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

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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 283,034 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.

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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.

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%. 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%. 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. 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. Most AIS patients receive standard VTE prophylaxis within 48 hours of admission. 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=13873) | AIS patients with non-hospitalised COVID-19 (N=12897) | AIS patients without COVID-19 (N=256264) | PR (95% CI)† comparing hospitalised COVID-19 AIS vs non-hospitalised COVID-19 AIS | PR (95% CI)† comparing non-hospitalised COVID-19 AIS vs non-COVID-19 AIS | P value* |
|--------------------|-------------|-------------------------------------------------|------------------------------------------------------|----------------------------------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|----------|
|                    |             | No with VTE | Prevalence (95% CI) | No with VTE | Prevalence (95% CI) | No with VTE | Prevalence (95% CI) |                               |                    |                                  |
| Total              | 283034      | 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              | 93060       | 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              | 106608      | 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+                | 83366       | 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               | 125356      | 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             | 157678      | 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| 230539      | 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| 27673       | 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           | 13702       | 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         | 11120       | 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.

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