Drivers of Costs Associated With Reperfusion Therapy in Acute Stroke

The Interventional Management of Stroke III Trial

Kit N. Simpson, DrPH; Annie N. Simpson, PhD; Patrick D. Mauldin, PhD; Michael D. Hill, MD; Sharon D. Yeatts, PhD; Judith A. Spilker, BSN; Lydia D. Foster, MS; Pooja Khatri, MD; Renee Martin, PhD; Edward C. Jauch, MD; Dawn Kleindorfer, MD; Yuko Y. Palesch, PhD; Joseph P. Broderick, MD; for the IMS III Investigators

Background and Purpose—The Interventional Management of Stroke (IMS) III study tested the effect of intravenous tissue-type plasminogen activator (tPA) alone when compared with intravenous tPA followed by endovascular therapy and collected cost data to assess the economic implications of the 2 therapies. This report describes the factors affecting the costs of the initial hospitalization for acute stroke subjects from the United States.

Methods—Prospective cost analysis of the US subjects was treated with intravenous tPA alone or with intravenous tPA followed by endovascular therapy in the IMS III trial. Results were compared with expected Medicare payments.

Results—The adjusted cost of a stroke admission in the study was $35 130 for subjects treated with endovascular therapy after intravenous tPA treatment and $25 630 for subjects treated with intravenous tPA alone (P<0.0001). Significant factors related to costs included treatment group, baseline National Institutes of Health Stroke Scale, time from stroke onset to intravenous tPA, age, stroke location, and comorbid diabetes mellitus. The mean cost for subjects who had routine use of general anesthesia as part of endovascular therapy was $46 444 when compared with $30 350 for those who did not have general anesthesia. The costs of embolectomy for IMS III subjects and patients from the National Inpatient Sample cohort exceeded the Medicare diagnosis-related group payment in ≥75% of patients.

Conclusions—Minimizing the time to start of intravenous tPA and decreasing the use of routine general anesthesia may improve the cost-effectiveness of medical and endovascular therapy for acute stroke.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00359424.

Key Words: brain ischemic ■ costs and cost analysis ■ hospitals ■ reperfusion ■ stroke

Costs for the initial hospital admission for patients with acute ischemic stroke are affected by stroke severity, presence of prestroke comorbid conditions, type of reperfusion treatment selected, response to therapy, including adverse events, hospital care processes, and hospital charging patterns related to the use of specific services. Understanding the relative contributions of these complex factors to the overall cost of stroke care is critical so that the processes of stroke care can be designed to be cost-effective.

Recent studies have reported the costs associated with the use of intravenous tissue-type plasminogen activator (tPA) alone. Brinjikji et al1 used 2001 to 2008 Healthcare Cost and Utilization Project National Inpatient Sample data to identify median charges for patients with acute ischemic stroke treated with intravenous tPA, as well as patient and hospital characteristics associated with variations in charges. Most previous US studies of tPA have used a decision analysis modeling approach. Fagan et al5 demonstrated that patients treated with intravenous tPA, when compared with placebo-treated patients, had a shorter length of stay in the hospital (10.9 versus 12.4 days; P=0.02), long-term health outcomes of 564 (3–850) quality-adjusted life-years saved ≥30 years of the model per 1000 patients, and a greater likelihood of discharge to home than to inpatient rehabilitation or a nursing home (48% versus 36%; P=0.002). However, length of stay at the time of the National Institute of Neurological Disorders and Stroke (NINDS) tPA
Trial (1991–1994) was much longer than length of stay today. A pooled analysis of data from three large trials revealed a strong relationship between the speed of initiation of intravenous tPA after stroke onset and improved functional outcome at 90 days but did not examine the economic effect.8 Luengo-Fernandez et al identified an inverted U-shaped relationship between initial National Institute of Health Stroke Scale (NIHSS) score and cost of care in the year subsequent to the initial stroke, with more severe patients expending more, but with costs attenuated for the sickest patients because of early death. A recent study compared mechanical thrombectomy as an adjunct to intravenous tPA using a Markov model and Monte Carlo simulation based on a hypothetical 68-year-old patient with large-vessel ischemic stroke.8 This simulation study reported an intervention strategy has the potential for being cost-effective, but the assumptions of the model have been questioned.8

The present economic study was planned as part of the Interventional Management of Stroke (IMS) III Trial—an international, multicenter, randomized, open-label clinical trial with a blinded outcome assessment at 3 months—that tested the approach of intravenous tPA followed by protocol-approved endovascular treatment when compared with standard intravenous tPA.10 The IMS III trial began enrollment in August 2006. In April 2012, after 656 of a planned 900 participants had undergone randomization, the Data and Safety Monitoring Board recommended to the sponsor (the National Institute of Neurological Disorders and Stroke) that enrollment be terminated owing to the crossing of the prespecified boundary for futility. The clinical trial analysis found no overall difference in outcomes for the 2 study arms. A prespecified subgroup analysis showed a statistical trend that patients with more severe stroke may do better with intravenous-intra-arterial, but this relationship did not achieve statistical significance (\(P=0.06\)). The current analysis compares initial hospital charges and costs estimated from the recorded charges for IMS III subjects treated in the United States with intravenous tPA alone and those treated with intravenous tPA followed by endovascular therapy (hereafter referred to as the endovascular-treated group) for whom UB04 billing data were prospectively collected as part of the clinical trial.

Methods

Study Population
The IMS III Trial planned to enroll a maximum of 900 subjects, aged 18 to 82 years, at 58 centers in the United States, Canada, Australia, and Europe. Eligibility criteria included receipt of intravenous tPA within 3 hours after symptom onset and a moderate to severe neurological deficit (defined as an NIHSS score, \(\geq 10\) or after approval of amendment 3, an NIHSS score of \(8–9\) with computed tomographic angiographic evidence of an occlusion of the first segment of the middle cerebral artery [M1], internal carotid artery, or basilar artery at institutions, where computed tomographic angiographic imaging at baseline was the standard of care for patients with acute stroke). Informed consent was obtained from the eligible patient or a legal representative before randomization. Detailed inclusion and exclusion criteria have been published.9 The original economic study of the IMS III Trial was designed with 80% power to detect a 10% reduction in cost \(\geq 1\) year after stroke.10 The present analysis has a shorter time horizon for the accumulation of cost difference and contains only US subjects’ UB04 charge data because UB04 data are not collected in Australia, Canada, or Europe. The results of this analysis of hospital cost differences should be interpreted in view of these limitations.

Determination of Cost
Cost of the initial hospital admission was estimated based on the actual hospital charges documented on UB04 billing forms provided by the treating hospitals. Total charges were summed if \(\geq 1\) UB04 form was present. Thus, study charges included cases where \(\geq 1\) bill was submitted from a hospital, as well as multiple individual bills submitted from referring and receiving hospitals. Subjects were not charged for the intra-arterial tPA (study drug provided by Genentech); thus, the cost of one 50-mg vial of tPA was added to the cost estimate for all subjects who received this therapy. Free devices, or hospital-requested device replacement, were provided to some vendors over parts or all of the trial period (EKOS, Concentric, and Johnson & Johnson). This variation was corrected by adding the cost of the primary device to the estimated cost for the affected bills. Charges were converted to costs using the treating hospital’s Medicare cost:charge ratio file with the CMS. All cost estimates were converted to 2012 US dollars using the Medical Care Services Consumer Price Index. Because hospital costs vary greatly across geographic regions in the United States based on differences in the cost of labor, we also estimated an adjusted cost value, using the CMS 70% labor adjustment factor for each of the hospitals in the study; however, this cost estimate modification did not significantly affect the results, so these data are not reported. Thus, 3 separate measures of the amount of hospital resources used for the initial ischemic stroke event were estimated in the cost analyses. These were charges as submitted in the year of the event, costs in currency of the year of the event, and present value costs (PVC) inflated to represent costs in 2012. All analyses were performed using SAS version 9.3 (Cary, NC).

Intent-to-treat analysis included data for all subjects randomized in the study, who had economic data collected for the initial stroke hospitalization. Basic descriptive statistics were used to compare costs of subjects randomized to endovascular treatment to subjects receiving intravenous tPA alone. The effects of differences in subject characteristics at baseline on observed charges, costs, and 2012 PVC were examined using generalized linear multivariable models with a \(\gamma\)-distributed log-link function. All cost models included as covariates any measures are listed in the online-only Data Supplement that were significant at \(P<0.05\). The distribution of hospital charges for the admissions was examined using the standard CMS charge groupings with the exception of the operating or procedure room charges and anesthesia charges, which we combined in the OR category, and blood charges, which we included in the Other category. Finally, the cost profiles of the IMS treatment groups were compared with the cost profiles of a sample of US patients, who were treated under usual care conditions using all payer data from the Healthcare Cost and Utilization Project National Inpatient Sample (NIS) for 2010. NIS patients were selected if they had a principal diagnosis International Classification of Diseases, Ninth Revision, code of acute ischemic stroke similar to the principal International Classification of Diseases, Ninth Revision, diagnosis codes observed for the IMS subjects, while also having a procedure code indicating receipt of tPA. Within this group, we then identified the subgroup of admissions with an International Classification of Diseases, Ninth Revision, procedure code of endovascular embolectomy (39.74). Although the NIS comparison group was selected to be as similar to the IMS stroke cohort as possible, it is likely that those treated with intravenous tPA had substantially lower stroke severity than the subjects in the IMS III Trial because the trial excluded patients with an NIHSS of \(<10\) except for patients with NIHSS of \(8\) to \(9\) with a larger artery occlusion on imaging. The charges for the NIS cohort were adjusted to costs using the cost:charge ratios for the discharging hospital. For consistency with the IMS III Trial cost analysis, the NIS data were then inflated to 2012 PVC using the Medical Care Services Consumer Price Index.

Results
A total of 430 (66% of subjects randomized in the study), of the 454 US subjects in the trial, had usable economic data collected for the initial stroke hospitalization. The 202 non-US subjects were not considered in this analysis (Appendix).
Table 1. Hospital Charges as Incurred, Costs as Incurred, and Costs in 2012 US Currency for the Initial Treatment of US Patients With Moderate or Severe Stroke Enrolled in the Study*

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Charges (Year of Stroke)</th>
<th>Costs (Year of Stroke)</th>
<th>Present Value Costs (2012 Value)</th>
<th>Estimated Mean Cost (2012 Cost)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endovascular therapy</td>
<td>Mean (SD)</td>
<td>$113,185 (8279)</td>
<td>$26,935 (6602–179491)</td>
<td>$29,848 (7856–205609)</td>
</tr>
<tr>
<td></td>
<td>Median (range)</td>
<td>$86,481 (23350–552279)</td>
<td>$18,134 (6602–179491)</td>
<td>$19,768 (5992–209299)</td>
</tr>
<tr>
<td>IV tPA alone</td>
<td>Mean (SD)</td>
<td>$86,880 (91057)</td>
<td>$23,833 (21799)</td>
<td>$26,266 (24042)</td>
</tr>
<tr>
<td></td>
<td>Median (range)</td>
<td>$58,247 (13701–830652)</td>
<td>$18,134 (6602–179491)</td>
<td>$19,768 (5992–209299)</td>
</tr>
</tbody>
</table>

* IV indicates intravenous; and tPA, tissue-type plasminogen activator.
† Costs in year of stroke indicate the actual costs at the time of patient enrollment. These costs are not adjusted for inflation.
‡ Multivariable model controlling for age, National Institute of Health Stroke Scale, time to IV tPA administration, stroke location, and diabetes mellitus.

The mean observed charges and costs for the subjects with moderate to severe stroke randomized to endovascular treatment and to intravenous tPA alone are provided in Table 1. The mean hospital charges per admission recorded on the UB04 form was $113,185, this amount is equal to $35,130 when adjusted to reflect the 2012 costs of a stroke admission (controlling for effects of age, stroke location, NIHSS, diabetes mellitus, and time to intravenous tPA administration). The $35,130 cost incurred for subjects treated with endovascular therapy and is compared with a cost of $25,630 for subjects treated with intravenous tPA alone, a difference of $9500 in 2012 currency (P<0.0001). The cost of the endovascular devices used to administer intra-arterial tPA or to perform thrombectomy in this population can range from $1250 to $11,000. Thus, the higher cost in the endovascular therapy arm may be largely explained by the cost of the device. As expected, treatment group (intravenous plus endovascular treatment) and baseline NIHSS (higher severity with higher costs) did affect costs, as did time to tPA (lower costs with earlier treatment), age (higher costs with older age), stroke location (higher cost with right hemispheric location), and comorbid diabetes mellitus (higher costs with diabetes).

The multivariable analysis assessing the effects of differences in subject characteristics at baseline on observed charges, PVC, and the other primary outcome revealed a significant effect of the study year on charges (P<0.0001) and costs (P<0.0002). However, the inflation-adjusted costs did not show a time effect over the course of the study. Sex, race, history of hypertension, coronary artery disease, congestive heart failure, hyperlipidemia, statin or antiplatelet use at baseline, atrial fibrillation, baseline systolic blood pressure, baseline international normalized ratio, withdrawal of care, or preexisting disability did not significantly affect the estimated cost of a hospital admission for stroke in subjects treated within the trial.

The effects of treatment group, stroke severity, and time to tPA administration on mean PVC of hospital care for stroke are shown in Figure 1. The adjusted mean cost of the initial hospital admission for stroke subjects randomized to endovascular therapy after intravenous tPA is, as expected, consistently higher than the mean cost of care for subjects treated with intravenous tPA alone, regardless of the timing of tPA administration. However, the mean cost of care for subjects randomized to endovascular therapy after intravenous tPA differed based on whether patients actually received an endovascular therapy. Multivariable model estimates (controlling for age, stroke severity, and early tPA administration) of mean cost for subjects randomized to endovascular therapy after intra-arterial tPA who did not receive the intra-arterial intervention was $30,313 when compared with $38,424 for subjects who were treated with intra-arterial tPA or an embolectomy device. For comparison, mean cost for the intravenous tPA alone group was $25,630.

Subjects with a severe stroke (NIHSS≥20) have $7000 greater hospital costs than subjects with a moderate stroke (Figure 1). However, in the group randomized to endovascular therapy, administration of tPA within 2 hours of stroke onset reduced the cost of a stroke by an estimated $3248 (P=0.0442) regardless of stroke severity. A different cost pattern was observed for subjects treated with intravenous tPA alone. Early administration of tPA made no significant difference ($1385) in observed cost for those with moderate stroke (P=0.1267) but reduced the mean cost by $7706 for those with severe stroke. Thus, the greatest cost savings for subjects treated with intravenous tPA alone may be expected from improvement in the time to tPA administration for subjects with severe stroke.

The pattern of adjusted mean length of hospital stay reflects those observed for the costs for subgroups of subjects defined...
by timing of tPA and stroke severity. Length of hospital stay was 2.4 days shorter for subjects who received tPA within 2 hours of stroke onset ($P<0.0001$); 1.5 days shorter for subjects with baseline NIHSS<20 ($P=0.0190$); and length of hospital stay was 1.3 days longer for subjects with a right hemispheric stroke ($P=0.0361$). We observed a trend toward slightly shorter mean hospital length of stay (1.0 day) for subjects who received endovascular therapy ($P=0.0848$) than the mean length of hospital stay observed for subjects who received intravenous tPA alone, after controlling for the effects of timing of tPA and baseline covariates. There was no statistical difference at 7 days after stroke ($P=0.57$) for the 2 study arms, so cost differences are unlikely to be because of survival. Thus, differences in length of hospital stay explain some, if not much, of the cost difference observed in the study.

When we examined the distribution of mean charges by charge category (Figure 2), we observed significantly higher charges billed for respiratory services ($P=0.02$), laboratory ($P=0.03$), operating or procedure room use (including anesthesia) ($P=0.0001$), radiology services ($P<0.0001$), and supplies ($P<0.0001$) for endovascular therapy subjects when compared with the mean charges for the intravenous tPA-alone group.

As expected, we observed some variations in mean cost across the treatment groups depending on the endovascular device types used and the choices made for the use of anesthesia. Some subjects who were randomized to receive endovascular therapy were not candidates for thrombectomy, and 3 subjects randomized to intravenous tPA alone received endovascular therapy. The mean cost observed for subjects by the use of intubation for general anesthesia, whether routinely used for the endovascular procedure or as medically indicated for control of airway and respiration, is presented in Table 2.

We examined the cost distributions by therapy type and compared the cumulative cost curves for the IMS III subjects

![Graph showing mean charges by category. Anesthesia is grouped with operating costs, and blood products are grouped with other costs. IA indicates intrarterial; and IV tPA, intravenous tissue-type plasminogen activator.](image)

**Table 2.** Adjusted Cost for IV tPA Alone and Anesthesia as Indicated by Intubation in First 7 Hours After Stroke

<table>
<thead>
<tr>
<th>Treatment Type and Anesthesia Status</th>
<th>n=430</th>
<th>Mean Cost Per Admission (SD)</th>
<th>Estimated Mean Cost Per Admission*</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV tPA alone, no intubation†</td>
<td>135</td>
<td>$22,982 ($14,745)</td>
<td>$23,027</td>
</tr>
<tr>
<td>IV tPA alone, with medically indicated intubation</td>
<td>9</td>
<td>$59,784 ($61,035)</td>
<td>$57,145</td>
</tr>
<tr>
<td>IV tPA alone, with procedural intubation</td>
<td>2</td>
<td>$97,137 ($57,114)</td>
<td>$95,829</td>
</tr>
<tr>
<td>Endovascular therapy, no intubation</td>
<td>186</td>
<td>$30,216 ($15,825)</td>
<td>$30,350</td>
</tr>
<tr>
<td>Endovascular therapy, with medically indicated intubation</td>
<td>45</td>
<td>$42,760 ($20,196)</td>
<td>$41,690</td>
</tr>
<tr>
<td>Endovascular therapy, with procedural intubation</td>
<td>53</td>
<td>$46,139 ($28,912)</td>
<td>$46,444</td>
</tr>
</tbody>
</table>

*IV indicates intravenous; and tPA, tissue-type plasminogen activator.

*Multivariable model adjusted for effects of National Institute of Health Stroke Scale and early tPA administration.

†No intubation groups include subjects missing intubation information.
with the cost curves for patients from the 2010 NIS inflating their costs to 2012 values to be comparable with the IMS III PVC presented here. The cumulative cost curves for the IMS subjects and the NIS patients are provided in Figure 3.

**Discussion**

The financial burden of stroke is large from all viewpoints: people, society, and payer. Although the cumulative costs of stroke care in the long term far exceed the costs of acute care, costs associated with acute care have not been well characterized using detailed billing information.\(^\text{13,14}\) As expected, emergency endovascular intervention using embolectomy devices in the IMS III Trial resulted in greater cost per subject when compared with subjects treated with intravenous tPA alone. This cost difference is explained primarily by the use of the embolectomy devices, intra-arterial tPA, and the angiographic procedure. However, the IMS III Trial also provides insights into 3 important drivers of acute care costs in subjects who undergo reperfusion therapy: baseline stroke severity, time from stroke onset to start of reperfusion therapy, and routine use of general anesthesia during endovascular stroke therapy.

Stroke prognosis and care needs are governed by stroke severity, and costs and outcomes are closely linked in our findings. Severe stroke was much more expensive in the acute hospital care than moderate stroke in the IMS III Trial, irrespective of treatment assignment. This is an intuitive result for clinicians because patients with severe stroke are less likely to be discharged quickly and to go home. It also complements the recent report by Fonarow et al\(^\text{2}\) using the Get With The Guidelines database in which baseline stroke severity is the most important driver of subject outcome and mortality.

![Figure 3. Subject treated with tissue-type plasminogen activator (tPA) alone and those treated with tPA followed by endovascular therapy using embolectomy devices in Interventional Management of Stroke (IMS) III and National Inpatient Sample (NIS) cohorts. Cumulative cost curves for patients with acute ischemic stroke (AIS) receiving IV tPA alone (red curves) included data from IMS III subjects randomized to tPA alone (IMS IV alone) and Healthcare Cost and Utilization Project NIS patients who received IV tPA but did not have an endovascular procedure code or a diagnosis-related group (DRG) classification indicating an endovascular intervention (NIS tPA). Cumulative cost curves for IMS III subjects who were randomized to endovascular treatment with embolectomy devices (black solid line) and NIS patients who had both a tPA procedure code (indicating received tPA) and an endovascular procedure code or DRG classification indicating embolectomy (black interrupted line) are provided. Medicare 2012 payment levels (without any hospital-specific payment for teaching or regional factors) for the DRGs most relevant to IMS III are indicated by the vertical lines. DRG 61 is national payment for AIS with the use of thrombolytic agent with major comorbid condition (MCC), DRG 62 is payment with comorbid condition (CC), and DRG 63 is payment without MCC or CC. To best reflect IMS III in this figure, DRG 23 is payment for AIS with embolectomy (craniotomy with major device implant or acute complex CNS PDX with MCC) and a tPA procedure code, and DRG 24 is payment for AIS with embolectomy as defined above without MCC and a tPA procedure code. Payment and cost of providing care are equal (on average) if the payment line crosses the cumulative cost curve at the 50% mark. Payments are inadequate for covering cost of care (on average) if the payment line crosses the cumulative cost curve at a point lower than 50%, and payment exceeds cost of care (on average) if the payment line crosses the cumulative cost curve above the 50% mark. The observed cost curves for IMS III subjects treated with IV tPA alone seem slightly higher than the cost curve for the NIS patients with stroke with an International Classification of Diseases, Ninth Revision, code of tPA, reflecting the exclusion of mild strokes from the trial. Furthermore, the expected Medicare payments for MS-DRGs 61, 62, and 63 fall below the 50th percentile on the cumulative cost curves, indicating that payment for these patients with stroke may be slightly less than the cost of care provided. A different pattern is observed for subjects who had embolectomy after tPA. Here, the cumulative cost curve for IMS III subjects fall to the left of the curve for NIS patients. This indicates that the IMS subjects have lower median cost than the costs estimated for the NIS patients. Furthermore, the expected payment for both groups fall far left of the median of the cost curves. This means that the typical Medicare DRG payment will be lower than what it costs a hospital to treat such a patient in a majority of cases. For the IMS III subjects, we may expect the care of 75% of subjects to cost more than the Medicare DRG payment will reimburse, whereas the expected DRG payment will not cover the cost of care for 85% of patients in the NIS cohort.
Evidence of a relationship between time to intravenous tPA and clinical outcome was found in only 1 of the 4 (US) subgroups examined: endovascular subjects with NIHSS ≥20. Interestingly, in the prespecified subgroup analyses of all IMS III subjects comparing intravenous tPA with intravenous tPA followed by endovascular therapy, there was a trend (non-significant) toward better overall outcomes among participants in the endovascular group in those patients treated with intravenous tPA within 2 hours after stroke onset.

Although we do not have evidence to show association of time to intravenous tPA and outcome in the subgroups with significantly different costs, this may be because of lack of power. In addition, the pattern of adjusted mean length of hospital stay reflects those observed for the costs for subgroups of subjects defined by timing of tPA and stroke severity.

Length of hospital stay was 2.4 days shorter for subjects who received tPA within 2 hours of stroke onset (P < 0.0001); 1.5 days shorter for subjects with baseline NIHSS < 20 (P = 0.0190, already in results). It is not clear why decreased costs are not seen in the subgroup of patients treated with intravenous tPA with NIHSS 8 to 19; imbalances in other variables related to both outcome and costs between patients treated early and late could be a factor, and small numbers can lead to differences simply related to chance because the confidence intervals include both positive and negative relationships.

This finding provides strong evidence to motivate physicians and hospitals to put into place systems of care that allow for and demand rapid treatment times with special focus on assuring that these systems are effective for both patients with moderate and severe stroke. Although we recognize the importance of a 60-minute door-to-needle time yet uncommonly meet that benchmark, the Helsinki group routinely manages treatment under 30 minutes. Thus, decreasing the time from stroke onset to start of reperfusion therapy currently saves money because it saves ischemic brain for patients with severe stroke. Additional work may be needed to assure that patients with moderate stroke have equal benefits.

Costs for endovascular therapy were substantially increased by the routine use of general anesthesia with intubation as part of an endovascular procedure. Increases in respiratory therapy, radiography, and anesthesia services were major drivers of the increased costs. Given the association of anesthesia and intubation with worse clinical outcomes in several previous reports, and the substantial increased costs with the use of general anesthesia and intubation, this practice needs great scrutiny going forward.

Importantly from the overall societal costs perspective, the charges for subjects in the intravenous tPA treatment group within the trial were close to charges for a similar cohort from the NIS. This suggests that these economic results from the IMS III Trial are generalizable to typical care in the United States. The costs for endovascular therapy with devices in IMS III were less than the NIS sample of patients treated with embolecomy, likely because embolecomy devices were used in a minority of IMS III–treated patients who received endovascular therapy when compared with those in the recent NIS sample. The costs for care for endovascularly treated patients far exceed typical remuneration patterns in the NIS, implying that these procedures are undersupported financially.

The current study has several limitations. First, we analyzed only hospital costs and did not include any physician costs in our analyses. It would be expected that the use of endovascular treatment and routine anesthesia would add a larger amount of separately billed physician costs to the overall total cost difference between the 2 approaches. Second, this analysis examines only the initial hospitalization and does not examine the costs over subsequent years that are highly correlated with disability after stroke. A subsequent article will address the 1-year costs and projected future costs in the IMS III cohort. Finally, we cannot generalize our cost estimates to other countries. However, we expect that the increase in costs associated with stroke severity, endovascular treatment, later treatment with intravenous tPA, and routine use of intubation will be mirrored in other countries as well.

Appendix

Enrolling Clinical Centers

University of Cincinnati College of Medicine (72 subjects): J. Broderick, T. Tomsick; University of Pittsburgh Medical Center (46): L. Wechsler, T. Jovin; Calgary Health Region/Foothills Medical Centre (44): A. Demchuk, M. Goyal; Toronto Western Hospital (29): F. Silver, K. Murphy; Hospital Vall d’Hebron (28): C. Molina, M. Ribó; Royal Melbourne Hospital (27): B. Yan, P. Mitchell; Mayo Clinic Arizona (26): B. Demaerschalk, B. Chung; Oregon Health Sciences University, Oregon Stroke Center (24): W. Clark, S. Barnwell; Riverside Methodist Hospital (24): R. Budzik; Alexian Brothers Hospital Network (23): T. Malisch; Froedert Hospital/Medical College of Wisconsin (23): O. Zaidat; Colorado Neurological Institute/Swedish Medical Center (21): C. Fanale, D. Frei; Allegheny General Hospital (18): A. Tayal, A. Ku; Dresden University of Technology (17): U. Bodechtel, R. von Kummer; Ruan Neurology/Mercy Medical Center (16): M. Jacoby, W. Young; Lehigh Valley Hospital (15): Y. Isayev, D. Shaff; UCLA Medical Center (14): S. Starkman, F. Vinuela; University of Louisville (11): A. Abou-Chebl; Martin Luther University (10): K. Wartenberg, K. Stock; Royal Prince Alfred Hospital (10): C. Anderson, G. Parker; Abington Memorial Hospital (9): Q. Shah; Vancouver General Hospital (9): A. Woolfenden, G. Redekop; Henry Ford Hospital (8): C. Lewandowski, W. Sanders; University of Virginia Health System (8): E. Clarke Haley, A. Evans; Washington University (8): P. Panagos, C. Derdeyn; Hoag Memorial Hospital Presbyterian (7): D. Brown, M. Brandt-Zawadzki; Morton Plant Mease Health Care (7): A. Arora, E. Lopez De Valle; PENN State M.S. Hershey Medical Center (7): K. Cockroft; University of Miami Miller School of Medicine/Jackson Memorial Hospital (7): D. Yavagal; Lahay Clinic Medical Center (6): In Sup Choi; Mission Hospitals/ Mission Neurology Services (6): A. Schneider, J. Short; Monash Medical Centre (6): T. Phan, W. Chong; University of North Carolina (5): D. Huang, S. Solander; University of Texas Medical School at Houston (5): J. Grotta, P. Chen; Upstate Medical University (5): Z. El Zommar, E. Deshaies; Bichat Stroke Centre and Paris Diderot University (4): P. Amarenco, M. Mazighi; Medical University of South Carolina (4): E. Jauch, A. Turk; Ottawa Hospital-Civic Campus (4): G. Stotts, C. Lum; Park Nicollet Institute (4): S. Hanson, M.

Nonenrolling Sites
Intercoastal Medical Group/Sarasota Memorial Hospital: M. Concha, N. Razack; University of Rochester Medical Center: C. Benesch, B. Jahromi; St. Louis University: R. Edgell, N. Vora; Reading Hospital and Medical Center: R. Chavali; Methodist Research Institute/Clariion Health Partners: J. Scott; Central DuPage Hospital: H. Shownkenn; QEII Health Sciences Centre, Dalhousie University: S. Phillips, E. Versnick; Hospital of the University of Pennsylvania: S. Kasner, R. Hurst; University of Alberta Stroke Program: A. Shuaib, D. Emery; Sutter Medical Facility of Sacramento: B. Varjavand, R. Atkinson; St. John Providence Medical Center: R. Fessler; University of Freiburg: W. Niesen, C. Hader; Ernst Moritz Arndt University: A. Khaw, S. Langner; University of Basel: F. Lyer, C. Stippich.

Executive Committee

University of Cincinnati Clinical Coordinating and Angiogram Image Analysis Center

Statistical and Data Coordination Unit at Medical University South Carolina

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Disclosures
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References


Drivers of Costs Associated With Reperfusion Therapy in Acute Stroke: The Interventional Management of Stroke III Trial
for the IMS III Investigators

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## Baseline Characteristics of Subjects With and Without Cost Data by Treatment Type

<table>
<thead>
<tr>
<th></th>
<th>Cost Group Endovasc. Therapy N=284</th>
<th>Cost Group IV t-PA N=146</th>
<th>No Cost Group Endovasc. Therapy N=150</th>
<th>No Cost Group IV t-PA N=76</th>
<th>Overall N=656</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age: median (min-max)</strong></td>
<td>69 (24-89)</td>
<td>66.5 (23-84)</td>
<td>71 (23-83)</td>
<td>70 (29-82)</td>
<td>69 (23-89)</td>
</tr>
<tr>
<td><strong>Male (%)</strong></td>
<td>139 (48.43)</td>
<td>83 (56.08)</td>
<td>80 (53.33)</td>
<td>40 (52.63)</td>
<td>340 (51.83)</td>
</tr>
<tr>
<td><strong>Black/African American/African (%)</strong></td>
<td>44 (15.33)</td>
<td>17 (11.49)</td>
<td>7 (4.67)</td>
<td>3 (3.95)</td>
<td>70 (10.67)</td>
</tr>
<tr>
<td><strong>Hispanic or Latino (%)</strong></td>
<td>9 (3.14)</td>
<td>6 (4.05)</td>
<td>3 (2.00)</td>
<td>6 (7.89)</td>
<td>23 (3.51)</td>
</tr>
<tr>
<td><em><em>Baseline NIHSS</em>: median (min-max)</em>*</td>
<td>17 (7-40)</td>
<td>16 (9-30)</td>
<td>17 (7-40)</td>
<td>17 (8-30)</td>
<td>17 (7-40)</td>
</tr>
<tr>
<td><strong>ASPECTS 8-10 (%)</strong></td>
<td>160 (56.54)</td>
<td>88 (59.46)</td>
<td>88 (59.86)</td>
<td>44 (57.89)</td>
<td>378 (57.62)</td>
</tr>
<tr>
<td><strong>Presumptive Stroke Location</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Left hemisphere (%)</strong></td>
<td>141 (49.13)</td>
<td>66 (44.59)</td>
<td>84 (56.00)</td>
<td>40 (52.63)</td>
<td>330 (50.3)</td>
</tr>
<tr>
<td><strong>Right hemisphere (%)</strong></td>
<td>136 (47.39)</td>
<td>76 (51.35)</td>
<td>63 (42.00)</td>
<td>35 (46.05)</td>
<td>306 (46.65)</td>
</tr>
<tr>
<td><strong>Brain Stem / Cerebellum (%)</strong></td>
<td>7 (2.44)</td>
<td>4 (2.70)</td>
<td>3 (2.00)</td>
<td>0 (0)</td>
<td>14 (2.13)</td>
</tr>
<tr>
<td><strong>Unknown / Multiple (%)</strong></td>
<td>3 (1.05)</td>
<td>2 (1.35)</td>
<td>0 (0)</td>
<td>1 (1.32)</td>
<td>6 (0.91)</td>
</tr>
<tr>
<td><strong>Atrial Fibrillation (%)</strong></td>
<td>100 (34.84)</td>
<td>47 (31.76)</td>
<td>55 (36.67)</td>
<td>24 (31.58)</td>
<td>223 (33.99)</td>
</tr>
<tr>
<td><strong>History of Hypertension (%)</strong></td>
<td>216 (75.26)</td>
<td>118 (79.73)</td>
<td>105 (70.00)</td>
<td>54 (71.05)</td>
<td>490 (74.70)</td>
</tr>
<tr>
<td><strong>History of Diabetes (%)</strong></td>
<td>64 (22.30)</td>
<td>42 (28.38)</td>
<td>32 (21.33)</td>
<td>12 (15.79)</td>
<td>148 (22.56)</td>
</tr>
<tr>
<td><strong>History of Congestive Heart Failure (%)</strong></td>
<td>34 (11.85)</td>
<td>24 (16.22)</td>
<td>18 (12.00)</td>
<td>7 (9.21)</td>
<td>81 (12.35)</td>
</tr>
<tr>
<td><strong>History of Coronary Artery Disease (%)</strong></td>
<td>80 (27.87)</td>
<td>52 (35.14)</td>
<td>22 (14.67)</td>
<td>20 (26.32)</td>
<td>174 (26.52)</td>
</tr>
<tr>
<td><strong>History of Hyperlipidemia (%)</strong></td>
<td>163 (56.79)</td>
<td>84 (56.76)</td>
<td>54 (36.00)</td>
<td>29 (38.16)</td>
<td>327 (49.85)</td>
</tr>
<tr>
<td><strong>Baseline Serum Glucose: mean (SD)</strong></td>
<td>7.42 (3.03)</td>
<td>7.70 (3.28)</td>
<td>7.29 (2.56)</td>
<td>7.34 (2.67)</td>
<td>7.45 (2.96)</td>
</tr>
<tr>
<td></td>
<td>Cost Group Endovasc. Therapy N=284</td>
<td>Cost Group IV t-PA N=146</td>
<td>No Cost Group Endovasc. Therapy N=150</td>
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</tr>
<tr>
<td><strong>Time from Onset to IV t-PA Initiation, minutes: mean (SD)</strong></td>
<td>124.8 (33.1)</td>
<td>123.0 (33.2)</td>
<td>117.5 (34.4)</td>
<td>117.0 (35.0)</td>
<td>121.8 (33.6)</td>
</tr>
<tr>
<td><strong>Pre-existing Disability</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No symptoms at all (%)</td>
<td>255 (88.85)</td>
<td>133 (89.86)</td>
<td>127 (84.67)</td>
<td>66 (86.84)</td>
<td>576 (87.80)</td>
</tr>
<tr>
<td>No significant disability despite symptoms (%)</td>
<td>18 (6.27)</td>
<td>12 (8.11)</td>
<td>17 (11.33)</td>
<td>9 (11.84)</td>
<td>53 (8.69)</td>
</tr>
<tr>
<td>Slight disability (%)</td>
<td>13 (4.53)</td>
<td>3 (2.03)</td>
<td>6 (4.00)</td>
<td>1 (1.32)</td>
<td>23 (3.51)</td>
</tr>
<tr>
<td>Moderate disability requiring some help (%)</td>
<td>1 (0.35)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (0.15)</td>
</tr>
<tr>
<td><strong>Baseline Systolic Blood Pressure, mmHg: mean (SD)</strong></td>
<td>148.19 (20.62)</td>
<td>147.50 (24.05)</td>
<td>147.65 (22.52)</td>
<td>146.26 (24.52)</td>
<td>147.68 (22.35)</td>
</tr>
<tr>
<td>Antiplatelet Use at Baseline (%)</td>
<td>131 (45.64)</td>
<td>71 (47.97)</td>
<td>57 (37.33)</td>
<td>37 (48.68)</td>
<td>294 (44.82)</td>
</tr>
<tr>
<td>Statin Use at Baseline (%)</td>
<td>112 (39.02)</td>
<td>59 (39.86)</td>
<td>45 (30.00)</td>
<td>24 (31.58)</td>
<td>238 (36.28)</td>
</tr>
</tbody>
</table>

IV = intravenous; t-PA = tissue plasminogen activator; INR = international normalized ratio; NIHSS = National Institutes of Health Stroke Scale; ASPECTS = Alberta Stroke Program Early CT Score.