

Published in final edited form as:

Stroke Vasc Neurol. 2016 March; 1(1): 8-15. doi:10.1136/svn-2015-000002.

Use of intravenous tissue plasminogen activator and hospital costs for patients with acute ischaemic stroke aged 18–64 years in the USA

Heesoo Joo, PhD1, Guijing Wang, PhD2, and Mary G. George, MD2

Abstract

Introduction—Intravenous tissue plasminogen activator (IV tPA) is a globally recommended treatment for acute ischemic stroke patients. We examined IV tPA use among patients aged 18-64 years with a primary diagnosis acute ischemic stroke in the US and inpatient costs per hospitalization by IV tPA use status among these patients.

Methods—Using 2010-2013 MarketScan Commercial Claims and Encounters Inpatient Data, we identified 39,149 hospitalizations with a primary diagnosis of acute ischemic stroke. We verified those with and without IV tPA by ICD-9 procedure code 99.10. We estimated trends in IV tPA use by applying logistic regression. The average inpatient costs per acute ischemic stroke hospitalization were assessed for sub-populations. We examined costs per acute ischemic stroke hospitalization using multivariate regression models controlling for IV tPA status, age, gender, urbanization, geographic region, Charlson Comorbidity Index, length of hospital stays (LOS) and discharge status.

Results—2,546 hospitalizations (6.5%) used IV tPA. IV tPA use increased over time (2010 vs. 2013; odds ratio 1.50). Average inpatient costs per acute ischemic stroke hospitalization was \$20,331 (\$31,369 for IV tPA group, \$19,563 for non-tPA group). From multivariate analyses, higher costs per acute ischemic stroke hospitalization were associated with longer LOS, non-home discharge destination, and IV tPA use, which might be correlated with severity of stroke.

Conclusions—Findings suggest that IV tPA use increased recent years while the inpatient costs per acute ischemic stroke hospitalization using IV tPA are substantial. Those findings are useful in better understanding the overall economic burden of stroke, short-term cost implications of using IV tPA, and for estimating the accurate cost-effectiveness of stroke treatments.

Corresponding: Dr. Guijing Wang, Senior Economist, 4770 Buford Hwy NE, Mailstop F75, Atlanta, GA 30341, USA, Tel: +1-770-488-4846, Fax: +1-770-488-8151, gbw9@cdc.gov, Dr. Heesoo Joo, Senior Health Economist, 4770 Buford Hwy NE, Mailstop F75, Atlanta, GA 30341, USA, Tel: +1-770-488-7093, Fax: +1-770-488-8151, hjoo@cdc.gov.

Sources of funding: None

Disclosures: None

Competing interests: None declared

¹ IHRC Inc., Atlanta, GA, USA

² Division for Heart Disease and Stroke Prevention, US Centers for Disease Control and Prevention (US CDC), Atlanta, GA, USA

Keywords

tPA; stroke; economics

Introduction

Intravenous (IV) infusion of tissue plasminogen activator (tPA) is the only US Food and Drug Administration (FDA) approved intravenous thrombolytic for acute ischemic stroke. After the FDA approval in 1996, the American Heart Association/American Stroke Association (AHA/ASA) recommended IV thrombolysis with tPA for acute ischemic stroke patients who are eligible to be treated within 0 to 3 hours after symptom onset and more recently expanded the recommendation to use IV tPA for selected patients within 3 to 4.5 hours after the onset of acute ischemic stroke. Other organizations have similarly recommended treatment within 0 to 4.5 hours after acute ischemic stroke onset.

The recommendations were based on a strong body of clinical evidence from several trials, including the National Institute of Neurological Disorders and Stroke tPA trial, Alteplase Thrombolysis for Acute Non-interventional Therapy in Ischemic Stroke trial, Stroke in Thrombolysis Study, and the European Cooperative Acute Stroke Study I, II, and III. These trials confirmed that the use of IV tPA within 0-4.5 hours after the onset of stroke could be used safely and improved clinical outcomes three months post stroke.

Although some studies examined inpatient costs of stroke by stroke type, diagnosis status, age group, and discharge destination, ^{13, 14} no study has examined the inpatient costs for acute ischemic stroke by IV tPA status, especially for patient younger than 65 years old. The purpose of this study is to estimate inpatient costs per acute ischemic stroke hospitalization from the health care payers' perspective by IV tPA use status and patient characteristics, and to examine socio-demographic factors affecting IV tPA use to identify characteristics of those who have limited access to IV tPA.

Methods

We identified all inpatient hospitalizations with a primary diagnosis of acute ischemic stroke (International Classification of Diseases, Ninth Revision, Clinical Modifications [ICD-9-CM] diagnosis codes 433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, and 436) from 2010-2013 MarketScan Commercial Claims and Encounters Inpatient Database. In each year, the data contains several million individuals, including employees, their spouses, and dependents covered by employer-sponsored private health insurance. The database has been used to estimate hospitalization cost for various health conditions. Because of a relatively low prevalence of acute ischemic stroke in adults younger than age 65 and a markedly low level of IV tPA use among those who have acute ischemic stroke, we pooled three years MarketScan data to increase our sample size for analyses.

In the selection process of the study sample (n=60,417, Figure 1), we excluded: 1) patients with repeat hospitalizations with primary diagnosis of acute ischemic stroke during study

period because patients with prior stroke within 3 months are not recommended for IV tPA¹ and patients with repeated hospitalization due to stroke may not typical patients and require intensive care;2) patients with missing variables of interest such as residence region or discharge destination, main independent variables in our study, and enrollee ID, which was used to define repeated acute ischemic stroke hospitalizations during study period; 3) patients younger than 18 or older than 64 years of age because the data is mainly covered patients younger than 64 years, and patients younger than 18 are not recommended for IV tPA¹; 4) hospitalizations associated with a capitated health insurance plan because total payment does not reflect the medical services provided for each health condition; 5) hospitalizations with intra-arterial tPA by using ICD-9-CM procedure code 99.10 (injection or infusion of thrombolytic agent) and 39.74 (endovascular removal of obstruction from head and neck vessels); and 6) hospitalizations with a cost below the 1st or above 99th percentiles to reduce the influence of extreme values on the cost estimates.

Hospitalizations associated with IV tPA were identified by using ICD-9-CM procedure code 99.10. Our main outcome measure was the total hospital cost per hospitalization from the health care payers' perspective, which was the sum of payments received by all providers associated with a hospitalization. All costs were inflated to 2013 US dollars using the Consumer Price Index (CPI) in Medical Care from the Bureau of Labor Statistics. ¹⁶

First, we examined factors affecting IV tPA use, including age, gender, urbanization, region, Charlson Comorbidity Index (CCI), and year of a hospitalization, by using logistic regression. Next, we examined average inpatient cost per hospitalization associated with acute ischemic stroke. We conducted univariate comparisons of the average inpatient cost per hospitalization for the IV tPA and the non-tPA groups using t-tests. Comparisons were conducted for each socio-demographic group as well as for all patients. Last, we examined factors affecting hospitalization cost associated with acute ischemic stroke using ordinary least squares. IV tPA use, age, gender, urbanization, region, LOS, CCI, discharge destination, and year of a hospitalization were used as independent variables. The CCI was derived by using secondary diagnosis codes of up to 18 different conditions, which partly captured the severity of overall health.¹⁷ We further examined the impact factors on the hospitalization cost by LOS, which could be highly correlated with severity of stroke. We used three categories of LOS (less than 2 days, 2 to 4 days, and 5 or more days) for analyses. All statistical analyses were performed using SAS version 9.3 (SAS Institute Inc, Cary, NC).

Results

Among the 39,149 hospitalizations during the study period, 2,546 hospitalizations received IV tPA (6.5%). This IV tPA group differed significantly from the non-tPA group (n = 36,603) across most socio-demographic characteristics (age, urbanization, region, CCI, LOS, and discharge destination) (Table 1). Those who received IV tPA were younger, more likely to live in an urban area, more likely to be discharged to a rehabilitation facility, less likely to be discharged to home, and had a longer LOS than those who did not receive tPA. Those who did not receive tPA had a higher CCI than those receiving tPA.

Patients aged 45-64 years, living in rural area, or who had a higher CCI were less likely to receive IV tPA (Table 2). Those who lived in Northeast or South regions (compared with those who lived in West) were also less likely to receive IV tPA (odds ratio 0.82 [95% CI=0.71-0.94] and 0.86 [0.76-0.97], respectively). Use of IV tPA had increased over time (year 2011 vs. year 2010; odds ratio 1.21 [95% CI=1.07-1.37]; year 2012 vs. year 2010; odds ratio 1.26 [95% CI=1.12-1.42]; year 2013 vs. year 2010; odds ratio 1.50 [95% CI=1.33-1.70]).

Across all hospitalizations, the average inpatient cost per hospitalization with a primary diagnosis of acute ischemic stroke was \$20,331 (Table 3). Cost for the non-tPA group averaged \$19,563 per hospitalization while the cost averaged \$31,369 per hospitalization among those who received IV tPA. The mean difference in inpatient cost per hospitalization between the IV tPA and the non-tPA groups was \$11,806 and increased with age and LOS.

LOS, discharge destination, and use of IV tPA were the three most significant factors in our analysis associated with inpatient costs per acute ischemic stroke hospitalization (Table 4). LOS of 5 or more days were associated with an additional \$18,822 per hospitalization compared to LOS of less than 2 days. Hospitalizations with a primary diagnosis of acute ischemic stroke that resulted in a non-home discharge destination were found to have a significantly higher hospital cost compared to those with a home discharge destination (\$5,002 for discharging to rehabilitation facility; \$6,407 for discharging to short-term hospital, skilled-nursing facilities, or other non-home facilities; \$19,438 for expired). Use of IV tPA was associated with increased hospital costs of \$9,195 (p-value <0.01, [95% CI= \$8,546 - \$9,844]) per acute ischemic stroke hospitalization. The average increase in the inpatient cost per hospitalization associated with IV tPA was \$7,453 [95% CI=\$6,328 - \$8,577] for LOS of less than 2 days; \$9,386 [95% CI= \$8,842 - \$9,929]) for LOS of 2-4 days; and \$9,409 [95% CI=\$7,656 - \$11,163] for LOS of 5 or more days.

Discussion

In this study, we found that estimated hospitalization costs for acute ischemic stroke patients were substantial. Average inpatient cost per hospitalization of acute ischemic stroke was \$20,331. The use of IV tPA was significantly associated with age, metropolitan statistical area, region, CCI, and year of hospitalization. Due to known contraindications for the use of IV tPA, the finding that those with a high CCI group were less likely to receive IV tPA than low CCI group was expected. Higher use of IV tPA among those who lived in a metropolitan statistical area is likely related to increased timely access to a stroke center.

We also found that IV tPA was one of the factors which affected hospitalization costs of acute ischemic stroke. The significant difference in hospitalization costs between the IV tPA and the non-tPA groups in the current study was consistent with previous estimates in cost-effectiveness of IV tPA studies from the United States. A previous study by Fagan and her colleagues estimated that the hospitalization cost among the IV tPA group was \$1,747 higher than the cost for the non-tPA group in 1996 US dollars. A more recent study estimated that the use of IV tPA increased the cost per hospitalization by \$4,423 (\$2,750 for tPA cost; \$467 for consult physician cost; and \$1,206 for intensive care unit (ICU) cost) than the non-tPA

group, using 2010 hospital billing data from South Carolina. ¹⁹ Also, a third study by Boudreau et al. showed that the estimated cost associated with IV tPA therapy, including drug, administration, and monitoring costs, was \$6,083 in 2011 US dollars by using Medicare reimbursement rates ²⁰ while the current study estimates are IV tPA associated costs including possible complications.

Another cost-effectiveness study by Tung et al. used the hospitalization costs with and without IV tPA from nationwide estimates of Medicare costs with a retrospective approach from a study by Young et al., which was similar to the approach in our study, for their model. ^{21, 22} The adopted hospital costs associated with IV tPA, was \$9,417 in 2010 US dollars. ²¹ The costs are closely akin to our results but are far different than the cost estimate from Boudreau et al. The higher cost of IV tPA group in our study and in the study by Tung et al. might be due to costs associated with IV tPA other than the drug, administration, and ICU monitoring costs. ^{20, 21}

When we compared inpatient cost estimates from our study with the cost estimates from the previous study by Fagan et al., we found a large increase in the inpatient costs per acute ischemic stroke hospitalizations, especially among those that received IV tPA therapy. ¹⁸ The short-term hospitalization cost for the IV tPA group increased from \$16,671 in 1996 dollars ¹⁸ to \$31,369 (Table 3) in 2013 dollars. The cost for hospitalizations not using tPA also increased (\$14,923 in 1996 US dollars ¹⁸ vs. \$19,563 (Table 3) in 2013 US dollars), but the hospital cost increase among hospitalizations not using tPA was much smaller than the increase among hospitalizations using IV tPA (non-tPA vs. IV tPA; \$4,640 vs. \$14,698). The short-term hospital cost increased by 31% and by 88% among non-tPA group and IV tPA group respectively, while there was an 86% increase of an average price of medical care between 1996 and 2013 in the US (CPI in Medical Care 228.2 in 1996 vs. 425.1 in 2012). ¹⁶

This asymmetric increase of hospital costs could be caused by multiple factors. First, the drug price of tPA has increased over time. The wholesale price of tPA was \$2,750 in 1996 dollars and was \$6,525 in 2013 dollars although tPA drug cost paid by hospitals could be lower than the wholesale price, the wholesale price can serve as an indicator of price paid by hospitals. Next, despite decreasing LOS for both the IV tPA and the non-tPA groups over time, LOS of non-tPA group decreased more than the LOS of IV tPA group during the past 20 years. acute ischemic stroke hospitalizations not using tPA reported average LOS of 12.4 days in 1995 and 4.1 days (Table 1) during 2010-2013, while acute ischemic stroke hospitalizations using IV tPA reported average LOS of 10.9 days in 1995 and 4.6 days (Table 1) during 2010-2013. Lastly, the in-hospital care after IV tPA likely increases hospital cost. After receiving IV tPA, most patients are monitored in an ICU or specialized stroke unit which adds to the cost.

Although this study and existing literature consistently found that acute ischemic stroke hospitalizations using IV tPA encountered higher hospital costs than acute ischemic stroke hospitalizations not using tPA, IV tPA within 0 to 3 hours after the onset of stroke has been shown to be a cost-saving strategy in the long-term because of long-term benefit of IV tPA resulting in less disability. ^{16, 18, 19} In addition, IV tPA improves the quality adjusted life years (QALYs) for acute ischemic stroke survivors. ^{16, 18-20}

Another positive finding is the increased use of IV tPA in recent years. Our study shows that on average, 6.5% of hospitalizations were associated with IV tPA therapy during 2010-2013. The odds ratio confirmed that, even in this short study period, the proportion of acute ischemic stroke patients who received IV tPA therapy increased each year, with the odds of receiving IV tPA increasing by 21% from 2010 to 2011, by 26% from 2010 to 2012, and by 50% from 2010 to 2013. In the late 1990s, nationally only 2-3% of stroke patient received IV tPA. ²³ In the 2000s, the national estimates increased from 1 to 5%²⁴⁻²⁶, but still few acute ischemic stroke patients received IV tPA. Our estimates of the use of IV tPA may be conservative due to the fact that most patients experiencing acute ischemic stroke are likely to be covered by Medicare and are not included in this study.

We want to emphasize that accurate hospital cost information can be used as a key input for cost-effectiveness analyses of treatments for acute ischemic stroke. Cost-effectiveness evaluations of public health programs are sensitive to cost information as well as health outcomes achieved from the programs. Unlike IV tPA from 0 to 3 hours after the onset of acute ischemic stroke, which consistently showed the improvement of health outcomes and the long-term cost-saving impact among patients with IV tPA, IV tPA from 3 to 4.5 hours after the onset of stroke increased short-term and long-term costs. Two studies examining cost-effectiveness of IV tPA between 3 and 4.5 hours after the onset of stroke in the US showed that IV tPA improved QALYs but increased lifetime cost. Although IV tPA from 3 to 4.5 hours after the onset of stroke are recommended by AHA/ASA, IV tPA use for extended time window did not get an approval from FDA yet²⁷.

In addition, inpatient cost per hospitalization with IV tPA is important baseline information for studying the cost-effectiveness of advanced stroke treatment, such as intra-arterial (IA) thrombectomy as an adjunct to IV tPA. Additional cost-effectiveness analyses of IV tPA are needed to provide more information, which will be helpful for decision makers, and the findings of current study could be an important input for further cost-effectiveness analyses of IV tPA.

There are some limitations in this study. First, while the median age of patients with stroke in stroke trials were 68 years old, ¹⁶ it is limited to patients aged 18-64 years old because of the characteristics of dataset we used. In addition, the study sample included only those who were covered by private insurance and does not reflect hospitalizations for those with Medicare or without any insurance. Because hospital costs with and without IV tPA for adult patients who were younger than 65 years old had not been included in previous study samples, we believe that this study is a reasonable complement to previous estimates using Medicare reimbursement rates. ²⁰

Second, MarketScan does not provide data about severity of stroke. Since IV tPA is not recommended to those who have very mild stroke, non-tPA group may include those for whom IV tPA is not recommended. However, we indirectly considered the severity of stroke through analyses with LOS categories and controlling for a CCI and hospital discharge destination. Last, hospitalizations with IA therapy could not be separately examined because of very low frequency (n=137). Despite these limitations, our study derived a reasonable estimate of hospitalization costs with and without IV tPA.

Conclusions

This study found that the IV tPA use, which can improve health outcomes of acute ischemic stroke survivors, increased in recent years. However, inpatient cost per acute ischemic stroke hospitalization is substantial, especially for those who received IV tPA. Despite the fact that many studies have claimed that IV tPA is cost-effective or cost-saving in a long-term, the immediate hospitalization costs by IV tPA use in a younger population have not been rigorously evaluated. Future cost-effectiveness studies of stroke treatments should consider such information as inputs, especially when studying the cost-effectiveness of IV tPA alone versus in combination with IA therapy.

Abbreviations

IV tPA intravenous tissue plasminogen activator

LOS length of hospital stays

FDA Food and Drug Administration

AHA/ASA American Heart Association/American Stroke Association

ICD-9-CM International Classification of Diseases, Ninth Revision, Clinical

Modifications

CPI Consumer Price Index

QALYs quality adjusted life years

IA intra-arterial

References

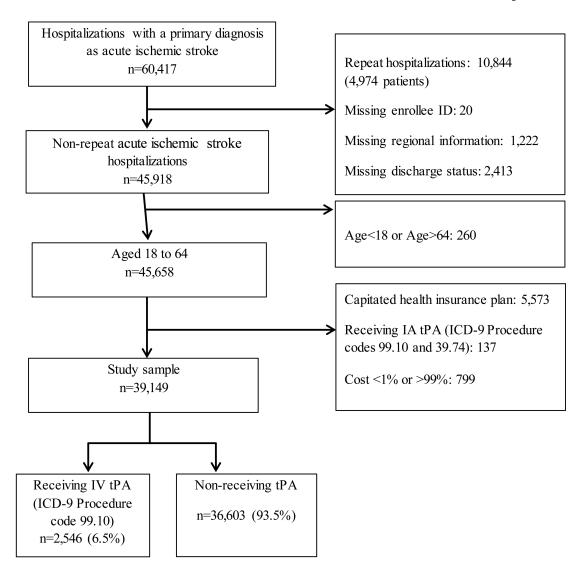
- Jauch EC, Saver JL, Adams HP Jr. Bruno A, Connors JJ, Demaerschalk BM, et al. Guidelines for the early management of patients with acute ischemic stroke: A guideline for healthcare professionals from the american heart association/american stroke association. Stroke; a journal of cerebral circulation. 2013; 44:870–947.
- Adams HP Jr. Brott TG, Furlan AJ, Gomez CR, Grotta J, Helgason CM, et al. Guidelines for thrombolytic therapy for acute stroke: A supplement to the guidelines for the management of patients with acute ischemic stroke. A statement for healthcare professionals from a special writing group of the stroke council, american heart association. Circulation. 1996; 94:1167–1174. [PubMed: 8790069]
- 3. Del Zoppo GJ, Saver JL, Jauch EC, Adams HP Jr. American Heart Association Stroke C. Expansion of the time window for treatment of acute ischemic stroke with intravenous tissue plasminogen activator: A science advisory from the american heart association/american stroke association. Stroke; a journal of cerebral circulation. 2009; 40:2945–2948.
- European Stroke Organisation Executive Committee, Committee ESOW. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. Cerebrovascular diseases. 2008; 25:457–507. [PubMed: 18477843]
- 5. National Institute for Health and Clincal Excellence. Alteplase for acute ischaemic stroke (nice technology appraisal guidance [ta264], review of technology appraisal guidance 122). 2012
- 6. National Stroke Foundation. Clinical guidelines for stroke management 2010. 2010

7. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. The New England journal of medicine. 1995; 333:1581–1587. [PubMed: 7477192]

- 8. Bluhmki E, Chamorro A, Davalos A, Machnig T, Sauce C, Wahlgren N, et al. Stroke treatment with alteplase given 3.0-4.5 h after onset of acute ischaemic stroke (ecass iii): Additional outcomes and subgroup analysis of a randomised controlled trial. The Lancet. Neurology. 2009; 8:1095–1102. [PubMed: 19850525]
- Hacke W, Donnan G, Fieschi C, Kaste M, von Kummer R, Broderick JP, et al. Association of outcome with early stroke treatment: Pooled analysis of atlantis, ecass, and ninds rt-pa stroke trials. Lancet. 2004; 363:768–774. [PubMed: 15016487]
- Brott T, Bogousslavsky J. Treatment of acute ischemic stroke. The New England journal of medicine. 2000; 343:710–722. [PubMed: 10974136]
- 11. Albers GW, Clark WM, Madden KP, Hamilton SA. Atlantis trial: Results for patients treated within 3 hours of stroke onset. Alteplase thrombolysis for acute noninterventional therapy in ischemic stroke. Stroke; a journal of cerebral circulation. 2002; 33:493–495.
- 12. Wahlgren N, Ahmed N, Davalos A, Hacke W, Millan M, Muir K, et al. Thrombolysis with alteplase 3-4.5 h after acute ischaemic stroke (sits-istr): An observational study. Lancet. 2008; 372:1303–1309. [PubMed: 18790527]
- Reed SD, Blough DK, Meyer K, Jarvik JG. Inpatient costs, length of stay, and mortality for cerebrovascular events in community hospitals. Neurology. 2001; 57:305–314. [PubMed: 11468317]
- 14. Wang G, Zhang Z, Ayala C, Dunet DO, Fang J, George MG. Costs of hospitalization for stroke patients aged 18-64 years in the united states. Journal of stroke and cerebrovascular diseases: the official journal of National Stroke Association. 2014; 23:861–868. [PubMed: 23954598]
- 15. Danielson E. Health research data for the real world: The marketscan database. 2014
- 16. Boudreau DM, Guzauskas GF, Chen E, Lalla D, Tayama D, Fagan SC, et al. Cost-effectiveness of recombinant tissue-type plasminogen activator within 3 hours of acute ischemic stroke: Current evidence. Stroke; a journal of cerebral circulation. 2014; 45:3032–3039.
- 17. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. Journal of chronic diseases. 1987; 40:373–383. [PubMed: 3558716]
- Fagan SC, Morgenstern LB, Petitta A, Ward RE, Tilley BC, Marler JR, et al. Cost-effectiveness of tissue plasminogen activator for acute ischemic stroke. Ninds rt-pa stroke study group. Neurology. 1998; 50:883–890. [PubMed: 9566367]
- 19. Kazley AS, Simpson KN, Simpson A, Jauch E, Adams RJ. Optimizing the economic impact of rtpa use in a stroke belt state: The case of south carolina. American health & drug benefits. 2013; 6:155–163. [PubMed: 24991353]
- Boudreau DM, Guzauskas G, Villa KF, Fagan SC, Veenstra DL. A model of cost-effectiveness of tissue plasminogen activator in patient subgroups 3 to 4.5 hours after onset of acute ischemic stroke. Annals of emergency medicine. 2013; 61:46–55. [PubMed: 22633340]
- Tung CE, Win SS, Lansberg MG. Cost-effectiveness of tissue-type plasminogen activator in the 3to 4.5-hour time window for acute ischemic stroke. Stroke; a journal of cerebral circulation. 2011; 42:2257–2262.
- 22. Young KC, Benesch CG, Jahromi BS. Cost-effectiveness of multimodal ct for evaluating acute stroke. Neurology. 2010; 75:1678–1685. [PubMed: 20926786]
- Alberts MJ, Hademenos G, Latchaw RE, Jagoda A, Marler JR, Mayberg MR, et al. Recommendations for the establishment of primary stroke centers. Brain attack coalition. Jama. 2000; 283:3102–3109. [PubMed: 10865305]
- Kleindorfer D, Lindsell CJ, Brass L, Koroshetz W, Broderick JP. National us estimates of recombinant tissue plasminogen activator use: Icd-9 codes substantially underestimate. Stroke; a journal of cerebral circulation. 2008; 39:924–928.
- 25. Fang MC, Cutler DM, Rosen AB. Trends in thrombolytic use for ischemic stroke in the united states. Journal of hospital medicine: an official publication of the Society of Hospital Medicine. 2010; 5:406–409.

26. Adeoye O, Hornung R, Khatri P, Kleindorfer D. Recombinant tissue-type plasminogen activator use for ischemic stroke in the united states: A doubling of treatment rates over the course of 5 years. Stroke; a journal of cerebral circulation. 2011; 42:1952–1955.

27. Marshall RS. Progress in intravenous thrombolytic therapy for acute stroke. JAMA Neurol. 2015



Notes:

IA tPA: Intra-arterial tissue plasminogen activator

IV tPA: Intravenous tissue plasminogen activator

Figure 1.Study population selection process from 2010-2013 MarketScan Commercial Claims and Encounters Inpatient Database

Table 1

Sample characteristics of patients aged 18-64 years with a primary diagnosis of acute ischemic stroke by IV tPA therapy status (%), 2010-2013 MarketScan Commercial Claim Inpatient Database

	T . 1 (2) (20 1 (0))	tPA status				
	Total (N=39,149)	Non-tPA group (N=36,603)	IV tPA group (N=2,546)	p-value		
Age						
18-44	12.7	12.6	14.7	< 0.01		
45-54	28.6	28.7	28.4	0.81		
55-64	58.6	58.7	56.8	0.06		
Average (years)	54.3	54.3	53.8	< 0.01		
Gender						
Female	41.6	41.6	41.6	0.99		
Male	58.4	58.4	58.4	0.99		
Metropolitan Statistical Area						
No	18.0	18.4	12.5	< 0.01		
Yes	82.0	81.6	87.5	< 0.01		
Region						
West	12.4	12.2	14.4	< 0.01		
Northeast	17.3	17.4	16.7	0.35		
North central	27.5	27.5	28.0	0.57		
South	42.8	43.0	41.0	0.05		
Charlson comorbidity index						
0-2	33.8	33.7	34.6	0.39		
3-4	44.7	44.4	49.2	< 0.01		
5 or higher	21.5	21.9	16.2	< 0.01		
Average (index)	3.25	3.26 3.14		< 0.01		
Length of Stay						
<2 days stay	16.6	17.2	7.5	< 0.01		
2-4 days stay	55.4	55.4	56.3	0.36		
5 days stay	28.0	27.4	36.2	< 0.01		
Average (days)	4.1	4.1	4.6	< 0.01		
Discharge destination						
Home	74.9	75.5	67.2	< 0.01		
Rehabilitation facility	14.0	13.5	21.1	< 0.01		
Short-term hospital/SNF/Other ^a	9.0	9.0	8.4	0.29		
Expired	2.1	2.0	3.3	< 0.01		

Note:

^{al}SNF stands for skilled-nursing facility. Other discharge status includes transferring to federal hospital, critical access hospital, hospice, long-term care facility, and all other discharge status.

Table 2

Odds ratio of receiving IV tPA for patients aged 18-64 years with primary diagnosis of acute ischemic stroke,

2010-2013 MarketScan Commercial Claim Inpatient Database (n=39,149)

	Odds Ratio	95% confidence interval
	Odds Ratio	95% confidence interval
Age		
18-44	1.00	
45-54	0.87*	[0.76-0.99]
55-64	0.86*	[0.76-0.97]
Gender		
Female	1.00	
Male	1.01	[0.93-1.10]
Metropolitan Statistical Area		
No	1.00	
Yes	1.58**	[1.40-1.78]
Region		_
West	1.00	
Northeast	0.82 ***	[0.71-0.94]
North central	0.90	[0.79-1.03]
South	0.86*	[0.76-0.97]
Charlson Comorbidity Index		
0-2	1.00	
3-4	1.08	[0.99-1.18]
5 or higher	0.72 ***	[0.64-0.82]
Year		
2010	1.00	
2011	1.21 **	[1.07-1.37]
2012	1.26**	[1.12-1.42]
2013	1.50 **	[1.33-1.70]

Note:

 $^{^{*}}$ denotes statistical significance at the p<0.05 and

 $^{^{**}}$ denotes statistical significance at the p<0.01.

Table 3

Average hospital costs (\$2013) for patients aged 18-64 years with primary diagnosis of acute ischemic stroke by IV tPA status, 2010-2013 MarketScan Commercial Claim Inpatient Database

	Total (N=39,149)	IV tPA status			
		Non-tPA group (A) (N=36,603)	IV tPA group (B) (N=2,546)	Differences (B-A) (p-value)	
Total	20,331	19,563	31,369	11,806 (<0.01)	
Age					
18-44	22,316	21,581	31,347	9,767 (<0.01)	
45-54	20,165	19,456	30,428	10,972 (<0.01)	
55-64	19,981	19,182	31,845	12,663 (<0.01)	
Gender					
Female	20,210	19,450	31,137	11,687 (<0.01)	
Male	20,417	19,644	31,534	11,891 (<0.01)	
Metropolitan Statistical Area					
No	18,683	18,091	31,220	13,129 (<0.01)	
Yes	20,693	19,895	31,390	11,495 (<0.01)	
Region					
West	24,419	23,572	34,735	11,164 (<0.01)	
Northeast	21,456	20,753	32,005	11,252 (<0.01)	
North Central	19,770	19,048	29,949	10,901 (<0.01)	
South	19,056	18,270	30,895	12,625 (<0.01)	
Charlson Comorbidity Index					
0-2	17,833	17,119	27,842	10,723 (<0.01)	
3-4	21,293	20,384	33,063	12,679 (<0.01)	
5 or higher	22,253	21,661	33,745	12,084 (<0.01)	
Length of Stay					
<2 days	11,882	11,638	19,934	8,296 (<0.01)	
2-4 days	16,218	15,560	25,525	9,965 (<0.01)	
5 days	33,469	32,611	42,822	10,211 (<0.01)	
Discharge destination					
Home	17,065	16,440	27,164	10,724 (<0.01)	
Rehabilitation facility	28,766	27,618	39,330	11,711 (<0.01)	
Short-term hospital/SNF/Other ^a	29,710	28,939	41,613	12,674 (<0.01)	
Expired	40,574	40,633	40,055	-578 (0.87)	

Note: All numbers except p-values are 2012 US dollar.

^aSNF stands for skilled-nursing facility. Other discharge status includes transferring to federal hospital, critical access hospital, hospice, long-term care facility, and all other discharge status.

Table 4

Marginal effect of receiving IV tPA on hospital costs (\$2013) for patients aged 18-64 years with primary diagnosis of acute ischemic stroke, 2010-2013 MarketScan Commercial Claim Inpatient Database

	T . 1 (N. 20 140)	Length of Stay		
	Total (N=39,149)	<2 days (N=6,489) 2-4 days (N=21,696) 5 days (N=		
tPA				
non-tPA group	Ref.	Ref.	Ref.	Ref.
IV tPA group	9,195***	7,453**	9,386 ***	9,409 ***
Age				
18-44	Ref.	Ref.	Ref.	Ref.
45-54	-1 , 860 **	-1,354 **	-1,078**	-3,722 ***
55-64	-2,555***	-1,817 ***	-1,610**	-4,948 ***
Gender				
Female	Ref.	Ref.	Ref.	Ref.
Male	724**	140	279*	1,934 ***
Metropolitan Statistical Area				
No	Ref.	Ref.	Ref.	Ref.
Yes	1,186***	382	630 **	2,982 ***
Region				
West	Ref.	Ref.	Ref.	Ref.
Northeast	-3,894**	1,409**	-2,523 ***	-10,853 **
North central	-4,737 **	-67	-3,660**	-11,129**
South	-5,879**	-461	-4,611**	-12,945 **
Charlson Comorbidity Index				
0-2	Ref.	Ref.	Ref.	Ref.
3-4	1,140***	511*	927**	2,045 **
5 or higher	739 ***	782**	939**	933
Length of Stay				
<2 days	Ref.	-	-	-
2-4 days	3,858**			
5 days	18,822***			
Discharge destination				
Home	Ref.	Ref.	Ref.	Ref.
Rehabilitation facility	5,002 ***	8,013 ***	4,171 **	6,642 ***

	Total (N=39,149)	Length of Stay		
		<2 days (N=6,489)	2-4 days (N=21,696)	5 days (N=10,964)
Short-term hospital/SNF/Other ^a	6,407 ***	873*	2,120 **	10,942 ***
Expired	19,438 ***	11,937***	19,058 ***	23,561 ***
Year				
2010	Ref.	Ref.	Ref.	Ref.
2011	502*	653*	608 **	77
2012	762**	934**	734 ***	396
2013	1,523 ***	1,507***	1,345 ***	1,659*
Constant	14,420 **	11,123**	17,507**	37,332 ***

Page 15

Notes:

Joo et al.

^{*} denotes statistical significance at the p<0.05 and

 $^{^{**}}$ denotes statistical significance at the p<0.01.

^aSNF stands for skilled-nursing facilities. Other discharge status includes transferring to federal hospital, critical access hospital, hospice, long-term care facility, and all other discharge status.