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Association between Stroke Center Hospitalization for Acute Ischemic Stroke and Mortality

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Abstract

Context—Although stroke centers are widely accepted and supported, little is known about their impact on patient outcomes.

Objective—To examine the association between admission to stroke centers for an acute ischemic stroke and mortality.

Design, Setting, and Participants—Observational study using data from the New York Statewide Planning and Research Cooperative System. We compared mortality for patients admitted with acute ischemic stroke (n=30,947) between 2005 and 2006 at designated stroke centers and non-designated hospitals using differential distance to hospitals as an instrumental variable to adjust for potential pre-hospital selection bias. Patients were followed for mortality for 1 year after the index hospitalization through 2007. To assess whether our findings were specific to stroke, we also compared mortality for patients admitted with gastrointestinal hemorrhage (n=39,409) or acute myocardial infarction (n=40,024) at designated stroke centers and non-designated hospitals.

Main Outcome Measure—Thirty-day all-cause mortality.

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AUTHOR CONTRIBUTIONS
Dr Xian had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Xian, Friedman, Holloway.
Acquisition of data: Xian, Friedman.
Analysis and interpretation of data: Xian, Friedman, Holloway, Noyes, Shah, Peterson, Chan, Ting, Chappel.
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Disclaimer: This study used a linked SPARCS-SSADMF database. The interpretation and reporting of these data are the sole responsibility of the authors.

Results—Among 30,947 patients with acute ischemic stroke, 15,297 (49.4%) were admitted to designated stroke centers. Using the instrumental variable analysis, admission to designated stroke centers was associated with greater use of thrombolytic therapy (4.8% vs. 1.7%; adjusted difference 2.2%, 95% CI, 1.6% to 2.8%; P<0.001) and lower 30-day all-cause mortality (10.1% vs. 12.5%; adjusted mortality difference: −2.5%, 95% CI, −3.6% to −1.4%; P<0.001). Differences in mortality also were observed at all time points, including at 1-day, 7-day, and 1-year follow-up. Moreover, the outcome differences were specific to stroke, as stroke centers and non-stroke centers had similar 30-day all-cause mortality rates among those with acute myocardial infarction (adjusted mortality difference: +0.3%, 95% CI, −0.5% to 1.0%; P=0.50) and/or gastrointestinal hemorrhage (adjusted mortality difference: +0.1%, 95% CI, −0.9% to 1.1%; P=0.83).

Conclusions—Admission to a designated stroke center for acute ischemic stroke was associated with more frequent use of thrombolytic therapy and lower mortality.

Keywords

quality improvement; outcome research; acute ischemic stroke

Stroke is the leading cause of serious long-term disability and the third leading cause of mortality in the United States.[1] Responding to the need for improvements in acute stroke care, the Brain Attack Coalition (BAC) published recommendations for the establishment of Primary Stroke Centers in 2000.[2] In December 2003, the Joint Commission began certifying stroke centers based on BAC criteria.[3] Now, nearly 700 of the 5,000 acute care hospitals in the U.S. are Joint Commission-certified stroke centers.[4] Some states, such as New York, Massachusetts, and Florida have established their own designation programs using the BAC core criteria.

Despite widespread support for the stroke center concept, there is limited empiric evidence demonstrating that admission to a stroke center is associated with lower mortality. Prior studies have largely focused on stroke processes of care, such as treatment timeline and use of thrombolytic therapy.[5–8] There is comparably less information on whether or not better care at stroke centers affects acute or long-term mortality.[9] Therefore, our goal was to evaluate the association between admission to stroke centers for acute ischemic stroke and mortality.

METHODS

Study Population

The primary data source was the New York Statewide Planning and Research Cooperative System (SPARCS), a comprehensive reporting system that collects patient-level data from every hospital admission in New York State. We identified 33,090 hospitalized patients, 18 years of age or older, with a principal diagnosis of acute ischemic stroke between January 1, 2005 and December 31, 2006. An ischemic stroke diagnosis was verified through the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes 433.x1, 434.x1 and 436. We limited our study sample to only patients presenting with an initial stroke admission during the study period. We excluded 548 (1.7%) patients who lived outside of New York State and 123 (0.4%) patients with missing data. To avoid a bias against non-designated hospitals, we also excluded 1,472 (4.4%) patients for whom the distance from their home residence to the admitting hospital was greater than 20 miles, since these patients would be less likely to receive thrombolytic therapy. Consistent with the Centers for Medicare and Medicaid Services (CMS), all transfer patients were assigned to the transferring hospital. The final sample included 30,947 patients.

New York State Stroke Center Designation

The New York State Stroke Center Designation program is collaboration between the New York State Department of Health (NYSDOH), the American Heart Association (AHA), and the New York State Quality Improvement Organization.[7,10] Beginning in 2004, all New York hospitals were invited to apply to the NYSDOH for stroke center designation if they met the BAC criteria. These criteria are organized around 11 aspects of stroke care, specifically: acute stroke teams, written care protocols, emergency medical services (EMS), emergency department, stroke units, neurosurgical services, commitment and support of the medical organization, neuro-imaging services, laboratory services, outcome and quality improvement activities, and continuing medical education.[2] Hospitals were evaluated for stroke center designation with an initial hospital survey, followed by an on-site review and inspection, to ensure hospital compliance with the BAC criteria and preparedness to operate as a stroke center.

Of 244 New York hospitals, 104 (42.6%) became state-designated stroke centers by the end of 2006 (seeeFigure). Considering some hospitals became stroke centers during the study period, we assigned stroke center status for each patient based on the hospital's designation at the time of admission.

Patient Follow-up and Outcome Measures

Evaluation of in-hospital mortality may be confounded by different lengths of stay between stroke centers and non-designated hospitals. Moreover, the CMS is considering including 30-day ischemic stroke mortality as one of its publicly-reported measures of hospital quality of care.[11] Therefore, as our primary outcome, we examined 30-day all-cause mortality among those who were and were not admitted to a stroke center. As secondary outcomes, we evaluated 1- and 7-day, and 1-year all-cause mortality for a sensitivity analysis. Follow-up ended on the date of death or 1 year after the index hospitalization through 2007, whichever came first. Mortality post-discharge was determined through the Social Security Administration Death Master File. Finally, we explored how the use of thrombolytic therapy (ICD-9-CM procedure code 99.10 and/or diagnosis-related group 559), discharge to skilled nursing facilities, and all-cause readmission within 30 days of the index hospital discharge differed by whether or not a patient was admitted to a designated stroke center. Patients who died during the index hospitalization were excluded from the readmission analyses.

Other Study Variables

The SPARCS reporting system provided data on patient characteristics, including socio-demographics (age, sex, race/ethnicity, and insurance status) and comorbidities (differentiated from complications using a present-on-admission indicator). Comorbidities included prior myocardial infarction, congestive heart failure, atrial fibrillation, peripheral vascular disease, diabetes mellitus with or without complications, renal insufficiency, cancer, metastatic carcinoma, liver disease, chronic obstructive pulmonary disease, dementia, connective tissue disease disorder, and peptic ulcer disease. These comorbidities were used to construct a modified version of the Charlson Comorbidity Index (CCI) tailored for ischemic stroke.[12] Hospital characteristics, such as size and academic affiliation, were obtained from the NYSDOH and the American Hospital Association Annual Survey. Finally, we determined whether a patient lived in a rural or urban area by applying the Rural-Urban Commuting Area Codes classification system to the patient's residential zipcode.[13]

Instrumental Variable

Because it would be impractical to randomize patients with acute ischemic stroke to designated stroke centers or non-designated hospitals, researchers must rely on observational data to assess the impact of stroke centers on mortality. However, both measured and unmeasured confounding inherent in observational studies may lead to selection bias for treatment. For example, EMS may systematically transport more severely-ill patients to stroke centers. Standard statistical approaches, such as multivariate logistic regression or propensity score analysis, cannot account for unmeasured confounding because they can only adjust for measured covariates.[14,15] One solution is to use instrumental variable (IV) analysis (an econometric method) to minimize unmeasured confounding.[16,17]

The key notion behind instrumental variable analysis is that the instrument is highly correlated with the treatment (stroke center vs. non-designated hospital), but is otherwise unrelated to observed or unobserved prognostic risk factors so that it does not directly or indirectly affect patient outcome except through the treatment itself.[16,17] This is similar to a randomized controlled trial where the randomization process assigns patients to treatment groups but the randomization itself is not directly associated with outcomes. In the case of stroke center admission, we used differential distance, which is an instrumental variable that has been used in prior studies of acute myocardial infarction and trauma.[16–20] Differential distance was calculated as the difference between the straight-line distance from a patient's residence to the nearest stroke center minus the straight-line distance from this patient's residence to the nearest hospital of any type. The differential distance is the additional distance, if any, beyond the nearest hospital to reach a stroke center. The choice of differential distance as an effective instrumental variable is based on two assumptions: (1) it is logical to assume that patient transported by a private vehicle will go to the nearest hospital. Importantly, the New York State Stroke Protocol requires EMS to transport stroke patients to the nearest stoke center if the pre-hospital time is less than 2 hours.[21] As one would expect, those who live close to a stroke center are more likely to be transported to the stroke center; and (2) patients cannot predict if and when they will have a stroke and, therefore, they do not choose their residence based on proximity to a given hospital. Thus, distance to each type of hospital is highly predictive of whether the patient was admitted to a stroke center but is not associated with disease characteristics such as stroke severity.

Statistical Analyses

Baseline characteristics were compared between patients admitted to designated and non-designated hospitals using the standardized difference. This method has been used to assess the comparability of study subjects in the literature.[22] An absolute standardized difference greater than 10 (approximately equivalent to $p<0.05$) indicates significant imbalance of a baseline covariate, while a smaller value supports the balance assumption between groups. We then assessed whether admission to a designated stroke center was associated with lower mortality using an instrumental variable analysis estimated by a simultaneous two-equation bivariate probit model.[23] The first equation estimated the probability of stroke center admission as a function of differential distance and other covariates. The second equation assessed the association of stroke center admission with mortality, adjusted for other patient and hospital factors. Estimating two equations jointly using a bivariate probit approach provides consistent estimates of the treatment effect.[23, 24] The IV-adjusted mortality estimate (technically, the average marginal effect) can be interpreted as the mean predicted difference in the probability of death for stroke patients who received treatment at designated stroke centers because they lived relatively closer to stroke centers versus patients who received treatment at non-designated hospitals because they lived further away.

We examined the robustness of our findings in several ways. First, we sought to determine whether admission to a designated stroke center was associated with lower 1- and 7-day, and 1-year all-cause mortality by repeating the analyses for these time points. Second, because the majority of stroke centers are located in New York City (see eFigure), we performed subgroup analyses for patients living in the New York metropolitan area and for those in upstate New York. Third, whites and minorities often live in different neighborhoods and may have systematically used different hospitals. We stratified the analysis by race and checked whether the effect of stroke centers varied by race/ethnicity group. Finally, to determine if our mortality findings were specific to stroke, we compared mortality among patients admitted at designated and non-designated hospitals for 2 other acute life-threatening conditions—gastrointestinal (GI) hemorrhage and acute myocardial infarction (AMI). Both conditions are quality indicators recommended by the Agency for Healthcare Research and Quality to assess a hospital's quality of care.[25] If mortality was lower for either of these 2 conditions in designated stroke centers, this would suggest that lower stroke mortality would be due to these hospitals' overall commitment to quality improvement, rather than to these hospitals' implementation of actions specific to stroke.

All tests were evaluated at a 2-sided significance level of $p<0.05$. The analyses were performed using SAS 9.2 (SAS Institute, Cary, North Carolina) and STATA 11 (StataCorp, College Station, Texas) software. This study was approved by the University of Rochester's institutional review board, with waiver of informed consent.

RESULTS

Among 30,947 stroke patients, 15,297 (49.4%) were admitted to designated stroke centers and 15,650 (50.6%) to non-designated hospitals. Table 1 compares baseline characteristics of the study cohort. Patients admitted to stroke centers were more frequently younger, non-Hispanic black, less likely to live in a rural area, and more likely to be admitted at a hospital with more beds and an academic affiliation. Patients admitted to stroke centers were relatively healthier with respect to the prevalence of comorbidities, although none of the differences were statistically significant.

As mentioned above, instrumental variables carry with them several assumptions. First, one assumes that the instrumental variable is highly correlated with the variable of interest. We found from a logistic regression model that the differential distance was highly predictive of whether a patient was admitted to a stroke center (C-statistic=0.88). Second, one assumes that the instrumental variable does not independently affect patient outcomes so that it is not associated with other potential confounders of the outcome. Although it is not possible to examine the unmeasured stroke severity, we were able to check the balance of observed health status according to the differential distance to a stroke center. Table 2 shows baseline characteristics relative to whether a patient lived closer to a stroke center (differential distance=0 or >0 mile). Although there were small differences in certain measures, age and the prevalence of most comorbidities were far more similar than were the groups in Table 1, as reflected by diminishing standardized differences. Despite the similarity in observed health status, the differential distance groups differed substantially in their probability of being admitted to a stroke center. The high correlation between differential distance and stroke center, as well as the balance in observable health status, provide validation of the key instrumental variable assumptions.

Stroke Mortality and Other Outcomes

Mortality rates among patients admitted to stroke centers and non-designated hospitals are summarized in Table 3. The overall 30-day all-cause mortality rate was 10.1% for patients admitted at stroke centers and 12.5% for patients admitted at non-designated hospitals

(unadjusted mortality difference, −2.4%, P<0.001). Using instrumental variable analysis, we found admission to a designated stroke center was associated with a 2.5% absolute reduction in 30-day all-cause mortality (adjusted mortality difference, −2.5%; 95% CI, −3.6% to −1.4%; P<0.001).

Use of thrombolytic therapy was 4.8% (739/15,297) for patients admitted at stroke centers and 1.7% (266/15,650) for patients admitted at non-designated hospitals (P<0.001). Admission to a stroke center was associated with the increased use of thrombolytic therapy (adjusted difference in thrombolysis use of 2.2%, 95% CI, 1.6% to 2.8%, P<0.001). However, further adjustment for use of thrombolysis in our instrumental variable models did not substantially alter the association of stroke center admission with lower 30-day mortality: adjusted mortality difference −2.7% (95% CI −3.8% to −1.6%, P<0.001). Among those surviving to hospital discharge, there was no difference in rates of 30-day all-cause readmission (14.8% vs. 14.2%, adjusted difference 1.1%, 95% CI −0.3% to 2.6%, p=0.12) and discharge to a skilled nursing facility (24.6% vs. 28.5%, adjusted difference −0.5%, 95% CI −2.1% to 1.2%, p=0.56).

Sensitivity Analyses

Our sensitivity analysis examined whether or not the effect of stroke center on mortality varied by race, location, or time points. Lower mortality was observed within the first hospital day and at 7 days. Importantly, the all-cause mortality difference also was sustained at 1-year after the index hospitalization (see Table 3). Subgroup analyses of the New York metropolitan area, upstate New York, and stratified analyses by race/ethnicity, found similar results of lower all-cause mortality at designated stroke centers (see Table 4).

Specificity Analyses

To examine whether the lower mortality at designated stroke centers was specific to stroke, we examined mortality rates for patients admitted with GI hemorrhage and AMI at stroke centers and non-designated hospitals. Thirty-day all-cause mortality for GI hemorrhage was comparable for patients admitted to stroke centers and non-designated hospitals (5.0% vs. 5.8%; adjusted mortality difference, +0.3%; 95% CI, −0.5% to 1.0%; P=0.50). Similarly, 30-day all-cause mortality for AMI did not significantly differ between the two groups (10.5% vs. 12.7%; adjusted mortality difference, +0.1%; 95% CI, −0.9% to 1.1%; P=0.83). For these 2 conditions, there also were no differences in 1-day or 7-day mortality (Table 5). Lastly, given our sample size and observed mortality rates, a retrospective power analysis indicated that our study had more than 90% statistical power to detect a 0.1% mortality difference for AMI and 70% power to detect a 0.3% mortality difference for GI hemorrhage.

COMMENT

Reduced mortality and increased use of acute stroke therapies are two expected benefits of primary stroke centers.[2] Nevertheless, limited empiric evidence supports the benefits of stroke centers—in particular, outcome-based quality measures.[9] In this large observational study, we found that patients admitted to stroke centers were more likely to receive thrombolytic therapy and less likely to die when compared to patients admitted to non-designated hospitals. This survival benefit was sustained for up to one year after stroke occurrence and was independent of patient and hospital characteristics. Importantly, the lower mortality at designated stroke centers was specific to stroke and was not found for other acute life-threatening conditions, which suggests that the mortality benefit was related to stroke center designation, rather than to overall quality improvement efforts at designated stroke centers. Collectively, our study provides evidence that the implementation and

establishment of a BAC-recommended stroke system of care was associated with improved outcomes for patients with acute ischemic stroke.

Previous evaluations of stroke center quality performance have primarily focused on process measures with limited information on patient outcomes.[5–8] To date, only one study in Finland has reported lower 1-year stroke case-fatality associated with stroke centers.[26] Our study extends the findings from this prior study, as systems of stroke care in the U.S. may differ substantially from other national healthcare systems (especially those with universal health coverage). Significantly, we were able to report both short-term and 1-year mortality outcomes. Finally, we were able to demonstrate that lower mortality was specific to stroke at designated stroke centers.

Importantly, geographic patterns of stroke triage are likely to be non-random. Designated stroke centers and non-designated hospitals may treat different groups of patients in terms of demographics and disease severity. For instance, it is possible that EMS may systematically transport more severely-ill patients to stroke centers,[4] which is consistent with our finding of a greater IV-adjusted mortality difference (in absolute value) compared to the unadjusted difference (e.g. 2.5% vs. 2.4% for 30-day all-cause mortality). Moreover, prior studies have reported that stroke centers are more likely to admit patients with hemorrhagic strokes, which are associated with higher mortality as compared to strokes with an ischemic etiology.[7,8] Indeed, we found a similar pattern, in which nearly 60% (4,193/7,243) of hemorrhagic stroke patients in New York were admitted to a stroke center during our study period. In the absence of randomized controlled trials, controlling for treatment patterns is often difficult and assessments of mortality outcomes may be biased given the presence of treatment selection. Our analysis sought to address these concerns by using an instrumental variable analysis to control for the selection bias (both measured and unmeasured) inherent in observational studies. After adjusting for patient and hospital characteristics and the potential for unmeasured selection bias with the instrumental variable analysis, we found that admission to a stroke center for an acute ischemic stroke was associated with a 2.5% absolute reduction in 30-day all-cause mortality.

The BAC recommendations serve as the cornerstone for the establishment of primary stroke centers. Previous studies have shown reduced mortality among patients who were treated by neurologists or who received organized care in a stroke care unit.[27–29] Although we cannot determine which individual components of the BAC criteria for stroke center designation were most important for the lower mortality observed in this study, it is likely that the BAC criteria cannot be examined as individually isolated units. Rather, the 11 core criteria, combined, establish the infrastructure and define a paradigm for optimizing care for acute ischemic stroke. By emphasizing an integrated and organized system of care with EMS, hospital emergency departments, acute stroke teams, stroke units, and neuro-imaging services, the BAC criteria facilitate rapid transportation, evaluation, and treatment. Moreover, availability of stroke protocols standardizes acute stroke care and minimizes protocol violation. These efforts are further enhanced by the BAC criteria's emphasis on surveillance of outcomes, quality initiatives, and continuing educational programs. Of equal importance are the improved performance measures which may also impact downstream care and outcomes. Studies have found association between process of care performance measures and mortality outcomes for patients with cardiovascular disease and stroke.[30, 31] It is certainly possible that improved guideline-based treatment, more frequent thrombolytic therapy, enhanced secondary prevention and risk factor management, early rehabilitation and patient education programs may also be responsible for the lower mortality rates among patients treated at stroke centers. However, these efforts may not have any appreciable short-term or immediate life-saving effect, which is consistent with our findings of minimal mortality difference at day 1 and similar readmission rates at 30 days compared to greater

survival benefit at the end of 1 year follow-up. Collectively, it is likely that the combinations of these efforts elevate the structure and process of stroke care and subsequently lead to improved patient outcomes.

Since stroke center certification is voluntary, it is possible that hospitals were already committed to quality improvement and would have achieved these results regardless of designation. A recent evaluation of the Joint Commission Certified Primary Stroke Centers found that certified hospitals had better outcomes than non-certified hospitals even before the certification program began.[32] Based on our data, we cannot definitively establish if the designation program resulted in reduced mortality or if higher quality hospitals participated in designation. However, this concern is largely mitigated by our specificity analysis, in which we examined mortality rates at designated and non-designated hospitals for 2 other life-threatening conditions—GI hemorrhage and AMI. Hospitals committed to quality improvement prior to stroke center designation would be expected to demonstrate lower mortality for other medical conditions, as well as for stroke. Nevertheless, the lower mortality observed in this study was specific to stroke, thus suggesting that the lower stroke mortality could not be explained simply by the fact that hospitals who received stroke designation were more likely to implement hospital-wide quality improvement.

Our study should be interpreted in the context of the following limitations. First, the SPARCS database did not include information on stroke severity. The differences in mortality may be due to patient case-mix, as opposed to variation in the quality of acute stroke care. This being said, selection bias is more likely to be against admission to a stroke center rather than favoring stroke centers.[4] Second, we were unable to assess other performance and outcomes such as eligibility and contradiction of thrombolytic therapy, thrombolysis related hemorrhage, quality of life, neurological and functional status at discharge, since these measures were not collected in the SPARCS database, nor were we able to assess cause-specific mortality. Nonetheless, our study was able to report on the relationship between stroke center admission and all-cause mortality—an outcome which has not been routinely reported. Third, while our sensitivity and specificity analyses suggest that lower mortality associated with stroke center admission may be due to the implementation of the BAC criteria as part of stroke center designation, other quality improvement initiatives (e.g., the AHA Get With The Guidelines-Stroke program), economic incentives from pay for performance, and public reporting could also impact stroke care and outcomes. Fourth, our study only included data from New York. The generalizability of our findings to other states and agencies certifying stroke centers remains to be established. Fifth, we were unable to assess acute treatments other than thrombolytic therapy, including the use of life-sustaining interventions and end-of-life care which may affect short-term or intermediate survival.[33] Sixth, many hospitals were transitioning to stroke center during our study period. Defining a stroke center based on designation status on the admission date may have underestimated the mortality differences with stroke center admission. Nonetheless, our conservative approach still demonstrates a lower risk of death associated with stroke centers. Finally, the instrumental variable approach assumes that differential distance has no independent effect on patient outcomes except through its impact on the likelihood of receiving treatment at the designated stroke center. The assumption by its very nature is unproven. However, this assumption would generally be satisfied if a patient's residence is not associated with stroke severity, which appears reasonable. Moreover, differential distance has been widely and successfully used as an instrument to control for selection bias in a variety of clinical settings.[16–20]

In conclusion, we found that admission to designated stroke centers in New York State was associated with a lower risk of death for patients with an acute ischemic stroke. The lower mortality in designated stroke centers was specific to stroke. Our findings suggest that a

rigorous process of designating stroke centers has the potential to improve the quality of stroke care and reduce stroke mortality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Baseline Characteristics of Study Cohort

Variable	Designated Stroke Center N=15,297 (%)	Non-Designated Hospital N=15,650 (%)	$\|d\|$*
Demographic			
Age			12.5
Mean (SD) years	72.3 (14.3)	74.0 (13.8)	
Median (IQR)	75 (63–83)	77 (65–84)	
Male	6,957 (45.5)	6,837 (43.7)	3.6
Race/ethnicity			
Non-Hispanic white	8,865 (58.0)	11,649 (74.4)	35.4
Non-Hispanic black	3,337 (21.8)	2,303 (14.7)	18.5
Hispanic	1,507 (9.9)	784 (5.0)	18.5
Other	1,588 (10.4)	914 (5.8)	16.7
Insurance			
Medicare	10,386 (67.9)	11,557 (73.9)	13.1
Medicaid	1,475 (9.6)	953 (6.1)	13.2
Private insurance	2,840 (18.6)	2,562 (16.4)	5.8
Other insurance	185 (1.2)	220 (1.4)	1.7
Self-pay	411 (2.7)	358 (2.3)	2.6
Rural	219 (1.4)	2,556 (16.3)	54.3
Comorbidity			
Charlson comorbidity index			6.6
Mean (SD)	1.1 (1.4)	1.2 (1.5)	
Median (IQR)	1 (0–2)	1 (0–2)	
Charlson comorbid conditions			
MI	1, 051 (6.9)	1,185 (7.6)	2.7
CHF	2,146 (14.0)	2,386 (15.3)	3.4
PVD	882 (5.8)	1,084 (6.9)	4.7
Dementia	947 (6.2)	1,083 (6.9)	2.9
COPD	1,936 (12.7)	2,503 (16.0)	9.5
Connective tissue disease	275 (1.8)	372 (2.4)	4.1
Peptic ulcer disease	126 (0.8)	144 (0.9)	1.0
DM without complications	4,557 (29.8)	4,322 (27.6)	4.8
DM with complications	442 (2.9)	586 (3.7)	4.8
Renal disease	1,150 (7.5)	1,063 (6.8)	2.8
Cancer	485 (3.2)	584 (3.7)	3.1
Metastatic carcinoma	189 (1.2)	258 (1.7)	3.5
Liver disease	116 (0.8)	133 (0.9)	1.0
Atrial fibrillation	3,046 (19.9)	3,485 (22.3)	5.8
Hospital			
Teaching hospital	11,264 (73.6)	7,998 (51.1)	47.8

Variable	Designated Stroke Center N=15,297 (%)	Non-Designated Hospital N=15,650 (%)	$\|d\|$*
Total number of beds (SD)	458 (221)	308 (181)	74.4
Distance to the hospital†, mile			10.8
Median (IQR)	2.7 (1.2–5.6)	3.1 (0.8–6.7)	
Differential distance to stroke center‡, mile			86.2
Median (IQR)	0 (0 to 0.2)	11.5 (2.0 to 46.7)	

Abbreviations: CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; IQR, interquartile range; MI, myocardial infarction; PVD, peripheral vascular disease; SD, standard deviation.

*Standardized difference $d=\frac{100 \times (\bar{x}_{sc}+\bar{x}_{nsc})}{\sqrt{\frac{S_{sc}^2+S_{nsc}^2}{2}}}$ for continuous variable.

$\bar{x}_{SC}$ and $\bar{x}_{NSC}$ denote the mean of a covariate in stroke center and non-stroke center patients, while s_{sc}^2 and s_{nsc}^2 denote the variance.

$$d=\frac{100 \times (P_{sc}-P_{nsc})}{\sqrt{\frac{P_{sc}(1-P_{sc})+P_{nsc}(1-P_{nsc})}{2}}}$$ for binary variable.

P_{SC} and P_{NSC} denote the prevalence of the binary variable.

A standardized difference >10 (approximately equivalent to $p<0.05$) indicates significant imbalance of a variable.

†Distance from the patient's residence to the admitting hospital (5-digit zip code centroid to 5-digit zip code centroid)

‡Distance from the patient's residence to the nearest New York State designated stroke center (5-digit zip code centroid to 5-digit zip code centroid) minus the distance from the patient's residence to the nearest hospital of any type. Differential distance equals 0 if the nearest hospital is a designated stroke center.

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Table 2

Patient Characteristics by Differential Distance to a Designated Stroke Center*

Variable	Non-Hispanic Whites			Non-Hispanic Blacks		
	Differential Distance=0 N=7,516 (%)	Differential Distance>0 N=12,998 (%)	|*d*|	Differential Distance=0 N=2,829 (%)	Differential Distance>0 N=2,811 (%)	|*d*|
Age			0.4			4.2
Mean (SD) years	75.8 (13.1)	75.9 (13.1)		66.7 (14.4)	67.3 (14.1)	
Median (IQR)	79 (68–85)	79 (69–85)		67 (57–78)	68 (57–78)	
Charlson Comorbidity Index			5.2			0.9
Mean (SD)	1.1 (1.4)	1.2 (1.5)		1.2 (1.4)	1.2 (1.4)	
Median (IQR)	1 (0–2)	1 (0–2)		1 (0–2)	1 (0–2)	
MI	560 (7.5)	1,107 (8.5)	3.9	134 (4.7)	147 (5.2)	2.2
CHF	1,178 (15.7)	2,023 (15.6)	0.3	352 (12.4)	422 (15.0)	7.5
PVD	508 (6.8)	980 (7.5)	3.0	142 (5.0)	106 (3.8)	6.1
Dementia	519 (6.9)	895 (6.9)	0.1	158 (5.6)	183 (6.5)	3.9
COPD	1,060 (14.1)	2,211 (17.0)	8.0	281 (9.9)	322 (11.4)	4.9
Connective tissue disease	148 (2.0)	325 (2.5)	3.6	49 (1.7)	53 (1.9)	1.2
Peptic ulcer disease	60 (0.8)	116 (0.9)	1.0	20 (0.7)	22 (0.8)	0.9
DM without complications	1,765 (23.5)	3,259 (25.1)	3.7	1,074 (38.0)	1,057 (37.6)	0.7
DM with complications	204 (2.7)	422 (3.3)	3.1	115 (4.1)	119 (4.2)	0.8
Renal disease	504 (6.7)	846 (6.5)	0.8	261 (9.2)	261 (9.3)	0.2
Cancer	299 (4.0)	507 (3.9)	0.4	73 (2.6)	60 (2.1)	2.9
Metastatic carcinoma	121 (1.6)	214 (1.7)	0.3	29 (1.0)	27 (1.0)	0.7
Liver disease	53 (0.7)	93 (0.7)	0.1	18 (0.6)	25 (0.9)	2.9
Atrial fibrillation	2,033 (27.1)	3,563 (27.4)	0.8	326 (11.5)	341 (12.1)	1.9
Admit to stroke center	6,286 (83.6)	2,579 (19.8)	165.8	2,279 (80.1)	1,058 (37.6)	97.0

*Abbreviations, standardized difference and differential distance are defined in Table 1.

Similar results for Hispanic and other race/ethnicity group (not shown in the table).

Table 3

Mortality at Designated Stroke Centers and Non-Designated Hospitals

Mortality Assessment	Designated Stroke Center N=15,297 (%)	Non-Designated Hospital N=15,650 (%)	Adjusted Mortality Difference*, (95% CI)	p value
1-day	90 (0.6)	134 (0.9)	−0.3 (−0.6 to −0.0)	0.04
7-day	665 (4.3)	842 (5.4)	−1.3 (−2.1 to −0.6)	0.001
30-day	1,543 (10.1)	1,951 (12.5)	−2.5 (−3.6 to −1.4)	<0.001
1-year	3,412 (22.3)	4,067 (26.0)	−3.0 (−4.4 to −1.5)	<0.001

* Negative values indicate lower mortality at designated stroke center vs. non-designated hospital. Adjusted for age, gender, race, health insurance status, rural status, 13 Charlson comorbid conditions, atrial fibrillation, hospital teaching status, and total number of hospital beds by using the instrumental variable analysis.

Table 4

Sensitivity Analysis: 30-Day Mortality at Designated Stroke Centers and Non-Designated Hospitals

Sensitivity Analysis	Designated Stroke Center (%)	Non-Designated Hospital (%)	Adjusted Mortality Difference*, (95% CI)	p value
By Location†				
Metropolitan New York	1,034/11,120 (9.3)	715/6,881 (10.4)	−2.0 (−3.4 to −0.5)	0.01
Upstate New York	509/4,177 (12.2)	1,236/8,769 (14.1)	−2.0 (−3.8 to −0.3)	0.02
By race/ethnicity‡				
Non-Hispanic white	1,091/8,865 (12.3)	1,635/11,649 (14.0)	−2.5 (−3.9 to −1.1)	<0.001
Non-Hispanic black	204/3,337 (6.1)	148/2,303 (6.4)	−2.4 (−4.8 to −0.0)	0.05
Hispanic	117/1,507 (7.8)	73/784 (9.3)	−5.2 (−9.4 to −0.9)	0.02
Other race/ethnicity	131/1,588 (8.3)	95/914 (10.4)	−3.2 (−7.3 to 0.9)	0.12

*Negative values indicate lower mortality at designated stroke center vs. non-designated hospital.

†Stratified by location

‡Stratified by race/ethnicity group

Table 5

Specificity Analysis: Mortality for Gastrointestinal Hemorrhage and Acute Myocardial Infarction at Designated Stroke Centers and non-Designated Hospitals

Mortality Assessment	Designated Stroke Center	Non-Designated Hospital	Adjusted Mortality Difference*, (95% CI)	p value
GI hemorrhage	N=17,481	N=21,928		
1-day	119 (0.7)	178 (0.8)	0.2 (−0.1 to 0.5)	0.24
7-day	352 (2.0)	523 (2.4)	0.2 (−0.3 to 0.7)	0.46
30-day	871 (5.0)	1, 261 (5.8)	0.3 (−0.5 to 1.0)	0.50
AMI	N=16,833	N=23,191		
1-day	363 (2.2)	688 (3.0)	−0.3 (−0.7 to 0.2)	0.30
7-day	983 (5.8)	1,689 (7.3)	−0.5 (−1.3 to 0.2)	0.17
30-day	1,775 (10.5)	2,950 (12.7)	0.1 (−0.9 to 1.1)	0.83

Abbreviations: GI, gastrointestinal; AMI, acute myocardial infarction.

* Negative values indicate lower mortality at designated stroke center vs. non-designated hospital. Adjusted for age, gender, race, health insurance status, rural status, Charlson comorbidity conditions, hospital teaching status, and total number of hospital beds by using the instrumental variable analysis.