with “mismatch” (i.e., small infarct volumes in the presence of large areas at risk) presenting >6 hours after the patient was last seen well (LSW).

The seemingly difficult to reconcile discrepancy between the finding of a strong relationship between timing of reperfusion and outcomes in the early time window and the finding of strong benefit from thrombectomy in the late time window can be explained by patient selection with respect to speed of infarct progression. Whereas the early time window trials enrolled largely unselected patients, the late time window trials restricted enrollment to “slow progressors,” a term derived from the recognition of 2 distinct phenotypes with respect to infarct growth rate following proximal large vessel occlusion, the slow and fast progressors.\textsuperscript{17} At a cellular level, the corresponding rate of neuronal loss following vessel occlusion has been described to be highly variable, ranging from <35,000 to >27 million neurons per minute.\textsuperscript{18} The variability in the rate of infarct growth in the setting of LVO is highly dependent on the individual degree of leptomeningeal collateral blood flow.\textsuperscript{19-21} Not surprisingly, leptomeningeal collaterals have also been shown to be an independent predictor of good outcome in LVO stroke.\textsuperscript{22} Factors influencing the presence and extent of collaterals and consequent susceptibility to ischemic damage include genetic factors, physiologic measures such as blood pressure, body position, CO\textsubscript{2} temperature, glucose, and demographics.\textsuperscript{17} Long-standing intracranial stenosis can lead to the development of more extensive collaterals, but comorbidities promoting their development (e.g., hypertension, diabetes) are associated with impaired collateral blood flow during acute stroke.\textsuperscript{23,24} Cerebral edema has also been shown to impair blood flow through collateral vessels, and this may explain the decreased final infarct size seen in studies evaluating sulfonylurea use for the reduction of cerebral edema.\textsuperscript{25}

When patients with proximal LVO are defined as fast progressors if harboring an infarct in the MCA territory greater than 70 mL within 6 hours of LSW, and as slow progressors if their infarct is less than 30 mL beyond 6 hours of LSW, the prevalence of slow progressors is approximately 50% and that of fast progressors is approximately 25%.\textsuperscript{26} This latter patient population experiences rapid infarct growth and represents the most sensitive group with respect to delays in time to recanalization.\textsuperscript{27}

**Time and Neuroimaging**

Consistent with current American Heart Association (AHA)/American Stroke Association guidelines,\textsuperscript{28} it is reasonable to guide the use of neuroimaging as a selection tool for thrombectomy according to the time from LSW to presentation. In the 0–6 hours window, a simplified approach to parenchymal imaging based on noncontrast CT to rule out intracerebral hemorrhage and (optionally) to estimate infarct size is supported by the HERMES derived data. In the HERMES meta-analysis, the vast majority of patients presented in the 0–6 hours time window and were largely unselected with regards to baseline infarct volumes. In these patients, net benefit was noted across all baseline infarct volume categories, and the strong relationship found between time to treatment and outcomes was largely driven by the high prevalence of fast progressors in this patient population. Thus, in the early time window, assuming the presence of salvageable brain may be the right strategy in nearly all patients. Emphasis should be placed on shortening the times from hospital arrival to treatment initiation, and advanced imaging should be forgone in most instances to avoid time delays.

In the 6–24 hours window, most data documenting benefit from thrombectomy are derived from the DAWN and DEFUSE 3 trials, in which patients were selected based on advanced imaging with CTP and MRI that identified a population with substantial mismatch, that is, a population consisting largely of slow progressors. In these trials, consistent with the slow progressor profile of most patients enrolled, time to treatment was not found to be strongly correlated to clinical outcomes, and therefore in patients meeting DAWN or DEFUSE 3 criteria presenting in the extended time window, delays in reperfusion caused by advanced imaging are less likely to be of consequence.

While CTP and diffusion-weighted imaging (DWI) MRI/magnetic resonance perfusion currently represent the standard imaging modality for selection of patients with LVO presenting in the 6–24 hours time window, emerging data suggest that assessment of mismatch based on clinical and infarct volume criteria, similar to the paradigm used in DAWN, can be obtained with reasonable accuracy based on noncontrast CT estimation of infarct volume. This is performed using either the Alberta Stroke Program Early CT Score (ASPECTS) or as a volumetric assessment of hypodense areas on CT. A simplified approach to baseline infarct estimation is less necessary from the standpoint of gains in time to reperfusion (such as in the case of the 0–6 hours time window patients) and more from the standpoint of accessibility to EVT, as most of the thrombectomy centers worldwide lack 24/7 CTP or MRI capability.

The DAWN investigators noted that when the prethrombectomy CT scans of patients enrolled in the trial were analyzed, only patients with ASPECTS >6 derived clear benefit from EVT.\textsuperscript{29} Similarly, analysis of the AURORA dataset, an individual level meta-analysis of randomized trials enrolling patients beyond 6 hours from LSW, revealed statistically significant benefit from EVT in patients with baseline ASPECTS scores of 8–10 and 6–7 but not in those with baseline ASPECTS scores of 0–5.\textsuperscript{30} A retrospective study supporting an ASPECTS score of ≥6 as cutoff for patient selection in the beyond 6-hour time window was reported by Desai et al.\textsuperscript{31} In the 185 patients with proximal LVO and
advanced imaging (CTP or DWI/perfusion-weighted imaging MRI) included in this study, clinical core mismatch, as defined in the DAWN trial, was present in 79% of patients with ASPECTS 6–10 presenting in the 6–24 hours time window, and the likelihood that clinical core mismatch was present for a given ASPECTS score was found to be constant throughout the 6–24 hours time window.31 Thus, given the strong benefit of thrombectomy in patients selected by DAWN criteria (number need to treat of 2 to reduce disability), it is reasonable to assume benefit of EVT for patients with ASPECTS 6–10 who otherwise meet DAWN criteria. The lack of CTP or MRI should not be a deterrent from thrombectomy in the beyond 6-hour time window for these patients. Whether benefit from thrombectomy exists in patients with proximal LVO and ASPECTS <6 or low National Institutes of Health Stroke Scale (NIHSS) presenting beyond 6 hours from LSW needs to be established through randomized trials.

**Neuroimaging for IV tPA and Thrombectomy Eligibility**

Acute clinical evaluation in the emergency department is typically followed by relevant neuroimaging, which is comprised at most centers of CT head, with or without CTA. Alternatively, MRI-based imaging (MRI and magnetic resonance angiography) is used instead at some centers. However, the use of magnetic resonance–based imaging, even at the most efficient centers, may be associated with delays compared to CT.32 This, along with implanted devices or other metallic structures that constitute absolute contraindications to MRI use, represent the main disadvantage of MRI use in acute stroke.

Originally, the main goal of acute imaging was to rule out intracerebral hemorrhage for the purpose of administering IV tissue plasminogen activator (tPA). However, since thrombectomy has become common practice in LVO stroke, imaging has been increasingly utilized to assess for thrombectomy eligibility by confirming the presence of an LVO, by ruling out a large infarction and by confirming the presence of reversible ischemic tissue (mismatch). While the exclusion of intracerebral hemorrhage is the main prerequisite with respect to IV thrombolysis administration, all other neuroimaging studies are essentially performed for screening purposes, with the ultimate goal of accurately identifying patients considered ineligible for thrombectomy for the purpose of excluding them from angiography. Furthermore, patients with stroke transferred to a thrombectomy-capable stroke center (TSC) from a non-TSC often undergo repeat evaluation and neuroimaging upon arrival in the TSC emergency department prior to activation of the thrombectomy team. In many instances, repeat imaging occurs despite already having established thrombectomy eligibility at the referring hospital, with the justification that the imaging study obtained at the referring hospital no longer accurately reflects tissue viability status.33 Even if in cases of long delays during transfer this may be appropriate, it remains unclear what time threshold would justify repeat imaging.

The need for IV thrombolytic administration in IV thrombolysis–eligible thrombectomy candidates presenting directly to a TSC has been called into question, as recent randomized trials showed no difference in outcomes when IV tPA was administered prior to thrombectomy compared to thrombectomy performed without IV tPA (although reperfusion rates on angiography were higher in the combination therapy group).34,35 If this finding is confirmed by other ongoing randomized trials, IV thrombolysis may no longer be indicated for certain thrombectomy candidates presenting directly to TSCs. In this setting, the issue of ruling out intracerebral hemorrhage for the purpose of IV thrombolysis administration may become less relevant.

**Large Ischemic Core Volume in the Early Time Window**

A long-held belief among stroke experts has been that reperfusion of large volumes of infarcted brain tissue is detrimental to patients’ outcomes due to the development of symptomatic intracerebral hemorrhage, malignant edema, or other reperfusion-related deleterious effects. Important unresolved questions related to this concept include the definition of large infarct and the accuracy of available imaging-based tools for infarct measurement. Definitive evidence against a net detrimental effect of reperfusion is lacking, but the results of recent studies have shed considerable doubt on this assumption, as to date no category of patients defined by imaging or otherwise has been found to be harmed by thrombectomy.

The most commonly used imaging-based methods to estimate the ischemic core in patients with LVO stroke are noncontrast CT, CTP, and MRI. Score of 7 on ASPECTS36 as the baseline infarct volume threshold associated with benefit from reperfusion was initially described in the first-generation endovascular trials.37,38 However, advances in technology and workflow have shifted this cutoff to lower values. Indeed, in the initial HERMES collaborators publication, a statistically significant benefit from mechanical thrombectomy could be demonstrated using an ASPECTS cutoff of 6 and above. Subsequent to this publication, in the prospective study ETIS, Panni et al.39 reported a rate of good outcome, defined as a modified Rankin Scale (mRS) score of 0–2 at 3 months, of 32% in the subgroup of patients with ASPECTS of 4–5. Similarly, analysis of patients with ASPECTS 0–5 who underwent thrombectomy in the BEYOND-SWIFT registry showed that 40% had favorable outcome (mRS 0–3) at 90 days.40 These outcome rates are superior to what would be expected in patients with nontreated LVO stroke with similar baseline ASPECTS scores.

CTP is considered superior to noncontrast CT in its ability to estimate the core, perhaps especially in clinical settings where calculation of ASPECTS may be less reliable than in clinical trials. When interrater reliability is good, studies have shown that with respect to its ability to estimate a large infarct (>70 mL), a noncontrast CT ASPECTS cutoff of <7 is equivalent to CTP when compared to the gold standard of DWI MRI.41

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Furthermore, in the era of modern thrombectomy, with fast and complete reperfusion achieved in an increasingly higher proportion of patients, CTP-derived thresholds defining infarct are being redefined and seem to be a “moving target.” It has been shown that cerebral blood flow (CBF) thresholds defining infarct are dependent on both the timing of reperfusion relative to the CTP study and on the timing of reperfusion relative to the stroke symptom onset. These findings were confirmed by Qiu et al. based on patients from the HERMES database. Earlier reperfusion necessitates lower CBF thresholds in order to estimate infarct volume with the same accuracy as those used in patients who achieve reperfusion later. However, even with these adjustments, thresholds used for infarct measurement on CTP lack strong reliability.

Improvements in stroke systems of care coupled with advances in thrombectomy technology make it likely that high-quality reperfusion will be achieved earlier in the future. As such, it is not clear that the thresholds defining infarct on CTP will achieve sufficient accuracy. Indeed, the final infarct volumes in patients who undergo successful reperfusion can be smaller than predicted by CTP imaging on the pre-thrombectomy CTP, especially when reperfusion is achieved very early (within 3 hours from LSW). DWI MRI is widely considered the most precise method for core estimation in clinical practice but it is associated with delays. Furthermore, even though superior to all other imaging modalities in clinical use, MRI is also prone to inaccurate characterization of the infarcted brain, especially in the context of reperfusion. The earlier the pre-reperfusion MRI scan is performed relative to ischemia onset, and the faster reperfusion occurs following completion of the MRI scan, the higher the likelihood that the DWI lesion noted on the initial MRI will no longer be demonstrated on a follow-up MRI scan. This phenomenon, termed DWI reversibility, has been noted to occur in up to a quarter of patients with acute stroke.

Data from the HERMES collaboration indicate strong signals of benefit in favor of thrombectomy in patients with large (>$70 mL) and even very large (>$100 mL) baseline infarct volumes. Thus, both the limitations of CTP and MRI in accurately measuring the true infarct core, and the lack of convincing evidence of lack of benefit (or harm) with thrombectomy in patients with large cores measured by these imaging modalities, call into question the utility of advanced imaging (CTP or MRI) in determining thrombectomy eligibility in the early time window.

Perhaps the most compelling data showing the benefit of EVT, even in patients with large baseline infarcts, come from the expanded dataset making up the HERMES collaboration, which included 7 randomized endovascular stroke trials showing superiority of EVT plus best medical therapy (that included IV thrombolysis in eligible patients) over best medical therapy alone. Although most of the participating trials’ protocols excluded patients with large baseline infarctions, some of these patients were inadvertently enrolled due to lack of recognition of large infarcts on initial imaging by local investigators. In a meta-analysis of these trials, of the 1,764 patients enrolled, 126 underwent thrombectomy with core laboratory–adjudicated baseline ASPECTS $<5$ on CT (61 patients) or MRI (65 patients). Both in the MRI and CT groups there was a trend in favor of benefit with EVT, while in the combined analysis of CT or MRI-imaged patients, the benefit from EVT reached statistical significance (odds ratio [OR], 2.15; 95% confidence interval [CI], 1.06–4.37). In 228 patients with evidence of hypodensity involving greater than 1/3 of the MCA territory, another measure of large baseline infarct, benefit from EVT was also demonstrated (OR, 1.70; 95% CI, 1.04–2.78). Using the same expanded HERMES dataset, similar results were seen on a CTP-based analysis of patients with large core infarcts ($>$70 mL and even $>$100 mL) with no significant reduction in absolute treatment effect with EVT and no net signals of harm despite a higher incidence of symptomatic intracerebral hemorrhage in the thrombectomy group compared to controls. Findings from these studies suggest that patients with LVO who have large baseline infarcts are likely to benefit from EVT compared to medical treatment alone, and that although a large baseline infarct represents a prognostic factor, it does not represent a treatment effect modifier.

Efforts to identify patients with large baseline infarcts for the purpose of exclusion from thrombectomy may lack justification not only due to the observed strong trends of benefit of thrombectomy for these patients, but also because in patients presenting in the early time window, the prevalence of large infarctions without significant salvageable tissue is exceedingly low, as demonstrated by the 95% of patients who had mismatch by SWIFT PRIME criteria and by the 78% of patients who had large penumbral volumes ($>$60 mL) in the HERMES collaboration–derived CTP-based study. In fact, the prevalence of large infarcts (ASPECTS 0–5) has been estimated to be no more than about 15% of patients with M1 MCA occlusion presenting within 6 hours after LSW, while within the first 3 hours after symptom onset the prevalence of ASPECTS 0–5 in patients with MCA occlusion is 4%. As such, not only is there a paucity of evidence to suggest a lack of benefit of EVT for LVO strokes with large baseline infarcts, but also the prevalence of large infarcts in the early time window is low.

### Tradeoff Between Advanced Imaging and Delays in Time to Reperfusion

Advanced imaging can require significant time for completion. In SWIFT PRIME, the median time from start of CT to postprocessing of CTP imaging was 24 minutes, while MRI-based selection was associated with a delay from door to groin puncture of a median of 16 minutes compared to CT-based selection. Considering that based on data derived from HERMES every 15 minutes of delay in reperfusion results in a 3.9% lower chance of reduction in disability, if the delay in
reperfusion caused by CTP in SWIFT PRIME was a conservative 15 minutes, this delay translates into 3.9% higher chance of disability in those patients who achieved reperfusion in the intervention arm of the trial. The delays incurred by advanced imaging can be inferred from the fact that in DAWN and DEFUSE-3, studies with protocol requirements of advanced imaging (CTP or MRI), median emergency department arrival to groin puncture times were 109 and 112 minutes, respectively, compared to 89 minutes in the ESCAPE trial, 60 minutes in the ESCAPE NA-1 trial, and 60 minutes in the ARISE II study,5,15,16,51,52 none of which required advanced imaging. Consistent with this observation, the AHA guidelines endorse thrombectomy as Level I evidence only for patients harboring an LVO and a limited core volume defined as an ASPECT score >5.28 However, based on data published after the publication of the AHA guidelines, in the early time window (0–6 hours), following exclusion of intracerebral hemorrhage (typically accomplished with a noncontrast head CT), it is justified to question the necessity for patient selection for thrombectomy based on any baseline infarct size.

### Is Vessel Imaging Always Necessary?

The vast majority of stroke centers perform CTA in a conventional CT scanner to confirm the presence of LVO prior to the decision to proceed with transport to the angiography suite. Studies examining workflow efficiency in intrahospital systems of care have shown that when only a plain CT is utilized in lieu of the standard CTA for the purposes of LVO diagnosis, the time required for imaging decreases by an average of 28 minutes, and the time elapsed from hospital presentation to access site puncture time decreases by 36 minutes.53 Thus, in situations where there is an a priori high likelihood of LVO, forgoing the CTA after head CT in favor of transport directly to the angiography suite may save substantial time to brain reperfusion. An NIHSS cutoff of 10 or above has been shown to predict the presence of LVO with 80% accuracy in the early time window.54 Furthermore, clinical information in combination with a plain CT has been found on AI applications to predict LVO with even higher accuracy (positive predictive value 88%).55

The tradeoff between the substantial reductions in time to reperfusion for the majority of patients with occlusion in favor of unnecessary mobilization of angiography suite resources for the minority of patients who do not harbor an LVO is a widely accepted paradigm in cardiology. Myocardial infarction with nonobstructive coronary arteries (MINOCA), characterized by patent coronary arteries during emergent cardiac catheterization despite clinical, electrocardiographic, and biomarker features consistent with myocardial infarction, is encountered with a frequency of 5%–25% and typically results in no coronary intervention at the time of the emergent cardiac catheterization procedure.56

Recent advances in flat panel angiography technology have made possible the identification of both intracranial hemorrhage and
LVO on the angiography table, which represents a noninvasive way of answering the questions relevant for triage of patients with LVO in the most time-efficient manner.\textsuperscript{57} Flat panel CT and CTA, obtained by low-dose contrast injection to create CTA-like images, demonstrated high accuracy in their respective ability to rule out hemorrhage and detect LVO in the neuroangiography suite.\textsuperscript{58,59} Most stroke centers do not employ flat panel CT and CTA, but with more widespread adoption, this technology may be a clinically useful tool in reducing reperfusion times. Other strategies adopted by some centers for reducing imaging-associated time delays include prenotification by first responders followed by immediate imaging on hospital arrival, or CT imaging performed on a mobile stroke unit en route to the hospital.

**Discussion**

Multiple randomized trials have shown that thrombectomy with or without IV thrombolysis is associated with the strongest clinical response in LVO stroke and that the benefit of this approach is exquisitely time dependent, especially in nonselected patients presenting in the early (0–6 hours) time window. Therefore, systems-based approaches aimed at reducing times from stroke onset to reperfusion have been a priority in the quest to improve acute stroke care. The DTA model represents a new paradigm to dramatically reduce reperfusion times through bypass of conventional pathways for early presenting LVO stroke. It consists of clinical and imaging evaluation on the angiography table using either no additional imaging prior to thrombectomy (in the cases of transferred patients) or flat panel technology (in the cases of patients presenting directly to a thrombectomy capable center). This model, which predominantly benefits patients presenting with severe stroke (NIHSS >9) in the early (0–6 hours) time window, a patient population enriched with fast progressors, relies on emerging data suggesting that knowledge of baseline infarct volume may no longer be necessary for patient selection in the early time window and that the presence of LVO can be estimated with high likelihood either based on the NIHSS or even more accurately with a flat panel CTA performed after patient arrival in the angiography suite. DTA has been shown to be feasible and safe and is associated with significant decreases in time to treatment initiation.

Conversely, patients presenting in the 0–6 hours time window with stroke of moderate severity (NIHSS 6–9) are less likely to harbor an LVO compared to those with more severe stroke at presentation. Even in the presence of an LVO, these patients are likely to fit the slow progressor profile due to favorable collaterals, and thus are less likely to benefit from a DTA approach. Judicious use of hospital resources renders the screening of these patients with CTA to confirm the presence of an LVO a reasonable option. We propose the preferred imaging algorithm prior to endovascular therapy based on symptom timing and severity in the Table. The benefit of thrombectomy in patients with LVO and NIHSS of 0–5 presenting in the 0–6 hours time window has not been established and randomized trials investigating its utility are underway. In patients with LVO presenting beyond 6 hours from LSW, the time delays caused by performance of advanced imaging are less consequential. However, several studies indicate that an ASPECTS score of 2–6 may be a reasonable baseline infarct cutoff in patients otherwise meeting DAWN criteria and may be used in lieu of CTP or MRI when these imaging modalities are not available. Whether there is a benefit from performing thrombectomy in patients with proximal LVO and ASPECTS <6 or low NIHSS (0–5) presenting beyond 6 hours from LSW needs to be established through randomized trials.

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**Appendix Authors**

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