eNeurologicalSci 26 (2022) 100392

Contents lists available at ScienceDirect

eNeurologicalSci

journal homepage: www.elsevier.com/locate/ensci

Demographic and institutional predictors of stroke hospitalization mortality among adults in the United States

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ARTICLE INFO

Keywords:
Stroke
Ischemic stroke
Hemorrhagic stroke
Mortality
Inpatient mortality

ABSTRACT

Introduction: Stroke remains a primary source of functional disability and inpatient mortality in the United States (US). Recent evidence reveals declining mortality associated with stroke hospitalizations in the US. However, data updating trends in inpatient mortality is lacking. This study aims to provide a renewed inpatient stroke mortality rate in a national sample and identify common predictors of inpatient stroke mortality.
Methods: In this cross-sectional study, we analyzed data from a nationwide database between 2010 and 2017. We included patient encounters for both ischemic (ICD9 433–434, ICD10 I630–I639) and hemorrhagic stroke (ICD9 430–432, ICD10 I600–I629). We performed an annual comparison of in-hospital stroke mortality rates, and a cross-sectional analytic approach of multiple variables identified common predictors of inpatient stroke mortality.
Results: Between 2010 and 2017, we identified 518,185 total stroke admissions (86.6% ischemic stroke and 13.4% hemorrhagic strokes). Stroke admissions steadily increased during the studied period, whereas we observed a steady decline in in-hospital mortality during the same time. The inpatient stroke mortality rate gradually declined from 4.8% in 2010 (95% CI 4.6–5.1) to 2.1% in 2017 (95% CI 2.0–2.1). Predictors of higher odds of dying from ischemic stroke were female (OR 1.059, 95% CI 1.015–1.105, $p = 0.008$), older age (OR 1.028, 95% CI 1.026–1.029, $p < 0.001$), and sicker patients (OR 1.091, 95% CI 1.089–1.093, $p < 0.001$). Predictors of higher odds of dying from hemorrhagic stroke were Hispanic ethnicity (OR 1.459, 95% CI 1.084–1.926, $p < 0.001$), older age (OR 1.021, 95% CI 1.019–1.023, $p < 0.001$), and sicker patients (OR 1.042, 95% CI 1.039–1.045, $p < 0.001$). All census regions and hospital types demonstrated improvements in in-hospital mortality.
Conclusion: This study identified a continuous declining rate in in-hospital mortality due to stroke in the United States, and it also identified demographic and hospital predictors of inpatient stroke mortality.

1. Introduction

The acute care of stroke has markedly evolved at many levels in the past decades, curtailing stroke mortality, especially in developed nations [1,2]. The adoption of intravenous thrombolysis and the advent of endovascular thrombectomy fueled by the completion of multiple randomized clinical trials have decreased the morbidity and mortality associated with ischemic stroke [3–12]. These therapies and the institution of neurocritical care units improved the outcomes of patients suffering from severe stroke independent of stroke etiology [13–15] .

Notwithstanding these promising trends, stroke remains a leading cause of disability and mortality in the United States (US). A high prevalence of vascular risk factors in the US and disparities in access to comprehensive stroke care are thought to be the main drivers of the morbidity and mortality of stroke [16]. Consequently, efforts to uncover demographic and institutional predictors of in-hospital stroke mortality remain central to inform systems of care that aim to mitigate stroke mortality [1,16].

This study sought to determine the in-hospital stroke mortality rate and its trend between 2010 and 2017 in a national sample. We also aimed to identify the most common predictors of inpatient mortality among adult patients admitted with stroke in the US.

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https://doi.org/10.1016/j.ensci.2022.100392
Received 12 July 2021; Received in revised form 24 December 2021; Accepted 13 January 2022
Available online 22 January 2022
2405-6502/

2. Methods

2.1. Study design

We conducted a cross-sectional study to determine the in-hospital mortality rate defined as the ratio of in-hospital stroke mortalities and all stroke admissions per year at each reporting hospital. We also compared the annual in-hospital mortality rates between 2010 and 2017. In addition, we analyzed the predictors of stroke mortality within the sample of patients through a cross-sectional analytic approach of multiple variables.

2.1.1. Study population or individuals

We initially identified 355,961,565 million encounters between 2010 and 2017. For the diagnosis, we used the International Classification of Diseases Version 9 (ICD 9) for 2008–2015 and ICD10 for 2016–2017. We categorized these visits into ischemic stroke (ICD9 433–434, ICD10 I630–I639) and hemorrhagic stroke (ICD9 430–432, ICD10 I600–I629). The sensitivity of ICD-9430–438/ICD-10 I60-I69 for any cerebrovascular disease is >82%, and specificity is >95% [17]. The PPV of these codes for any cerebrovascular disease is >81% [17]. We included both stroke subtypes in the final analysis. We only included a patient's first visit if we identified multiple encounters for the same patient. We excluded patients under 18 years old, patients with comorbid cerebral arteriovenous malformation, nontraumatic extradural hemorrhage, subdural hemorrhage, traumatic and non-traumatic subarachnoid hemorrhage, skull fractures, multiple fractures involving skull or face, and a brain tumor in line with Williams et al. [18]. We included all 518,185 unique encounters with stroke as their primary or secondary diagnosis in the final analysis after applying inclusion and exclusion criteria.

2.1.2. Source of data

The Cerner Health Facts® Database is an automated electronic medical record system that captures hospital procedures, diagnostic information, demographics, medical history, admission, discharge, drug prescriptions, and laboratory tests over time. Seven hundred fifty facilities contributed de-identified information on 69 million patients seen between January 2001 and July 2018. The Cerner Health Facts® Database is a HIPAA compliant, de-identified, longitudinal collection of individual-level information generated from the Cerner® electronic medical record system utilized by community and academic hospitals across the US. We collected data from the Cerner Health Facts® database from 2010 to 2017.

2.1.3. Stroke mortality predictors and trends

We gathered patients' information from the database, including gender, race, age (in years), and comorbidities. We calculated the patient's Van Walraven comorbidity index; an Elixhauser-based comorbidity summary score [19,20] previously validated as a predictor of in-hospital mortality [21]. To use an updated version of these scores, we applied an updated method previously validated on the Cerner Health Facts® database [22]. Finally, we used a year look back period to determine the presence of these comorbidities, as this period is most effective at determining in-hospital death and sickness [23,24]. We obtained information about the hospital setting (rural vs. urban), hospital type (academic vs. non-academic), and census region (North, South, West, and Northeast) to be included in the multivariate analysis. Data on comprehensive stroke center or primary stroke center designation was not available. We determined trends in the use of alteplase and endovascular thrombectomy (EVT) for ischemic stroke visits. We identified thrombolytic use according to previously established methodology using the ICD-9-CM PCS code (9910), a secondary ICD-9-CM code (V4588), the ICD-10-PCS code (3E03317), a secondary ICD-10-CM code (Z9282), and CPT codes (37,195, 37,201, 37,202) [25–27]. We identified endovascular thrombectomy procedures using the association of the visit with either one of the following, per Zachrison et al. [27]: ICD-9-PCS code (3974, 1753, 1754), ICD-10-PCS code (03CG3ZZ, 03CH3ZZ, 03CJ3ZZ, 03CK3ZZ, 03CL3ZZ, 03CM3ZZ, 03CN3ZZ, 03CP3ZZ, 03CQ3ZZ). We also noted trends inpatient discharges to skilled nursing facilities (SNF) and hospice to provide information on patient discharge disposition.

2.2. Statistical analysis

We estimated the in-hospital mortality rate by dividing the number of in-hospital stroke admissions that resulted in patient death by the total number of admissions due to stroke yearly between 2010 and 2017. We calculated the stroke hospitalization incidence by the ratio of hospital admissions for stroke per 100,000 of the census populations served by each reporting hospital. We determined the trends in in-hospital stroke mortality between 2010 and 2017 using a multivariate logistical model while adjusting for covariates to identify independent predictors of in-hospital stroke mortality. We adjusted for age, race, gender, comorbidities, van Walraven comorbidity score, hospital region, hospital bed size, hospital type, and hospital setting. We conducted all data analyses using logistic regression to determine the factors predicting inpatient mortality in our sample of cases. For this, we created two regression models. The first focused on patient factors and included variables based on age, gender, race, comorbidities, and van Walraven score. The second focused on hospital and regional situations with variables describing the hospital's teaching status, urban or rural setting, and census region. We tested our hypotheses statistically against the $p < 0.05$ level of statistical significance. We performed statistical analysis using R version 3.6.1. (The R Foundation, Vienna, Austria).

3. Results

During the studied period, 518,185 total stroke admissions were observed. The mean patient age was 67.3 (SD 14.7) in the ischemic cohort and 63.5 (SD 16.6) in the hemorrhagic stroke cohort. Patients aged over 60-years-old compromised 69.0% of the general cohort. The ischemic stroke cohort had a significant female predominance. Caucasians constituted 69.4% and 67.9% of the ischemic and hemorrhagic stroke cohort. The three most frequently encountered comorbidities were hypertension, uncomplicated diabetes, and cardiac arrhythmias (data not shown). Most admitted strokes occurred at hospitals in the South region, urban areas, and designated as teaching hospitals. Table 1 summarizes the cohort's general characteristics by stroke subtype.

Stroke admissions steadily increased between 2010 and 2017 independent of etiology, as demonstrated in Fig. 1A. Of all stroke hospitalizations, 86.6% were due to ischemic stroke, as shown in Fig. 1B. Of all ischemic stroke admissions, 2.1% resulted in patient deaths, whereas 9.7% of hemorrhagic stroke admissions resulted in inpatient deaths. Inpatient stroke mortality gradually declined during the study period decreasing from 4.8% in 2010 (95% CI 4.6–5.1) to 2.1% in 2017 (95% CI 2.0–2.1), a trend independent of stroke etiology, as observed in Fig. 2A-B. Ischemic stroke mortality decreased by 1.4%, and hemorrhagic stroke mortality decreased by 6.7% throughout the studied period.

Table 2 summarizes the logistical regression results by stroke subtype. The odds of dying from ischemic stroke were higher in female patients (OR 1.059, 95% CI 1.015–1.105, $p = 0.008$), older age (OR 1.028, 95% CI 1.026–1.029, $p < 0.001$), and sicker patients (OR 1.091, 95% CI 1.089–1.093, $p < 0.001$) identified by the higher van Walraven score. African Americans had significantly lower odds of dying from ischemic stroke. For admissions due to hemorrhagic stroke, Hispanic ethnicity (OR 1.459, 95% CI 1.084–1.926, $p < 0.001$), older age (OR 1.021, 95% CI 1.019–1.023, p < 0.001), and sicker patients (OR 1.042, 95% CI 1.039–1.045, p < 0.001) had higher odds of dying in the hospital. Comorbid diagnosis of cardiac arrhythmia, congestive heart failure, renal failure, and liver disease had higher odds of dying from a stroke while inpatient independent of stroke etiology.

Table 1
Patient and hospital characteristics by stroke pathological subtype. (*n* = 518,185).

	Ischemic (*N* = 449,199)	Hemorrhagic (*N* = 68,986)	*P*-value
Gender			
Female	230,076 (51.2%)	36,602 (53.1%)	<0.001
Male	219,123 (48.8%)	32,384 (46.9%)	
Race			
African American	95,510 (21.3%)	12,685 (18.4%)	<0.001
Asian	7256 (1.6%)	2172 (3.1%)	
Caucasian	311,548 (69.4%)	46,815 (67.9%)	
Hispanic	1756 (0.4%)	513 (0.7%)	
Other	33,129 (7.4%)	6801 (9.9%)	
Age (years)			
Mean (SD)	67.3 (14.7)	63.5 (16.6)	<0.001
Median [Min, Max]	68.0 [18.0, 90.0]	64.0 [18.0, 90.0]	
Region			
Midwest	98,011 (21.8%)	11,148 (16.2%)	<0.001
Northeast	79,957 (17.8%)	17,805 (25.8%)	
South	195,818 (43.6%)	27,881 (40.4%)	
West	75,413 (16.8%)	12,152 (17.6%)	
Hospital Size (beds)			
<5	60,813 (13.5%)	4221 (6.1%)	<0.001
6–99	55,773 (12.4%)	5075 (7.4%)	
100–199	66,485 (14.8%)	8187 (11.9%)	
200–299	74,858 (16.7%)	10,711 (15.5%)	
300–499	90,832 (20.2%)	14,342 (20.8%)	
500+	100,438 (22.4%)	26,450 (38.3%)	
Hospital Setting			
Rural	80,328 (17.9%)	11,099 (16.1%)	<0.001
Urban	368,871 (82.1%)	57,887 (83.9%)	
Hospital Type			
Non-Teaching	200,372 (44.6%)	21,123 (30.6%)	<0.001
Teaching	248,827 (55.4%)	47,863 (69.4%)	
Patient Status (in hospital)			
Expired	9252 (2.1%)	6665 (9.7%)	<0.001
Survived	439,947 (97.9%)	62,321 (90.3%)	
van Walraven Scores			
Mean (SD)	6.74 (8.55)	6.82 (8.71)	0.0462
Median [Min, Max]	5.00 [−16.0, 69.0]	5.00 [−14.0, 57.0]	
Vascular comorbidities			
Hypertension	279,456 (62.2%)	37,663 (54.6%)	<0.001
Dyslipidemia	145,265 (32.3%)	13,279 (19.2%)	<0.001
Uncomplicated diabetes	113,200 (25.2%)	11,447 (16.6%)	<0.001
Complicated diabetes	39,217 (8.7%)	2568 (3.7%)	<0.001
Cardiac arrhythmia	110,147 (24.5%)	13,882 (20.1%)	<0.001
Congestive heart failure	58,423 (13.0%)	5782 (8.4%)	<0.001
Valvular heart disease	40,141 (8.9%)	40,141 (8.9%)	<0.001
Peripheral vascular disease	41,749 (9.3%)	5998 (8.7%)	<0.001
Renal failure	51,553 (11.5%)	5681 (8.2%)	<0.001
Liver disease	8804 (2.0%)	1909 (2.8%)	<0.001

%: percentages are sample, not population, proportions.
SD: standard deviation.
[Min, Max]: range of values.
$p < 0.05$ level of statistical significance.

All census regions demonstrated improvements in in-hospital mortality. The odds of dying from ischemic and hemorrhagic stroke were higher in the West region (OR for ischemic 2.292, 95% CI 2.127–2.471 and OR for hemorrhagic 1.540, 95% CI 1.411–1.680, $p < 0.001$), teaching hospitals (OR for ischemic 2.233, 95% CI 2.127–2.344 and OR for hemorrhagic 1.945, 95% CI 1.825–2.075, $p < 0.001$), and in an urban setting (OR for ischemic 1.107, 95% CI 1.044–1.175 and OR for hemorrhagic 1.116, 95% CI 1.035–1.205, $p < 0.001$). Notably, hospitals in the West region reported a 4.4% decline, the greatest of all subgroups.

Fig. 3A illustrates the increasing trend of alteplase use in the population admitted for ischemic stroke during the analyzed period. Simultaneously, an increasing trend in endovascular thrombectomies in ischemic stroke visits was observed in the studied period, as illustrated in Fig. 3B. Fig. 4 illustrates the trends in discharge disposition to hospice (Fig. 4A) and SNF (Fig. 4B) during the studied period per stroke etiology.

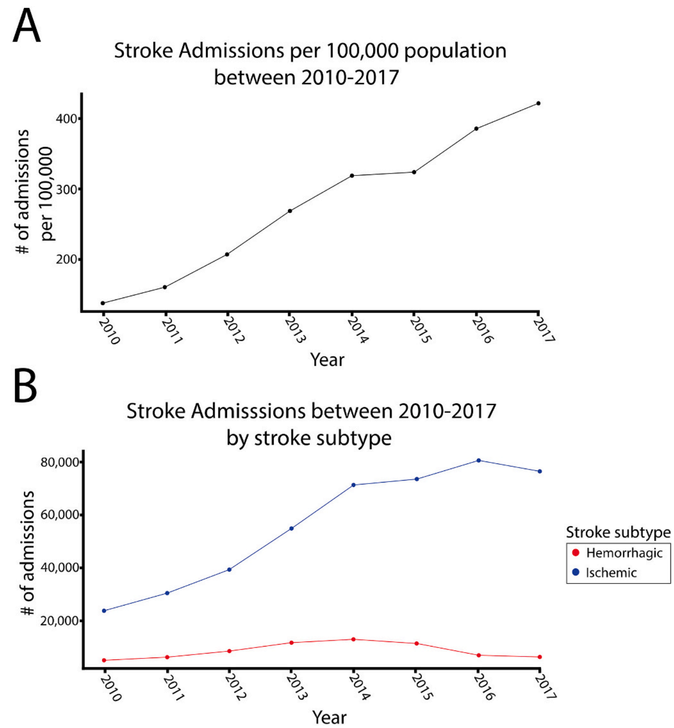

Fig. 1. Total stroke admissions prevalence by 100,000 population between 2010 and 2017 (A) and admission frequency by stroke pathological subtype (B).

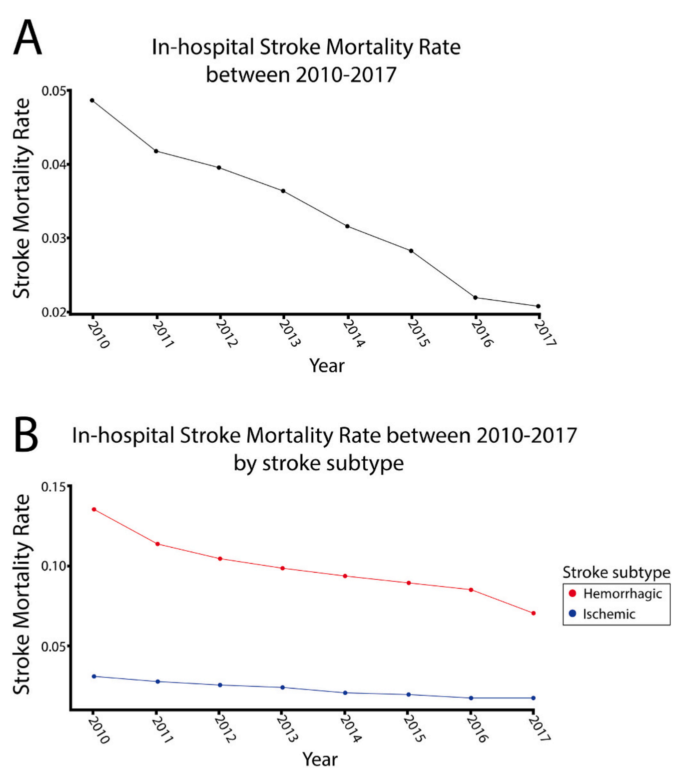

Fig. 2. In-hospital stroke mortality rate between 2010 and 2017 (A) and proportional stroke mortality by stroke pathological subtype (B).

Discharges to hospice and SNF steadily increased between 2010 and 2017, whereas discharges to hospice and SNF peaked in 2013–2014 and slowly decreased after that.

Table 2
Regression analysis of predictors of in-hospital patient mortality by stroke pathological subtype between 2010 and 2017 in the United States.

	Ischemic OR (95% CI)	P-value	Hemorrhagic OR (95% CI)	P-value
Gender				
Female	1.059 (1.015–1.105)	0.008	0.994 (0.944–1.047)	0.824
Race				
African American	0.816 (0.769–0.865)	<0.001	0.999 (0.930–1.073)	0.983
Asian	1.013 (0.858–1.187)	0.878	0.878 (0.748–1.025)	0.107
Hispanic	1.072 (0.716–1.537)	0.719	1.459 (1.084–1.926)	<0.001
Other	1.211 (1.118–1.311)	<0.001	1.085 (0.991–1.185)	0.074
Age (years)				
Age (in years)	1.028 (1.026–1.029)	<0.001	1.021 (1.019–1.023)	<0.001
van Walraven Scores				
Score	1.091 (1.089–1.093)	<0.001	1.042 (1.039–1.045)	<0.001
Region				
Northeast	2.179 (2.033–2.336)	<0.001	0.938 (0.863–1.021)	0.139
South	1.564 (1.464–1.672)	<0.001	1.053 (0.973–1.141)	0.202
West	2.292 (2.127–2.471)	<0.001	1.540 (1.411–1.680)	<0.001
Hospital Setting				
Urban	1.107 (1.044–1.175)	<0.001	1.116 (1.035–1.205)	0.005
Hospital type				
Teaching	2.233 (2.127–2.344)	<0.001	1.945 (1.825–2.075)	<0.001
van Walraven Scores				
Score	1.091 (1.089–1.093)	<0.001	1.042 (1.039–1.045)	<0.001
Vascular comorbidities				
Hypertension	0.991 (0.942–1.042)	0.716	1.547 (1.480–1.673)	<0.001
Dyslipidemia	1.019 (0.974–1.066)	0.405	1.132 (1.063–1.205)	<0.001
Uncomplicated diabetes	0.982 (0.935–1.032)	0.478	1.061 (0.993–1.134)	0.078
Complicated diabetes	0.905 (0.841–0.974)	0.008	0.902 (0.793–1.023)	0.111
Cardiac arrhythmia	2.290 (2.186–2.398)	<0.001	1.531 (1.440–1.627)	<0.001
Congestive heart failure	1.754 (1.665–1.846)	<0.001	1.112 (1.020–1.212)	0.015
Valvular heart disease	0.885 (0.830–0.942)	<0.001	0.824 (0.739–0.917)	<0.001
Peripheral vascular disease	1.065 (1.001–1.134)	0.046	0.741 (0.673–0.814)	<0.001
Renal failure	1.516 (1.435–1.601)	<0.001	1.364 (1.253–1.483)	<0.001
Liver disease	2.469 (2.235–2.721)	<0.001	2.080 (1.833–2.354)	<0.001

OR: odds ratio.
95% CI: 95% confidence interval.
$p < 0.05$ level of statistical significance.

4. Discussion

In this analysis of in-hospital stroke mortality between 2010 and 2017 in the US, we show that stroke in-hospital mortality decreased over time. This finding agrees with previously published reports that observed a decreased mortality secondary to stroke [28–30]. Notably, the observed decline of in-hospital mortality was independent of stroke etiology. Previous work attributed this observation to improvements in

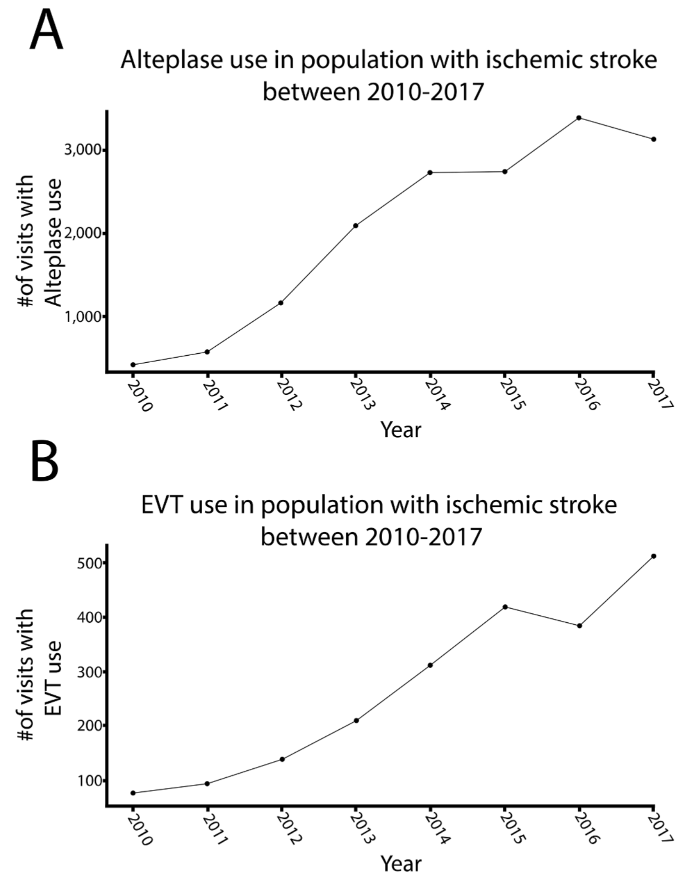

Fig. 3. Alteplase (A) and endovascular thrombectomy (EVT) (B) use in ischemic stroke admissions between 2010 and 2017.

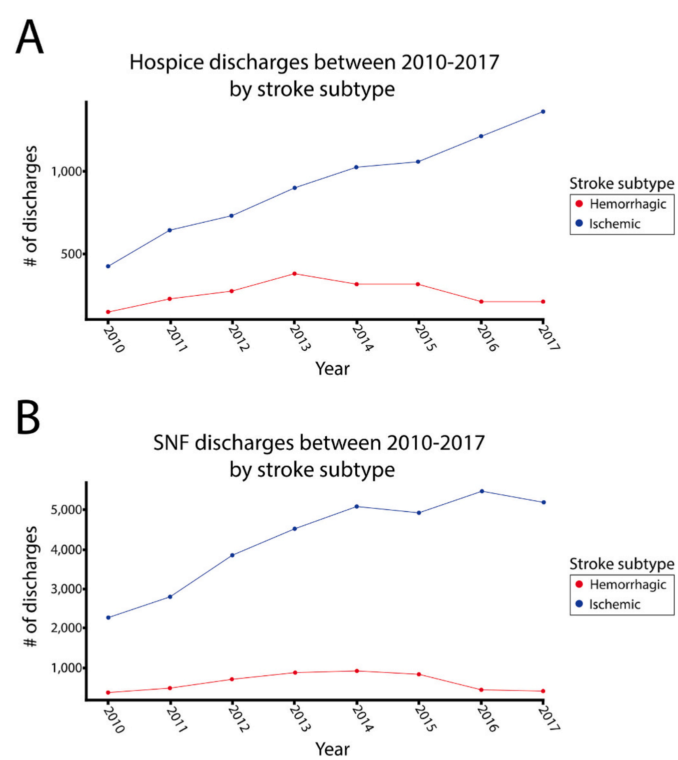

Fig. 4. Discharges to hospice (A) and skilled nursing facilities (SNF) (B) by stroke pathological subtype between 2010 and 2017.

risk factor control, higher adherence to secondary stroke prevention, earlier stroke detection, and advanced acute stroke care [31,32]. Indeed, we uncovered a timely association of decreased stroke mortality with increases in thrombolytic and thrombectomy usage. Hypertension, diabetes, and cardiac arrhythmias were the most identified comorbidities in the analyzed cohort. These comorbidities remain important stroke risk factors that warrant more attention from systems of care. A recent study identified that close to 1 in 4 patients with hypertension was untreated or undertreated, showing a disappointingly low rate of treatment of this severe stroke risk factor [33]. Also, in two recent trials investigating early blood pressure control for intraparenchymal hemorrhage, only 1 in 2 patients was on anti-hypertensives at the time of hemorrhagic stroke [34,35]. We also noted a proportional increase in discharges to SNF and hospice during the studied period. This finding is notable considering the decreasing trend in in-hospital mortality as some of the reporting hospitals may have discharged patients to in-hospital hospices, thus artificially increasing hospital survivorship and, subsequently, decreasing in-hospital stroke mortality [36].

We also observed that stroke admissions steadily increased between 2010 and 2017 primarily driven by ischemic stroke admissions. This observation may be due to a growing population in the regions served by the reporting hospitals or increased stroke diagnosis rates, although we did not test these hypotheses directly. Previous projections estimated an increase in 3.4 million people suffering from a stroke in 2030 relative to 2012 [1]. These estimates were based primarily on an aging population. For example, risks from cardioembolic stroke increase from 1.5% in patients aged between 50 and 59 to 23.5% in those aged from 80 to 89 [37]. Similarly, Kamal et al. identified that Canadian provinces with the highest population increases had an increasing burden of all-cause stroke-related admissions [38]. While we noted a disproportionate increase in ischemic stroke admissions compared to their hemorrhagic counterparts, future work should continue to elucidate the frequency of different stroke subtypes, as this is also anticipated to change as the population ages [1].

Our regression analysis revealed that sicker, older, and female patients have a higher chance of death from a stroke during their in-hospital stay. While it is not surprising that sicker and older patients have higher odds of dying from stroke, females' higher likelihood of death in the present study is noteworthy. Women have higher stroke fatality rates than men [39]. However, recent work showed that middle-aged women survive after stroke more than middle-aged men [40]. This discrepancy in demographic stroke mortality continues to merit further research. We also identified that comorbid diagnosis of cardiac arrhythmia, congestive heart failure, renal failure, and liver disease are key predictors of inpatient mortality in the studied cohort.

Our study also adds to the existing literature that regional disparities in stroke mortality across the US continue to exist. We noted the most considerable incidence of stroke admissions in our study in the South region, previously coined as the "Stroke Belt," in agreement with the NHANES I Epidemiologic Follow-up Study and *posthoc* analysis of the Reasons for Geographic and Racial Differences in Stroke (REGARDS) national cohort study [41–44]. Although all regionalities demonstrated graded improvement in stroke mortality over time, temporal trends in stroke mortality were mostly improved in hospitals in the West region. The Midwest and South regions were associated with higher inpatient stroke mortality.

We also observed that the risk of stroke death differs with hospital characteristics. In urban and teaching hospitals, hospitalizations for stroke were significantly associated with higher mortality even after controlling for age, gender, location, and comorbidities. This observation contrasts with previously published work that suggested rural settings and non-teaching hospitals have higher odds of stroke mortality [45,46]. Patient transfers from rural to urban settings could have contributed to these results, as rural facilities may not be well equipped to handle sicker patients [47]. Furthermore, we cannot exclude that the included teaching hospitals were designated as poor performers because we could not control for stroke severity [48–50].

5. Limitations

Our study is not free of limitations as it is both a retrospective study and relies on electronic medical and health records as its data source. Data can be limited when coming in an electronic medical record, as it may contain coding errors or incomplete records. The number of variables to be included is limited to those available and reported from the Cerner® system. For example, we were unable to control for stroke severity or note for stroke center designations. We were also not able to stratify admissions by first-ever or recurrent strokes. This limitation also may theoretically improve stroke mortality, as recurrent strokes are often associated with higher morbidity and mortality [51]. We also excluded a significant number of patients seeking attention in hospitals using a different EMR system. In addition, post-discharge data is not available in a group of patients; hence stroke deaths in the immediate or delayed discharge period were not accounted for, reflecting in conservative estimates.

6. Conclusion

Examining regional trends in in-hospital stroke mortality and hospital characteristics influencing stroke mortality have essential public health, health care, and policy-making implications. The present study corroborated the ongoing improvement in stroke mortality regardless of stroke etiology. It also identified important patient demographics, regions, and hospital characteristics that are affected disproportionately by stroke.

Funding source

None.

Institutional ethics committee clearance

Not applicable.

Author contributions

G.N., T.C., J.L., T.B., C.S., and V.M. contributed to the design and implementation of the research, to the analysis of the results, and to the writing of the manuscript.

Disclosures

The authors declare no conflict of interest.

Declaration of Competing Interest

None.

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