Pretreatment Advanced Imaging in Patients with Stroke Treated with IV Thrombolysis: Evaluation of a Multihospital Data Base

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ABSTRACT

BACKGROUND AND PURPOSE: CT angiography, CT perfusion, and MR imaging have all been advocated as potentially useful in treatment planning for patients with acute ischemic stroke. We evaluated a large multihospital data base to determine how the use of advanced imaging is evolving in patients treated with intravenous thrombolysis.

MATERIALS AND METHODS: Patients with acute ischemic stroke receiving IV thrombolytic therapy from 2008 to 2011 were identified by using the Premier Perspective data base. Mortality and discharge to long-term care rates were compared following multivariate logistic regression between patients who received head CT only versus those who received CTA without CT perfusion, CT perfusion, or MR imaging.

RESULTS: Of 12,429 included patients, 7305 (59%) were in the CT group, 2359 (19%) were in the CTA group, 848 (7%) were in the CTP group, and 1917 (15%) were in the MR group. From 2008 to 2011, the percentage of patients receiving head CT only decreased from 64% to 55%, while the percentage who received cerebral CT perfusion increased from 3% to 8%. The use of CT angiography and MR imaging marginally increased (1%–2%). Outcomes were similar between CT only and advanced imaging patients, except discharge to long-term care was slightly more frequent in the CTP group (OR = 1.17 [95% CI, 0.96–1.43]; $P = .0412$) and MR group (OR = 1.14 [95% CI, 1.01–1.28]; $P = .0177$) and mortality was lower in the MR group (OR = 0.64 [95% CI, 0.52–0.79]; $P < .0001$).

CONCLUSIONS: Use of advanced imaging is increasing in patients treated with IV thrombolysis. While there were differences in outcomes among imaging groups, the clinical effect of advanced imaging remains unclear.

The potential benefit of intravenous thrombolytic therapy for acute ischemic stroke decreases rapidly with time. Because of wide variability in collateral circulation, time elapsed since onset is a crude indicator of the potential benefit of treatment in each patient. Advanced imaging might provide a means to refine selection of patients who could potentially benefit from revascularization therapy. The advanced imaging techniques that might add clinically useful information in the setting of acute ischemic stroke include CT angiography, CT perfusion, and MR imaging. CT angiography can be used to identify patients with large-artery occlusions potentially amenable to intra-arterial therapy,[1-3] and CT angiography source images have been proposed as a means of evaluating collateral circulation.[4-6] CT perfusion may potentially allow discrimination between salvageable brain ("penumbra") and brain already doomed to infarction ("ischemic core")[2,7-10] and thus may be useful in helping to refine selection of patients for IV thrombolysis[11,12] or intra-arterial thrombectomy.[13-15] MR perfusion and diffusion imaging have also been reported to be useful in screening patients for intravenous therapy.[16-22]

While advanced imaging techniques hold promise for the evaluation of patients with acute ischemic stroke, there is variation in techniques and definitions of parameters that limit wide application and acceptance of these techniques.[4,23-25] There is currently no consensus on a standard imaging approach for acute ischemic stroke. We studied a large data base of hospitals in the United States to assess the recent of advanced imaging in patients with acute ischemic stroke treated with intravenous thrombolysis, including an evaluation of the use of advanced imaging, with respect to patient outcome.

MATERIALS AND METHODS

Data Source and Study Population

The Perspective data base is a voluntary, fee-supported collection of data developed by Premier Inc (Charlotte, North Carolina) to

assess quality and resource use. As of 2011, the Perspective data base consisted of approximately 15% of hospitalizations nationwide and represented >600 US hospitals. Detailed information of a patient's hospitalization, including patient demographics, hospital information, diagnoses, procedures, discharge status, payer, and all billed items are recorded.

Patients who presented with acute ischemic stroke (ICD-9-CM diagnostic codes 433.x1 and 434.x1) from 2008 through 2011 were identified from the Perspective data base. Patients were included only if the stroke code was listed as the primary hospitalization diagnosis to avoid including patients with a history of stroke. Patients in this cohort who received IV thrombolysis during their hospitalization were identified by using the ICD-9 procedural code 99.10.

Relevant imaging performed during hospitalization was retrieved by using billing information. Imaging was included if it was performed before or on the day of thrombolysis. Patients were included if they underwent a noncontrast head CT during hospitalization. Advanced imaging modalities of head CT angiography, cerebral CT perfusion, head MR imaging, and head MR angiography were also retrieved.

Outcome Analysis

The outcomes examined in this study were in-hospital mortality and discharge to long-term care (discharge to a rehabilitation facility, long-term care hospital, or nursing facility). Patients were divided into the following subgroups on the basis of imaging received: noncontrast head CT only (CT group), CT with cerebral CT angiography but no CT perfusion (CTA group), CT with cerebral CT perfusion (CTP group), and CT with head MR imaging or MR angiography (MR group). Statistical analyses were performed by using JMP, Version 9, and SAS, Version 9.3 (SAS Institute, Cary, North Carolina). Differences among imaging groups and admit years were compared by using the Pearson χ^2 test and linear regression, respectively. The likelihood of mortality or discharge to long-term care was compared among imaging subgroups following multivariate logistic regression to minimize differences in clinical characteristics among groups. The generalized estimating equation was used to adjust for the possible clustering effect of hospitals in the patient population.[26] Models were estimated by using the SAS GENMOD procedure (http://www.math.wpi.edu/saspdf/stat/chap29.pdf). Two models were created, a full model that encompassed all patient and hospital characteristics as shown in On-line Table 1 and a reduced model that encompassed only significant characteristics as determined by the stepwise selection option in the SAS LOGISTIC procedure (http://support.sas.com/documentation/cdl/en/statug/63347/HTML/default/viewer.htm#logistic_toc.htm).

RESULTS

Of the 176,991 patients identified who were hospitalized from 2008 to 2011 with acute ischemic stroke listed as a primary diagnostic code, 15,470 patients (8.7%) received IV thrombolytic therapy during hospitalization. Of that group, 12,429 patients (80%) underwent a head CT during hospitalization. Within that group, 2359 patients (19%) also underwent a head CT angiography; 848 patients (6.8%), cerebral CT perfusion; and 1917 pa-
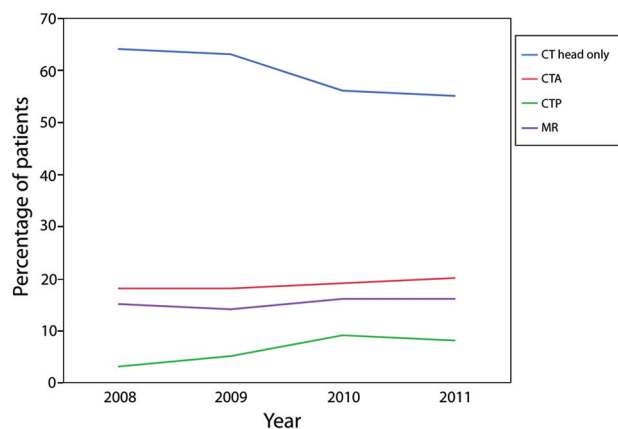

FIG 1. Trends in the use of head CT and advanced imaging in patients treated with IV thrombolysis from 2008 to 2011. Patients who received only head CT (*blue line*), head CT with CT angiography (*red line*), head CT with CT perfusion (*green line*), or head CT with MR imaging (*purple line*) are shown.

tients (15%), MR imaging. Patient and hospital characteristics of the 4 imaging subgroups are shown in On-line Table 1.

Trends in the use of head CT and advanced imaging are shown in Fig 1. From 2008 to 2011, the percentage of patients treated with thrombolysis who only underwent a noncontrast head CT decreased slightly from 64% to 55% ($P = .0570$), while the percentage of patients who underwent cerebral CT perfusion increased from 3% to 8% ($P = .11$). Use of CT angiography and MR imaging each increased slightly from 18% to 20% ($P = .0561$) and from 15% to 16% ($P = .33$), respectively, during this time.

The incidence of in-hospital mortality was lower in the MR group (6.2%) than in the CT, CTA, and CTP groups (10.2%, 12.4%, and 12.4%, respectively; $P < .0001$) (Table 1). The incidence of discharge to long-term care was slightly higher in the CTP group (47%) compared with the CT, CTA, and MR groups (43%, 41%, and 43%, respectively; $P = .0352$). Following multivariate logistic regression by using the full model, the likelihood of mortality was significantly lower in the MR group compared with the CT group (OR = 0.64 [95% CI, 0.52–0.79]; $P < .0001$) but was similar between the CTA and CT groups ($P = .99$) and between the CTP and CT groups ($P = .20$) (Table 2). The likelihood of discharge to long-term care was significantly higher in the MR group compared with the CT group (OR = 1.14 [95% CI, 1.01–1.28]; $P = .0177$), was slightly higher in the CTP group compared with the CT group (OR = 1.17 [95% CI, 0.96–1.43]; $P = .0412$), and was similar between the CT and CTA groups ($P = .31$). Similar findings were observed by using the reduced regression models.

DISCUSSION

Our analysis of a large, multihospital data base found wide variation in the use of imaging in patients with acute ischemic stroke. From 2008 to 2011, the percentage of patients treated with thrombolysis who received only a head CT decreased slightly from 64% to 55%. If this trend continues, more than half of the patients treated with thrombolysis will receive some form of advanced imaging during their hospitalization. This growth in the use of

Table 1: Outcome incidences by imaging subgroup

	CT Group	CTA Group	CTP Group	MR Group
In-hospital mortality	748/7305 (10.2%)	241/2359 (12.4%)	105/848 (12.4%)	119/1917 (6.2%)
Discharge to long-term care	3170/7305 (43%)	975/2359 (41%)	399/848 (47%)	828/1917 (43%)

Table 2: Patient outcomes following logistic regression analysis

	Odds Ratio (95% CI)	P Value
In-hospital mortality		
Full model		
CT	1.00 (reference)	–
CTA	1.00 (0.83–1.21)	.99
CTP	1.17 (0.93–1.47)	.20
MRI	0.64 (0.52–0.79)	<.0001
Reduced model		
CT	1.00 (reference)	–
CTA	1.03 (0.86–1.24)	.75
CTP	1.14 (0.92–1.40)	.22
MRI	0.65 (0.53–0.79)	<.0001
Discharge to long-term care		
Full model		
CT	1.00 (reference)	–
CTA	0.95 (0.83–1.09)	.31
CTP	1.17 (0.96–1.43)	.0412
MRI	1.14 (1.01–1.28)	.0177
Reduced model		
CT	1.00 (reference)	–
CTA	0.89 (0.66–1.18)	.59
CTP	1.33 (1.00–1.77)	.12
MRI	1.15 (0.73–1.83)	.0471

Note:— –indicates no P value was calculated for the CT reference group.

advanced imaging is primarily attributable to increased use of CT perfusion but also to increased use of CT angiography and MR imaging.

Imaging has been an essential part of stroke treatment planning since the introduction of CT.[27] Unenhanced CT has been useful for demonstrating acute hemorrhage or other mimicking lesions, as well as showing cytotoxic edema from evolving infarction. CT is standard for trauma patients in emergency departments and has been the historical standard for patients with acute neurologic conditions, so CT is already fully integrated into emergency department culture and is readily available to patients with acute ischemic stroke. In fact, readily available head CT is a defining characteristic of a primary stroke center in the United States.[28] If the patient is already going to the CT scanner for the standard unenhanced imaging, it is generally not very time-consuming to add additional CT angiography and/or CT perfusion studies.[2] However, advanced CT, including high-quality CT perfusion and CT angiography, requires hardware and software that are not available at every hospital treating patients with stroke; this circumstance might limit adoption of these imaging techniques. As CT scanners are replaced and upgraded with time, advanced CT techniques are becoming uniformly available; this availability might account for some of the increased use demonstrated in our study. The clinical utility of such advanced CT imaging, however, is not universally accepted.

Our study showed that from 2008 to 2011, screening with MR imaging had a negligible increase from 15% to 16% of patients undergoing IV thrombolysis. These results suggest that MR imaging has not been widely adopted. MR imaging has been proposed as an effective means of identifying candidates for intrave-

nous thrombolysis in the 3- to 4.5-hour time window.[16-22] The exact time of onset relative to the time of imaging or the time of thrombolytic administration is not available in the Perspective data base, so we cannot determine how often MR imaging was used for screening patients in the 3- to 4.5-hour time window. In addition, MR imaging is not typically as readily available as CT in an emergency setting. Safety screening for implants can slow down the process of acquiring MR imaging, especially if it is not possible to immediately obtain an accurate and complete history, which occurs reasonably often in the setting of acute ischemic stroke. Another impediment is that rapid, emergent acquisition of MR imaging is not part of the culture at many hospital emergency departments.

We found that patients who underwent MR imaging had lower in-hospital mortality rates compared with patients who underwent a head CT only or other types of advanced imaging. However, patients who received MR imaging or CT perfusion had a higher rate of being discharged to long-term care compared with the head CT group. These findings suggest that the use of advanced imaging may affect these patient outcomes; however, a causal link cannot be confirmed from our observational study. It is likely that patients treated with IV thrombolysis who underwent imaging with only unenhanced CT were clinically different from those who underwent additional imaging. Patients who underwent only CT were more likely to be admitted from the emergency department compared with patients who also underwent advanced imaging. While we performed multivariate logistic regression to minimize these differences in clinical characteristics between imaging groups, differences in unmeasured clinical variables may affect our results. For example, patients treated with IV thrombolysis who underwent additional imaging were probably more likely to have severe stroke compared with patients who only underwent CT imaging, with the additional imaging used to help determine whether mechanical embolectomy was warranted. We cannot quantify such a trend because we cannot assess stroke severity at presentation.

Our study of a national cohort of inpatients who received IV thrombolysis did not show that the use of CT angiography or CT perfusion significantly improved patient outcomes. However, these findings do not suggest that these imaging examinations are not useful in specific clinical settings, such as studies comparing IV thrombolysis with combined IV and intra-arterial treatments. In such studies, CT angiography may be useful in both identifying and characterizing pretreatment arterial occlusive lesions and in identifying post treatment recanalization effects.

This study has several additional limitations. We acknowledge that coding inaccuracies occur, which can affect a retrospective study of any administrative data base; however, it is unlikely that such inaccuracies would be more prevalent in one imaging group over another. As noted above, we cannot assess stroke severity at the time of presentation. We are unable to identify patients with similar stroke severity who did not receive intravenous thrombol-

ysis, so we do not have a control group to allow assessment of the benefit from different treatments. We cannot determine whether screening imaging was used uniformly at each center and thus was not subject to selection bias. We also are unable to assess the time of presentation, but the patients undergoing intravenous thrombolysis would typically be expected to have presented early enough for initiation of intravenous therapy within 3 hours of symptom onset. However, some patients may have been evaluated with imaging specifically for broadening of the time window to 4.5 hours, especially with MR imaging.[16-22] Our study focused on the use of advanced imaging before or on the day of thrombolysis; the use of advanced imaging after treatment was not examined. Additional studies are needed to examine the use of advanced imaging in patients treated with IV thrombolysis and to examine the effect of this imaging on patient outcomes.

CONCLUSIONS

Significant variation occurs in imaging of patients with acute ischemic stroke treated with intravenous thrombolysis in the United States. The use of advanced imaging is increasing in these patients. While there were differences in outcome among the imaging groups, the clinical effect of advanced imaging remains unclear.

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