SVN Stroke & Vascular Neurology

Venous thromboembolism among Medicare acute ischaemic stroke patients with and without COVID-19

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To cite: Tong X, Yang Q, Asaithambi G, *et al*. Venous thromboembolism among Medicare acute ischaemic stroke patients with and without COVID-19. *Stroke & Vascular Neurology* 2023;**8**: e001814. doi:10.1136/svn-2022-001814

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/svn-2022-001814).

Received 16 June 2022
Accepted 2 September 2022
Published Online First 15 November 2022

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ABSTRACT

Background COVID-19 is associated with an increased risk of venous thromboembolism (VTE). This study examined the prevalence of VTE among acute ischaemic stroke (AIS) patients with and without a history of COVID-19.

Methods We identified AIS hospitalisations of Medicare fee-for-service (FFS) beneficiaries aged ≥65 years from 1 April 2020 to 31 March 2022. We compared the prevalence and adjusted prevalence ratio of VTE among AIS patients with and without a history of COVID-19.

Results Among 283 034 Medicare FFS beneficiaries with AIS hospitalisations, the prevalence of VTE was 4.51%, 2.96% and 2.61% among those with a history of hospitalised COVID-19, non-hospitalised COVID-19 and without COVID-19, respectively. As compared with patients without a history of COVID-19, the prevalence of VTE among patients with a history of hospitalised or non-hospitalised COVID-19 were 1.62 (95% CI 1.54 to 1.70) and 1.13 (95% CI 1.03 to 1.23) times greater, respectively.

Conclusions There appeared to be a notably higher prevalence of VTE among Medicare beneficiaries with AIS accompanied by a current or prior COVID-19. Early recognition of coagulation abnormalities and appropriate interventions may help improve patients' clinical outcomes.

INTRODUCTION

Several studies have suggested that infection with SARS-CoV-2, the virus that causes COVID-19 may predispose patients to an increased risk of venous thromboembolism (VTE), especially among hospitalised patients.[1 2] VTE is a common medical complication in patients with acute ischaemic stroke (AIS) and is recognised as a negative quality indicator of stroke care.[3] Few studies have examined the association between COVID-19 and VTE among AIS patients.[4] We examined this relationship among Medicare fee-for-service (FFS) beneficiaries aged ≥65 years who were hospitalised with AIS from 1 April 2020 to 31 March 2022.

METHODS

We used the real-time Medicare monthly files to identify the beneficiaries for this retrospective study. AIS was defined as having a hospital admission with primary diagnosis of International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) code I63. The final analytical study population had 283 304 Medicare FFS beneficiaries diagnosed with AIS (figure 1). We obtained the first diagnosis of COVID-19 (ICD-10-CM U07.1) through claims from any type of healthcare setting and classified by hospitalisation status to reflect the severity of COVID-19. If the first occurrence of COVID-19 was identified through the inpatient setting claims, it was defined as hospitalised COVID-19. We defined AIS patients with a history of COVID-19 if the dates of the first COVID-19 diagnoses were earlier than AIS admission dates. For each AIS admission, we identified the beneficiaries with VTE through secondary diagnoses codes (ICD-10-CM I80–I82, I26).

We calculated the median age and IQR and the distribution of age group, sex, race/ethnicity, National Institutes of Health Stroke Scale (NIHSS) scores, VTE, death and medical history of comorbidity conditions among AIS patients by three groups: with history of hospitalised COVID-19; with history of non-hospitalised COVID-19 and without COVID-19. About 37% of AIS patients had missing NIHSS scores, and we used the multiple imputation to impute the missing values with 25 imputed datasets using PROC MI in SAS. We used SAS PROC GENMOD's log-binomial regression to estimate the prevalence ratio (PR) and 95% CIs for all patients and by age group, sex and race/ethnicity group. We calculated the adjusted PR (adjusted for age, sex, race/ethnicity, NIHSS score, history of stroke/transient ischaemic attack, ischaemic heart disease, hypertension, hypercholesterolaemia, diabetes, atrial fibrillation, heart failure, chronic kidney disease, acute myocardial infarction, peripheral vascular disease, chronic obstructive pulmonary disease and tobacco use) of VTE by comparing: AIS patients with a history of hospitalised COVID-19 or non-hospitalised COVID-19 versus those without COVID-19.

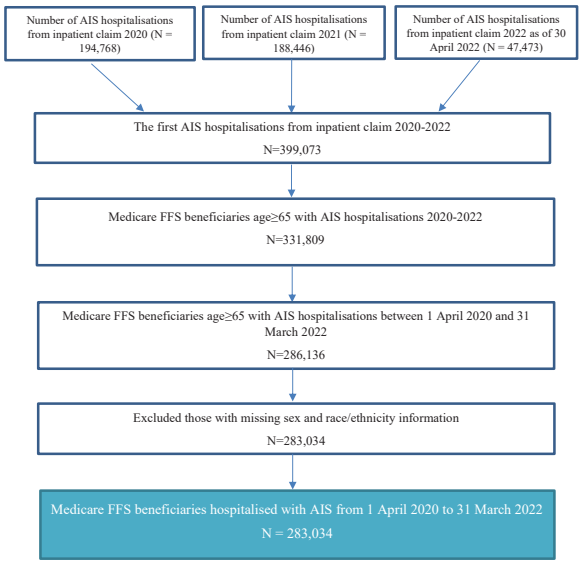

Figure 1 Study flowchart of Medicare fee-for-service (FFS) beneficiaries aged ≥65 years hospitalised with acute ischaemic stroke (AIS) in the USA, 2020–2022

DATA AVAILABILITY

The Medicare data used in this study cannot be shared by authors because of the data usage agreement, but the investigators can access to these data by application to Centers for Medicare and Medicaid Services.

RESULTS

Among total of 283 034 Medicare FFS beneficiaries with AIS admissions, 9.5% patients had a history of COVID-19, while 52% of them classified as hospitalised, and 2.7% patients had VTE (online supplemental table 1). The stroke severity measured by NIHSS score was higher among AIS patients with a history of COVID-19 than those without COVID-19. AIS patients with a history of hospitalised COVID-19 had the mortality rate of 41.0%, compared with 31.9% with a history of non-hospitalised COVID-19, and 30.8% among those without COVID-19. Among 26 770 AIS patients with a history of COVID-19, the median days between COVID-19 and AIS dates were 97 days (IQR 9–275 days).

VTE prevalence was 4.51%, 2.96% and 2.61% among AIS patients with a history of hospitalised, non-hospitalised COVID-19 and without COVID-19, respectively (table 1). As compared with AIS patients without COVID-19, adjusted PRs of VTE was 1.62 (95% CI 1.54 to 1.70) and 1.13 (95% CI 1.03 to 1.23) among those with a history of hospitalised or non-hospitalised COVID-19, respectively. Patients aged 65–74 years had the highest prevalence of VTE as compared with those aged 75–84 years and those aged ≥85 years. Compared with other race/ethnicity groups, non-Hispanic black patients had the highest prevalence of VTE at 6.53% among those with a history of hospitalised COVID-19, 3.86% among those with non-hospitalised COVID-19 and 3.97% among those without COVID-19.

DISCUSSION

Our findings suggested a notably higher prevalence of VTE among AIS patients with a history of COVID-19 among Medicare FFS beneficiaries aged ≥65 years. Compared with AIS patients without COVID-19, the prevalence of VTE among AIS patients with a history of hospitalised or non-hospitalised COVID-19 were 1.62 and 1.13 times greater, respectively. Non-Hispanic black AIS patients had the highest prevalence of VTE consistent with the findings of other studies.[5 6]

Many studies reported significant increases in incidence of VTE among hospitalised COVID-19 patients ranging from 1.0% to 85% with an average of 17%.[1 2 7] Our study showed a 4.51% of VTE among AIS patients with a history of hospitalised COVID-19, which was lower than the average reported previously. However, if studies were restricted to those that included ≥200 patients with COVID-19, then the pooled incidence of VTE was approximately 4%.[1] While most studies focused on thrombotic complications among the hospitalised patients with COVID-19, especially among those ICU admissions, we are not aware of any study that examined the association between AIS patients with history of non-hospitalised COVID-19. Our findings suggested that the prevalence of VTE among AIS patients is notably higher among those with milder symptoms of COVID-19 that do not require hospitalisation when compared with those without history of COVID-19.

VTE is a serious complication among AIS patients and is associated with poor prognosis.[8] VTE prophylaxis is one of the 10 evidence-based stroke core measures endorsed by the Joint Commission, American Heart Association and Centers for Disease and Control and Prevention.[9] Most AIS patients receive standard VTE prophylaxis within 48 hours of admission.[9 10] In the context of COVID-19, vigilance in identifying opportunities for early VTE prophylaxis or interventions to help improve patients' clinical outcomes is recommended based on perceived coagulation abnormalities among AIS patients with a history of COVID-19.

This study has several limitations. We may have missed some beneficiaries with diagnosed COVID-19, VTE and AIS, or incorrect diagnoses dates, due to the usage of preliminary Medicare monthly data. NIHSS scores were based on the ICD-10 codes, which may not be accurate. We are unable to determine whether a history of COVID-19 may affect the severity and comorbidities of stroke, or it may directly affect the incidence of VTE. Finally, VTE was identified through the secondary diagnostic fields, and we cannot determine if VTE was a pre-existing or incident diagnosis.

CONCLUSIONS

Our findings suggested that AIS patients with a history of COVID-19 had a notably higher prevalence of VTE,

Table 1 Prevalence and adjusted prevalence ratios of VTE among AIS patients with and without COVID-19 by demographic characteristics

Variables	Total N (%)	AIS patients with hospitalised COVID-19 (N=13 873)		AIS patients with non-hospitalised COVID-19 (N=12 897)		AIS patients without COVID-19 (N=256 264)		P value*	PR (95% CI)† Hospitalised COVID-19 vs non-COVID-19 AIS	PR (95% CI)† Non-hospitalised COVID-19 vs non-COVID-19 AIS
		No with VTE	Prevalence (95% CI)	No with VTE	Prevalence (95% CI)	No with VTE	Prevalence (95% CI)			
Total	283 034	626	4.51 (4.18 to 4.87)	382	2.96 (2.68 to 3.27)	6697	2.61 (2.55 to 2.68)	<0.001	1.62 (1.54 to 1.70)	1.13 (1.03 to 1.23)
Age in groups										
65–74	93 060 (32.9)	231	5.39 (4.75 to 6.10)	149	3.62 (3.09 to 4.23)	2458	2.90 (2.79 to 3.02)	<0.001	1.69 (1.56 to 1.83)	1.24 (1.08 to 1.40)
75–84	106 608 (37.7)	249	4.82 (4.27 to 5.44)	122	2.54 (2.13 to 3.02)	2603	2.69 (2.59 to 2.80)	<0.001	1.68 (1.55 to 1.81)	0.94 (0.76 to 1.12)
85+	83 366 (29.5)	146	3.31 (2.82 to 3.88)	111	2.79 (2.32 to 3.36)	1636	2.18 (2.08 to 2.29)	<0.001	1.44 (1.27 to 1.60)	1.27 (1.08 to 1.46)
Sex										
Male	125 356 (44.3)	311	5.18 (4.65 to 5.77)	160	2.91 (2.50 to 3.39)	2915	2.56 (2.47 to 2.65)	<0.001	1.89 (1.77 to 2.00)	1.13 (0.98 to 1.29)
Female	157 678 (55.7)	315	4.00 (3.59 to 4.46)	222	3.00 (2.63 to 3.41)	3782	2.66 (2.57 to 2.74)	<0.001	1.43 (1.31 to 1.54)	1.13 (1.00 to 1.27)
Race/ethnicity										
Non-Hispanic white	230 539 (81.5)	451	4.36 (3.98 to 4.77)	313	2.99 (2.68 to 3.34)	5211	2.48 (2.42 to 2.55)	<0.001	1.70 (1.61 to 1.80)	1.21 (1.09 to 1.32)
Non-Hispanic black	27 673 (9.8)	125	6.53 (5.51 to 7.73)	45	3.86 (2.89 to 5.14)	976	3.97 (3.73 to 4.22)	<0.001	1.56 (1.37 to 1.74)	0.95 (0.66 to 1.24)
Hispanic	13 702 (4.8)	32	2.94 (2.07 to 4.13)	15	1.91 (1.13 to 3.15)	310	2.62 (2.35 to 2.93)	0.388	1.06 (0.70 to 1.42)	0.72 (0.21 to 1.24)
Other race	11 120 (3.9)	18	3.41 (2.13 to 5.36)	9	1.86 (0.93 to 3.56)	200	1.98 (1.72 to 2.27)	0.109	1.60 (1.11 to 2.08)	0.93 (0.27 to 1.59)

*P value comparing the difference in prevalence of VTE between the Medicare FFS beneficiaries hospitalised with AIS across three groups of COVID-19 status based on t-test.
†PRs were estimated using the log-binomial regression models adjusting for age, sex, race/ethnicity, NIHSS score, history of medical conditions and tobacco use.
AIS, acute ischaemic stroke; NIHSS, National Institutes of Health Stroke Scale; PR, prevalence ratio; VTE, venous thromboembolism.

especially among those with more severe COVID-19. Clinicians should be aware of this increased risk regardless of standard VTE prophylaxis provided to AIS patients. Early recognition of coagulation abnormalities and appropriate interventions may help improve patients' clinical outcomes.

Contributors All authors have contributed to this manuscript, including study design, writing the manuscript and significant editing of manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval The Centers for Disease Control and Prevention Human Subjects Coordinator determined that this study did not require review for human subjects protections because the data did not contain personal identifiers and were not originally collected specifically for this study. Therefore, the requirement of informed consent was waived.

Provenance and peer review Not commissioned; externally peer reviewed.

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