Journal of Vascular and Interventional Neurology
OFFICIAL JOURNAL OF THE ZEENAT QURESHI STROKE INSTITUTE

Journal of Vascular and Interventional Neurology, Vol. 14

Thrombolytic treatment for in-hospital ischemic strokes in United States

Tenbit Emiru, M.D., PH.D*, **Malik M Adil, M.D.**, **M Fareed K Suri, M.D.**, and **Adnan I Qureshi, M.D.**

Zeenat Qureshi Stroke Research Center, Departments of Neurology, University of Minnesota, Minneapolis, MN, USA

Abstract

Background—Despite the recent emphasis on protocols for emergent triage and treatment of in-hospital acute ischemic stroke, there is little data on outcomes of patients receiving thrombolytics for in-hospital ischemic strokes. The objective of this study was to determine the rates of patients with in-hospital ischemic stroke treated with thrombolytics and to compare outcomes with patients treated on admission.

Methods—We analyzed an 8-year data (2002-2010) from the National Inpatient Survey. We identified patients who had in-hospital ischemic strokes (thrombolytic treatment after 1 day of hospitalization) and those treated on admission day. We compared demographics, clinical characteristics, in hospital complications and procedures, length of stay, hospitalization charges, and discharge disposition between the two groups.

Results—A total of 25193 (19%) and 109784 (81%) patients received thrombolytics for in-hospital and on admission acute strokes, respectively. In-hospital complications including intracerebral hemorrhage, pneumonia, deep venous thrombosis, pulmonary embolism and sepsis and in-hospital procedures such as cerebral angiography, endovascular thrombectomy, carotid artery stent placement, carotid endarterectomy, intubation, mechanical ventilation, gastrostomy, transfusion of blood products were significantly higher in the in-hospital stroke group. In a multivariate analysis, those who were treated following in-hospital stroke had higher rates of in-hospital mortality (odds ratio (OR) 1.1, 95% confidence interval (CI) 1.0–1.3, p = 0.05), and post-thrombolytic ICH (OR 1.2, CI 1.0–1.3, p = 0.03).

Conclusion—One out of every five acute ischemic stroke patients treated with thrombolytics is receiving the treatment for in-hospital stroke. The higher mortality and complicated hospitalization in such patients needs to be recognized.

Keywords

Acute stroke; in-hospital stroke; thrombolysis; stroke treatment; stroke complications; thrombolytic treatment

Introduction

Hospitalized patients have high rates of co morbidities such as advanced age, recent myocardial infarction, coronary artery disease, cardiac failure, diabetes mellitus, history of cigarette smoking, and impaired renal function [1–4]. Therefore, occurrence of ischemic stroke during hospitalization is not uncommon. In-hospital strokes represents 5%–15% of all hospitalized acute stroke cases [4]. Eligibility for thrombolytic treatment is confounded by concurrent medical illnesses and surgical procedures performed as part of nonstroke admission diagnosis. Despite the recent emphasis on protocols for emergent triage and treatment of in-hospital acute ischemic stroke [5–7], there is little data on rates and outcomes of patients receiving thrombolytics for in-hospital ischemic strokes. The objective of this study was to determine the rates of in-hospital ischemic stroke treated with thrombolytics and to compare outcomes with patients treated with thrombolytics on admission.

Published December, 2014.

***Correspondence to:** Tenbit Emiru, Zeenat Qureshi Stroke Institute, 519 2nd St NE, St. Cloud, MN 56303, USA, Tel.: +1-320-281-5545; Fax: +1-320-281-5547, emir0001@umn.edu

Methods

We used the data files from National Inpatient Sample (NIS) from 2002 to 2010 for our analysis. NIS is the largest all-payer database in the United States and derives the data from 20% of nonfederal hospitals. Using appropriate sampling weights, national estimates can be derived. The database contains information on patients' demographic and clinical characteristics, in-hospital procedures, hospital characteristics and charges, and discharge outcomes. A comprehensive synopsis on NIS data is available at http://www.hcup-us.ahrq.gov. We used the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) primary diagnosis codes 433-437.1 to identify the patients admitted with ischemic stroke. Patients who underwent thrombolytic treatment were identified by procedure code 99.10. The procedure code, 99.10, was designated for injection or infusion of thrombolytic agents permitting estimation of national and state-wide use since 1998. The patients were divided into two categories on the basis of the day thrombolytics were administered using a variable procedure day. Those patients who received the thrombolytics on the day of admission (day 0) were included in stroke on admission category while those who received thrombolytics after the day of admission (after day 0) were included in in-hospital stroke category. Study variables included were patient's age, gender, race/ethnicity, and co-morbidities obtained from AHRQ co-morbidity data files including congestive heart failure, diabetes mellitus, hypertension, renal failure, and chronic lung disease. ICD-9-CM secondary diagnosis codes were used to identify those with stroke associated complications such as post-thrombolytic intracerebral hemorrhage (ICH) (431 and 432), pneumonia (486, 481, 482.8, and 482.3), urinary tract infection (599.0, 590.9), sepsis (995.91, 996.64, 038, 995.92, and 999.3), deep venous thrombosis (451.1, 451.2, 451.81, 451.9, 453.1, 453.2, 453.8, and 453.9), pulmonary embolism (415.1), and myocardial infarction (410.0–410.9). We also used ICD-9-CM procedure codes to estimate the percentage of stroke patients who underwent in-hospital procedures such as cerebral angiography (88.41), mechanical ventilation (96.72), intubation (96.04), carotid angioplasty/stent placement (00.63/00.64), carotid endarterectomy (38.12), blood transfusion (99.04), tracheostomy (31.10, 31.20, 31.21, or 31.29), and gastrostomy (431.1–431.9). Patients undergoing mechanical thrombectomy were identified using the ICD-9 procedure code 39.74 and DRG 543. If a patient received ICD-9 CM code 99.10 and subsequent ICD-9 CM 00.41 to 00.43, then the patient also was labeled as receiving endovascular treatment [8].

We determined the length of stay and hospital charges for each patient. Discharge status is categorized into routine, home health care, short-term hospital, and other facilities including intermediate care and skilled nursing home, or death in NIS database. We categorized routine discharge as none to minimal disability, any other discharge status as moderate to severe disability as previously described [9].

Statistical analysis

The SAS 9.1 software (SAS Institute, Cary, NC) was used to convert NIS data into weighted counts to generate national estimates, following Healthcare Cost and Utilization Project (HCUP) recommendations (HCUP, Rockville, MD). Overview is available at, http://www.hcup-us.ahrq.gov/nisoverview.jsp accessed January 17, 2010. We performed univariate analysis, chi-square for categorical and *t*-test for continuous variables to identify differences in study variables and endpoints between two groups. To assess the effect of outcomes of in-hospital stroke versus stroke on-admission, two logistic regression models were created. All variables that were significant in the univariate analysis were included in the logistic regression model. Model one included all patients; logistic regression analysis was used to identify the association between in-hospital stroke and odds of in-hospital mortality and post-thrombolytic intracerebral hemorrhage among all thrombolytic treated patients. Potential confounders included age (continuous), gender (men/women), hypertension, and atrial fibrillation (yes/no). Model two included patients who were discharged alive; logistic regression analysis was used to identify the association between in-hospital stroke and odds of moderate to severe disability. Potential confounders included age (continuous), gender (men/women), hypertension, and atrial fibrillation (yes/no) as potential confounders.

Results

A total of 25193 (19%) and 109784 (81%) patients received thrombolytics for in-hospital and on admission acute ischemic strokes, respectively. Table 1 shows univariate analysis comparing demographics, co morbidities, in-hospital complications and procedures, and outcomes between the two groups. There were no differences in age, gender or ethnicity; with mean age in years [±SD] of 68 (±33) and 69 (±33), and women constituted 48% and 50% for the in-hospital versus on admission groups, respectively. Patients who were given thrombolytics following in-hospital strokes had lower rates of hypertension (71% versus 75%, $p < 0.0001$), and atrial fibrillation (28% versus 30%, $p = 0.04$) than those who

Table 1. Univariate analysis of demographics, clinical characteristics, in-hospital complications, and outcome for in-hospital stroke and stroke on admission.

	Patients with in-hospital ischemic stroke	Patients with ischemic stroke on-admission	*p*-value
Overall number (%)	25193	109784	
Age (mean ±SD)	68±33	69±33	0.5
Women	12153 (48)	54594 (50)	0.1
Race/ethnicity			
White	10141 (76)	71632 (73)	
African Americans	1722 (13)	14127 (15)	
Hispanic	691 (5)	6469 (7)	
Other	742 (6)	5320 (5)	0.1
Co-morbid conditions			
Hypertension	17760 (71)	82413 (75)	<.0001
Diabetes mellitus	5264 (21)	24372 (22)	0.1
Dyslipidemia	2436 (10)	11139 (10)	0.5
Atrial fibrillation	7275 (28)	33789 (30)	0.04
Congestive heart failure	4100 (16)	16581 (15)	0.1
Chronic lung disease	3481 (14)	15099 (14)	0.9
Renal failure	2190 (9)	9023 (8)	0.4
Alcohol	1037 (4)	4214 (4)	0.5
Nicotine dependence	3446 (14)	16658 (15)	0.06
In hospital complications			
Pneumonia	1284 (5)	3792 (3)	0.0001
Deep venous thrombosis	467 (2)	743 (0.7)	<.0001
Urinary tract infection	3697 (15)	14745 (13)	0.07
Sepsis	601 (2)	1642 (1)	0.01
Pulmonary embolism	235 (0.9)	569 (0.5)	0.01
Myocardial infarction	796 (3)	3081 (3)	0.3
Post-thrombolytic ICH	1575 (6)	5932 (5)	0.04
In hospital procedures			
Cerebral angiography	7770 (31)	21405 (19)	<.0001
Mechanical thrombectomy	2040 (8.1)	6175 (5.6)	0.01
Gastrostomy	3003 (12)	9668 (9)	<.0001
Intravenous thrombolysis only	22780 (90.4)	103082 (93.3)	0.001
Intra-arterial thrombolysis	2412 (9.6)	6702 (6.1)	0.001
Carotid angioplasty and stent	1311 (5)	1841 (2)	<.0001
Carotid endarterectomy	868 (3)	1157 (1)	<.0001
Tracheostomy	78 (0.3)	180 (0.1)	0.1
Intubation	3569 (14)	11540 (10)	<.0001
Transfusion	1152 (5)	3215 (3)	0.0008
Withdrawal of care	679 (2.7)	3579 (3.2)	0.2
Hospital bed size			
Small	1053 (4)	6014 (5)	
Medium	4050 (16)	23526 (22)	
Large	19855 (80)	78966 (73)	0.04
Teaching status			
Nonteaching	7966 (32)	46787 (43)	
Teaching	16993 (68)	61719 (57)	0.002
Length of stay (mean ±SD)	8±25	7±15	<.0001
Hospital charges (mean ±SD)	74713±197337	68429±159803	<.0001
Discharge disposition			
None to minimal disability	9210 (36)	41868 (38)	0.1
Moderate to severe disability	12990 (51)	55867 (51)	0.5
In hospital mortality	2799 (11)	11091 (10)	0.1
Outcome			
Post-thrombolytic ICH	1575 (6)	5932 (5)	0.04

ICH: intracerebral hemorrhage, SD: standard deviation.

were given thrombolytics on admission. The rates of other co-morbidities including diabetes mellitus, dyslipidemia, congestive heart failure, chronic lung disease, or renal failure were similar between the two groups. The two groups were also similar in rates of previous history of alcohol use and nicotine dependence. In hospital complications such as pneumonia (5% versus 3%, $p = 0.0001$), deep venous thrombosis (2% versus 0.7%, $p < 0.0001$), pulmonary embolism (0.9% versus 0.5%, $p = 0.01$), and sepsis (2% versus 1%, $p = 0.01$) were significantly higher in those who were treated with thrombolytics following in-hospital stroke compared with those who were treated on admission. Although statistically significant, no clinically meaningful difference in rate of post thrombolytic ICH was identified between patients with stroke on admission and those with in hospital stroke.

Endovascular treatment was more frequently used in patients with in hospital stroke compared with those with stroke on admission (9.6% versus 6.1%, $p = 0.001$). In-hospital procedures such as cerebral angiography (31% versus 19%, $p < 0.0001$), carotid artery stent placement (5% versus 2%, $p < 0.0001$), mechanical

Table 2. Multivariate analysis evaluating effect of in-hospital stroke occurrence on outcomes of ischemic stroke patients who underwent thrombolytic treatment.

	Patient outcome	Unadjusted		Adjusted for age and gender		Adjusted for age, gender, medical co-morbidities*	
		Odds ratio (95% confidence interval)	*p*-Value	Odds ratio (95% confidence interval)	*p*-Value	Odds ratio (95% confidence interval)	*p*-Value
Model 1	**Analysis comprising of all patients**						
	Discharged alive	**Reference**		**Reference**		**Reference**	
	In-hospital mortality	1.13 (0.91-1.23)	0.1	1.22 (1.08-1.32)	0.03	1.17 (1.07-1.34)	0.05
	No post-thrombolytic ICH	**Reference**		**Reference**		**Reference**	
	Post-thrombolytic ICH	1.17 (1.07-1.33)	0.04	1.22 (1.08-1.41)	0.02	1.24 (1.08-1.34)	0.03
Model 2	**Analysis comprising of alive patients**						
	None to minimal disability	**Reference**		**Reference**		**Reference**	
	Moderate to severe disability	1.02 (0.92-1.16)	0.2	1.17 (1.04-1.22)	0.06	1.17 (1.07-1.34)	0.04

OR: odds ratio, CI: confidence interval, ICH: Intracerebral hemorrhage.

*Hypertension and atrial fibrillation.

thrombectomy (8.1% versus 5.6%, $p = 0.01$), carotid endarterectomy (3% versus 1%, $p < 0.0001$), intubation (14% versus 10%, $p < 0.0001$), mechanical ventilation (8% versus 4%, $p < 0.0001$), gastrostomy (12% versus 9%, $p < 0.0001$), and transfusion of blood products (5% versus 3%, $p = 0.0008$) were significantly higher in those who were treated with thrombolytics following in-hospital stroke. More patients in the in-hospital group were hospitalized in large hospitals compared with those in on admission group (80% versus 73%, $p = 0.04$). Mean hospital length of stay (8 ± 25 days versus 7 ± 15 days, $p < 0.0001$) and mean hospital charges were significantly higher ($74713 ± 197337 versus $68429 ± 159803, $p < 0.0001$) among patients treated following in-hospital stroke. There was no difference in rates of none to minimal disability, moderate to severe disability, and in-hospital mortality between patients who were treated with thrombolytics for in-hospital versus those treated for on admission strokes. In a multivariate analysis of all patients, those who were treated following in-hospital stroke had higher rates of in hospital mortality (odds ratio (OR) 1.17, 95% confidence interval (CI) 1.07–1.34, $p = 0.05$), and higher rates of post-thrombolytic ICH (OR 1.24, CI 1.08–1.34, $p = 0.03$) after adjustment for age, gender, and baseline risk factors (see Table 2).

In addition, when analyzing only patients who were discharged alive, those who were treated for in-hospital stroke had higher rates of moderate to severe disability (OR 1.17 [CI] 1.07–1.34, $p = 0.04$) after adjustment for age, gender, and baseline risk factors.

Discussion

We found that patients who were treated with thrombolytics for in-hospital strokes had complex hospitalization associated with higher rates of complications and higher rate of in-hospital mortality compared with those who were treated on admission. This finding is consistent with previous studies that reported higher in-hospital medical complications, higher disability at discharge and/or in-hospital mortality among patients with in-hospital strokes [4,10–13]. A prospective cohort study of patients with in-hospital strokes and strokes on admission from a statewide acute stroke registry of 15 representative hospitals found that 177 (6.5%) of the 2,743 cases in the registry were in-hospital strokes associated with higher mortality rate (14.6% versus 6.9%), greater functional impairment (mRS ≥ 4) (61% versus 36%), and lower rate of discharge to home (23% versus 52%) when compared with those who had stroke on admission [4]. Bhalla *et al* [14], reported that patients with in-hospital strokes were more likely to be incontinent, dysphagic, have either a motor deficit, or altered level of consciousness. Patients with in-hospital stroke were more likely to have difficulty in performing activities of daily living and have higher 3-month mortality compared with patients with stroke on admission. The complex hospitalization is attributed to a higher incidence of severe strokes such as cardio-embolic strokes, concurrent hospital procedures for which patients were originally admitted, and/or high rate of baseline medical co morbidities. An aspect of in-hospital stroke that has been relatively understudied is rates and patterns of acute thrombolytic treatment as a potential explanation for higher rates of poor outcomes.

The complex pattern of multisystem involvement and its relationship to in-hospital outcomes has been reported in patients with in-hospital stroke in previous studies [15]. The most common in-hospital ischemic stroke etiologic subtype is cardio-embolic followed by those related to systemic hypotension [13]. Cardio-embolic strokes are associated with greater neurological disability and high rates of early recurrence and hemorrhagic transformation [16, 17]. The disproportionate representation of cardio-embolic etiology in patients with in-hospital ischemic strokes may explain the higher complication rates and mortality in these patients. A multicenter, 1-year prospective study of in-hospital strokes in 13 hospitals found that of 273 patients with in-hospital stroke, cardiac sources of embolism were present in 138 (50.5%), withdrawal of antithrombotic drugs in 77 (28%), and active cancers in 35 (12.8%); in addition, reasons for admission were programmed or urgent surgery in 70 (25%), cardiac diseases in 50 (18%), transient ischemic attacks or stroke in 30 (11%) and other medical illnesses in 71 (26%). A study that looked at 111 consecutive patients who developed in-hospital stroke during a 5-year period at a single hospital found that 46% of patients were admitted to the department of cardiology or cardiovascular surgery and 60% of the strokes were associated with surgery or procedures. In addition, when compared to patients who were admitted with stroke, the in-hospital stroke group had longer mean hospital stay (30.1 ± 41.1 days versus 11.0 ± 14.1 days), and showed an increased frequency of cardiac disease, leukocytosis, and anemia with up to a tenfold higher mortality rates, with sepsis being the most common cause of death [2]. We found significantly higher rates of complications such as pneumonia, deep venous thrombosis, pulmonary embolism, and sepsis among the in-hospital stroke group. Previous studies [15] have highlighted the important contribution of medical complications on overall patient outcome in stroke patients. In one study of patients with stroke and length of stay >7 days, age and stroke severity accounted for 44.1%, whereas pneumonia (12.2%), other complications (12.6%), and increased intracranial pressure (8.3%) contributed to one-third of in-hospital deaths [15].

Another explanation for the higher mortality in patients with in-hospital stroke is greater delay in the evaluation of patients who are already in the hospital suspected of having stroke when compared with such patients presenting with stroke symptoms on admission [6]. These delays are due to sedation, pharmacological paralysis, delirium, absence of specific training in the recognition of stroke or treatment options amongst referring physicians and complexities of within hospital triage practices [2, 13]. Confounding medical illness, less efficient care processes on hospital wards compared with the emergency department, and distance to the computed tomography scanner have all been proposed as reasons for slower response to in-hospital stroke, time to CT scan and treatment for patients with in-hospital stroke [18]. Such delays even in the time window of 4.5 h from the symptom onset result in higher rates of disability [19]. The higher rate of use of mechanical thrombectomy in patients with in-hospital stroke may be consequent to unique characteristics such as delay in diagnosis or contra-indication to IV rt-PA frequently observed in these patients. Several studies have consistently observed a higher rate of death and disability among patients treated with mechanical thrombectomy due to greater time intervals between symptom onset and treatment [20–22]. We also evaluated the possibility of disproportionate use of withdrawal of care among patients with in-hospital stroke. Although there was no significant difference between the two groups in the rate of withdrawal of care in our study, a higher likelihood of decision to withdrawal of care by family based on patients' underlying medical condition combined with severe stroke, longer length of hospitalization, higher rates of in-hospital complications such as infections and ICH can be expected. A study that reviewed all ischemic stroke mortalities at an academic medical center to understand the causes of inpatient stroke mortality found that among 37 deaths or discharges to hospice in a 1-year period, 36 occurred after a patient/family decision to withdraw/withhold potentially life-sustaining interventions. Furthermore, an independent survey of three vascular neurologists at that institution revealed that some early deaths could have been delayed beyond 30 days if patients or families had agreed to more aggressive measures concluding that acute stroke mortality may be more reflective of patient/family preferences than the provision of evidence-based care [23].

There are some modifiable factors in improving the higher rates of death and disability seen in patients with in-hospital strokes. For example, the development of inpatient stroke code teams with trained specialists evaluating patients suspected of having stroke within a few minutes with neurological triage capability would reduce unnecessary delays such as pathways to CT scan and greatly improved the response times, quality of care and treatment provided for those in-hospital patients [7, 24]. Previous data has shown that thrombolytic treatment is safe and effective in patients with in-hospital strokes in presence of inpatient stroke code teams [6]. A single center study analyzed the treatment procedures, safety, and efficacy of IV rt-PA in patients with in-hospital strokes compared with out-of-hospital strokes. The study found that while no differences were observed in safety or efficacy of the treatment with appropriate and well defined triage pathways, in-hospital delays were significantly longer in the in-hospital stroke group for door-to-CT (39.5± 18.7 versus 22.6 ±19.7 min, $p <$ 0.0001) and CT-to-treatment time (92.0 ± 26.1 versus 65.4 ± 25.8 min, $p < 0.0001$) [6]. Future studies would have to determine that whether further reduction in time to treatment is possible in patients with in-hospital stroke using new care pathways.

This study is limited by the information that cannot be retrieved from the NIS database. For example, although data on all stroke patients who received thrombolytic treatment either on the day of admission or thereafter were collected from the NIS database, it is difficult to be certain that thrombolytic treatment was specifically for stroke. In addition, the accuracy of the codes for thrombolysis and thrombectomy in identifying every patient with such procedures for stroke can be questioned. We observed a relatively high proportion of inpatients who received IV rt-PA. In-hospital stroke comprises between 6.5% and 15.0% of all strokes [3]. In a multicenter prospective registry, almost 10% of patients who received IV rt-PA were already admitted to the hospital [6]. The procedure date assigned to the thrombolysis is based on local hospital coding and is subject to variations in coding practices. There is also an unknown component of miscoding due to difference in dates of admission to ED and thrombolytic assignment in patients presenting to ED in after 10 PM. We acknowledge the possibility of overestimating in hospital strokes secondary to limitations of our methodology. Use of ICD 9 codes to identify medical complications such as pneumonia or DVT is limited due to inability to differentiate between pre- or post-stroke occurrence in the hospital. It is also not possible to compare the initial severity of neurological deficits between the two groups. In addition, it is difficult to establish the etiology of ischemic stroke for each patient in each of the two cohorts. Furthermore, it is difficult to estimate the time from diagnosis to thrombolytic treatment for each patient in each group.

Conclusion

In current practice, a prominent proportion of acute ischemic stroke patients treated with thrombolytics is receiving the treatment for in-hospital stroke. Further efforts are required to reduce the high mortality and complicated hospitalization in such patients.

References

1. Vera R, Lago A, Fuentes B, Gallego J, Tejada J, Casado I, et al. 2011;In-hospital stroke: a multi-centre prospective registry. *European Journal of Neurology: The official journal of the European Federation of Neurological Societies* 18:170–6.
2. Park HJ, Cho HJ, Kim YD, Lee DW, Choi HY, Kim SM, et al. 2009;Comparison of the characteristics for in-hospital and out-of-hospital ischaemic strokes. *European Journal of Neurology: The Official Journal of the European Federation of Neurological Societies* 16:582–8.
3. Blacker DJ. 2003;In-hospital stroke. *Lancet Neurology* 2:741–6.
4. Farooq MU, Reeves MJ, Gargano J, Wehner S, Hickenbottom S, Majid A. 2008;In-hospital stroke in a statewide stroke registry. *Cerebrovasc Dis* 25:12–20.
5. Meretoja A, Strbian D, Mustanoja S, Tatlisumak T, Lindsberg PJ, Kaste M. 2012;Reducing in-hospital delay to 20 minutes in stroke thrombolysis. *Neurology* 79:306–13.
6. Masjuan J, Simal P, Fuentes B, Egido JA, Diaz-Otero F, Gil-Nunez A, et al. 2008;In-hospital stroke treated with intravenous tissue plasminogen activator. *Stroke; A Journal of Cerebral Circulation* 39:2614–6.
7. Cumbler E, Zaemisch R, Graves A, Brega K, Jones W. 2011;Improving stroke alert response time: Applying quality improvement methodology to the inpatient neurologic emergency. *Journal of Hospital Medicine* 2012:137–41.
8. Hassan AE, Chaudhry SA, Grigoryan M, Tekle WG, Qureshi AI. 2012;National trends in utilization and outcomes of endovascular treatment of acute ischemic stroke patients in the mechanical thrombectomy era. *Stroke* 43:3012–7.
9. Qureshi AI, Chaudhry SA, Hassan AE, Zacharatos H, Rodriguez GJ, Suri MF, et al. 2011;Thrombolytic treatment of patients with acute ischemic stroke related to underlying arterial dissection in the united states. *Archives of Neurology* 68:1536–42.
10. Kimura K, Minematsu K, Yamaguchi T. 2006;Characteristics of in-hospital onset ischemic stroke. *European Neurology* 55:155–9.
11. Aly N, McDonald K, Leathley M, Sharma A, Watkins C. 2000;Retrospective case note review of acute and inpatient stroke outcomes. *BMJ* 320:1511–2.
12. Nadav L, Gur AY, Korczyn AD, Bornstein NM. 2002;Stroke in hospitalized patients: Are there special risk factors? *Cerebrovasc Dis* 13:127–31.
13. Alberts MJ, Brass LM, Perry A, Webb D, Dawson DV. 1993;Evaluation times for patients with in-hospital strokes. *Stroke; A Journal of Cerebral Circulation* 24:1817–22.
14. Bhalla A, Smeeton N, Rudd AG, Heuschmann P, Wolfe CD. 2010;A comparison of characteristics and resource use between in-hospital and admitted patients with stroke. *Journal of Stroke and Cerebrovascular Diseases: The Official Journal of National Stroke Association* 19:357–63.
15. Koennecke HC, Belz W, Berfelde D, Endres M, Fitzek S, Hamilton F, et al. 2011;Factors influencing in-hospital mortality and morbidity in patients treated on a stroke unit. *Neurology* 77:965–72.
16. Kolominsky-Rabas PL, Weber M, Gefeller O, Neundoerfer B, Heuschmann PU. 2001;Epidemiology of ischemic stroke subtypes according to toast criteria: Incidence, recurrence, and long-term survival in ischemic stroke subtypes: a population-based study. *Stroke; A Journal of Cerebral Circulation* 32:2735–40.
17. Petty GW, Brown RD Jr, Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO. 2000;Ischemic stroke subtypes : a population-based study of functional outcome, survival, and recurrence. *Stroke; A Journal of Cerebral Circulation* 31:1062–8.
18. Cumbler E, Anderson T, Neumann R, Jones W, Brega K. 2010;Stroke alert program improves recognition and evaluation time of in-hospital ischemic stroke. *Journal of Stroke and Cerebrovascular Diseases* 19:494–6.
19. Strbian D, Soinne L, Sairanen T, Happola O, Lindsberg PJ, Tatlisumak T, et al. 2010;Ultraearly thrombolysis in acute ischemic stroke is associated with better outcome and lower mortality. *Stroke; A Journal of Cerebral Circulation* 41:712–6.
20. Smith WS, Sung G, Starkman S, Saver JL, Kidwell CS, Gobin YP,

et al. 2005;Safety and efficacy of mechanical embolectomy in acute ischemic stroke: results of the merci trial. *Stroke; A Journal of Cerebral Circulation* 36:1432–8.

21. Smith WS. 2006;Safety of mechanical thrombectomy and intravenous tissue plasminogen activator in acute ischemic stroke. Results of the multi mechanical embolus removal in cerebral ischemia (MERCI) trial, Part I. *AJNR. American Journal of Neuroradiology* 27:1177–82.
22. Smith WS, Sung G, Saver J, Budzik R, Duckwiler G, Liebeskind DS, et al. 2008;Mechanical thrombectomy for acute ischemic stroke: Final results of the multi merci trial. *Stroke; A Journal of Cerebral Circulation* 39:1205–12.
23. Kelly AG, Hoskins KD, Holloway RG. 2012;Early stroke mortality, patient preferences, and the withdrawal of care bias. *Neurology* 79:941–4.
24. Gomez CR, Malkoff MD, Sauer CM, Tulyapronchote R, Burch CM, Banet GA. 1994;Code stroke: an attempt to shorten inhospital therapeutic delays. *Stroke; A Journal of Cerebral Circulation* 25:1920–3.