Cost-effectiveness of Perfusion Imaging With Computed Tomography to Identify Patients for Intravenous Thrombolysis: A Hospital Perspective

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INTRODUCTION

- Stroke is the leading cause of serious long-term disability and the third leading cause of death in the United States.[1]
- Brain imaging with unenhanced computed tomography (CT) is the standard diagnostic imaging test used to distinguish between hemorrhagic and nonhemorrhagic stroke so that appropriate thrombolytic treatment can be administered.[2,3]
- Studies of penumbral brain imaging via magnetic resonance imaging (MRI) have shown potential advantages for identifying patients who may benefit from intravenous recombinant tissue plasminogen activator (IV tPA) treatment beyond 3 hours (e.g., perfusion lesion greater than diffusion lesion volume by ≥ 20%).[4,5]
- However, MRI is costly and labor intensive, and often is not readily available.
- CT perfusion (CTP) is the use of CT with a contrast medium that shows cerebral blood flow, which may help identify ischemic regions of the brain.
- Although the use of CTP may not be as accurate as MRI,[6] it is capable of determining penumbra and may be more practical to administer in hospitals.

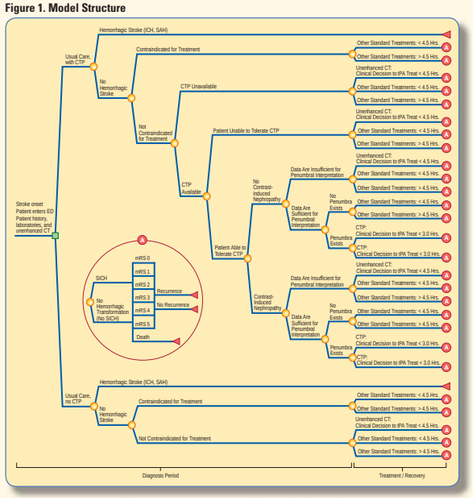
OBJECTIVE

Examine the cost-effectiveness of adding penumbral-based selection to usual care through the use of CTP to identify patients for IV tPA treatment compared with current usual care selection using only unenhanced CT.

METHODS

A decision tree model was developed to simulate a cohort of patients through the acute stroke treatment process, which includes the use of CT, CTP, and treatment with IV tPA when indicated (Figure 1).

Figure 1. Model Structure



ED = emergency department; ICH = intracranial hemorrhage; mRS = modified Rankin Score; SAH = subarachnoid hemorrhage; SICH = secondary hemorrhagic transformation.

- Patients were similar to those observed in the pooled analysis of ATLANTIS, ECASS, and NINDS IV tPA trials[6] and in Schellinger et al.[5]: baseline National Institute of Health Stroke Scale scores ranged from 11 to 14, mean age was 68 years, and 85% were white, non-Hispanic.[5,6]
- Comparators included:
  - CT selection: Patients selected for IV tPA treatment based on results of unenhanced CT, patient history, and time since onset of stroke symptoms.
  - CTP selection: Patients selected for IV tPA treatment based on results of unenhanced CT, patient history, and penumbral-based imaging via CTP.
- Patients entered the model at stroke onset at which time they proceeded to the ED. Patient history was obtained, and patients were assumed to get standard acute stroke workup and an unenhanced CT.
- Imaging assumptions included:
  - All patients undergoing diagnostics will produce interpretable scan images.
  - Interpretation of unenhanced CT in combination with patient history diagnoses hemorrhage/nonhemorrhage stroke with 100% certainty.
  - Unenhanced CT scan cannot detect disturbances in blood flow.
  - All patients undergo unenhanced CT scan first, even those who later undergo CTP.
  - CTP and CT scans are available 24 hours a day for 7 days a week for stroke patients.
  - Patients are assumed not to have contraindications for CTP or CT scanning.
- Based on the sensitivity, specificity, and accuracy, CTP was assumed to accurately image penumbra 89.2% of the time compared with MRI, which was assumed accurate 100% of time.[6]
- Patterns of penumbra were assumed to exist in 61.7% of ischemic stroke cases.[8]
- Other standard treatments were given based on results from the unenhanced CT and patient history when penumbra was not found.
- 43.2% of patients admitted to the hospital had contraindications for IV tPA.[9]
- After discharge from the hospital, a proportion of patients experienced recurrent stroke hospitalization (applicable to modeling time horizons extending beyond hospital discharge).
- Patients with recurrent stroke were assumed to return to the same hospital for the recurrent stroke hospitalization as seen in the index stroke hospitalization
- Time since stroke onset to the arrival at ED and time from ED until completion of obtaining patient history and interpretation of CT were estimated from the published literature.[10,11]
- Administration of CTP added 15 minutes to the total time from onset of stroke symptoms to completion of typical diagnostics.
- Based on mean time and standard deviations, a gamma distribution was used to estimate the percentage of patients eligible for treatment within each treatment time window.
- Patient eligibility and dose of IV tPA administered was obtained from FDA labeling.[12]
- IV tPA drug costs were estimated based on the wholesale acquisition price at $3,442.[7,13]
- Hospital costs were obtained from the Healthcare Utilization Project[14] and considered cost of the index hospitalization, occurrence of SICH and contrast induced nephropathy, and recurrent stroke when applicable.
- Costs were reported in 2008 US dollars, and all costs and outcomes were discounted at 3% per annum where appropriate.
- Utility weights by mRS group status were obtained from the published literature.[15]

Clinical Benefits

- Based on results from ECASS 3,[16] when a patient qualified, IV tPA was allowed to be administered within 4.5 hours from onset of stroke when penumbra was not examined or seen. IV tPA was allowed to be administered within 6 hours from onset of stroke when penumbra was seen.
- CT selection with no IV tPA treatment: Distribution of favorable outcome (mRS) given no acute stroke treatment was similar to the placebo arm of the pooled analysis of ATLANTIS, ECASS, and NINDS IV tPA trials[7] (Table 1).
- CT selection with IV tPA treatment: Compared with no treatment, adjusted odds ratios of favorable outcome (mRS < 2) when treated within the following time window after onset of stroke are:
  - ≤ 1.5 hours: 2.81 (95% confidence interval [CI]: 1.75-4.50; *P* value not reported)
  - 1.5 to ≤ 3.0 hours: 1.55 (95% CI: 1.12-2.15; *P* value not reported)[7]
  - 3.0 to ≤ 4.5 hours: 1.34 (95% CI: 1.02-1.76; *P* value = 0.04).[16]
- CTP selection with IV tPA treatment: Compared with CT selection with IV tPA treatment, odds ratios of favorable outcome (mRS < 2) when treated within the following time window after onset of stroke are:
  - > 3 hours: 1.467 (95% CI: 1.017-2.117; *P* value = 0.04)
  - ≤ 3 hours: 1.136 (95% CI: 0.841-1.534; *P* value > 0.05).[5]

Clinical Risks

- CT selection with no IV tPA treatment: Risk of SICH was obtained from the placebo arm of the pooled analysis of IV tPA trials[7] (Table 1).
- CT selection with IV tPA treatment: Risk of SICH when treated within the following time window after onset of stroke was:
  - ≤ 1.5 hours 3.1% (95% CI: 1.6%-5.6%)
  - 1.5 to ≤ 3.0 hours 5.6% (95% CI: 3.9%-7.9%)
  - 3.0 to ≤ 4.5 hours: 5.9% (range: 2.1%-8.7%).[7,16]
- CTP selection with IV tPA treatment: Risk of SICH when treated within the following time window after onset of stroke was:
  - > 3 hours: 2.8% (±20%)
  - ≤ 3 hours: 4.4% (±20%)[17]
- Incidence of contrast-induced nephropathy was 0.5% (range: 0.0%-2.0%) in patients receiving CTP.[18]
- Mortality with SICH was 46.7% in patients not treated with IV tPA and 62.2% in patients treated with IV tPA.[5,7]

Table 1. Distribution of 90-Day mRS and Incidence SICH Within Each Time Window When Treating With No IV tPA

Model Parameter	CT-Based Selection		
	No IV tPA < 1.5 Hours	No IV tPA 1.5 to ≤ 3.0 Hours	No IV tPA 3.0 to ≤ 4.5 Hours
Efficacy (90-day disease severity by mRS score)			
mRS 0	10.0%	16.0%	11.0%
mRS 1	19.0%	14.0%	21.0%
mRS 2	13.0%	10.0%	11.0%
mRS 3	12.0%	17.0%	16.0%
mRS 4	21.0%	20.0%	20.0%
mRS 5	5.0%	9.0%	10.0%
mRS 6	21.0%	16.0%	12.0%
Incidence of SICH	0.0% (95% CI: not applicable)	1.0% (95% CI: 0.4%-2.0%)	1.7% (95% CI: 1.0%-2.9%)

RESULTS

Figures 2 and 3 present the percentage of patients with favorable outcome (i.e., mRS ≤ 1), life years, and quality-adjusted life years (QALYs) for CT and CTP selection. Figure 4 presents the total hospital cost for CT- and CTP-selected stroke patients.

Figure 2. Percentage of Patients With Favorable Outcome for CT and CTP Selection

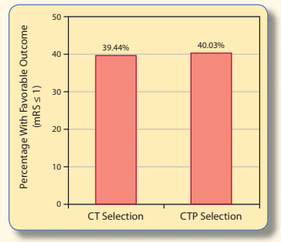


Figure 3. Life Years and QALYs of Patients With CT and CTP Selection

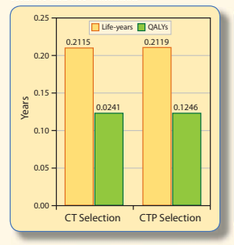
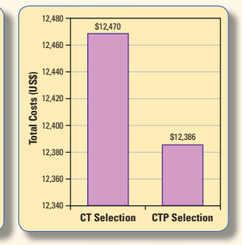


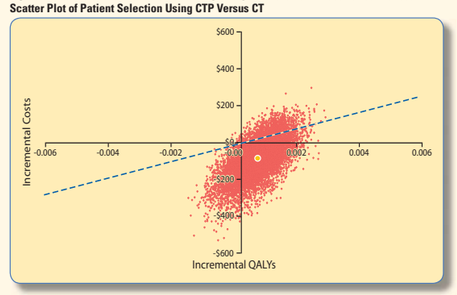
Figure 4. Total Costs to Hospitals Per Patient for CT and CTP Selection



Sensitivity Analyses

Results were robust to changes to all parameters. Probabilistic sensitivity analysis (Figure 5) showed that CTP selection was cost-effective in 89.2% of the simulation runs; it remained cost-saving in 78.4% of runs.

Figure 5. Results of Probabilistic Sensitivity Analysis: Incremental Cost-effectiveness Scatter Plot of Patient Selection Using CTP Versus CT



Dotted line represents an incremental cost/QALY = $50,000. Points to right of dotted line are considered cost-effective. Gray dots represent simulations. Black dot represents base-case result.

CONCLUSIONS

- Penumbral-based CTP selection decreases mortality and improves functional outcome in patients upon discharge from the hospital.
- Overall costs to the hospital given CT and CTP selection are comparable.
- Using penumbral-based CTP selection after routine CT is cost-effective for hospitals.
- Diagnostic imaging with CTP may provide hospitals and clinicians with greater access and a more cost-efficient alternative to improve stroke outcomes with IV tPA based on penumbral selection.

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