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Identification of imaging selection patterns in acute ischemic stroke patients and the influence on treatment and clinical trial enrollment decision making

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Abstract

Background and Purpose—The purpose of this study was to collect precise information on the typical imaging decisions given specific clinical acute stroke scenarios. Stroke centers

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worldwide were surveyed regarding typical imaging used to work up representative acute stroke patients, make treatment decisions, and willingness to enroll in clinical trials.

Methods—STroke Imaging Research and Virtual International Stroke Trials Archive-Imaging circulated an online survey of clinical case vignettes through its website, the websites of national professional societies from multiple countries as well as through email distribution lists from STroke Imaging Research and participating societies. Survey responders were asked to select the typical imaging work-up for each clinical vignette presented. Actual images were not presented to the survey responders. Instead, the survey then displayed several types of imaging findings offered by the imaging strategy, and the responders selected the appropriate therapy and whether to enroll into a clinical trial considering time from onset, clinical presentation, and imaging findings. A follow-up survey focusing on 6 h from onset was conducted after the release of the positive endovascular trials.

Results—We received 548 responses from 35 countries including 282 individual centers; 78% of the centers originating from Australia, Brazil, France, Germany, Spain, United Kingdom, and United States. The specific onset windows presented influenced the type of imaging work-up selected more than the clinical scenario. Magnetic Resonance Imaging usage (27–28%) was substantial, in particular for wake-up stroke. Following the release of the positive trials, selection of perfusion imaging significantly increased for imaging strategy.

Conclusions—Usage of vascular or perfusion imaging by Computed Tomography or Magnetic Resonance Imaging beyond just parenchymal imaging was the primary work-up (62–87%) across all clinical vignettes and time windows. Perfusion imaging with Computed Tomography or Magnetic Resonance Imaging was associated with increased probability of enrollment into clinical trials for 0–3 h. Following the release of the positive endovascular trials, selection of endovascular only treatment for 6 h increased across all clinical vignettes.

Keywords

Computed Tomography scan; clinical trial; ischemic stroke; Magnetic Resonance Imaging; stroke; thrombolysis

Introduction

The use of imaging in treatment and clinical trial enrollment decision-making has been well investigated.[1–11] The current recommended uses of imaging in stroke clinical trials were put forth in the Acute Stroke Imaging Research Roadmap II by the STroke Imaging Research (STIR) and Virtual International Stroke Trials Archive (VISTA)-Imaging groups.[12] Specifically, these uses outlined the selection of patients with imaging-confirmed diagnosis of stroke, selection of appropriate patients with treatment-relevant acute imaging target (TRAIT), and exclusion of patients based on imaging-defined futility of therapeutic intervention.[12] However, some multi center studies of acute stroke trial imaging practicalities suggest that the substantial enthusiasm to use Magnetic Resonance Imaging (MRI) including perfusion imaging in trials, and greater availability of MRI in stroke centers, is not matched by actual use in practice.[13,14]

To better inform trial design, more precise information regarding the clinician's preferences with respect to typical imaging of standard acute stroke patients as a function of clinical presentation across a spectrum of scenarios encountered in daily practice would be useful. We surveyed stroke centers worldwide to quantify the consistency of typical imaging selection in acute stroke treatment decisions and willingness to enroll into clinical trials. We attempted to understand the amount of consistency across centers when imaging-based definitions were applied. We included clinical vignettes with varying stroke severity and across multiple time windows to understand the impact of these factors in terms of selection of imaging work-up, treatment, and trial enrolment decisions. Multiple imaging modalities and typical findings were included in the survey to allow for specific imaging optimization for each clinical vignette. This has been previously studied; however, it has been limited as far as scope including the number of clinical scenarios considered, imaging protocols, and participating stroke centers.[15]

Our study attempted to collect data on imaging selection practices worldwide to identify some of the unresolved issues with these biomarkers.[12] These issues included the usage of MRI versus Computed Tomography (CT) on patient selection, the added value of vascular and perfusion imaging, the effect of additional imaging on treatment and enrollment rates, and whether imaging selection varied depending on the time window and clinical presentation.

Methods

STIR and VISTA circulated an online survey of clinical vignettes during the summer of 2014 through its website (https://stir.seton.org) and its email distribution list, through the websites and email distribution lists of national professional societies from multiple countries including Australia, Brazil, France, Germany, Italy, South Korea, Spain, United Kingdom, and United States (American Society of Neurology, British Society of Neuroradiology, European Stroke Organization, etc). The survey was distributed in preparation for and prior to the Thrombolysis and Thrombectomy in Acute Stroke Treatment meeting. The initial survey was conducted prior to the release of the positive results of the endovascular trials including MR CLEAN (a Multi center Randomized CLinical trial of Endovascular treatment for Acute ischemic stroke in the Netherlands).[16] We circulated using the same mechanisms described above a follow-up survey after the release of the positive endovascular trials[16] to understand the potential impact on treatment and enrollment rates.

The survey included 14 unique clinical vignettes covering up to 21 typical scenarios with varying imaging findings encountered in daily practice. Each clinical vignette displayed the patient's age, onset time window, a brief description of clinical symptoms, and the corresponding National Institutes of Health Stroke Scale (NIHSS) score. There were four clinical descriptions, linked to four stroke onset-to-presentation times, namely 0–3, 6, or 10 h or wake-up, save for two scenarios. The follow-up survey included the same four clinical descriptions at 6 h only. Table 1 contains the clinical scenarios descriptions. The responder was presented with all scenarios across the same time window before being presented with the next time window.

Responders were then asked what typical imaging they would request in a standard patient with the clinical description just displayed. Actual images were not presented to the survey responders. Responders were allowed to select as many imaging options as applicable across multiple modalities and parameters. The imaging options provided for each clinical vignette were: (a) CT non-contrast head; (b) Computed Tomography Angiography (CTA) head and neck; (c) CT perfusion; (d) Brain MR including Diffusion-Weighted Imaging (DWI), FLuid Attenuated Inversion Recovery (FLAIR), and Gradient Recalled Echo (GRE)/Susceptibility-Weighted Imaging (SWI), Magnetic Resonance Angiography (MRA) of the head; (e) Gadolinium (GAD) MRA of the aortic arch and cervical arteries, and/or (f). MR perfusion (Dynamic Susceptibility Contrast (DSC) or Arterial Spin Labeling (ASL)). Based on the specific imaging options selected, the corresponding modality specific imaging findings were displayed to the responder. If parenchymal imaging was selected, then the DWI lesion volume or CT Alberta Stroke Program Early CT Score (ASPECTS) was disclosed for MRI or CT, respectively. For time windows greater than 0–3 h, a possible subtle FLAIR abnormality in the imaging findings was also included. If vascular imaging was selected, then the location of the occlusion (Internal Carotid Artery (ICA), M1, M2, basilar, or no occlusion) was disclosed. If perfusion imaging was selected, then the size: large, small, or no penumbra including the penumbral volume, percent of the ischemic volume relative to the total perfusion deficit volume, total perfusion deficit volume, and specific penumbral location in case of basilar artery territory involvement were disclosed. All applicable imaging findings were displayed to the responder at once.

Responders were then asked the typical treatment they would administer in a standard patient with the imaging findings just displayed. Responders were asked to select only one option from the treatment options: (1) no revascularization therapy, (2) intravenous (IV) tPA alone, (3) endovascular/intra-arterial (IA) alone, or (4) IV tPA possibly followed by endovascular/IA. Next, responders were asked whether they would enroll this patient in an image-guided clinical trial comparing endovascular and/or IV tPA versus best medical therapy with yes or no options. Responders were not allowed to go back to change their answers to any clinical vignette questions. Therefore, after specific imaging findings were provided, the responders were not able to modify their treatment or clinical enrollment decisions for prior clinical vignettes. Responders were not required to answer all clinical vignettes, however, complete versus partial responses were tracked.

As many interested responders at each participating center were asked to answer the survey. At the end of the survey, responders were asked if they belonged to a stroke network, a collaborative group of stroke centers, and if so to specify, if the current work-up of their acute ischemic stroke patients used the imaging modality that they considered to be optimal or the imaging modality that is practical, as well as their specialty: stroke neurologist, i.e. medical specialty dealing with stroke, stroke physician, emergency physician, diagnostic neuroradiologist, interventionalist, and diagnostic and interventional neuroradiologist or other.

Unless noted otherwise for the majority of results presented in this study, only one response from each participating center was included. One response per center was included to weigh results equally across centers rather than to have results biased toward the highest

responding centers. If more than one response was provided by a center, then one response was selected from all complete responses across all specialties. The selection was performed in blinded fashion to the actual answers of the clinical vignettes. The survey software automatically tracked a status of “complete” or “partial” for each response based on whether the responder answered all of the clinical vignettes. If an individual center had both complete and partial responses, then the complete response was chosen. If more than one complete response per center was available, then just one was chosen blinded to the actual answers including specialty. Participating centers were asked to provide their site name and country with responder name as optional. In addition, all responses were automatically tracked by the survey software based on location parameters: city, state, country, and network location: internet protocol address. This tracking information was used as necessary to identify multiple responses from individual centers.

Nonparametric binomial tests were used to calculate significance of probability between responses with IBM SPSS Statistics Version 19.0.

Results

We received 548 responses from 35 countries including 282 individual centers; 78% of the centers originating from Australia, Brazil, France, Germany, Spain, United Kingdom, and United States. Specialty was not reported by 45% of the 548 responses. Of the remaining that reported specialty, stroke neurologists were the primary responders (39%) with the remaining responders by stroke physician (5%), emergency physician (1%), diagnostic neuroradiologist (4%), interventionalist (1%), diagnostic and interventional neuroradiologist (5%), and other (1%). Approximately 450 individuals were emailed and asked to respond to the surveys. The subsequent analyses were limited to one representative response from each of the 282 individual centers unless otherwise specified. Of the 282 responses, 56% were from neurologists, 24% were from the other six specialties, and 20% did not specify. The representative response rate by country is provided for both surveys (supplemental Table I). Of the 160 responders who answered the stroke network question, 49% reported yes to belonging to one whereas 51% reported no. Of the 201 responders who answered the optimal versus practical imaging modality usage, 44% indicated that they were using the optimal imaging modality whereas 56% indicated that they were using the practical imaging modality.

For the follow-up survey, we received 202 responses from 22 countries including 119 individual centers: 73% of the centers originating from Australia, France, Germany, Japan, The Netherlands, South Korea, United Kingdom, and United States. In comparison with the original survey, 76% of the same centers responded to the follow-up survey. Of the 119 responses, 60% were from neurologists, 28% were from the other six specialties, and 12% did not specify.

Table 1 contains the breakdown of CT versus MRI selection across the four clinical scenarios and time windows. The majority of responders (65–71%) selected CT rather than MRI across all clinical scenarios in the 0 - to 3-h time window ($p < 0.0001$). The selection of MRI was substantial in the time windows of 6 h, 10 h, and wake-up stroke, especially if the

CT followed by MRI option is accounted for, even within the 0–3 window. For wake-up stroke, the selection of MRI or combination CT and MRI (56–59%) was higher than CT only selection (41–44%, p=0.030, 0.008 for clinical scenarios #1 and #4). Responders selected both CT and MRI for the imaging strategy rather than just one modality (21–31%). Overall, the specific onset windows influenced the type of imaging work-up selected more than the clinical scenario. For the follow-up survey of 6 h, the imaging strategy did not change substantially across clinical scenarios, but there was a minor trend for increased MRI only selection (2–6%).

Table 2 reports the specific selections of parenchymal, vascular, and perfusion imaging using either CT or MRI across the four clinical scenarios and time windows. Usage of perfusion imaging increased with time window across the majority of clinical scenarios except at 10 h, reaching a maximum with wake-up stroke (49–59%, p=0.010 for wake-up). Vascular imaging was consistently highest (32–38%) at 0–3 h across all clinical scenarios compared with the other time windows. The follow-up survey for 6 h demonstrated an increase (7–13%) in the selection of perfusion imaging (CT or MRI) and a decrease (5–11%) in parenchymal only imaging (CT or MRI) across all clinical scenarios.

Tables 3 and 4 contain the treatment decisions across clinical scenarios and time windows. For scenarios with no penumbra, small penumbra or normal perfusion, no treatment was the major selection (37–67%). No treatment was also the primary selection at 10 h for large and small penumbra scenarios (54–71%). For 0- to 3-h time window, combination therapy (IV tPA possibly followed by endovascular/IA) dominated the clinical scenarios with large penumbra (59–67%). In contrast for the scenarios with M2 occlusion with small penumbra (42%) or no vascular occlusion and normal perfusion (38%), IV only dominated in 0–3 h but did not reach 100%. Endovascular treatment dominated at 6 h for scenarios with large penumbra and basilar artery occlusion (35–39%). For wake-up stroke, none (46%) dominated for small penumbra. The follow-up survey results for 6 h demonstrated an increase in endovascular only treatment (6–15%, p=0.01 for clinical scenarios #1 (large penumbra, M1), #2 (small penumbra, M1), and #3 (small penumbra, M2)).

In comparison, supplemental Tables II and III contain the treatment decisions when using CT only selections including just non-contrast or multiparametric. For responses where CT only was used for imaging, treatment selection did not vary compared with results reported in Tables 3 and 4. The follow-up survey results for 6 h reflected an increase in endovascular only treatment (4–21%, $p < 0.001$ for clinical scenario #2 (small penumbra, M1)). In supplemental Tables IV and V where MRI only was used, endovascular treatment (48%) did dominate at 6 h for scenarios with large penumbra in contrast to CT only decisions. Also, in wake-up stroke with large penumbra using MRI, combination treatment dominated (45%) with endovascular still as the primary treatment for basilar artery occlusion (48%). Contrary to CT only, MRI only selection yielded minimal to no increase in the endovascular only treatment with one exception, an 11% increase for clinical scenario #3 (small penumbra, M2).

Supplemental Tables VI and VII summarize the treatment decisions when perfusion imaging using CT or MRI was included. The selection of combination treatment for large penumbra

increased when using perfusion imaging in 0–3 h whether using CT or MRI. Usage of perfusion imaging (CT or MRI) yielded various results with the follow-up survey for endovascular only treatment selection with the only significant increase of 13% for clinical scenario #3 (small penumbra, M2, $p < 0.01$). For the scenarios with small infarct, IV only treatment dominated in 0–3 h for parenchymal only imaging decisions; however, selection of combination therapy dominated once vascular or perfusion imaging was included. None was the major treatment selection at 6 h (50–98%) across all clinical scenarios when using parenchymal only imaging. Once perfusion imaging was added, endovascular therapy dominated for large penumbra and basilar artery occlusion scenarios (50–61%). For parenchymal only imaging decisions, endovascular only treatment decisions for 6 h increased significantly (6–17%) across clinical scenarios #1, #2 with small infarct, $p < 0.001$, and #4 with hemiparesis, $p < 0.001$.

No treatment was the exclusive selection at 10 h for scenarios when parenchymal only imaging was used. Once vascular or perfusion imaging was selected, endovascular therapy was selected for basilar artery occlusion (28–69%). Similarly for wake-up stroke, parenchymal only imaging lead to none as the primary treatment selection. Once vascular and perfusion imaging was added, endovascular only (7–58%) and combination therapy (7–41%) increased. With the follow-up survey results for 6 h when vascular imaging was added, endovascular only (16–32%) decisions increased even further across all scenarios, in particular, for small infarct clinical scenarios #1 (M1, $p<0.01$; ICA, $p<0.001$), #2 ($p<0.01$), #3 (M1, $p<0.0001$), and basilar artery occlusion clinical scenario #4 ($p<0.0001$). Treatment decisions when using parenchymal only, and parenchymal and vascular using CT or MRI are summarized in supplemental Tables VIII, IX, X, and XI. As noted in the table heads, for the basilar artery occlusion scenario (#4), if parenchymal imaging only using either CT or MRI was selected, then it was not actually known to be a basilar artery occlusion.

Table 5 breaks down the clinical trial enrollment decisions across clinical scenario and time window. Positive enrollment rate was highest for ICA/M1 occlusion with large penumbra (58–66%) for 0–3 h. There was still willingness (50–55%) to enroll for this scenario at 6 h and wake-up. Equipoise was demonstrated consistently for M1/small penumbra, normal perfusion, and basilar artery occlusion scenarios across all time windows except at 10 h. At 10 h, rates were reduced further, demonstrating unwillingness to enroll in this time window. For the follow-up survey of 6 h, willingness to enroll across small penumbra scenarios increased (10–23%, $p < 0.001$ for clinical scenario #3 (small penumbra, M2)).

In comparison, supplemental Tables XII and XIII contain the clinical trial enrollment decisions when using CT only or MRI only selections. In supplemental Table XII, positive enrollment rates across time windows were consistent with the results reported in Table 5. However, in supplemental Table XIII, for responses where MRI only was used for imaging, positive enrollment rates across all time windows were higher except at 10 h and for basilar artery occlusion scenarios across all time windows. There was 100% agreement to not to enroll normal perfusion cases when using MRI only for clinical scenario #3.

For comparison with Table 5, supplemental Tables XIV and XV contain the clinical trial enrollment decisions when using parenchymal only, and parenchymal and vascular imaging

using CT or MRI. The enrollment decisions were comparable with those summarized in Table 5. However, Table 6 contains the clinical trial enrollment decisions including perfusion imaging using CT or MRI. Similar to MRI only based decisions, positive enrollment rates across all time windows were higher for perfusion imaging-based decisions. Positive enrollment rates were maximized (53–79%) for wake-up stroke across all scenarios when perfusion imaging was required. For the follow-up survey of 6 h, willingness to enroll across large penumbra scenarios decreased significantly (24–30%, $p < 0.001$) when perfusion imaging (CT or MRI) was selected. Conversely, there was a significant increase in willingness to enroll in clinical scenario #3 (M2, small penumbra) (18%, $p < 0.01$).

Discussion

One response per center was included to weigh results equally across centers rather than have results biased toward the highest responding centers. However, to illustrate the differences between all responses and individual responses, the percentages are reported for 282 (versus range of all 548) centers below.

The typical imaging modality selected was CT in making treatment decisions across all clinical vignettes and time windows. For instance, imaging strategy varied for 0–3 h versus all the other time windows. MRI selection, or CT followed by MRI, was substantial, nearly 50% (48–58%) for the 6-h window regardless of the clinical scenario. This trend for MRI selection increased slightly following the release of the positive endovascular trials. Even for the 0- to 3-h window, it was approximately 30% (27–36%). MRI only usage (27–28% (31–32%)) was substantial for wake-up stroke. The design of future image-guided trials in wake-up stroke should consider MRI-based imaging protocols when dependent TRAITs are required.[12]

The specific onset windows presented influenced the type of imaging work-up selected more than the clinical scenarios. This is probably due to the trend of multiparametric imaging being selected regardless of clinical scenario. Usage of vascular or perfusion imaging by CT or MRI beyond just parenchymal imaging was the primary work-up (62–87% (70–90%)) across all clinical vignettes and time windows. For the clinical scenarios of small infarct and large penumbra, 59–67% (56–67%) of responders selected IV tPA possibly followed by endovascular. When selecting IV tPA, 75% (64–67%) of these responders selected vascular or perfusion imaging in the 0- to 3-h window to make the treatment decision. Likewise for the clinical scenarios without early improvement, with small infarct and small penumbra, 42–54% (34–47%) of responders selected IV tPA alone. When selecting IV tPA alone, 81% (78%) of these responders selected vascular or perfusion imaging, in the 0- to 3-h window. There was an increase in selection of endovascular only treatment at 6 h following the release of the endovascular trials but specific to large penumbra, M1 occlusion or small penumbra, M1 or M2 occlusion. However, at 10 h, the majority of responders (54–71% (64–86%)) chose not to treat except in the case of basilar artery occlusion. The majority of these responders (62–63% (61–63%)) still selected multiparametric imaging when making the treatment decisions.

Perfusion imaging with CT or MRI was associated with increased probability of enrollment into clinical trials across 0–3 and 6 h. More than 2/3 responders would enroll patients with treatable penumbra into an image-guided clinical trial comparing endovascular (± IV tPA) versus IV tPA alone when perfusion imaging was selected. Compared with perfusion imaging with CT or MRI, selection of MRI only including parenchymal, vascular, or perfusion imaging was associated with comparable enrollment rates into clinical trials across 0–3 and 6 h. Further with the release of the positive endovascular trials, the selection of perfusion imaging increased at 6 h with a decrease in parenchymal only imaging. This suggests an overall willingness to utilize multiparametric CT or MRI when enrolling patients, in particular, small penumbra cases that need further investigation for promising therapies.

There are limitations to the survey and the results generated. Even though the survey was emailed indistinctly to unselected member listings of professional societies worldwide, the responders did not fully represent the medical community involved in acute stroke imaging work-up decisions. For instance, the majority of responders were neurologists, which is not representative of all the specialties. Furthermore, the majority of results (78%) were from seven countries limiting the generality of the findings. Although we tried to reach as wide a range of centers as possible with the survey, the responders are likely to represent enthusiasts and academic centers, and, therefore, may not reflect more common approaches to imaging or treatment decisions in stroke in non-expert or less interested centers. Further when centers are actively enrolling into clinical trials, the default imaging protocols are likely comprehensive already. In addition, imaging selections were potentially biased due to known efficacy of treatments, rather than imaging selections guiding these decisions. For instance, the initial survey was conducted prior to the release of the positive results of the endovascular trials including MR CLEAN. Given the positive results of these trials, the responses to the treatment decisions posed in the survey for the onset time window of 6 h were expected to change, and as a result, a follow-up survey was conducted. The majority of responses (76%) from the follow-up survey were from the same centers as the initial survey. However, responders were not required to enter their individual name in the survey and the majority did not. Therefore, it was not feasible to link and compare responses from individuals for the two surveys. Furthermore, there were still some geographical differences and a smaller response rate in the follow-up survey, potentially limiting the global representation of the results. The scope of the survey was limited to acute treatment and clinical trial enrollment decisions and did not address secondary prevention practices.

In conclusion, usage of vascular or perfusion imaging by CT or MRI beyond just parenchymal imaging was the primary work-up across all clinical vignettes and time windows. MRI usage was substantial, in particular, for wake-up stroke. Following the release of the positive trials, selection of perfusion imaging significantly increased for imaging strategy. Selection of endovascular only treatment for 6 h increased across all clinical vignettes, in response to the positive results of the endovascular trials. To conclude, the results from these surveys are intended to serve in the design of future image-guided trials.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

CT versus MRI selection across clinical scenarios and time windows

	Clinical scenario #1: Patient is 65 years old Altered level of consciousness, aphasia, dense right hemiplegia with sensory deficit NIHSS of 21			Clinical scenario #2: Patient is 65 years old Altered level of consciousness, aphasia, dense right hemiplegia with sensory deficit NIHSS of 21 with early improvement to 5			Clinical scenario #3: Patient is 65 years old Facial weakness, mild limb weakness NIHSS of 5			Clinical scenario #4: Patient is 65 years old Facial weakness, hemiparesis NIHSS of 10		
	CT	**MRI**	**CT and MRI**	**CT**	**MRI**	**CT and MRI**	**CT**	**MRI**	**CT and MRI**	**CT**	**MRI**	**CT and MRI**
0–3 h	71% (575)	8% (65)	21% (167)	67% (170)	10% (24)	23% (58)	65% (357)	9% (52)	26% (141)	68% (166)	9% (21)	23% (55)
6 h	55% (387)	19% (136)	26% (184)	55% (129)	19% (45)	25% (59)	51% (197)	24% (92)	25% (99)	54% (125)	19% (45)	27% (61)
6-h post ET	53% (173)	21 % (68)	26% (87)	50% (53)	25% (26)	25% (27)	45% (87)	26% (51)	29% (56)	49% (51)	25% (26)	26% (29)
10 h	58% (133)	18% (42)	24% (56)	Scenario not surveyed at this time window			58% (133)	20% (45)	22% (51)	55% (128)	19% (43)	26% (60)
Wake-up	43% (98)	27% (62)	30% (70)	Scenario not surveyed at this time window			44% (100)	27% (63)	29% (66)	41% (93)	28% (63)	31% (70)

CT: Computed Tomography; MRI: Magnetic Resonance Imaging; NIHSS: National Institutes of Health Stroke Scale.

Table 2

Parenchymal, vascular, and perfusion imaging selection using either CT or MRI across clinical scenarios and time windows

	Clinical scenario #1: Patient is 65 years old Altered level of consciousness, aphasia, dense right hemiplegia with sensory deficit NIHSS of 21			Clinical scenario #2: Patient is 65 years old Altered level of consciousness, aphasia, dense right hemiplegia with sensory deficit NIHSS of 21 with early improvement to 5			Clinical scenario #3: Patient is 65 years old Facial weakness, mild limb weakness NIHSS of 5			Clinical scenario #4: Patient is 65 years old Facial weakness, hemiparesis NIHSS of 10		
	Parenchymal	**Vascular**	**Perfusion**	**Parenchymal**	**Vascular**	**Perfusion**	**Parenchymal**	**Vascular**	**Perfusion**	**Parenchymal**	**Vascular**	**Perfusion**
0–3 h	25% (203)	37% (299)	38% (305)	21% (53)	37% (92)	42% (107)	19% (102)	38% (210)	43% (238)	28% (68)	32% (77)	40% (97)
6 h	19% (138)	23% (160)	56% (394)	18% (43)	28% (64)	54% (126)	19% (74)	28% (110)	53% (238)	19% (44)	27% (62)	54% (126)
6-h post ET	12% (38)	25% (83)	63% (207)	11% (12)	22% (23)	67% (71)	10% (19)	26% (50)	64% (125)	8% (9)	25% (26)	67% (71)
10 h	37% (85)	24% (55)	39% (91)	Scenario not surveyed at this time window			38% (88)	28% (63)	34% (78)	32% (73)	29% (68)	39% (89)
Wake-up	15.5% (36)	25.5% (59)	59% (135)	Scenario not surveyed at this time window			27% (62)	24% (55)	49% (112)	18% (42)	24% (54)	58% (131)

CT: Computed Tomography; ET: Endovascular Trial; MRI: Magnetic Resonance Imaging; NIHSS: National Institutes of Health Stroke Scale.

Table 3

Treatment decisions across clinical scenario #1 and time windows

	Clinical scenario #1: M1 occlusion, small infarct, large penumbra					Clinical scenario #1: ICA occlusion, small infarct, large penumbra					Clinical scenario #1: M1 occlusion, large infarct, no penumbra				
	None	**IV only**	**Endo only**	**IV plus possible endo (combo)**	**No response**	**None**	**IV only**	**Endo only**	**IV plus possible endo (combo)**	**No response**	**None**	**IV only**	**Endo only**	**IV plus possible endo (combo)**	**No response**
0–3 h	0% (0)	28% (79)	2% (7)	67% (190)	2% (6)	<1% (1)	27% (76)	7% (21)	59% (166)	6% (18)	24% (68)	32% (91)	5% (13)	30% (85)	9% (25)
6 h	26% (74)	2% (7)	35% (98)	20% (56)	17% (47)	26% (74)	4% (10)	38% (108)	14% (40)	18% (50)	67% (190)	1% (4)	10% (28)	4% (12)	17% (48)
6-h post ET	18% (22)	1% (1)	50% (59)	23% (27)	8% (10)	26% (31)	0% (0)	47% (56)	18% (21)	9% (11)	68% (81)	3% (3)	13% (15)	7% (8)	10% (12)
10 h	54% (152)	1% (3)	22% (62)	5% (13)	18% (52)	Scenario not surveyed at this time window					Scenario not surveyed at this time window				
Wake-up	20% (57)	10% (27)	24% (69)	26% (73)	20% (56)	Scenario not surveyed at this time window					Scenario not surveyed at this time window				

Table 4

Treatment decisions across clinical scenarios #2–4 and time windows

	Clinical scenario #2: M1 occlusion, small infarct, small penumbra					Clinical scenario 3: M1 occlusion, small infarct, small penumbra					Clinical scenario #3: M2 occlusion, small infarct, small penumbra					Clinical scenario #3: No occlusion, small infarct, normal perfusion					Clinical scenario #4: Basilar occlusion				
	None	**IV only**	**Endo only**	**IV plus possible endo (combo)**	**No response**	**None**	**IV only**	**Endo only**	**IV plus possible endo (combo)**	**No response**	**None**	**IV only**	**Endo only**	**IV plus possible endo (combo)**	**No response**	**None**	**IV only**	**Endo only**	**IV plus possible endo (combo)**	**No response**	**None**	**IV only**	**Endo only**	**IV plus possible endo (combo)**	**No response**
0–3 h	6% (16)	38% (106)	2% (6)	44% (124)	11% (30)	4% (11)	54% (151)	1% (4)	29% (81)	12% (35)	1% (2)	42% (118)	1% (2)	11% (30)	46% (130)	14% (39)	38% (108)	<1% (1)	1% (2)	47% (132)	<1% (1)	22% (62)	7% (20)	56% (157)	15% (42)
6 h	41% (115)	7% (20)	24% (68)	10% (28)	18% (51)	51% (143)	6% (18)	17% (48)	8% (22)	18% (51)	37% (104)	12% (33)	6% (16)	2% (5)	44% (124)	Scenario not surveyed at this time window					18% (51)	1% (3)	39% (109)	24% (69)	18% (50)
6-h post ET	31% (37)	3% (3)	39% (46)	17% (20)	11% (13)	45% (53)	3% (4)	27% (32)	14% (17)	11% (13)	38% (46)	11% (13)	17% (20)	8% (9)	26% (31)	Scenario not surveyed at this time window					13% (15)	2% (2)	45% (54)	28% (34)	12% (14)
10 h	Scenario not surveyed at this time window					71% (199)	2% (7)	7% (19)	2% (5)	18% (52)	Scenario not surveyed at this time window					Scenario not surveyed at this time window					35% (98)	1% (2)	36% (101)	10% (29)	18% (52)
Wake-up	Scenario not surveyed at this time window					46% (130)	11% (32)	10% (29)	11% (32)	21% (59)	Scenario not surveyed at this time window					Scenario not surveyed at this time window					19% (53)	4% (10)	36% (101)	22% (62)	20% (56)

Table 5

Clinical trial enrollment decisions across clinical scenarios and time window

	Clinical scenario #1: M1 occlusion, small infarct, large penumbra			Clinical scenario #1: ICA occlusion, small infarct, large penumbra			Clinical scenario #1: M1 occlusion, large infarct, no penumbra			Clinical scenario #2: M1 occlusion, small infarct, small penumbra			Clinical scenario #3: M1 occlusion, small infarct, small penumbra			Clinical scenario #3: M2 occlusion, small infarct, small penumbra			Clinical scenario #3: No occlusion, small infarct, normal perfusion			Clinical scenario #4: Basilar occlusion		
	Yes	**No**	**No response**	**Yes**	**No**	**No response**	**Yes**	**No**	**No response**	**Yes**	**No**	**No response**	**Yes**	**No**	**No response**	**Yes**	**No**	**No response**	**Yes**	**No**	**No response**	**Yes**	**No**	**No response**
0–3 h	66% (187)	31% (88)	3% (7)	58% (163)	35% (100)	7% (19)	37% (104)	54% (152)	9% (26)	47% (132)	41% (117)	12% (33)	37% (106)	50% (140)	13% (36)	17% (49)	37% (103)	46% (130)	3% (10)	50% (140)	47% (132)	43% (121)	42% (118)	15% (43)
6 h	55% (156)	29% (82)	16% (44)	50% (141)	33% (93)	17% (48)	25% (69)	58% (164)	17% (49)	42% (119)	40% (113)	18% (50)	39% (109)	43% (121)	18% (52)	22% (61)	34% (96)	44% (125)	Scenario not surveyed at this time window			37% (106)	45% (126)	18% (50)
6-h post ET	50% (59)	41% (49)	9% (11)	48% (57)	41% (49)	11% (13)	34% (41)	54% (64)	12% (14)	52% (62)	35% (42)	13% (15)	49% (58)	38% (46)	13% (15)	45% (54)	27% (32)	28% (33)	Scenario not surveyed at this time window			44% (53)	43% (51)	13% (15)
10 h	35% (100)	46% (129)	19% (53)	Scenario not surveyed at this time window			Scenario not surveyed at this time window			Scenario not surveyed at this time window			24% (69)	57% (160)	19% (53)	Scenario not surveyed at this time window			Scenario not surveyed at this time window			32% (91)	49% (139)	19% (52)
Wake-up	56% (158)	25% (70)	19% (54)	Scenario not surveyed at this time window			Scenario not surveyed at this time window			Scenario not surveyed at this time window			39% (110)	41% (116)	20% (56)	Scenario not surveyed at this time window			Scenario not surveyed at this time window			40% (114)	40% (112)	20% (56)

Table 6

Clinical trial enrollment decisions across clinical scenario and time window including perfusion imaging selections using CT or MRI

	Clinical scenario #1: M1 occlusion, small infarct, large penumbra		**Clinical scenario #1: ICA occlusion, small infarct, large penumbra**		**Clinical scenario #1: M1 occlusion, large infarct, no penumbra**		**Clinical scenario #2: M1 occlusion, small infarct, small penumbra**		**Clinical scenario #3: M1 occlusion, small infarct, small penumbra**		**Clinical scenario #3: M2 occlusion, small infarct, small penumbra**		**Clinical scenario #3: No occlusion, small infarct, normal perfusion**		**Clinical scenario #4: Basilar occlusion**	
	Yes	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**
0–3 h	76% (76)	24% (24)	67% (68)	33% (34)	33% (33)	67% (67)	58% (61)	42% (44)	58% (46)	42% (33)	39% (31)	61% (49)	5% (4)	95% (74)	48% (46)	52% (49)
6 h	78% (102)	22% (29)	72% (93)	28% (37)	27% (36)	73% (95)	59% (74)	41% (51)	61% (62)	39% (39)	45% (45)	55% (56)	Scenario not surveyed at this time window		50% (63)	50% (63)
6-h post ET	48% (32)	52% (34)	48% (32)	52% (35)	32% (22)	68% (47)	59% (41)	41% (29)	54% (33)	46% (28)	63% (40)	37% (23)	Scenario not surveyed at this time window		49% (34)	51% (36)
10 h	65% (59)	35% (32)	Scenario not surveyed at this time window		Scenario not surveyed at this time window		Scenario not surveyed at this time window		51% (40)	49% (38)	Scenario not surveyed at this time window		Scenario not surveyed at this time window		49% (44)	51% (45)
Wake-up	79% (107)	21% (28)	Scenario not surveyed at this time window		Scenario not surveyed at this time window		Scenario not surveyed at this time window		60% (67)	40% (44)	Scenario not surveyed at this time window		Scenario not surveyed at this time window		53% (70)	47% (61)

CT: Computed Tomography; MRI: Magnetic Resonance Imaging.