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Seasonal Variation in Ischemic Stroke Hospitalization: Results From a Large Health System in Six Western States of the United States

Reza Bavarsad Shahripour[a, b, j], Datis Azarpazhooh[c], Elizabeth Baraban[d], Horia Marginean[e], Sima Osouli Meinagh[f], Sholeh Faezi[g], Jasen Tarpley[h, i]

Abstract

Background: Evidence of seasonal variations in the number of stroke admission is inconsistent with some studies reporting no association and some a significant rise in different months of the year. In addition, less is known about how seasonality impacts the admission according to stroke subtype.

Methods: This was a cross-sectional, observational study of data from a hospital-based registry (n = 40 hospitals) affiliated with Providence Health and Services in Alaska, California, Montana, Oregon, Texas, and Washington state. We included all cases with acute ischemic stroke admitted from March 1, 2017, to February 29, 2020. Admission data were categorized according to four meteorological seasons: winter, spring, summer, and fall. Acute ischemic stroke was categorized into two sub-types as large vessel occlusion (LVO) or non-LVO. We calculated the aggregate number of individuals admitted with stroke by season. Using linear regression models with generalized estimating equations (GEEs), we assessed the relationship between meteorological season and daily hospitalization number. We used R version 4.0.4 (2021-02-15) for both the descriptive and inferential analyses and the R gee pack package (version 1.2-1) to perform GEEs.

Results: During the study period, we identified 18,886 patients with acute ischemic stroke (median age: 73; 48.7% women). Acute ischemic stroke was more commonly observed during winter compared with other seasons with some variations between the selected regions. Based on a GEE model, stroke hospitalization increased during winter, with an additional 3.3 cases per day in comparison with spring in the whole population (beta: 3.3, 95% confidence interval (CI): (2.4, 4.1), P < 0001). Winter is also associated with a higher number of LVO.

Conclusions: The total number of ischemic stroke admissions, including cases of LVO, increased during the winter months. The results are important for human resource allocation for better management of cases with ischemic strokes.

Keywords: Ischemic stroke; Incidence; Hospitalization; Season; Stroke subtypes; Etiology; Large vessel occlusion

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[a]Department of Neurology, Comprehensive Stroke Center, Loma Linda University, Loma Linda, CA, USA
[b]Comprehensive Stroke Center, University of California San Diego (UCSD), San Diego, CA, USA
[c]Department of Medical Sciences, University of Western Ontario, London, ON, Canada
[d]Providence Saint John's Health Center, Neurovascular and Stroke Center, Santa Monica, CA, USA
[e]Providence Brain and Spine Institute, Providence St Joseph Health, Portland, OR, USA
[f]Department of Neurology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[g]Department of Clinical Neurological Sciences, University of Western Ontario, London, ON, Canada
[h]Providence St Johns Health Science Center, Santa Monica, CA
[i]Department of Neurology, Pacific Neuroscience Institute, Santa Monica, CA, USA
[j]Corresponding Author: Reza Bavarsad Shahripour, Department of Neurology, Comprehensive Stroke Center, Loma Linda University, Loma Linda, CA, USA. Email: nbavar@yahoo.com

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Introduction

Evidence of seasonal changes in the incidence of stroke is inconsistent. While some studies showed no association between seasons and strokes [1], hospitalization rate in most studies peaked in different seasons including, spring [2], summer [3], autumn [4, 5], and winter [6, 7]. These variations in findings can be explained partially by the different sample sizes [8], study design (hospital vs. population-based) [2], short observation periods [8], statistical model for data analysis, regional vs. national data selection [9], and geographical location of the study population [3]. In addition, less is known about how seasonality impacts the incidence of stroke subtype [10].

With recent advances in hyper-acute stroke care including thrombolytic and endovascular therapy, we hope the data help hospitals to identify seasons with the highest number of stroke codes and admissions. Also, it may help and guide human resources for a more time-based approach in the future.

The current study was designed to identify seasonal changes in the number of stroke hospitalization and stroke subtype in the western USA.

Materials and Methods

Ethics

This study was approved by the Institutional Review Board of Providence Health and Services with a waiver of informed consent. We followed the reporting guidelines of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for observational studies [11].

Setting

This was a cross-sectional study of data from a hospital-based registry focused on improving care for patients diagnosed with a stroke. Data were collected for clinical care and quality improvement by 40 hospitals affiliated with Providence Health and Services. Providence Health System is a large healthcare system located in Alaska, California, Montana, Oregon, Texas, and Washington. All adult inpatients with a diagnosis of acute ischemic stroke at admission within Providence Health and Services from March 1, 2017, to February 29, 2020, were included.

We excluded patients younger than 18 years old, where target lesion was not recorded, patients who were diagnosed with a transient ischemic attack (TIA), and patients with stroke mimics. Exploratory data analysis was carried out before formal analysis through inspection of graphical data of the hospitalization of acute ischemic stroke over time for each hospital. We excluded patients from sites that showed inconsistent data collection reflected in scattered missing data. We also excluded patients from sites with small stroke patient volume (averaged fewer than 60 patients per year). In addition, we excluded cases from time periods and sites where annual data collection was incomplete or where data for full seasons were not available. In clinical registries, there is a recognized time lag between the event occurrence and data entry [12]. As a result, our final analytic cohort represents cases admitted for stroke from March 1, 2017, to February 29, 2020.

Study variables and definitions

Ischemic stroke was defined according to the updated definition of stroke for the 21st century [13]. Acute ischemic stroke was categorized into two sub-types as large vessel occlusion (LVO) or non-LVO. LVO was identified based on the clinical history of acute ischemic stroke and neurovascular imaging findings. We classified our centers based on their stroke center certification status into primary stroke centers, comprehensive stroke centers, thrombectomy-capable stroke centers, and centers without any certification.

The daily number of acute ischemic stroke admissions was calculated from the date of patient arrival at the hospital. Admission data were categorized according to four meteorological seasons. Winter was defined as December 1, to February 28 (29 in a leap year), spring from March 1, to May 31, summer from June 1, to August 31, and fall from September 1, to November 30. We selected the meteorological season classification because it is based on seasonal temperature patterns. Since the western USA includes states with diverse regional climates ranging from subarctic to warm desert climates, we made a commonsense judgment about weather patterns and grouped states into three regions accordingly: 1) Alaska; 2) California and Texas; and 3) Montana, Washington, and Oregon. In this exploratory analysis, we included well-recognized risk factors for acute ischemic stroke: demographic (age at arrival, sex, and race), and comorbidity (hypertension, dyslipidemia, atrial fibrillation or flutter, previous stroke, diabetes mellitus, obesity).

Statistical analysis

Baseline characteristics and comorbidities were described by season. Categorical variables were described using percentages. Continuous variables were summarized using medians and interquartile ranges. Differences in these characteristics were compared using Pearson's Chi-squared test or Fisher's exact test where appropriate for categorical variables and Wilcoxon's matched pairs test and paired *t*-tests for continuous variables.

Our primary outcome was the aggregate number of individuals admitted with acute ischemic stroke by season. Linear regression models with generalized estimating equations (GEEs) were used to model the relationship between meteorological season and daily presentation with acute ischemic stroke. GEE allowed us to account for the repeated measurement of stroke hospitalization over time. The daily number of stroke admissions was set as the dependent variable in the model. Demographic, region, stroke center certification status, and comorbidities defined above were included as the independent variables. An exchangeable working correlation structure was selected based on the quasi-likelihood under the independence model criterion.

We used GEE to report increase or decrease on daily admission number of stroke patients according to different seasons. All differences are reported based on adjusted beta after controlling the effect of possible risk factors.

We selected GEE as this model can represent changes in number of admissions. This is an appropriate model for our data analysis as our data have a normal pattern of distribution. In addition, clinicians and administrative authorities in hospitals can understand easily changes in number based on season and allocate their resources accordingly. The clinical outcome was the estimated day change in average acute ischemic stroke occurrence when progressing from one season to another.

Our secondary outcome was the number of ischemic stroke admission stratified according to LVO. For our subgroup analysis of stroke subtype based on the presence of vessel occlusion, we only considered patients with the time of onset to admission within 24 h. The objective of this analysis was to identify seasonal variation in the number of treatment-eligible stroke patients with thrombolytic therapy or endovascular treatment, as these patients represent the greatest healthcare resource utilization. To this end, we excluded cases that were admitted to the hospital more than 24 h after the last known-well time because these patients are typically ineligible for revascularization therapy.

Regression coefficient estimates and 95% confidence intervals (CIs) are reported. Two-tailed P values were reported, and P values less than 0.05 were considered significant. R version 4.0.4 (2021-02-15) was used for both the descriptive and inferential analyses. The GEEs were run using the R gee pack package (version 1.2-1).

Results

The registry enrolled 138,836 patients of which 119,950 were excluded from the analysis. Our analytic sample consisted of 18,886 patients with acute ischemic stroke who were admitted over a 3-year period (Fig. 1). The demographic and clinical characteristics of our cohort are shown in Table 1. We estimated the seasonality in the overall ischemic cohort (n = 18,886) and separately for each of the two subtypes, LVO (n = 4,382) and non-LVO (n = 9,571).

Seasonality of acute ischemic stroke

Overall, the seasonal pattern of acute ischemic stroke over the 3-year analysis period in the western USA shows a steady increase in the number of stroke hospitalization (Fig. 2).

Acute ischemic stroke was more frequent during the winter compared with other seasons (spring 4,565 (24.2%), summer 4,482 (23.7%), fall 4,692 (24.8%), winter 5,147 (27.3%)) (Table 1). There were differences in the hospitalization of stroke between seasons by region. In Alaska, the season with the highest number of strokes was summer (n = 275) (Table 1). In contrast, winter was the season with the highest number of strokes for the region of California and Texas (n = 2,361) and the region of Montana, Washington, and Oregon (n = 2,573) (Table 1). The relative distribution of strokes between regions also differed by season. In Alaska, the season with the highest relative frequency of stroke was summer, with 6.1% of all strokes occurring during the summer admitted to sites in Alaska. In the region of Montana, Washington, and Oregon, spring was the season with the highest relative frequency of stroke, with 54.7% (n = 2,499) of all strokes occurring during spring admitted to sites in this region. In California and Texas, winter had the highest relative frequency of strokes, with 45.9% (n = 2,361) of strokes occurring during winter admitted to sites in California and Texas (P value < 0.0001) (Table 1). Patient demographics and clinical characteristics were balanced between seasons.

We next investigated the seasonal variation of ischemic stroke, using the GEE model with acute ischemic stroke as the response variable. As Figure 2 demonstrates the average daily admission of acute ischemic stroke from 2018 to 2020, which is around 15 - 25 events per day, using the beta coefficient test and adjusting based on stroke risk factors revealed the most significant increase in daily admission of acute ischemic stroke between spring and winter, which was 3.3 more cases per day.

The results indicate that there were strong seasonal patterns of acute ischemic stroke admissions (Table 2). In the unadjusted model, the total admission per day of acute ischemic stroke increased by about one case per day between spring and fall (95% CI: (0.05, 1.6), P value = 0.04) (Table 2), and by 3.6 cases per day between spring and winter (95% CI: (2.7, 4.4), P value < 0.001) (Table 2). After controlling for stroke risk factors, there was no significant difference in the number of admissions between spring and fall (beta: 0.66, 95% CI: (-0.14, 1.5), P value = 0.10) (Table 2). However, between spring and winter, the daily admission of acute ischemic stroke increased (beta: 3.3 patients per day; 95% CI: (2.4, 4.1), P value < 0.001).

In sequential comparisons between seasons using the multivariate GEE model, no significant relationships were observed between spring and summer (slope: -0.1; 95% CI: (-0.9, 0.7), P value < 0.8) nor between summer and fall (slope: -0.1; 95% CI: (-0.1, 1.6), P = 0.08). However, between fall and winter, the total admission per day in acute ischemic stroke increased by 2.6 patients per day (95% CI: (1.7, 3.5), P value < 0.001).

We next examined seasonal admission of stroke by ischemic stroke subtypes, i.e., LVOs vs. those without LVO. Similar to the whole cohort, the number of admitted cases with LVO was lower in the spring and summer, increased in fall, and highest during the winter (Table 3).

Discussion

Our study has important clinical applications for stroke centers. In a large data of 18,886 patients with acute ischemic stroke in six states of the USA, we found a significant variation in the number of stroke hospitalization with a higher admission during winter. Likewise, the number of cases with LVO was significantly higher during this period.

Stroke hospitalization rates varied by season in different studies with most of them indicating an association between cold weather and the occurrence of ischemic strokes [6, 14-17]. In the line of these studies, we found a significant rise in the hospitalization of ischemic strokes during wintertime. Higher hospitalization is not the only clinical challenge during cold weather. From the pooled systematic analysis of ambient temperature effect in stroke, older age was more vulnerable to the lower temperature [18]. During colder months, strokes are also likely to be more severe with a higher rate of mortality [15, 16, 19, 20]. Consequently, stroke centers may have more challenges in the management and workflow of cases with stroke during this period of time.

With recent advances in endovascular therapy, it is crucial to identify any possible changes in the incidence of LVO in stroke centers. The current evidence regarding LVO hospitalization according to season/month is scarce. In a Japanese study (n = 12,660, between May 1999 and April 2000), cardioembolic stroke was more frequent during wintertime [21]. Likewise, another Japanese study revealed a higher incidence of hemorrhagic stroke and cardioembolic stroke in winter and non-cardioembolic strokes in summer [22]. In a hospital-based study (n = 2,628), Bucke et al noticed more mechanical

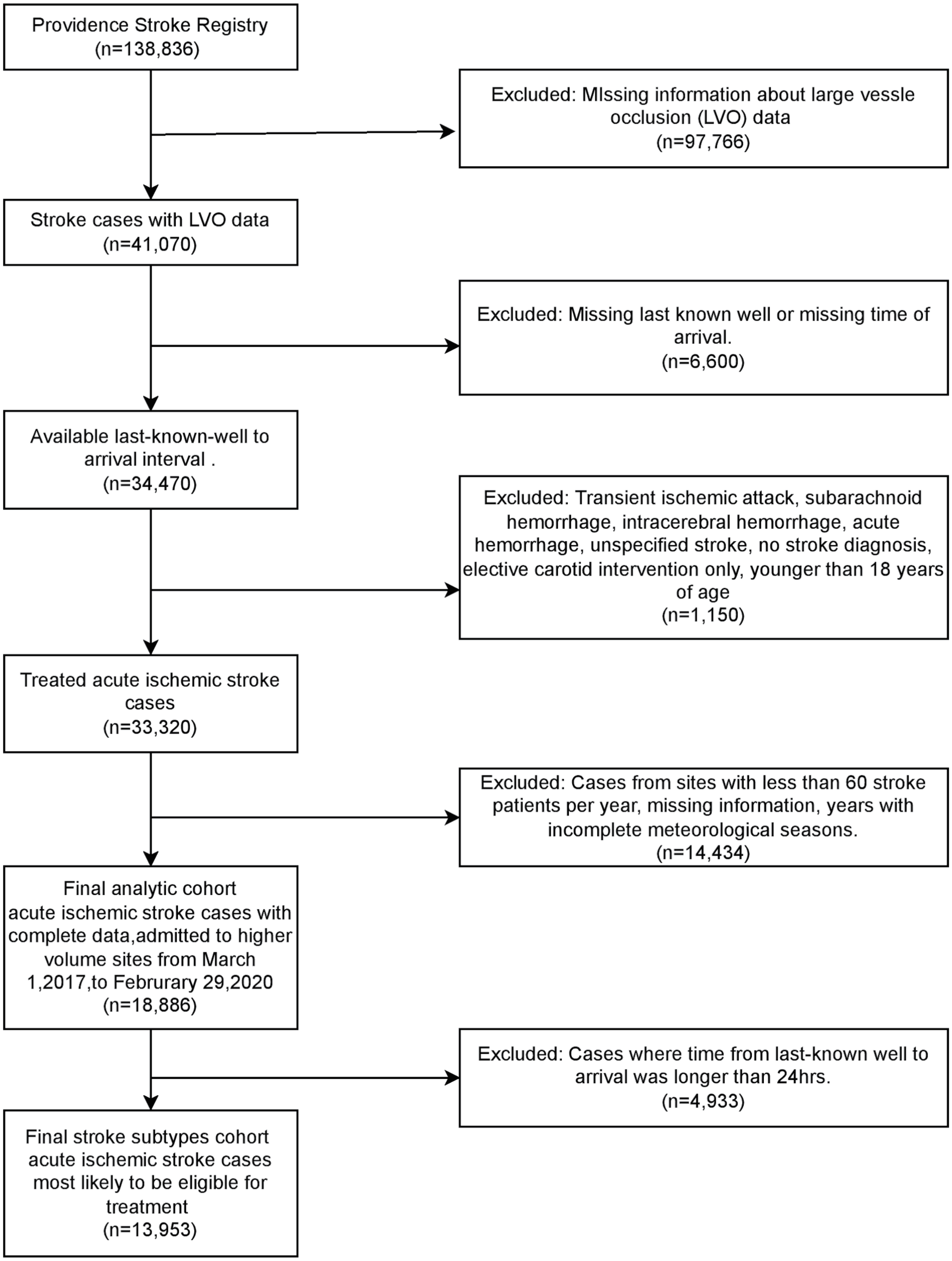

Figure 1. Flow chart of cohort selection. LVO: large vessel occlusion.

thrombectomy in spring and early autumn [23]. In our study, we found a higher number of LVO during winter.

There are many hypotheses about the risk factors of ischemic stroke in cold months. Atrial fibrillation, which is an important risk factor for ischemic stroke especially LVO, is reported more frequent in colder months because of higher rate of hypertension, symptomatic activation, and higher platelet count and blood viscosity in lower temperatures [24-26]. In our study, atrial fibrillation rate did not show a significant difference between seasons nor between the LVO and non-LVO groups.

Table 1. Patient Characteristics by the Season of Admission for Ischemic Stroke

Variables	LVO	Non-LVO	Total population	Spring	Summer	Fall	Winter	P
	4,382	9,571	18,886 (100)	4,565 (24.2)	4,482 (23.7)	4,692 (24.8)	5,247 (27.3)	
Age (years), median (IQR)	74.0 (20, 103) (21)	73.0 (18, 108) (21)	73.0 (18, 108) (21)	73.0 (18, 106) (20)	72.0 (21, 108) (20)	73.0 (19, 103) (21)	73.0 (19, 107) (21)	0.25
Sex (female), n (%)	2,182 (49.8%)	4,585 (47.9%)	9,192 (48.7%)	2,207 (48.3%)	2,145 (47.9%)	2,291 (48.8%)	2,549 (49.5%)	0.40
Race, n (%)								
Native American/Alaska Native	39 (0.9%)	79 (0.8%)	166 (0.9%)	52 (1.1%)	28 (0.6%)	42 (0.9%)	44 (0.9%)	0.22
Asian	285 (6.5%)	523 (5.5%)	1,069 (5.7%)	267 (5.8%)	274 (6.1%)	237 (5.1%)	291 (5.7%)	
Black/African American	168 (3.8%)	397 (4.1%)	771 (4.1%)	178 (3.9%)	189 (4.2%)	192 (4.1%)	212 (4.1%)	
Native Hawaiian/Pacific Islander	24 (0.5%)	52 (0.5%)	108 (0.6%)	23 (0.5%)	29 (0.6%)	28 (0.6%)	28 (0.5%)	
Unable to determine	430 (9.8%)	783 (8.2%)	1,628 (8.6%)	362 (7.9%)	378 (8.4%)	435 (9.3%)	453 (8.8%)	
White	3,436 (78.4%)	7,737 (80.8%)	15,144 (80.2%)	3,683 (80.7%)	3,584 (80.0%)	3,758 (80.1%)	4,119 (80.0%)	
Center certification, n (%)								
None	340 (7.8%)	687 (7.2%)	1,214 (6.4%)	289 (6.3%)	255 (5.7%)	305 (6.5%)	365 (7.1%)	0.27
Comprehensive stroke center	1,804 (41.2%)	3,317 (34.7%)	6,594 (34.9%)	1,617 (35.4%)	1,553 (34.6%)	1,624 (34.6%)	1,800 (35.0%)	
Primary stroke center	1,217 (27.8%)	3,495 (36.5%)	6,864 (36.3%)	1,627 (35.6%)	1,677 (37.4%)	1,701 (36.3%)	1,859 (36.1%)	
Thrombectomy capable center	1,021 (23.3%)	2,072 (21.6%)	4,214 (22.3%)	1,032 (22.6%)	997 (22.2%)	1,062 (22.6%)	1,123 (21.8%)	
Region, n (%)								
Alaska	168 (3.8%)	436 (4.6%)	923 (4.9%)	202 (4.4%)	275 (6.1%)	233 (5.0%)	213 (4.1%)	< 0.001
Montana/Washington/Oregon	2,261 (51.6%)	4,721 (49.3%)	9,939 (52.6%)	2,499 (54.7%)	2,383 (53.2%)	2,484 (52.9%)	2,573 (50.0%)	
California/Texas	1,953 (44.6%)	4,414 (46.1%)	8,024 (42.5%)	1,864 (40.8%)	1,824 (40.7%)	1,975 (42.1%)	2,361 (45.9%)	
Comorbidity[a], n (%)								
Atrial fibrillation	1,422 (32.5%)	1,950 (20.4%)	4,241 (22.5%)	1,042 (22.8%)	941 (21.0%)	1,085 (23.1%)	1,173 (22.8%)	0.06
Diabetes mellitus	1,122 (25.6%)	3,029 (31.6%)	5,910 (31.3%)	1,394 (30.5%)	1,443 (32.2%)	1,481 (31.6%)	1,592 (30.9%)	0.34
Hypertension	3,137 (71.6%)	7,134 (74.5%)	14,039 (74.3%)	3,382 (74.1%)	3,327 (74.2%)	3,506 (74.7%)	3,824 (74.3%)	0.91
Dyslipidemia	2,161 (49.3%)	5,002 (52.3%)	9,828 (52.0%)	2,394 (52.4%)	2,325 (51.9%)	2,401 (51.2%)	2,708 (52.6%)	0.49
Previous stroke	974 (22.2%)	2,666 (27.9%)	4,986 (26.4%)	1,224 (26.8%)	1,144 (25.5%)	1,265 (27.0%)	1,353 (26.3%)	0.40
Obesity/overweight	2,175 (49.6%)	4,842 (50.6%)	9,606 (50.9%)	2,287 (50.1%)	2,274 (50.7%)	2,391 (51.0%)	2,654 (51.6%)	0.55

[a]Multiple comorbidities allowed. IQR: interquartile range; LVO: large vessel occlusion.

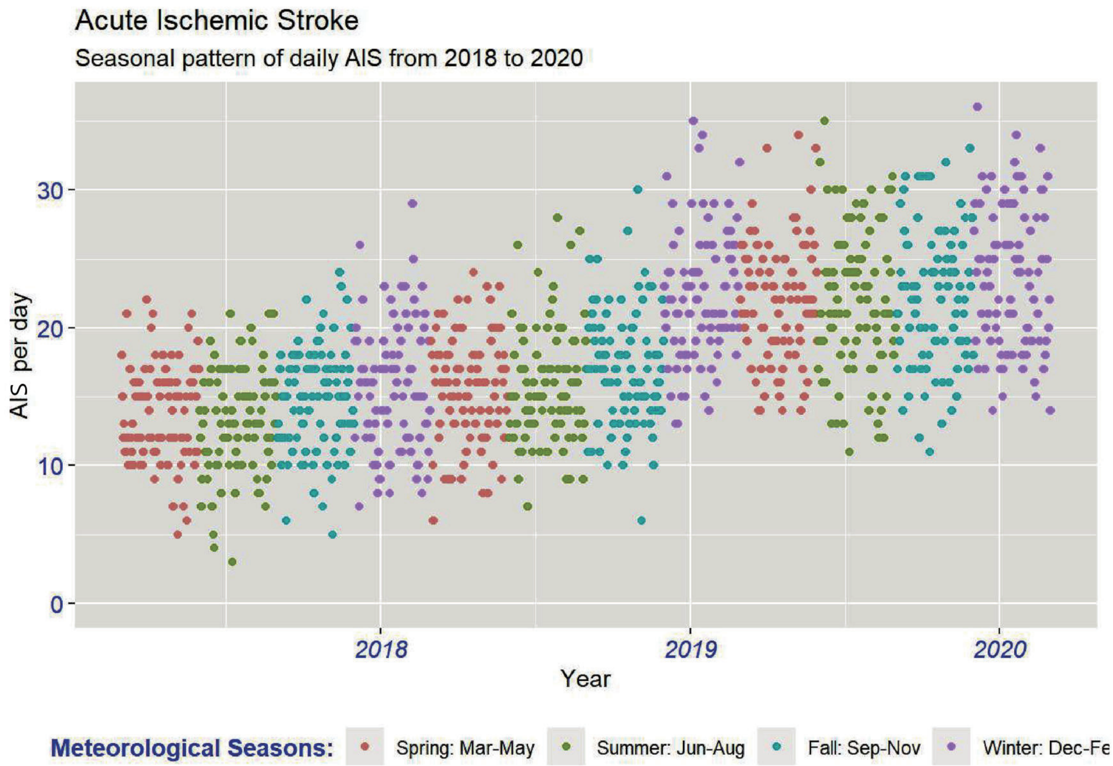

Figure 2. Seasonal pattern of daily acute ischemic stroke hospitalization in six western states of the USA. AIS: acute ischemic stroke.

Influenza and influenza like symptoms are another hypothesis on the increased risk of cardiovascular events in winter [27]. Kulick et al reported higher rate of ischemic stroke after influenza like illnesses, which is more common in cold weather, especially in men and people living in rural areas [28].

Air pollution as another meteorological factor can although affect the incidence of stroke. In a systematic review, admission to hospital or mortality from stroke was associated with increased level of gaseous pollutants and particulate matters especially on the exposure day [29]. These findings were confirmed with another more recent meta-analysis which has reported positive association of all six air pollutants and stroke hospital admission [30].

Our study has some limitations. There was missing information about LVO data in the majority population of the providence health registry and we have excluded them from our analysis. We do not have access to the severity of stroke at admission and therefore we cannot comment on the difference in stroke severity based on the season. The occurrence of coronavirus disease 2019 (COVID-19) may affect the hospitalization rates since the pandemic [31]. Despite an overall decline in the stroke hospitalization after the pandemic, the pattern of hospitalization based on season remained stable with a higher number of admissions in winter even during the pandemic. We have access to hospital-based information which is not representative of our community. Patients admitted to the hospital are more likely to have severe stroke with LVO as compared to lacunar strokes. However, this is a systematic limitation across all provinces/seasons and may not affect our final findings. Our major strength is having access to large data from 40 hospitals in the USA, which provides an opportunity to perform the current study and follow changes in hospitalization in detail.

In summary, we found that the number of stroke hospitalization increased over time overall, with a higher admission number peaking annually during the winter months. Because effective stroke treatment is a race against time, it is crucial for healthcare systems to identify seasons with the highest number of admissions. This information will provide a rational approach for human resource allocation, will help avoid staff burnout, and may lead to better stroke outcomes for patients.

Acknowledgments

None to declare.

Financial Disclosure

None to declare.

Conflict of Interest

None to declare.

Table 2. Estimation Results From the Generalized Estimating Equations (GEE) Model, the Association of Season With the Number of Acute Ischemic Stroke Admission

Variables	β	95% CI	P
Unadjusted model			
Spring	Reference		
Summer	-0.05	-0.86, 0.76	0.94
Fall	0.84	0.05, 1.6	0.04
Winter	3.60	2.7, 4.4	< 0.001
Adjusted model			
Age (years)	0.00	-0.01, 0.01	0.91
Sex			
Male	Reference	-0.16, 0.12	0.80
Female	-0.02		
Race			
Native American/Alaska Native	Reference	-1.3, 0.25	0.20
Asian	-0.52	-1.0, 0.49	0.50
Black/African American	-0.27	-1.9, 0.48	0.20
Native Hawaiian/Pacific Islander	-0.69	-0.69, 0.74	0.92
Unable to determine	0.02	-1.1, 0.32	0.30
White	-0.37	-1.3, 0.25	0.20
Center certification			
None	Reference		
Comprehensive stroke center	0.11	-0.21, 0.43	0.50
Primary stroke center	0.94	0.60, 1.3	< 0.001
Thrombectomy capable center	0.59	0.23, 1.0	0.001
Region			
Alaska	Reference		
Montana/Washington/Oregon	0.41	0.05, 0.77	0.03
California/Texas	1.30	0.92, 1.7	< 0.001
Comorbidity[a]			
Atrial fibrillation	-0.14	-0.34, 0.05	0.20
Diabetes mellitus	0.02	-0.13, 0.17	0.80
Hypertension	-0.14	-0.32, 0.03	0.11
Dyslipidemia	0.29	0.13, 0.46	< 0.001
Previous stroke	-0.24	-0.40, -0.08	0.004
Obesity/overweight	0.53	0.36, 0.69	< 0.001
Seasons			
Spring	Reference		
Summer	-0.10	-0.92, 0.71	0.80
Fall	0.66	-0.14, 1.5	0.10
Winter	3.30	2.4, 4.1	< 0.001

[a]Multiple comorbidities allowed. CI: confidence interval; β: beta coefficient.

Table 3. Estimation Results From the Generalized Estimating Equations (GEE) Model, the Association of Season With the Number of Acute Ischemic Stroke Subtypes Admission

Variables	Large vessel occlusion			Non-large vessel occlusion		
	Adjusted model			Adjusted model		
	β	95% CI	P value	β	95% CI	P value
Unadjusted model						
Spring	Reference			Reference		
Summer	-0.11	-0.94, 0.71	0.80	-0.10	-0.88, 0.68	0.80
Fall	0.73	-0.10, 1.6	0.08	0.80	0.04, 1.6	0.04
Winter	3.40	2.6, 4.2	< 0.001	3.50	2.6, 4.3	< 0.001
Adjusted model						
Age (years)	0.00	-0.01, 0.01	0.91	0.01	-0.00, 0.01	0.2
Sex						
Male	Reference	-0.16, 0.12	0.80	Reference		
Female	-0.02			0.10	-0.11, 0.30	0.40
Race, n (%)						
Native American/Alaska Native	Reference	-1.3, 0.25	0.20	Reference		
Asian	-0.52	-1.0, 0.49	0.50	-0.43	-1.45, 0.601	0.40
Black/African American	-0.27	-1.9, 0.48	0.20	0.06	-1.06, 1.17	0.92
Native Hawaiian/Pacific Islander	-0.69	-0.69, 0.74	0.92	-0.56	-2.33, 1.22	0.50
Unable to determine	0.02	-1.1, 0.32	0.30	0.42	-0.62, 1.46	0.40
White	-0.37	-1.3, 0.25	0.20	-0.23	-1.22, 0.758	0.60
Center certification						
None	Reference			Reference		
Comprehensive stroke center	0.11	-0.21, 0.43	0.50	-0.37	-0.81, 0.08	0.11
Primary stroke center	0.94	0.60, 1.3	< 0.001	0.62	0.16, 1.08	0.01
Thrombectomy capable center	0.59	0.23, 1.0	0.001	0.36	-0.14, 0.86	0.20
Region						
Alaska	Reference			Reference		
Montana/Washington/Oregon	0.41	0.05, 0.77	0.03	0.07	-0.43, 0.58	0.80
California/Texas	1.30	0.92, 1.7	< 0.001	1.25	0.72, 1.78	< 0.001
Comorbidity[a]						
Atrial fibrillation	-0.14	-0.34, 0.05	0.20	-0.26	-0.54, 0.02	0.06
Diabetes mellitus	0.02	-0.13, 0.17	0.80	-0.14	-0.36, 0.09	0.20
Hypertension	-0.14	-0.32, 0.03	0.11	-0.23	-0.48, 0.02	0.07
Dyslipidemia	0.29	0.13, 0.46	< 0.001	0.49	0.27, 0.72	< 0.001
Previous stroke	-0.24	-0.40, -0.08	0.004	-0.31	-0.53, -0.08	0.007
Obesity/overweight	0.53	0.36, 0.69	< 0.001	0.66	0.45, 0.87	< 0.001
Season						
Spring	Reference			Reference		
Summer	-0.13	-1.10, 0.81	0.80	-0.14	-0.95, 0.66	0.70
Fall	0.56	-0.41, 1.5	0.30	0.712	-0.084, 1.51	0.08
Winter	3.20	2.20, 4.10	< 0.001	3.25	2.40, 4.10	< 0.001

[a]Multiple comorbidities allowed. CI: confidence interval; β: beta coefficient.

Informed Consent

Not applicable.

Authors Contributions

Reza Bavarsad Shahripour: study design, writing the first draft. Datis Azarpazhooh: revising the manuscript. Elizabeth Baraban: data collection. Horia Marginean: data analysis. Sima Osouli: literature review, revising the manuscript. Sholeh Faezi: revising the manuscript. Jasen Tarpley: study design.

Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author.

Abbreviations

AIS: acute ischemic stroke; TIA: transient ischemic attack; CIs: confidence intervals; LVO: large vessel occlusion; IQR: interquartile range; AF: atrial fibrillation; GEE: generalized estimating equation; B: beta confident; STROBE: Strengthening the Reporting of Observational Studies in Epidemiology

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