Increasing Use of Computed Tomographic Perfusion and Computed Tomographic Angiograms in Acute Ischemic Stroke From 2006 to 2010

Achala Vagal, MD; Karthikeyan Meganathan, MS; Dawn O. Kleindorfer, MD; Opeolu Adeoye, MD, MS; Richard Hornung, PhD; Pooja Khatri, MD, MSc

Background and Purpose—Our objective was to study nationwide utilization trends of computed tomographic (CT) angiogram (CTA) and CT perfusion (CTP) in acute ischemic stroke and particularly in the context of use of reperfusion therapies.

Methods—We reviewed the Premier Perspective Database for ischemic stroke–related hospitalizations of adult patients during a 5-year period, 2006 to 2010. Use of multimodal CT-based imaging and reperfusion therapies was determined through the procedure and billing codes. Logistic regression was used to identify predictors of utilization of imaging studies and reperfusion treatments.

Results—An increasing proportion of ischemic strokes received CTA each year: 3.8% in 2006, 5.6% in 2007, 6.5% in 2008, 7.5% in 2009, and 9.1% in 2010 (P<0.0001). The proportion of acute strokes that were imaged with CTP imaging also increased each year: 0.05% in 2006, 0.05% in 2007, 0.9% in 2008, 2.2% in 2009, and 2.9% in 2010 (P<0.0001). Reperfusion treatment was more common among those who were imaged with CTA (13.0%) and CTP (17.6%) compared with those with CT head alone (4.0%; P<0.0001). Specifically, higher rates of recombinant tissue-type plasminogen activator were observed in CTA (10.2%) and CTP (11.4%) compared with those with CT head alone (3.8%; P<0.0001). Similarly, higher rates of mechanical embolectomy were observed in CTA (2.8%) and CTP (6.3%) compared with those with CT head alone (0.2%; P<0.0001).

Conclusions—There was a marked increase in the rate of CTA and CTP studies in setting of acute ischemic stroke from 2006 to 2010, and both modalities were associated with increased reperfusion therapy use. (Stroke. 2014;45:1029-1034.)

Key Words: perfusion imaging ■ reperfusion ■ utilization

Acute ischemic stroke is the leading cause of serious long-term disability, and on average, 1 American dies from stroke every 4 minutes.1 Intravenous thrombolysis treatment with recombinant tissue-type plasminogen activator (rt-PA) is the only Food and Drug Administration–approved treatment and is used in only 5% of patients with acute stroke attributable to a narrow 4.5-hour treatment window.2,3 Multimodal computed tomography (CT) and MRI including perfusion studies have offered the promise of increasing eligibility for acute reperfusion therapies for ischemic stroke, including the possibility of extending the time window for intravenous rt-PA and better selecting patients for endovascular therapies.

To date, the majority of randomized controlled trials using multimodal imaging for thrombolytic treatment selection have used magnetic resonance (MR)-based imaging.4,4 Although favorable trends were seen in some of the MR selection–based trials, no clinical benefit was demonstrated.4 A prospective cohort study using MR selection demonstrated favorable clinical outcomes.7 However, most recently, the randomized controlled phase II MR Rescue trial tested imaging selection for endovascular therapy using both MR and CT perfusion (CTP) and showed no evidence for the imaging selection hypothesis.8 No clinical trials have tested CT-based multimodal imaging exclusively, and thus the usefulness of CT-based imaging in making acute stroke treatment decisions is especially lacking.

Although randomized studies regarding its usefulness have been limited, CT-based multimodal imaging, including CT angiogram (CTA) and CTP, can be easily assimilated into routine clinical practice of stroke evaluation and treatment. As compared with MRI, CT scanners are typically more widely available, more easily accessible to most emergency departments, faster to complete, less medically contraindicated, and have lower costs. Utilization data on CT-based neuroimaging for acute stroke in the United States have been limited.

Received December 29, 2013; final revision received December 29, 2013; accepted January 14, 2014.

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The online-only Data Supplement is available with this article at http://stroke.ahajournals.org/lookup/suppl/doi:10.1161/STROKEAHA.113.004332/-/DC1.

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Stroke is available at http://stroke.ahajournals.org DOI: 10.1161/STROKEAHA.113.004332
We hypothesized that both CTA and CTP use in acute stroke setting may be increasing in the United States during the last few years, despite the lack of evidence supporting their use in acute treatment decisions. In support of its use for treatment decisions, we hypothesized that imaging rates particularly for CTP would be higher among cases treated with acute stroke reperfusion compared with those not treated with reperfusion therapies. We sought to determine nationwide utilization trends of CTA and CTP imaging in acute ischemic stroke and particularly in the context of reperfusion therapies.

Methods

Data

We reviewed a national hospital administrative database (Premier Perspective Database, Charlotte, NC). The Premier Hospital data set is the largest clinical and operational data warehouse in the nation developed for measuring quality and use of health care and contains longitudinal inpatient and ambulatory data pertaining to all discharges from >600 hospitals representing ~20% of all discharges nationwide (https://www.premierinc.com/wps/portal/premierinc/public/transforminghealthcare/improvingperformance/servicesprograms/researchservices). Participating hospitals represent all regions of the United States and are predominantly small-to-midsize nonteaching facilities that serve largely urban patient populations. This nationally representative database is as follows: rural (25%); nonteaching (72.6%) versus teaching (27.4%); number of beds, 0 to 99 (18.2%); 100 to 299 (43.3%), 300 to 499 (26.2%), 500+ (7.3%); and location (urban/rural). 

Descriptive analyses involving frequencies and percentages were used to describe trends in utilization of imaging studies and reperfusion treatments for fiscal years 2006 to 2010. Temporal trends of bimodal proportions were assessed using the Cochran–Armitage trend test. Associations between categorical variables were assessed using the χ² test, and mean values of continuous variables were compared across groups using the ANOVA test. Logistic regression was used to identify predictors of utilization of imaging studies and reperfusion treatments. SAS version 9.3 (SAS Institute Inc, Cary, NC) was used for all calculations, and the significance level was set at 0.05.

Table 1. Temporal Trend of CT-Based Imaging in Acute Ischemic Stroke

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic strokes</td>
<td>59,386</td>
<td>58,224</td>
<td>59,366</td>
<td>62,847</td>
<td>60,223</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>All CT imaging</td>
<td>46,830 (78.9)</td>
<td>45,957 (78.9)</td>
<td>47,327 (79.7)</td>
<td>50,838 (80.9)</td>
<td>48,788 (81.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CTH only</td>
<td>44,553 (75.0)</td>
<td>42,665 (73.3)</td>
<td>42,921 (72.3)</td>
<td>44,782 (71.3)</td>
<td>41,565 (69.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CTA</td>
<td>2250 (3.8)</td>
<td>3282 (5.6)</td>
<td>3852 (6.5)</td>
<td>4702 (7.5)</td>
<td>5460 (9.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CTP</td>
<td>27 (&lt;0.1)</td>
<td>20 (&lt;0.1)</td>
<td>554 (9.9)</td>
<td>1354 (2.2)</td>
<td>1763 (2.9)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CTP: This category includes patients who underwent CTP and CTA. CT indicates computed tomography; CTA, CT angiogram; CTH, CT head; and CTP, CT perfusion.
Temporal Trends of Use of CTA/CTP

During 2006 to 2010, we identified a total of 300,046 ischemic stroke discharge diagnoses. Of these, 239,740 (79.9%) patients were imaged with CT studies, 216,476 (72.1%) received CT head only, 19,546 (6.5%) received CTA, and 3718 (1.2%) received CTP imaging. Of the 3718 patients who received CTP, 3606 (97%) had also received CTA; these patients were included in the CTP group but not in the CTA group for all analyses. An increasing proportion of ischemic strokes received CTA each year: 3.8% in 2006, 5.6% in 2007, 6.5% in 2008, 7.5% in 2009, and 9.1% in 2010 (P<0.0001). The proportion of acute strokes that were imaged with CTP imaging also increased each year: 0.05% in 2006, 0.05% in 2007, 0.9% in 2008, 2.2% in 2009, and 2.9% in 2010 (P<0.0001; Figure 1 and Table 1).

Baseline Characteristics of Population

Patients with ischemic stroke who received CTA and CTP, as compared with CT head alone, were younger, more frequently males, of white race, were less likely to be on Medicare insurance, were similarly distributed between urban and rural hospitals, and were more frequent at teaching hospitals (Table 2, Table I in the online-only Data Supplement).

Reperfusion Trends in Study Population

Reperfusion treatment was more common among those who were imaged with CTA (13.0%) and CTP (17.6%) compared with those with CT head alone (4.0%; P<0.0001). Specifically, higher rates of r-tPA were observed in those imaged with CTA (10.2%) and CTP (11.4%) compared with those with CT head alone (3.8%; P<0.0001). Similarly, higher rates of mechanical embolectomy were observed in those imaged with CTA (2.8%) and CTP (6.3%) compared with those with CT head alone (0.2%; P<0.0001; Table 3 and Figure 2). The total number of patients who received overall reperfusion among CTA group was higher in teaching versus nonteaching hospitals: 146 versus 113 in 2006, 305 versus 106 in 2007, 358 versus 128 in 2008, 382 versus 239 in 2009, and 436 versus 334 in 2010. The total number of patients who received overall reperfusion among CTP group was also higher in teaching versus nonteaching hospitals: 4 versus 0 in 2006, 4 versus 0 in 2007, 83 versus 4 in 2008, 211 versus 26 in 2009, and 240 versus 84 in 2010 (Table II in the online-only Data Supplement).

Logistic regression analysis demonstrated that the odds of utilization of CTA and CTP increased temporally during the study period and was higher in males, whites, younger patients, and those with non-Medicare insurance. Utilization was also
higher at teaching hospitals. Similarly, odds of reperfusion treatment with r-tPA and mechanical embolectomy were higher in males, whites, younger patients, those with non-Medicare insurance, and those at teaching hospitals (Table 4).

**Discussion**

We found a marked increase in CTA/CTP use; there was a 142% increase in CTA and a 6429% increase in CTP use in the United States during a 5-year period (2006–2010) as compared with only a 1.40% increase in the total number of hospitalized ischemic strokes. These results suggest that CTA and CTP imaging are being rapidly assimilated into clinical practice and that patients with CTA/CTP have a higher association with reperfusion treatments.

The increased rates of CTA/CTP in this study are consistent with prior studies showing a marked nationwide overall increase in use of CT and MR imaging in the past decade. However, to the best of our knowledge, this is the first study showing utilization trends of CTA and CTP for evaluation of acute ischemic stroke. Tripling of CTP from 2007 to 2010 as seen in our study also mirrors the technological advances in CT scanners in the past few years. The newer scanners are faster, and they provide increased brain coverage suitable for perfusion imaging along with more sophisticated postprocessing tools.

The one stop shop of CT head, CTA, and CTP providing information about intracranial hemorrhage, vascular occlusion, and tissue at risk, along with speed and the ubiquitous availability of CT scanners, gives CT a distinct advantage over MRI in evaluation of acute stroke. However, CT-based multimodal imaging has some greater risks including radiation and a small risk of nephrotoxicity, and study of its clinical implications has been limited compared with MRI. The majority of the current evidence supporting the use of CTP comes from case series and case registries and not from definitive trials. A recent phase 2 randomized trial of tenecteplase versus alteplase for acute stroke used CTP as an eligibility criteria; however, the trial did not include a study arm of patients without CTP imaging. One of the challenges of using CTP is wide variability in the quantitative methods used for CTP analysis and poor reliability in measuring irreversible cerebral infarction. Given this lack of standardization and validation of perfusion imaging and the fact that using imaging to guide acute stroke treatment remains unproven, the increased rates of imaging observed raise important questions about current practice.

Increased use of imaging and its associated costs is a growing concern among the payers and policy makers. The cost of inpatient stroke care climbed by 42% between 1997 and 2007, and neuroimaging was the fastest growing component of the hospitalization cost. Recent imaging guidelines in acute stroke suggest CTA may be considered, provided it does not delay time to treatment (class I, level A evidence), but caution against routine use of CTP for clinical decision making.

**Table 4. Logistic Regression Analysis Evaluating the Association Between CTA and CTP and Reperfusion Treatments With Year, Age, Sex, Race, Insurance Status, and Type of Hospital**

<table>
<thead>
<tr>
<th>Demographic Characteristics</th>
<th>CTA/CTP OR (95% CI)</th>
<th>Overall Reperfusion OR (95% CI)</th>
<th>r-tPA Alone OR (95% CI)</th>
<th>Mechanical Embolectomy OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Year</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2006 Reference</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>1.54 (1.46–1.63)</td>
<td>1.14 (1.06–1.22)</td>
<td>1.08 (1.00–1.15)</td>
<td>2.40 (1.86–3.17)</td>
</tr>
<tr>
<td>2008</td>
<td>2.07 (1.96–2.18)</td>
<td>1.38 (1.30–1.47)</td>
<td>1.28 (1.20–1.37)</td>
<td>3.27 (2.52–4.21)</td>
</tr>
<tr>
<td>2009</td>
<td>2.70 (2.56–2.83)</td>
<td>1.58 (1.49–1.68)</td>
<td>1.45 (1.36–1.54)</td>
<td>4.13 (3.23–5.29)</td>
</tr>
<tr>
<td>2010</td>
<td>3.49 (3.31–3.66)</td>
<td>1.86 (1.74–1.97)</td>
<td>1.65 (1.55–1.75)</td>
<td>5.74 (4.91–7.31)</td>
</tr>
<tr>
<td><strong>Age, y</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>0.98 (0.97–0.98)</td>
<td>0.99 (0.99–0.99)</td>
<td>0.99 (0.99–0.99)</td>
<td>0.98 (0.97–0.98)</td>
</tr>
<tr>
<td><strong>Male (vs female)</strong></td>
<td>1.17 (1.14–1.20)</td>
<td>1.07 (1.03–1.11)</td>
<td>1.09 (1.05–1.37)</td>
<td>0.95 (0.86–1.07)</td>
</tr>
<tr>
<td><strong>White (vs other race)</strong></td>
<td>1.71 (1.66–1.77)</td>
<td>1.28 (1.23–1.33)</td>
<td>1.24 (1.19–1.30)</td>
<td>1.60 (1.42–1.81)</td>
</tr>
<tr>
<td><strong>Medicare (vs non-Medicare)</strong></td>
<td>0.86 (0.83–0.89)</td>
<td>0.84 (0.80–0.88)</td>
<td>0.84 (0.79–0.89)</td>
<td>0.81 (0.70–0.94)</td>
</tr>
<tr>
<td><strong>Teaching hospital</strong></td>
<td>2.86 (2.78–2.95)</td>
<td>1.47 (1.41–1.52)</td>
<td>1.34 (1.29–1.39)</td>
<td>2.87 (2.55–3.22)</td>
</tr>
</tbody>
</table>

The variables of urban location vs rural and number of beds of the admitting hospital were not included because they correlate highly with teaching status of the hospital. CI indicates confidence interval; CTA, computed tomographic angiogram; CTP, CT perfusion; OR, odds ratio; and r-tPA, recombinant tissue-type plasminogen activator.
making (class IIb, level B evidence).22,23 It could be argued that the increase in rates of CTA studies in our study could potentially be unrelated to decisions about endovascular interventions because CTA can also help in diagnostic evaluation or to guide long-term management. CTP would typically be done on patients with acute stroke who are potential candidates for endovascular therapies. However, we found that reperfusion treatments including r-tPA and mechanical embolectomy were more common in both CTA and CTP groups as compared with those with CT head alone. The finding that CTA and CTP were more frequently used at larger teaching hospitals is not surprising given that large academic centers are better equipped with neurointerventional stroke treatment options. Because the database used in this study has a heavy representation of small-to-midsized community nonacademic hospitals, the numbers may actually underestimate the percentage of CTA and CTP performed in the United States.

Our study has several important limitations. Because we used an administrative data set without specific clinical information on the patients, CTA/CTP studies were neither linked to physician rationale for ordering the imaging study nor linked to patient outcomes; the clinical indications for reperfusion therapies were also unavailable. Therefore, it is not clear whether high utilization of CTA/CTP translates to improved health outcomes, although controlled studies suggest no clinical benefit. Also, we could not correlate the use of CTP with CTA variables including vascular status. Transfer between hospitals was difficult to evaluate, and only the final receiving acute care hospital’s use of imaging was included in this analysis. Another limitation is that we did not compare the utilization rates of CT and MR perfusion studies. The lack of a current procedural terminology or billing code for MR perfusion studies made it difficult to make an accurate comparison. We did not address the costs and cost-effectiveness analysis of CTA/CTP; however, this was not the focus of our study. Additional limitations include the use of small, retrospective database, and future prospective studies using a larger data set are needed to confirm our findings. Although the concordance between administrative coding data and medical records for stroke has been validated, we recognize that administrative coding data relies on the accuracy of the diagnosis, quality of included data elements, and missing data elements.24–26 Despite these intrinsic limitations, nationwide administrative databases are a practical and cost effective tool for studying national practice patterns.

Our documentation of utilization rates and associated factors provide the critical benchmarks to understand current practice patterns, do cost studies, and plan future clinical trials related to multimodal imaging. Given the discrepancy of increasing use and lack of evidence-based guidelines, CT-based multimodal imaging needs to be investigated further in large randomized controlled trials to determine its efficacy to guide treatment decisions and improve patient outcomes; this is an urgent need and a fertile ground for further research.

Conclusions

CTA use tripled and CTP use increased >50-fold from 2006 to 2010, and both were associated with increased reperfusion therapy use. Given limited healthcare resources, the well-publicized risks of increased radiation, along with limited evidence for clinical benefit of this approach, it becomes imperative that CT-based multimodal imaging selection for acute ischemic strokes be studied in controlled clinical trials.

Acknowledgments

All authors made substantial contribution including data collection, analysis of data, drafting, and critical revision of the manuscript.

Disclosures

Dr Vagal is an American Roentgen Ray Society (ARRS) scholar and received research support from an ARRS scholarship award. Dr Kleindorfer is on the Speaker’s bureau of Genentech (modest level) and serves as a consultant for Genentech (modest level). Dr Adeoye is on the Speaker’s bureau of Genentech (modest level). Dr Khatri is a member of National Institutes of Health (MSIII) Executive committee and received research support from Penumbra (Assess the Penumbra System in the Treatment of Acute Stroke [THERAPY] Trial Neurology Principal Investigator) and Genentech (Potential of rPA for Ischemic Strokes With Mild Symptoms [PRISMS] Trial Principal Investigator). The other authors report no conflicts.

References


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*Stroke*. 2014;45:1029-1034; originally published online February 25, 2014; doi: 10.1161/STROKEAHA.113.004332

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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/45/4/1029

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Supplementary Tables:

### Table I. Temporal Trends of CTA and CTP by type of institution

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<thead>
<tr>
<th>Year</th>
<th>Type of Institution</th>
<th>2006</th>
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<th>2007</th>
<th></th>
<th>2008</th>
<th></th>
<th>2009</th>
<th></th>
<th>2010</th>
<th></th>
<th>Trend</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CTA</td>
<td>2006</td>
<td>No. (%)</td>
<td>2007</td>
<td>No. (%)</td>
<td>2008</td>
<td>No. (%)</td>
<td>2009</td>
<td>No. (%)</td>
<td>2010</td>
<td>No. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nonteaching</td>
<td>876</td>
<td>2.5%</td>
<td>1068</td>
<td>3.1%</td>
<td>1360</td>
<td>3.9%</td>
<td>2059</td>
<td>5.6%</td>
<td>2437</td>
<td>7.0%</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Teaching</td>
<td>1374</td>
<td>5.5%</td>
<td>2214</td>
<td>9.4%</td>
<td>2492</td>
<td>10.2%</td>
<td>2643</td>
<td>10.1%</td>
<td>3023</td>
<td>11.8%</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CTP</td>
<td>2006</td>
<td>No. (%)</td>
<td>2007</td>
<td>No. (%)</td>
<td>2008</td>
<td>No. (%)</td>
<td>2009</td>
<td>No. (%)</td>
<td>2010</td>
<td>No. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nonteaching</td>
<td>1</td>
<td>0%</td>
<td>5</td>
<td>0%</td>
<td>21</td>
<td>0.1%</td>
<td>85</td>
<td>0.2%</td>
<td>275</td>
<td>0.8%</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Teaching</td>
<td>26</td>
<td>0.1%</td>
<td>15</td>
<td>0.1%</td>
<td>533</td>
<td>2.2%</td>
<td>1269</td>
<td>4.9%</td>
<td>1488</td>
<td>5.8%</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CTA, CT angiogram; CTP, CT perfusion.
CTP: This category includes patients who got CTP and CTA

### Table II. Rates of overall reperfusion treatments by type of institution

<table>
<thead>
<tr>
<th>Year</th>
<th>Type of Institution</th>
<th>2006</th>
<th>No.</th>
<th>%</th>
<th>2007</th>
<th>No.</th>
<th>%</th>
<th>2008</th>
<th>No.</th>
<th>%</th>
<th>2009</th>
<th>No.</th>
<th>%</th>
<th>2010</th>
<th>No.</th>
<th>%</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>CTH only</td>
<td>2006</td>
<td>No.</td>
<td>%</td>
<td>2007</td>
<td>No.</td>
<td>%</td>
<td>2008</td>
<td>No.</td>
<td>%</td>
<td>2009</td>
<td>No.</td>
<td>%</td>
<td>2010</td>
<td>No.</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nonteaching</td>
<td>710</td>
<td>2.7</td>
<td>818</td>
<td>3.1</td>
<td>950</td>
<td>3.6</td>
<td>1129</td>
<td>4.1</td>
<td>1196</td>
<td>4.7</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Teaching</td>
<td>703</td>
<td>3.9</td>
<td>635</td>
<td>3.8</td>
<td>778</td>
<td>4.8</td>
<td>858</td>
<td>5.0</td>
<td>886</td>
<td>5.5</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CTA</td>
<td>2006</td>
<td>No.</td>
<td>%</td>
<td>2007</td>
<td>No.</td>
<td>%</td>
<td>2008</td>
<td>No.</td>
<td>%</td>
<td>2009</td>
<td>No.</td>
<td>%</td>
<td>2010</td>
<td>No.</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nonteaching</td>
<td>113</td>
<td>12.9</td>
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Overall Reperfusion includes both rtPA and mechanical embolectomy