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Original Article

Trends in Venous Thromboembolism Readmission Rates after Ischemic Stroke and Intracerebral Hemorrhage

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Background and Purpose Venous thromboembolism (VTE) is a life-threatening complication of stroke. We evaluated nationwide rates and risk factors for hospital readmissions with VTE after an intracerebral hemorrhage (ICH) or acute ischemic stroke (AIS) hospitalization.

Methods Using the Healthcare Cost and Utilization Project (HCUP) Nationwide Readmission Database, we included patients with a principal discharge diagnosis of ICH or AIS from 2016 to 2019. Patients who had VTE diagnosis or history of VTE during the index admission were excluded. We performed Cox regression models to determine factors associated with VTE readmission, compared rates between AIS and ICH and developed post-stroke VTE risk score. We estimated VTE readmission rates per day over a 90-day time window post-discharge using linear splines.

Results Of the total 1,459,865 patients with stroke, readmission with VTE as the principal diagnosis within 90 days occurred in 0.26% (3,407/1,330,584) AIS and 0.65% (843/129,281) ICH patients. The rate of VTE readmission decreased within first 4–6 weeks (P<0.001). In AIS, cancer, obesity, higher National Institutes of Health Stroke Scale (NIHSS) score, longer hospital stay, home or rehabilitation disposition, and absence of atrial fibrillation were associated with VTE readmission. In ICH, longer hospital stay and rehabilitation disposition were associated with VTE readmission. The VTE rate was higher in ICH compared to AIS (adjusted hazard ratio 2.86, 95% confidence interval 1.93–4.25, P<0.001).

Conclusions After stroke, VTE readmission risk is highest within the first 4–6 weeks and nearly three-fold higher after ICH vs. AIS. VTE risk is linked to decreased mobility and hypercoagulability. Studies are needed to test short-term VTE prophylaxis beyond hospitalization in high-risk patients.

Keywords Acute stroke; Deep venous thrombosis; Venous thromboembolism; Pulmonary embolism

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Introduction

Stroke is a leading cause of mortality and morbidity.[1] Advancements in acute stroke treatments and improved inpatient stroke care have led to decreased stroke-related mortality, but patients remain at risk for secondary complications.[2]

Despite current preventative strategies, clinically evident venous thromboembolism (VTE) is an important post-stroke complication that occurs in up to 5% of immobile stroke patients within the first 30-days[3] and contributes to post-stroke mortality.[4] Therefore, understanding factors associated with such complications is of paramount importance to identify patients at risk and ultimately improve therapeutic measures to reduce VTE-associated morbidity and mortality after stroke.

While current treatments such as mechanical or chemical VTE prophylaxis, are generally utilized in hospitalized stroke patients,[5] quality efforts do not generally oversee the use of such measures in the post-hospitalization phase, i.e., acute rehabilitation units and skilled nursing facilities. Furthermore, in patients with high risk of major bleeding such as patients with intracerebral hemorrhage (ICH), chemical prophylaxis is considered based on risk of VTE,[6] and may be avoided or delayed.[7] Therefore, it is crucial to identify patients at high-risk for VTE after their initial stroke hospitalization who may benefit from continued VTE prophylactic measures beyond their initial inpatient hospital stay. In this study, we aim to determine predictors of VTE readmissions in both hemorrhagic and ischemic stroke patients and compare VTE risk in patients with ICH to those with acute ischemic stroke (AIS).

Methods

IRB approval was waived by Lifespan Institutional Review Board since our analysis used de-identified publicly available data. Informed consent was waived by the IRB as the dataset used is a publicly available de-identified. The Nationwide Readmissions Database (NRD) used for this analysis is publicly available through the Healthcare Cost and Utilization Project (HCUP) at https://www.hcup-us.ahrq.gov/.

Patient population

We included adult patients 18 years or older hospitalized with a principal diagnosis of AIS or non-traumatic ICH using the HCUP Nationwide Database between January 1st, 2016 and December 31st, 2019. Diagnoses were identified based on ICD-10-CM (International Classification of Diseases, Tenth Revision, Clinical Modification) codes (Supplementary Table 1). For stroke, when used as a primary diagnosis, ICD-10 code has a positive predictive value of 99.8% and a sensitivity of 87.2%.[8] We excluded patients with a new VTE diagnosis at the time of index stroke admission, a prior history of VTE, and patients who died during the index admission. Due to the inability of following patients across different years, patients who were discharged from October to December were excluded each year to allow a follow-up duration of 90 days. Since we are interested in the short-term risk of a VTE readmission in stroke patients, we also excluded patients whose index admission exceeded 30 days in duration (Figure 1).

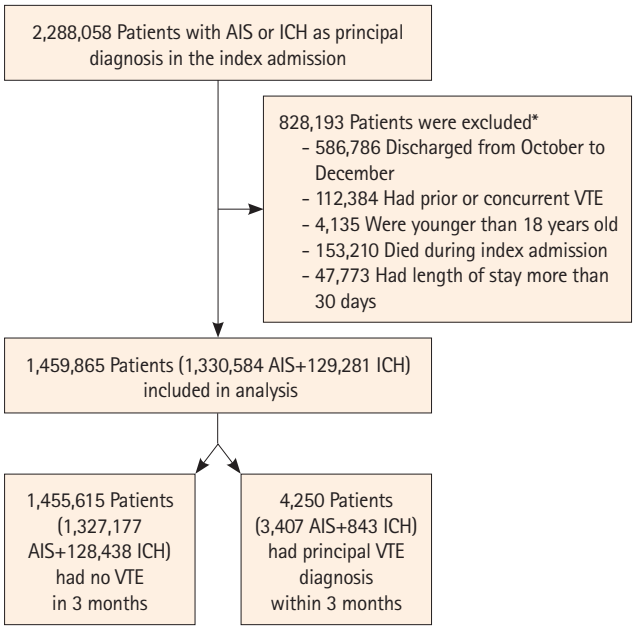

Figure 1. Flow chart of the study. AIS, acute ischemic stroke; ICH, intracerebral hemorrhage; VTE, venous thromboembolism. *Patients may have more than one exclusion reason.

Predictors

The variables of interest were abstracted from the list of diagnoses during the index hospitalization. These included:

(1) Demographic variables: age, sex, insurance status (Medicaid, Medicare, private insurance, and self-pay), median income by zip code (divided into quartiles according to HCUP thresholds), and hospital type (metropolitan teaching, metropolitan non-teaching, non-metropolitan).

(2) Clinical variables: history of hypertension, diabetes, cancer, congestive heart failure, obesity, and peripheral vascular disease generated with Elixhauser Comorbidity Software (Version 3.7), available on the HCUP website. History of coronary artery disease, history of atrial fibrillation or atrial flutter, National Institutes of Health Stroke Scale (NIHSS) score (continuous variable), hospital length of stay (continuous variable), and discharge disposition.

(3) In-hospital treatments: intravenous thrombolytics and mechanical thrombectomy.

Outcomes

The primary outcome was a hospital readmission within 90-days with a principal diagnosis of VTE. ICD-10 codes of pulmonary embolism and deep vein thrombosis (DVT) hospitalization were

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shown to have a good positive predictive value (87%).[9] We did not consider non-principal VTE readmission in the VTE outcome since VTEs occurring during a readmission could possibly be secondary to other etiologies.

Analytical plan

Patients were divided into two groups based on the occurrence of primary outcome. We compared baseline characteristics between the two weighted groups using univariate logistic regression. We identified variables with $P<0.1$ from the univariate analysis and included them in weighted Cox regression analyses to determine potentially relevant predictors of the primary outcome.

We also performed weighted Cox regression with unadjusted and adjusted propensity score weighting[10] to compare the risk of VTE readmission in ICH compared to AIS. We adopted propensity score methods in combination with survey weighting in order to obtain unbiased treatment effect estimates.[10] Two different methods were used to estimate the propensity score weight. The first "propensity score matching" method utilized nearest neighbor one-to-one propensity score matching, where the matched weight was derived by multiplying the survey weights with the propensity score weights. Alternatively, the second "propensity weighted analysis" method was similar to the inverse probability of treatment weighting. Patients were re-weighted using the matched weight, which was derived by multiplying the survey weights with the doubly robust estimation weights.[11] For adjustment and weighting, we included all variables associated with VTE readmissions in Cox regression models in patients with AIS and ICH. For Cox regression models, proportionality was assessed using Schoenfeld's residuals and parametric survival models were used when proportionality was not met.

Kaplan-Meier survival estimates were performed in both groups. Furthermore, to determine the risk of VTE over time, VTE readmission rates per day over 90-day were estimated with linear splines and the breakpoint was identified by joinpoint regression.

Finally, a risk scoring system for post-stroke VTE was developed with nomogram, which was generated using risk factors identified in Cox regression (Supplementary Table 2). NIHSS and the length of stay were dichotomized using the Youden Index cut-point. Area under the curve (AUC) was used to assess predictive accuracy. We then categorized patients into different risk groups and compared their absolute risk of post-stroke VTE readmission. All analyses were performed using Stata version 15 (StataCorp., College Station, TX, USA) and $P<0.05$ was considered statistically significant.

Results

Study cohort and overall VTE rates

Of the 2,288,058 patients with AIS or ICH as their principal diagnosis in their index admission, 1,459,865 met the inclusion criteria (Figure 1 depicts the study flow chart). Among the 1,330,584 included AIS patients, the mean age was 70.0±0.1 years, 49.6% (660,175/1,330,584) were women, and 3,407 (0.26%) had VTE as the principal diagnosis for readmission within 90 days of initial hospital discharge. Among the 129,281 included ICH patients, the mean age was 68.5±0.1 years, 47.9% (61,967/129,281) were women, and 0.65% (843) had VTE as the principal diagnosis for a readmission within 90 days of initial hospital discharge. The VTE readmission rate per day declined over the 90-day period and the trend significantly decelerated after day 30 for AIS patients ($P<0.001$) and day 46 for ICH patients ($P<0.001$) (Figure 2).

Factors associated with VTE readmission on univariate analyses in AIS

In univariate analyses, when compared to AIS patients without a VTE readmission, those with a VTE readmission were more likely to be older (71.1±0.3 years vs. 70.0±0.1 years, $P=0.002$), women (54.6% vs. 49.6%, $P<0.001$), have a cancer diagnosis (10.8% vs. 4.0%, $P<0.001$), have congestive heart failure (17.6% vs. 15.5%,

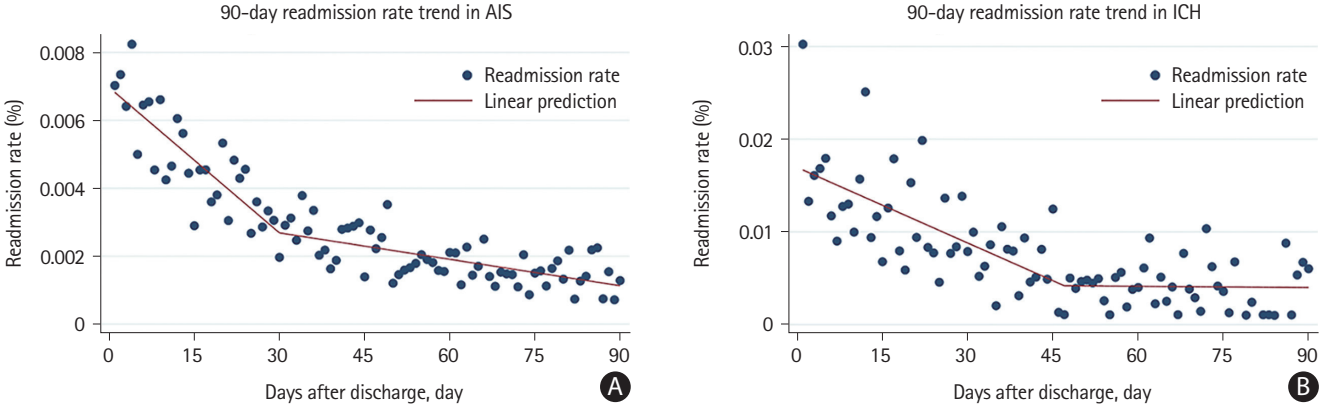

Figure 2. Trends in venous thromboembolism readmissions in (A) acute ischemic stroke (AIS) and (B) intracerebral hemorrhage (ICH) over 90 days.

P=0.020), obesity (18.3% vs. 14.0%, *P*<0.001), have a higher NIHSS score (median [interquartile range, IQR]: 6 [3–14] vs. 4 [1–8], *P*<0.001), have Medicare insurance (71.7% vs. 66.7%, *P*<0.001), be treated at a metropolitan teaching hospital (73.1% vs. 70.6%, *P*=0.027), receive intravenous thrombolysis (11.2% vs. 9.4%, *P*=0.020), mechanical thrombectomy (5.8% vs. 3.5%, *P*<0.001), have a longer length of stay (median [IQR]: 5 days [3–8] vs. 3 days [2–6], *P*<0.001), and be discharged to a rehabilitation or skilled nursing facility (56.6% vs. 34.9%, *P*<0.001), and less likely to have atrial fibrillation or flutter (19.9% vs. 24.2%, *P*<0.001). Other characteristics were not significantly different between the two groups (Table 1).

Table 1. Baseline characteristics across patients with vs. without VTE readmission in AIS and ICH

Variable	AIS			ICH		
	VTE readmission (n=3,407)	No VTE readmission (n=1,327,177)	*P*	VTE readmission (n=843)	No VTE readmission (n=128,438)	*P*
Age (yr)	71.1±0.3	70.0±0.1	0.002	69.5±0.7	68.5±0.1	0.187
Female sex	1,861/3,407 (54.6)	658,313/1,327,177 (49.6)	<0.001	436/843 (51.7)	61,531/128,438 (47.9)	0.140
Insurance						
Private insurance	503/3,404 (14.8)	239,487/1,325,252 (18.1)	0.001	161/841 (19.1)	25,000/128,210 (19.5)	0.872
Medicare	2,439/3,404 (71.7)	883,509/1,325,252 (66.7)	<0.001	576/841 (68.5)	80,725/128,210 (63.0)	0.028
Medicaid	293/3,404 (8.6)	117,642/1,325,252 (8.9)	0.708	67/841 (8.0)	13,811/128,210 (10.8)	0.152
Self-pay	169/3,404 (5.0)	84,614/1,325,252 (6.4)	0.023	37/841 (4.4)	8,674/128,210 (6.8)	0.057
Household income						
Zip income 1st quartile	1,097/3,363 (32.6)	407,405/1,309,721 (31.1)	0.203	229/828 (27.7)	37,027/126,804 (29.2)	0.530
Zip income 2nd quartile	890/3,363 (26.5)	357,907/1,309,721 (27.3)	0.476	182/828 (22.0)	33,722/126,804 (26.6)	0.043
Zip income 3rd quartile	788/3,363 (23.4)	312,421/1,309,721 (23.9)	0.682	240/828 (29.0)	30,800/126,804 (24.3)	0.051
Zip income 4th quartile	588/3,363 (17.5)	231,988/1,309,721 (17.7)	0.811	177/828 (21.4)	25,255/126,804 (19.9)	0.488
Hospital type						
Metropolitan non-teaching	710/3,407 (20.8)	283,763/1,327,177 (21.4)	0.589	109/843 (12.9)	17,173/128,438 (13.4)	0.785
Metropolitan teaching	2,491/3,407 (73.1)	936,359/1,327,177 (70.6)	0.027	723/843 (85.8)	107,773/128,438 (83.9)	0.302
Non-metropolitan hospital	206/3,407 (6.0)	107,055/1,327,177 (8.1)	0.005	11/843 (1.3)	3,492/128,438 (2.7)	0.194
Hypertension	2,928/3,407 (85.9)	1,142,372/1,327,177 (86.1)	0.874	738/843 (87.5)	111,794/128,438 (87.0)	0.776
Diabetes	1,275/3,407 (37.4)	517,927/1,327,177 (39.0)	0.200	245/843 (29.1)	36,838/128,438 (28.7)	0.890
Coronary artery disease	957/3,407 (28.1)	355,676/1,327,177 (26.8)	0.288	181/843 (21.5)	25,620/128,438 (19.9)	0.465
Cancer	367/3,407 (10.8)	52,584/1,327,177 (4.0)	<0.001	82/843 (9.7)	7,726/128,438 (6.0)	<0.001
Congestive heart failure	598/3,407 (17.6)	205,231/1,327,177 (15.5)	0.020	102/843 (12.1)	15,046/128,438 (11.7)	0.837
Peripheral vascular disease	350/3,407 (10.3)	137,762/1,327,177 (10.4)	0.909	53/843 (6.3)	8,868/128,438 (6.9)	0.653
Atrial fibrillation or flutter	679/3,407 (19.9)	321,784/1,327,177 (24.2)	<0.001	208/843 (24.7)	26,021/128,438 (20.3)	0.048
Obesity	624/3,407 (18.3)	186,417/1,327,177 (14.0)	<0.001	172/843 (20.4)	14,943/128,438 (11.6)	<0.001
NIHSS	6 [3–14]	4 [1–8]	<0.001	10 [4–16]	5 [2–13]	0.001
NIHSS ≥10	475/1,218 (39.0)	87,414/435,424 (20.1)	<0.001	100/188 (53.2)	7,660/22,244 (34.4)	<0.001
IV thrombolytics	380/3,407 (11.2)	125,168/1,327,177 (9.4)	0.020			
Thrombectomy	196/3,407 (5.8)	45,915/1,327,177 (3.5)	<0.001			
Length of stay (day)	5 [3–8]	3 [2–6]	<0.001	8 [4–14]	5 [3–11]	<0.001
Length of stay >7 days	1,002/3,407 (29.4)	232,586/1,327,177 (17.5)	<0.001	449/843 (53.3)	46,548/128,438 (36.2)	<0.001
Discharge disposition						
Home without services	806/3,407 (23.7)	578,363/1,327,090 (43.6)	<0.001	116/843 (13.8)	38,954/128,432 (30.3)	<0.001
Home with services	581/3,407 (17.1)	250,927/1,327,090 (18.9)	0.053	92/843 (10.8)	20,840/128,432 (16.2)	0.004
Rehab or nursing home	1,927/3,407 (56.6)	463,394/1,327,090 (34.9)	<0.001	617/843 (73.2)	64,444/128,432 (50.2)	<0.001
Other	93/3,407 (2.7)	34,406/1,327,090 (2.6)	0.708	18/843 (2.3)	4,194/128,432 (3.3)	0.246

Data are presented as mean±standard deviation, number (percentage), or median [interquartile range]. Percentages may not total 100% due to rounding.
VTE, venous thromboembolism; AIS, acute ischemic stroke; ICH, intracerebral hemorrhage; NIHSS, National Institutes of Health Stroke Scale; IV, intravenous.

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Factors associated with VTE readmission in univariate analyses in ICH

In univariate analyses, when compared to ICH patients without a VTE readmission, those with a VTE readmission were more likely to have atrial fibrillation (24.7% vs. 20.3%, *P*=0.048), have obesity (20.4% vs. 11.6%, *P*<0.001), have a higher median NIHSS score (median [IQR]: 10 [4–16] vs. 5 [2–13], *P*=0.001), have longer length of stay (median [IQR]: 8 days [4–14] vs. 5 days [3–11], *P*<0.001), and be discharged to a rehabilitation or skilled nursing facility (73.2% vs. 50.2%, *P*<0.001). On the contrary, VTE readmission was less common in patients in the 2nd quartile of the estimated median household income zip code (22.0% vs. 26.6%, *P*=0.043), home discharge (13.8% vs. 30.3%, *P*<0.001) or home with services discharge (10.8% vs. 16.2%, *P*=0.004). Other characteristics were not significantly different between the two groups (Table 1).

Factors associated with VTE readmission in AIS and ICH in Cox regression models

In Cox regression models, factors associated with increased rates of VTE readmission in patients with AIS were cancer (adjusted hazard ratios [aHR] 2.17, 95% confidence interval [CI] 1.63–2.90, *P*<0.001), obesity (aHR 1.73, 95% CI 1.42–2.10, *P*<0.001), higher NIHSS score (aHR 1.03 per point, 95% CI 1.02–1.04, *P*<0.001), longer hospital length of stay (aHR 1.03 per day, 95% CI 1.02–1.04, *P*<0.001), and disposition to home with services (aHR 1.60,

Table 2. Variables associated with venous thromboembolism readmission in AIS and ICH patients in Cox regression analysis

Variable	AIS (n=435,906)			ICH (n=22,096)		
	Adjusted hazard ratio	95% confidence interval	*P*>|t|	Adjusted hazard ratio	95% confidence interval	*P*>|t|
Age	1.01	1.00–1.02	0.143	NA	NA	NA
Female sex	1.09	0.93–1.27	0.304	NA	NA	NA
Insurance						
Private insurance	Ref	Ref	Ref	Ref	Ref	Ref
Medicare	0.86	0.67–1.11	0.241	1.16	0.67–1.99	0.596
Medicaid	0.95	0.66–1.35	0.758	0.41	0.15–1.10	0.075
Self-pay	1.14	0.77–1.68	0.518	1.12	0.39–3.24	0.828
Household income						
Zip income 1st quartile	NA	NA	NA	Ref	Ref	Ref
Zip income 2nd quartile	NA	NA	NA	1.12	0.62–2.02	0.719
Zip income 3rd quartile	NA	NA	NA	1.39	0.77–2.51	0.278
Zip income 4th quartile	NA	NA	NA	0.92	0.49–1.70	0.781
Hospital type						
Metropolitan non-teaching	Ref	Ref	Ref	NA	NA	NA
Metropolitan teaching	1.03	0.83–1.28	0.775	NA	NA	NA
Non-metropolitan hospital	0.80	0.49–1.30	0.358	NA	NA	NA
Cancer	2.17	1.63–2.90	<0.001	1.76	0.69–4.50	0.236
Congestive heart failure	1.05	0.84–1.31	0.679	NA	NA	NA
Atrial fibrillation or flutter	0.57	0.45–0.71	<0.001	1.40	0.87–2.28	0.169
Obesity	1.73	1.42–2.10	<0.001	1.61	0.96–2.70	0.072
NIHSS score	1.03	1.02–1.04	<0.001	1.01	0.99–1.03	0.367
IV thrombolytics	1.04	0.82–1.31	0.758	NA	NA	NA
Thrombectomy	1.12	0.85–1.47	0.414	NA	NA	NA
Length of hospital stay	1.03	1.02–1.04	<0.001	1.04	1.01–1.06	0.005
Discharge disposition						
Home without services	Ref	Ref	Ref	Ref	Ref	Ref
Home with services	1.60	1.22–2.11	0.001	1.35	0.58–3.16	0.489
Rehab or nursing home	2.74	2.18–3.44	<0.001	2.77	1.34–5.76	0.006
Other	1.81	1.04–3.15	0.037	1.87	0.42–8.37	0.412

AIS, acute ischemic stroke; ICH, intracerebral hemorrhage; NIHSS, National Institutes of Health Stroke Scale; IV, intravenous.

95% CI 1.22–2.11, *P*=0.001) or rehabilitation or nursing home (aHR 2.74, 95% CI 2.18–3.44, *P*<0.001) as opposed to disposition to home without services. On the other hand, atrial fibrillation was associated with a lower VTE readmission risk (aHR 0.57, 95% CI 0.45–0.71, *P*<0.001) (Table 2).

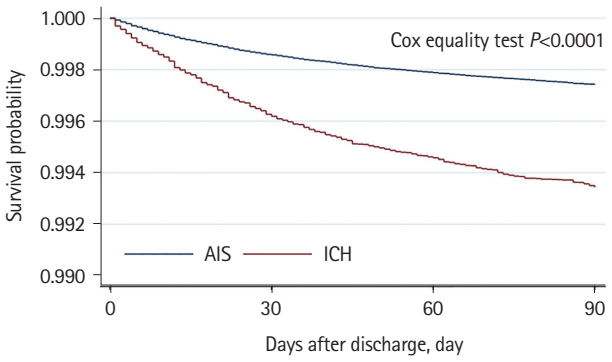
In ICH patients, factors significantly associated with increased rates of VTE readmission were longer hospital length of stay (aHR 1.04 per day, 95% CI 1.01–1.06, *P*=0.005) and disposition to rehabilitation or nursing home (aHR 2.77, 95% CI 1.34–5.76, *P*=0.006) (Table 2).

Comparing VTE readmission risk between AIS and ICH

In the unadjusted analysis, when compared to AIS, ICH conferred a higher risk of VTE readmission (HR 2.56, 95% CI 2.28–2.87, *P*<0.001) (Figure 3). This finding persisted after adjusting for potential confounders (aHR 2.10, 95% CI 1.67–2.65, *P*<0.001), propensity score matching (aHR 1.89, 95% CI 1.34–2.66, *P*<0.001), and propensity weighted adjusted analyses (aHR 2.86, 95% CI 1.93–4.25, *P*<0.001) (Table 3).

Post-stroke VTE risk score

Derived from the nomogram, the post-stroke VTE risk score (AUC: 0.70 [0.68–0.72]) used total 7 factors: ICH during index event, cancer, no history of atrial fibrillation, obesity, higher NIHSS (>4 points), longer length of stay (>3 days), and disposition to home with services, rehabilitation or nursing home. For those patients in the low (0–14), medium (15–34), and high risk (35–45) categories, the VTE readmission rates were 1,625/951,656 (0.2%), 2,617/ 507,868 (0.5%), and 8/343 (2.3%), respectively (*P*<0.001).



Number at risk

AIS	1,330,584	1,321,434	1,315,717	1,311,743
ICH	129,281	127,910	127,150	126,625

Figure 3. Kaplan-Meier survival estimates of venous thromboembolism readmission in acute ischemic stroke (AIS) vs. intracerebral hemorrhage (ICH).

Discussion

In this nationwide analysis of post-stroke patients, we found that the 90-day risk of VTE readmission is associated with factors linked to immobility and hypercoagulability. Furthermore, the risk of VTE readmission was highest in the first 30 days in AIS and 46 days in ICH and significantly decreased thereafter.

Some of our findings differed from prior studies. For instance, atrial fibrillation was shown to be associated with VTE after ischemic stroke in prior studies.[12,13] In our study atrial fibrillation was associated with lower risk of post-stroke VTE. The prior studies were conducted in the early 1990s when only 1.5% of their patients were treated with anticoagulation.[13] In current practice, these rates are substantially higher, particularly with anticoagulation by discharge being a joint commission quality measure in AIS patients with atrial fibrillation. Therefore, early initiation of oral anticoagulation in patients with atrial fibrillation according to current joint commission quality measures may be an important driver of reduced VTE risk in such patients. This notion is further supported by our observation that atrial fibrillation was not independently associated with VTE readmission risk after ICH, presumably because in such patients, initiation of oral anticoagulation may be delayed or considered contraindicated depending on the ICH etiology. Which again implies that the lower risk of VTE in atrial fibrillation patients may be due to anticoagulation therapy. Furthermore, the association between cancer and VTE risk in stroke patients is in line with studies suggesting

Table 3. Association of stroke type (ICH vs. AIS) with venous thromboembolism readmission in Cox regression models

	Hazard ratio	95% Confidence interval	*P*>|t|
Unadjusted model			<0.001
AIS	1.00	Ref.	
ICH	2.56	2.28–2.87	
Adjusted* model			<0.001
AIS	1.00	Ref.	
ICH	2.10	1.67–2.65	
Propensity score* matching†			<0.001
AIS	1.00	Ref.	
ICH	1.89	1.34–2.66	
Propensity weighted* analysis			<0.001
AIS	1.00	Ref.	
ICH	2.86	1.93–4.25	

ICH, intracerebral hemorrhage; AIS, acute ischemic stroke; NIHSS, National Institutes of Health Stroke Scale.
*Adjusted, matched, and weighted for obesity, cancer, NIHSS score, atrial fibrillation or flutter, length of hospital stay, and discharge disposition; †Without replacement.

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the occurrence of hypercoagulability in the setting of cancer,[14,15] which increases the risk of VTE.[16] Moreover, many risk factors for VTE readmission in our study have previously been linked to impaired mobility, such as increased hospital length of stay, stroke severity, discharge to a rehabilitation or skilled nursing facility, and obesity.[17-20] That said, there may be surveillance bias for facility disposition where VTE patients may more likely be sent to the hospital, and this finding should be interpreted with caution. Several studies have investigated extended VTE prophylaxis use in acutely ill medical patients and demonstrated decreased rate of VTE at a cost of increased rate of major bleeding. Stroke patients may have different coagulopathy (inherent disease or medication) and immobility than acutely ill medical patients. Further studies in this special subgroup patients are needed to test interventions such as early mobilization of stroke patients,[21] reducing the length of hospital stay to reduce the VTE rates, short-term use of mechanical and/or chemical DVT prophylaxis after hospital discharge, particularly in high-risk patients. Furthermore, standard doses of chemical prophylactic agents may not be as effective in obese patients.[19,22]

Similar to prior studies,[23,24] our study also showed that the risk of VTE was three-fold higher in ICH patients when compared to those with AIS. One possible explanation is the lower rates and delay in initiation of chemical VTE prophylaxis in ICH compared to AIS. Despite guidelines recommending chemical prophylaxis to be initiated between 1 and 4 days after ICH onset provided cessation of active bleeding,[7] one study showed that less than 20% of patients with ICH received chemical VTE prophylaxis, of whom less than half of them received it within 2 days after ICH onset.[24] Patients with ICH are also more likely to require an intensive care unit admission, have higher morbidity, and have a longer length of hospital stay than patients with AIS, all of which may contribute to the higher risk of VTE in patients with ICH compared to those with AIS. Nevertheless, our findings suggesting higher rates of VTE in ICH patients persisted even after adjusting for these factors.

Finally, we found that rates of VTE are highest during the first 30 days after ischemic stroke and 46 days from ICH, which is consistent with prior studies.[25,26] This is in line with findings from prior studies showing the risk of VTE in stroke patients extends into the acute rehabilitation phase.[12,27] Thus studies are needed to investigate the efficacy and safety of continued mechanical and chemical prophylaxis beyond the hospital setting in high-risk patients and up to these time points with AIS and ICH. Furthermore, given the risk of VTE is significantly lower beyond these time points, long-term chemical or mechanical prophylaxis may not be beneficial and is not recommended by clinical guidelines.[28]

There are several limitations to our study. Although this national database allows analysis of a very large number of patients, it lacks specific patient-level data. For example, despite accounting for multiple comorbidities, certain clinically relevant measures such as the use of anticoagulation and intermittent pneumatic compression are not available in this dataset. The national readmission database only provides disposition in limited categories, and it combines acute rehabilitation and skilled nursing facilities into one category. This is particularly important as patients who were discharged to long-term care have the most disability and the least potential for a good recovery than those discharged to acute rehabilitation. That said, the general criteria for discharge to acute rehabilitation are being unable to walk independently even with the use of an assistive device, which would imply a modified Rankin Scale score of 4 or 5 and thus have decreased mobility and are still at risk for VTE.

Importantly, we only considered patients who were hospitalized with VTE, and thus VTEs diagnosed and treated in the outpatient setting were not included. The rate of post-stroke VTE was reported to be up to 17% for asymptomatic and symptomatic patients and about 1% for clinically relevant events in prior studies.[29,30] Furthermore, patients with sudden death from an undiagnosed pulmonary embolus were also not included. These factors may have contributed to a lower rate of VTE in our study compared to prior studies.[3] Another limitation of our study is the exclusion of patients hospitalized between October and December. We however do not expect the variables and findings used in this study to vary based on this exclusion.

Conclusion

Although patients with stroke have a low rate of readmission for VTE, ICH and factors related to decreased mobility and/or hypercoagulability can put them at a higher risk of VTE. Further studies are needed to determine whether early mobilization and mechanical and/or short-term chemical prophylaxis post-discharge reduce the risk in high-risk patients.

Supplementary materials

Supplementary materials related to this article can be found online at https://doi.org/10.5853/jos.2022.02215.

Disclosure

The authors have no financial conflicts of interest.

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None

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Supplementary Table 1. Diagnoses based on International Classification of Diseases, Tenth Revision (ICD-10) code

Diagnosis	ICD-10 codes
DVT	I801 I802 I803 I808 I809 I82210 I82220 I82290 I824 I8262 I82890 I82A1 I82B1 I82C1 O223 O871
PE	I26
AIS	I63
ICH	I61
CAD	I20 I240 I248 I249 I251 I252 I255 I256 I257 I258 I259 Z951 Z955 Z9861
AF	I48
tPA	3E03317
Mechanical thrombectomy	03CG3Z6 03CG3Z7 03CG3ZZ 03CG4Z6 03CG4ZZ 03CH3Z6 03CH3Z7 03CH3ZZ 03CH4Z6 03CH4ZZ 03CJ3Z6 03CJ3Z7 03CJ3ZZ 03CJ4Z6 03CJ4ZZ 03CK3Z6 03CK3Z7 03CK3ZZ 03CK4Z6 03CK4ZZ 03CL3Z6 03CL3Z7 03CL3ZZ 03CL4Z6 03CL4ZZ 03CP3Z6 03CP3Z7 03CP3ZZ 03CP4Z6 03CP4ZZ 03CQ3Z6 03CQ3Z7 03CQ3ZZ 03CQ4Z6 03CQ4ZZ
History of VTE	Z8671
NIHSS	R297

DVT, deep vein thrombosis; PE, pulmonary embolism; AIS, acute ischemic stroke; ICH, intracerebral hemorrhage; CAD, coronary artery disease; AF, atrial fibrillation; tPA, tissue plasminogen activator; VTE, venous thromboembolism; NIHSS, National Institutes of Health Stroke Scale.

Supplementary Table 2. Post-stroke venous thromboembolism score

Variables	Score
ICH during index admission	
No	0
Yes	7
Cancer	
No	0
Yes	8
No atrial fibrillation	
No	0
Yes	3
Obesity	
No	0
Yes	6
NIHSS >4	
No	0
Yes	5
Length of stay >3 days	
No	0
Yes	6
Disposition	
Home without services	0
Home with services	5
Rehabilitation/nursing home	10
Total	45

ICH, intracerebral hemorrhage; NIHSS, National Institutes of Health Stroke Scale.