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Utilization of Emergent Neuroimaging for Thrombolysis-Eligible Stroke Patients

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Abstract

Background—Advances in diagnostic imaging of stroke include multimodal techniques such as noninvasive angiography and perfusion imaging. We aimed to characterize trends in neuroimaging utilization among acute stroke patients. Utilization of multimodal imaging for acute stroke in the community has remained largely uncharacterized despite its increased adoption at academic medical centers.

Methods—We quantified neuroimaging utilization in the emergency department for 1700 hyperacute stroke patients presenting <2 hours after symptom onset who participated in the National Institutes of Health Field Administration of Stroke Therapy Magnesium (FAST-MAG) study throughout Los Angeles and Orange Counties. FAST-MAG provided no recommendation as to imaging utilization.

Results—1700 cases were imaged a median (Interquartile range: IQR) of 92 (74–120) minutes after last known well time and 28 (19–41) minutes after ED arrival. The initial scanner used in the ED was CT in a preponderance of cases (N=1612, 95%), with MRI in 88 cases (5%). CT angiography was obtained in 192 (11%) and perfusion CT in 91 (5.4%) cases. MRI imaging was universally obtained using diffusion-weighted images, 60% with MR angiography and 33% included perfusion imaging. Rates of concomitant CTA or CTP use increased in the later years of the study from 4% in 2005–2006, 2% in 2007–2008, 8% in 2009–2010 and 26% in 2011–2012 (p for trend <0.001).

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Conclusions—Among acute stroke patients, non-contrast CT was the most common initial imaging strategy in clinical practice in the 2005–2012 time period, though use of concomitant CTA grew to one-quarter of cases, suggestive of an upward trend.

Keywords

imaging; prehospital; stroke; emergency medical services

Introduction

Hyperacute stroke patients presenting to the emergency department (ED) within 2 hours of symptom onset require urgent neuroimaging to determine eligibility for thrombolysis.[1] Neuroimaging is often repeated during hospitalization for confirmation of diagnosis and determination of mechanism.[2] Over the past decade advances in imaging of stroke include increasing utilization of multimodal magnetic resonance imaging (MRI) and computed tomography (CT), which have contributed to a better understanding of cerebrovascular pathophysiology.[3–6] It is not clear how frequently multimodal imaging is used in the ED during the hyperacute evaluation of stroke in the United States.

Multimodal CT typically includes non-contrast head CT, CT angiogram (CTA) of the head and neck and in some cases CT perfusion imaging. Multimodal MRI includes standard sequences such as T1, T2, diffusion-weighted imaging (DWI), perfusion imaging, fluid-attenuated inversion recovery (FLAIR), and gradient recalled echo (GRE) sequences combined with MR angiography of the head and neck.[2] These multimodal imaging modalities have provided stroke care providers with better visualization of the brain and its vasculature and important information about brain perfusion and tissue viability. Multimodal imaging of stroke has an important role in selecting therapies most appropriate for a given patient, considering additional factors such as initial presentation, risk factors, and the evolution of the disease process.

Despite adoption of multimodal imaging at many academic stroke centers and increasing publication regarding diagnostic neuroimaging advances in stroke care, the current standard practice of imaging utilization among hyperactue stroke patients in the community and how quickly such multimodal imaging modalities are being adopted by hospitals remains unclear. Description of imaging utilization in the community may highlight practices with potential for increased standardization, improved efficiency, and reduced costs.

We sought to describe neuroimaging modalities utilized in thrombolysis-eligible cases presenting to the ED throughout a large urban region encompassing small community and large academic hospitals. We aimed to better understand the penetration of multimodal imaging in acute stroke as well as describe trends in diagnostic neuroimaging use over the past decade. We utilized subjects participating in the Field Administration of Stroke Therapy-Magnesium (FAST-MAG) trial who received usual care aside from the magnesium sulfate vs. placebo study agent infusion. The study provided no recommendation as to what type of imaging should be used. All patients were enrolled <2 hours from symptom onset and transported to their usual care hospital. Los Angeles and Orange Counties encompass a large urban area accounting for more than 13 million inhabitants.

Materials and Methods

Dataset and Study Population

All subjects were participating in the Field Administration of Stroke Therapy Magnesium trial, a phase 3, National Institutes of Health-sponsored, randomized, placebo-controlled, clinical trial of field-initiated magnesium sulfate in hyperacute stroke patients within the first two hours of defined symptom onset.[7–9] Randomization was to 4 grams of magnesium sulfate in the field followed by 16 grams over 24 hours or matched placebo. Participating sites included 353 ambulances and 59 acute receiving hospitals in the Los Angeles and Orange Counties with a total of over 3300 paramedics and over 400 Emergency Physicians. The study was active and recruiting from January 2005 to December 2012.

Subjects were enrolled in the field using explicit informed consent by cell phone from either the potential subject or a legally authorized representative.[10, 11] After enrollment in the field, participants were taken to their usual hospital and, other than continuation of the study agent, usual care was provided. Inclusion criteria included the patient having a suspected stroke identified by the Los Angeles Prehospital Stroke Screen (LAPSS), being of the ages 40–95, inclusive, having a last known well time within 2 hours of treatment with the study drug, and having a deficit present for 15 minutes or longer. Relevant exclusion criteria included the patient being in a coma; having a rapidly improving neurologic deficit; or having a pre-existing neurologic, psychiatric, or advanced systemic disease that would confound the neurological or functional outcome evaluations. The 59 receiving hospitals included a few academic medical centers (University of California Los Angeles [UCLA], Los Angeles County + University of Southern California [LAC+USC], University of California Irvine [UCI] medical centers), hospitals with training programs (Cedars-Sinai, Huntington Memorial, and Hoag Harbor-UCLA, Olive-View UCLA), and a majority of community centers.

Quantifying Neuroimaging Utilization

All neuroimaging utilization in the ED was quantified for each subject into categories as CT and MRI. For the CT imaging group, data was collected on whether CT angiography was performed and whether perfusion imaging was performed. If MRI was obtained in the ED, all imaging sequences performed were recorded. There was no recommendation as to what type of imaging should be utilized. All subsequent imaging obtained throughout hospitalization was recorded along with a date and time of first image acquisition of each study.

Statistical Analysis

The number and proportion of total cases who first received non-contrast CT, CT angiography (CTA), CT perfusion, and MRI were determined. Mean time from ED arrival to imaging acquisition was compared between acute MRI and CT using t-test. Rates of multimodal imaging utilization for CT and MRI by year were compared by ANOVA, and rates of multimodal imaging in primary certified stroke centers vs. non-stroke centers from 2005–2012 were also calculated and compared.

Results

Study Population

There were 1700 consecutive cases with a mean age was 69±13 years and 42.6% were women. Final diagnoses of the qualifying event were cerebral ischemia in 73.3%, intracranial hemorrhage in 22.8%, and cerebrovascular disease mimic in 3.9%. Initial assessment in the field by paramedics was a median of 23 minutes (IQR 14–42) after last known well (LKW) time. The median time from LKW to start of study infusion was 45 minutes (IQR 35–62). Subjects were transported to 59 hospitals in southern California (Figure 1), arriving in the ED 58 minutes (IQR 46–79) minutes after LKW.

Neuroimaging Utilization

Initial imaging obtained in the ED was CT in a majority of cases, (Table 1, N=1612, 95%) and MRI in 88 cases (5%). Parenchymal CT scan was almost always performed without contrast and most commonly as the only study obtained in the ED. CT angiography was obtained in 192 (11%) and perfusion CT in 91 (5.4%). When CT perfusion was performed, it was combined with CTA 80% of the time (n=72). MR imaging was universally obtained using diffusion-weighted sequences, accompanied by MR angiography 60%, and MR perfusion 33% of the time.

The 1700 cases were imaged at a median (IQR) of 92 (74–120) minutes after last known well time and 28 (19–41) minutes after ED arrival. Mean time from ED arrival to imaging acquisition was significantly longer for acute MRI than CT (56 vs. 25 minutes, p=0.030). A majority of patients with a final diagnosis of ischemic stroke (n=859, 69%) received MRI at some point during admission. The majority of MRI scans in the study were not obtained urgently, at a mean (SD) 21.0 (20.9) and median (IQR) 18 (7–27) hours after ED arrival.

Rates of multimodal (non-contrast CT plus CTA and/or CTP) CT imaging utilization increased in the later years of the study from 4% in 2005–2006, 2% in 2007–2008, 8% in 2009–2010 and 26% in 2011–2012 (p <0.001, Figure 2). There was no change in rates of multimodal MRI imaging as one academic medical center accounted for >80% of all studies. In the subgroup of MRI cases obtained outside this one academic medical center (n=17), there was no increase in use over the study period.. When combining multimodal CT utilization with multimodal MRI utilization, a total of 294 cases (17%) had any form of multimodal imaging in the ED evaluation of acute stroke (Table 1). Cases with multimodal imaging were more likely to be evaluated at a hospital designated as a PSC, were imaged sooner, had more severe stroke, and were more likely to be treated with tPA (tissue plasminogen activator) and receive endovascular therapies. Multimodal imaging was more common in the subset of ischemic stroke cases treated with intravenous tPA (148/450, 33%) and endovascular therapy (43/76, 57%). During the period of study, rates of multimodal imaging in the subgroup of tPA-treated cases increased (11% 2005–2006, 11% 2007–2008, 27% 2009–2010, 53% 2011–2012, P<0.001).

In an analysis of multimodal imaging use in certified primary stroke centers (PSCs) vs. non-stroke centers from 2005–2012, we found that rates of multimodal imaging in PSCs were significantly higher than non-stroke centers from 2005–2010 (2005–2006: p < 0.001, 2007–

2008: $p < 0.001$, 2009–2010: $p < 0.004$). However, in the 2011–2012 period, the proportion of patients who received multimodal imaging in both primary stroke centers and non-stroke centers was comparable ($p= 0.903$) (Figure 3).

Discussion

The primary goals of imaging in the evaluation of acute ischemic stroke beyond the use of a routine non-contrast CT scan should be to 1) exclude the presence of hemorrhage, 2) identify the presence of an intravascular thrombus eligible for treatment with thrombolysis or thrombectomy, 3) demonstrate the presence and size of a core of irreversibly infarcted tissue and 4) identify the penumbra or hypoperfused tissue at risk for infarction unless perfusion is restored in a timely manner.[12] TPA administration in the setting of acute stroke is highly time-sensitive, as previous research has demonstrated that reduced time from symptom onset to reperfusion with endovascular therapies is highly associated with better clinical outcome.[13] It therefore becomes important to consider the ability of multimodal imaging to guide or change management, limit complications, or improve efficacy when determining whether multimodal imaging is necessary in the evaluation and treatment of an acute stroke patient pending endovascular therapy. In the recent 2015 American Heart Association/American Stroke Association Focused Update of the 2013 Guidelines for the Early Management of Patients With Acute Ischemic Stroke Regarding Endovascular Treatment, it strongly recommends a noninvasive intracranial vascular study during the initial imaging evaluation only if it does not delay IV TPA administration. Otherwise, initiating IV tPA before noninvasive vascular imaging is recommended and such imaging should be obtained as soon as possible following administration.[14] With literature validating the use of clinical scores and screening tools to evaluate stroke patients and further expedite care and mobilize resources, the judicious use of multimodal imaging becomes imperative in ensuring good outcomes in patients eligible for endovascular therapies.[15]

There has been recent interest in the use of multimodal CT imaging in acute ischemic stroke patients. Certain studies suggest that perfusion CT can provide accurate markers of tissue viability and help predict the degree of improvement following reperfusion, with the potential to add relevant clinical information compared with only non-contrast CT and CTA.[16, 17] Another recent study using baseline Alberta Stroke Program Early CT Score (ASPECTS) applied to CT angiography source images (CTA-SI) strongly predicted futile recanalization, thus carrying the potential to affect treatment decisions regarding the indication for revascularization therapies in particular cases.[18] However, the American Heart Association/American Stroke Association states that, at this time, the benefits of additional imaging beyond CT and CTA, such as CT perfusion, in selecting patients for endovascular therapy is still not well characterized and merits further research.[14] While our investigation cannot comment on the reasons for which perfusion CT and CTA were used emergently in acute stroke patients, this investigation observed a significant increase in the proportion of acute ischemic stroke patients receiving CTA and perfusion CT over the past decade in the Southern California region. Therefore, while non-contrast CT was still the most frequently used initial imaging modality, the use of CTA and perfusion CT has been gaining popularity.

Previous studies have suggested that because MRI is more sensitive than CT for detection of acute ischemia, it should be the preferred test for accurate diagnosis of patients referred for emergency assessment of suspected acute stroke.[19]. Recommendations by the American Heart Association favored routine use of MR-DWI or CTA over non-contrast CT alone for acute stroke patients given no subsequent delay of IV tPA administration.[12] Increased implementation of standardized, rapid stroke MRI protocols among stroke care teams may minimize utilization of resources, while remaining a feasible and effective option for appropriately diagnosing and treating the patient. [20] Despite these more favorable recommendations regarding MRI or CTA use among stroke patients, our study revealed that non-contrast CT alone remained the most frequently used initial imaging modality. It is likely that the widespread use of MRI in the emergent evaluation of acute stroke patients currently remains impractical due to the cost of the scans and its decreased availability in many community centers. In addition, the use of MRI may be impractical when evaluating an unstable patient with a large intracerebral hemorrhage (ICH), particularly if scan times are lengthy. Stroke teams comprised of multiple neurologist subspecialists or radiologists are likewise more impractical to assemble outside of large academic institutions, thereby decreasing the feasibility of implementing standardized, rapid stroke protocols. Those patients with pacemakers, claustrophobia, or other contraindications to MRI would also be unable to obtain the scan, further precluding its emergent use in acute stroke patients. Until MRI scans become more cost-effective and equally as or more rapid than CT, there will likely be several barriers preventing its widespread use in the evaluation of acute stroke.

In agreement with previous research, we also found a significant trend of increased rates of CTA and CT perfusion in the setting of acute ischemic stroke over the past decade, including in the subgroup of patients treated with IV tPA. [6, 22] However, our study revealed no significant increase in the use of multimodal MRI from 2005–2012, differing from other studies that suggest an increased use of MR angiography and diffusion-weighted MRI. [22, 23] Our finding may differ in this manner because one academic medical center accounted for >80% of all multimodal MR imaging studies. This finding may reflect the low rate of adoption of multimodal MR imaging in a majority of community hospitals in the geographic area of study.

Primary stroke centers (PSCs) had an overall greater rate of multimodal imaging use among hyperacute stroke patients than non-stroke centers from 2005–2012, though in the period 2011–2012, the proportion of patients who received multimodal imaging were comparable between PSCs and non-stroke centers. Multimodal imaging has the potential to more accurately evaluate those patients with acute stroke who are eligible for endovascular therapy and may also have more successful outcomes after thrombectomy, facilitating improved therapeutic decision-making with these noninvasive studies.[24, 25] While rates of multimodal imaging use continue to be relatively low, their increase over the last decade may reflect a trend toward their use for not only diagnostic purposes, but also therapeutic decision-making in the thrombectomy era.

In Los Angeles County after November 2009, patients were transported by paramedics to the nearest certified stroke center instead of being routed to the nearest community hospital. Because the criteria for being routed to a stroke center were similar to the inclusion and

exclusion criteria of this investigation, following November 2009, most of the data on neuroimaging utilization reflected the practice of these stroke centers, and thus this study may lack information on neuroimaging utilization among stroke patients in non-stroke center community hospitals after 2009. We also recognize the low stroke mimic rate observed in this study as another limitation. The stroke mimic rate in this study was 3.9%, which is likely artificially low due to the screening criteria of the FAST-MAG study and the use of stroke neurologist-led consent over telephone. The low stroke mimic rate is therefore less representative of the population seen and evaluated in most communities for possible stroke, where stroke mimics are much more common. Nevertheless, given the large sample size and the inclusion of a representative number of academic medical centers, hospitals with training programs, and a majority of community centers, we still believe that the study population has many similarities to the general population with hyperacute stroke.

Despite the frequent discussions of improved applications for advanced, multimodal imaging use in acute ischemic stroke patients, particularly the use of perfusion studies and specific MRI sequences, low rates of multimodal CT and MRI imaging of acute stroke reflect practice in the community of Los Angeles and Orange Counties, and likely throughout the country. [26, 27] Non-contrast CT alone remains the most frequently used acute brain imaging modality, utilized in >90% of stroke patients presenting <2 hours of onset. Less than a quarter of the centers obtained any type of multimodal imaging during the time the patient was in the emergency room. While diagnostic neuroimaging has made advances in recent years, stroke care teams can better implement these techniques with more precise definition of imaging protocols and increased standardization. [21] Standardization of neuroimaging practices serves as a potential area for improving the efficiency of stroke care among community medical centers in Southern California.

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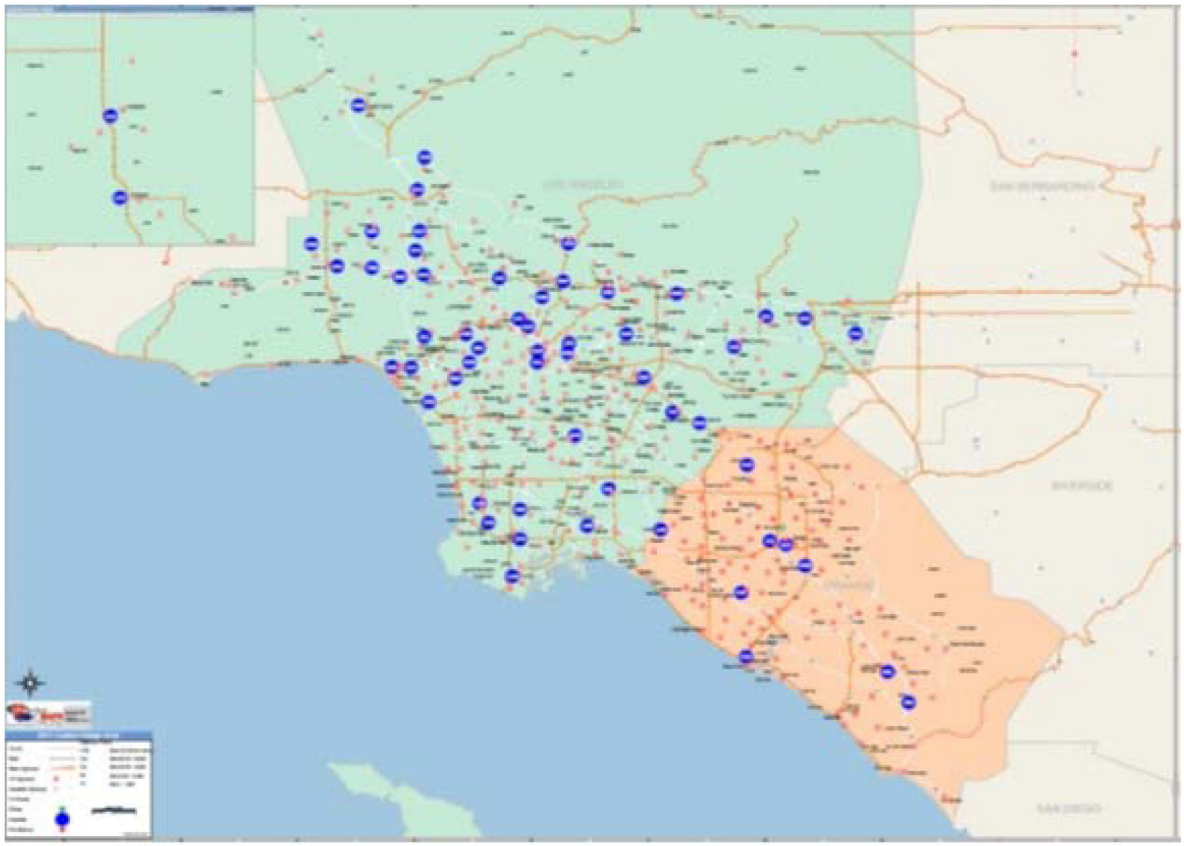
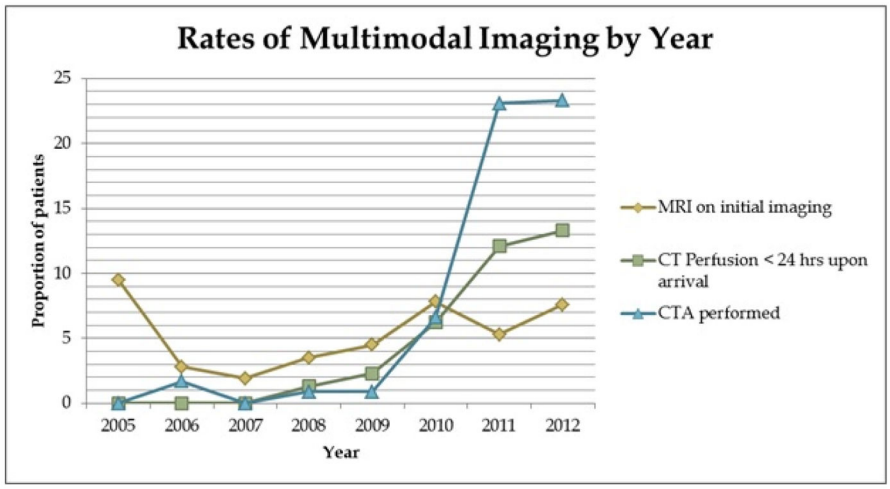


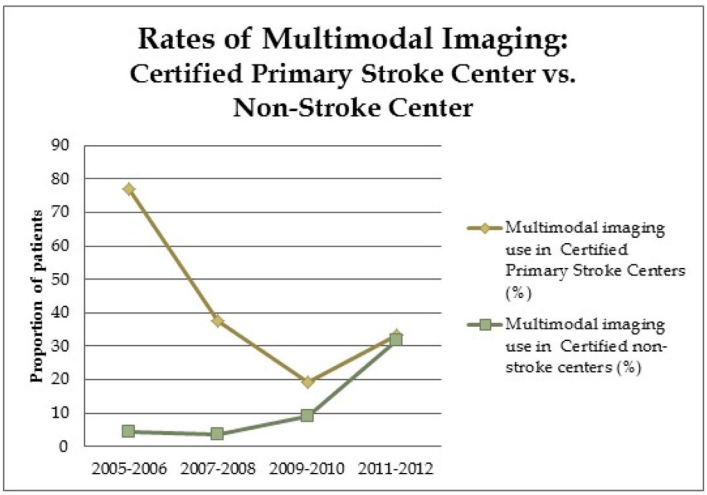
Figure 1.
Map of participating hospitals in Los Angeles and Orange Counties in the National Institutes of Health Field Administration of Stroke Therapy Magnesium investigation



	2005	2006	2007	2008	2009	2010	2011	2012
MRI as initial imaging (%)	9.5	2.8	1.9	3.5	4.5	7.8	5.3	7.6
CT perfusion < 24 hours upon arrival (%)	0	0	0	1.3	2.3	6.2	12.1	13.3
CTA performed during hospitalization	0	1.7	0	0.9	0.9	6.6	23.1	23.3

Figure 2.

Proportion of patients receiving multimodal imaging, including Magnetic Resonance Imaging (MRI), Computed tomography (CT) perfusion and CT angiography (CTA), by year from 2005–2012



	2005-2006	2007- 2008	2009- 2010	2011-2012
Certified PSCs (%)	76.9	37.5	19.1	33.1
Non- stroke centers (%)	4.2	3.4	9.0	31.8

Figure 3.

Proportion of patients receiving multimodal imaging, including Magnetic Resonance Imaging (MRI), Computed tomography (CT) perfusion and CT angiography (CTA), in certified primary stroke centers (PSCs) vs. non-stroke centers from 2005–2012

Table 1

Characteristics of patients who underwent multimodal imaging vs. those with non-contrast CT

	Multimodal Imaging (n= 294)	Non-Contrast CT (n=1406)	Significance
Age (years, SD)	69 (13)	69 (24)	0.547
Gender	45%	42%	0.323
White race	75%	79%	0.208
Latino Ethnicity	18%	25%	0.013
Minutes LKWT to ED [median, IQR]	59 [46–79]	58 [46–81]	0.560
Minutes ED arrival to imaging [median, IQR]	27 [19–40], mean 34	31 [20–39] mean 47	0.011
NIHSS in the ED [median, IQR]	9 [3–18] mean 10.0	8 [3–16] mean 11.6	0.013
Evaluated at PSC hospital *	248 (85%)	613 (44%)	0.001
Number treated with IV thrombolysis	149 (51%)	305 (22%)	0.001
Endovascular therapy	43 (14.6%)	33 (2.3%)	0.001
Time to treatment (mean, SD)	78 (32) minutes	92 (39) minutes	0.001

* at the time of enrollment the destination hospital was certified as a primary stroke center (PSC) by the Joint Commission or Det Norske Veritas

SD: standard deviation, ED: Emergency Department, IQR: interquartile range, LKWT: last known well time