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International survey of acute Stroke imaging used to make revascularization treatment decisions

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site.

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Abstract

Background—To assess the differences across continental regions in terms of stroke imaging obtained for making acute revascularization therapy decisions, and to identify obstacles to participating in randomized trials involving multimodal imaging.

Methods—Stroke Imaging Repository (STIR) and Virtual International Stroke Trials Archive (VISTA)-Imaging circulated an online survey through its website, through the websites of national professional societies from multiple countries as well as through email distribution lists from STIR and the above mentioned societies.

Results—We received responses from 223 centers (2 from Africa, 38 from Asia, 10 from Australia, 101 from Europe, 4 from Middle East, 55 from North America, 13 from South America). In combination, the sites surveyed administered acute revascularization therapy to a total of 25 326 acute stroke patients in 2012. Seventy-three percent of these patients received intravenous (IV) tissue plasminogen activator (tPA), and 27%, endovascular therapy. Vascular imaging was routinely obtained in 79% (152/193) of sites for endovascular therapy decisions, and also as part of standard IV tPA treatment decisions at 46% (92/198) of sites. Modality, availability and use of acute vascular and perfusion imaging before revascularization varied substantially between geographical areas. The main obstacles to participate in randomized trials involving multimodal imaging included: mainly insufficient research support and staff (50%, 79/158) and infrequent use of multimodal imaging (27%, 43/158).

Conclusion—There were significant variations among sites and geographical areas in terms of stroke imaging work-up used to make decisions both for intravenous and endovascular revascularization. Clinical trials using advanced imaging as a selection tool for acute revascularization therapy should address the need for additional resources and technical support, and take into consideration the lack of routine use of such techniques in trial planning.

Keywords

CT; MRI; penumbra; perfusion imaging; stroke; vascular imaging

Introduction

In their second Research Roadmap (1), the Stroke Imaging Research (STIR) and Virtual International Stroke Trials Archive (VISTA)-Imaging groups recommended the creation and implementation of a stroke neuroimaging network that will facilitate the use of advanced neuroimaging-based studies in large stroke clinical trials. As a first step towards this goal, STIR and VISTA-Imaging identified the need to track the imaging work-up used to make acute revascularization therapy decisions at potential participating centers, including the ability to do acute CT, CTA, MRI, MRA, perfusion imaging as well as the number of acute

stroke patients seen per year. Having this information readily available would provide a mechanism for identifying potential centers that are capable of integrating advanced imaging into stroke clinical trials and to participate in multicenter studies of standardizing, testing and validating multimodal imaging to assess clot, ischemic core, ischemic penumbra and collaterals. In the spirit of this STIR recommendation, we conducted an international survey to assess the differences across continental regions in terms of stroke imaging work-up used for making acute revascularization therapy decisions.

Methods

STIR circulated an online survey through its website (<https://stir.seton.org>) and its email distribution list, through editorials in *Stroke* and in the *American Journal of Neuroradiology*, as well as through the websites and email distribution list of national professional societies (American Society of Neurology, Canadian Stroke Consortium, European Stroke Organization, European Society of Neuroradiology, European Society of Minimally Invasive Neurological Therapy, British Society of Neuroradiology, Association of British Neurologists, UK Stroke Forum, British Association of Stroke Physicians, Brazilian Stroke Network, Mexican Stroke Association, Japan Stroke Society, Swiss Stroke Society, Israel Stroke Society Australasian/New Zealand Stroke Trials Network, Chinese Stroke Society) from multiple countries.

The survey, <https://www.surveymonkey.com/s/VY9GJBG>, asked for one responder at each participating institution to provide general contact information about their center, information about the number of stroke patients they treated with revascularization therapy in 2012, for the number of stroke patients who received intravenous (IV) recombinant tissue plasminogen activator (tPA) and/or endovascular revascularization, with specific details asked about the tPA therapeutic time window used and the number of endovascular treatments of posterior fossa arterial occlusions. Each site was asked whether or not they were logistically equipped to perform MRI in hyperacute stroke patients prior to revascularization therapy. They were asked about whether they obtained vascular imaging and/or perfusion imaging as part of the routine for stroke patients, and how they use the resulting information including core and penumbra estimations for treatment decisions. They were asked about their typical follow-up imaging of stroke patients. Finally, each site was asked specific details on their imaging scanners including the mechanism to archive and blind images, how many acute stroke treatment clinical trials they were currently involved and involved in the last five-years, type of institutional review board (IRB) and also what their main obstacles were to participate in randomized acute stroke treatment trials involving multimodal imaging.

Results

The survey was distributed to colleagues from a total of approximately 1000 institutions, and we sent an initial request by email followed by three reminders. We received responses from 223 centers, corresponding to a response rate of 20–25% (2 from Africa, 38 from Asia, 10 from Australia, 101 from Europe, 4 from the Middle East, 55 from North America, 13 from

South America). The database containing all survey results is available at STIR and can be made available upon request to investigators planning their clinical trials.

In combination, the sites surveyed administered acute revascularization therapy to a total of 25 326 acute stroke patients in 2012 (0 in Africa, 2602 in Asia, 585 in Australia, 14 895 in Europe, 217 in the Middle East, 6654 in North America, 373 in South America). Seventy-three percent of these patients received intravenous tPA (29% in Asia, 87% in Australia, 79% in Europe, 68% in the Middle East, 74% in North America, 81% in South America), and 27% endovascular therapy (71% in Asia, 13% in Australia, 21% in Europe, 32% in the Middle East, 26% in North America, 19% in South America). Twenty percent of the endovascular treatments targeted posterior fossa arterial clots (24% in Asia, 26% in Australia, 20% in Europe, 12% in the Middle East, 15% in North America, 21% in South America). Standard therapeutic time window for intravenous tPA administration was <3 h at 7% of the sites and <4.5 h at 96% of the sites (which included the 7% of sites using a <3 h time window). Four percent of the sites administered intravenous tPA beyond 4.5 h in selected patients. Standard time window for endovascular therapy was <8 h at 93% of the sites and <9 h at 95% of the sites (which included the 93% of sites using a <8-h time window). Five percent of the sites performed endovascular therapy beyond nine-hours in selected patients.

CT is the primary routine modality for acute stroke imaging work-up prior to endovascular therapy, except in Asia where MRI predominates (Fig. S1). Seventy-two percent (139/192) of the sites indicated that they are equipped to perform hyperacute MRIs (Fig. S2).

Vascular imaging is routinely obtained as part of the routine imaging work-up of acute stroke patients before IV thrombolysis and endovascular therapy decisions in 46% and 79%, respectively of sites (Figs. S3 and S4). CTA is routinely obtained as part of the routine imaging work-up in 60% (115/193) of sites, with the remaining vascular imaging consisting of MRA. Perfusion CT imaging is routinely performed as part of standard of care for stroke patients in 34% (66/193) of sites while PWI (dynamic susceptibility contrast DSC) MR imaging and arterial spin labeling (ASL) imaging are performed in 19% (37/193) and 11% (21/193), respectively of sites (Fig. S5).

Ischemic core and ischemic penumbra assessments are used at 35% (68/197) (Fig. S6) and 16% (31/198) (Fig. S7), respectively, of sites for IV tPA treatment decisions. Ischemic core and ischemic penumbra assessments are used at 53% (103/193) (Fig. S8) and 39% (75/193) (Fig. S9), respectively, of sites for standard endovascular therapy decisions.

Typical routine follow-up imaging in stroke patients is obtained at 24 h at 38% (78/203) of sites, 48–72 h at 27% (54/203) of sites, three- to five-days at 20% (40/203) of sites, at discharge at 6% (12/203) of sites, 30 days at 3% (7/203) of sites and 90 days at 6% (12/203) of sites (Table 1). This information is relevant to predict likely adherence to imaging protocols in clinical trials based on the follow-up visit requirements.

On average, each site was involved in 4 acute stroke treatment clinical trials over the last five-years (Asia: 2, Australia: 5, Europe: 5, Middle East: 2, North America: 7, South America: 1). At the time of the survey, each site was involved in 2 ongoing acute stroke

treatment clinical trials (Asia: 2, Australia: 4, Europe: 2, Middle East: 1, North America: 3, South America: 0). The main obstacles to participate in randomized acute stroke treatment trials involving multimodal imaging included: insufficient research support and staff (50%, 79/158), infrequent use of multimodal imaging (27%, 43/158), poor collaboration between different subspecialties which is 12% (19/158) and lack of equipoise (11%, 17/158), in decreasing order of frequency (Fig. S10).

Discussion

The necessary imaging work-up of acute ischemic stroke patients prior to making revascularization treatment decisions is still very much debated. Some advocate for the minimal imaging possible, typically a plain noncontrast head CT, in order to minimize the time from symptom onset to treatment, while others recommend a more comprehensive imaging work-up in order to select patients more likely to respond favorably to treatment and exclude those likely to develop treatment complications. The proposed imaging work-up includes variable combinations of vascular, core and/or penumbral imaging. Two recent trials (DIAS 2 (2) and MR RESCUE) (3) using such imaging selection approaches failed, but one even more recent trial (MR CLEAN) (4) had positive results, reinforcing the need to investigate the optimal imaging work-up for stroke patients, including the optimal modality (CT vs. MRI). The goal of this survey was to establish a lay of the land of how sites currently image their acute stroke patients, with the next goal being to engage these sites in clinical trials comparing different acute stroke imaging work-ups.

The imaging work-up of patients suspected of acute ischemic stroke and how this imaging is used to make treatment decisions vary considerably from site to site and across geographical regions. CT is the mainstay for the imaging work-up of acute stroke patients prior to endovascular therapy at many sites, except in Asia, where MRI is the first line imaging modality at many sites. More than two thirds of the sites indicated that they have the capability of performing MRI in the hyperacute setting, prior to a revascularization therapy decision. However, if CT remains the routine imaging modality for stroke patients at these sites, it is likely because using MRI as the first line of imaging for patients requires an organization, logistics and resources that go beyond having an MRI scanner open 24/7. Indeed, in order for an MRI work-up not to delay treatment decisions, an efficient process to screen patients for their ability to undergo an MRI, a prioritization system for patients scheduled to undergo MRI, a physical proximity of the MRI scanners to the emergency room, and an excess MRI scanning capacity able to accommodate unscheduled patients at all hours of day or night are required to offer hyperacute MRI screening of patients suspected of acute ischemic stroke.

Information extracted from vascular imaging is used at a majority of sites prior to and in order to make endovascular therapy decisions. Interestingly, vascular imaging is also very frequently obtained before and used for intravenous tPA decisions in Asia, Australia, Europe and the Middle East. This finding may reflect a selection bias and be explained by the fact that the sites that took the survey are likely academically orientated, as illustrated by the large number of acute stroke treatment clinical trials these sites are involved in. As a reminder, current guidelines for tPA administration only require a noncontrast head CT to

rule out intracranial hemorrhage and assess the extent of acute cerebral ischemic changes (5,6).

Another interesting observation from the survey was the mismatch between the large number of acute stroke patients receiving acute revascularization therapy at the sites surveyed (25 326 treated patients for 223 sites) and the known difficulties in enrolling stroke patients in clinical trials, reflected by the typical long duration or interruption of acute stroke treatment trials. A number of explanations exist for this mismatch, including the heterogeneity of stroke (7). From an imaging perspective, the main obstacle to participate in randomized acute stroke treatment trials involving multimodal imaging related to insufficient research support and staff, in line with previous similar reports (7). Infrequent use of multimodal imaging was also mentioned, describing the difficulty at a site becoming proficient at a certain imaging technique if they do not get to practice this technique on a routine basis. As mentioned above, performing hyperacute MRI or perfusion-CT in a fashion that does not delay treatment decisions requires more than having an MRI or CT scanner open 24/7. MRI and CT technologists need to be trained, including those working night and weekend shifts. Processes need to be implemented to deal with contrast issues and MRI screening, and to coordinate the timing of imaging with the clinical care and the treatment decisions.

As a limitation to our survey/study, we want to acknowledge that the numbers of survey answers is small compared to the number of sites surveyed (only 20–25% responders) and the total number of sites treating stroke patients. Our sample is definitely biased in favor of sites that are very active in terms of stroke imaging work-up, and the number report likely overestimate the proportion of sites using vascular and/or tissue viability imaging routinely for the acute assessment of their stroke patients.

In conclusion, the imaging work-up for stroke patients and how it is used to make acute revascularization decisions vary from site to site, and is usually based on individual site preferences rather than evidence-based guidelines. Clinical trials are required to better understand the role of different imaging modalities as a selection tool for acute revascularization therapy. Acute stroke treatment trials involving multimodal imaging require appropriate support and resources for the implementation of these imaging techniques. Also, sites need to practice these techniques on a routine basis in order for them and their staff to be ready for use in acute stroke treatment clinical trials.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Timing of typical routine follow-up imaging in stroke patients

	24 h	48–72 h	3–5 days	discharge	30 days	90 days
All together (<i>n</i> = 203)	38%	27%	20%	6%	3%	6%
Asia (<i>n</i> = 43)	28%	21%	35%	7%	0%	9%
Australia (<i>n</i> = 10)	30%	30%	20%	0%	10%	10%
Europe (<i>n</i> = 82)	30%	30%	18%	7%	6%	7%
Middle East (<i>n</i> = 4)	50%	0%	0%	25%	25%	0%
North America (<i>n</i> = 54)	61%	26%	11%	0%	0%	2%
South America (<i>n</i> = 10)	30%	30%	20%	20%	0%	0%