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Stroke

CLINICAL AND POPULATION SCIENCES

Risk, Clinical Course, and Outcome of Ischemic Stroke in Patients Hospitalized With COVID-19

A Multicenter Cohort Study

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BACKGROUND AND PURPOSE: The frequency of ischemic stroke in patients with coronavirus disease 2019 (COVID-19) varies in the current literature, and risk factors are unknown. We assessed the incidence, risk factors, and outcomes of acute ischemic stroke in hospitalized patients with COVID-19.

METHODS: We included patients with a laboratory-confirmed SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2) infection admitted in 16 Dutch hospitals participating in the international CAPACITY-COVID registry between March 1 and August 1, 2020. Patients were screened for the occurrence of acute ischemic stroke. We calculated the cumulative incidence of ischemic stroke and compared risk factors, cardiovascular complications, and in-hospital mortality in patients with and without ischemic stroke.

RESULTS: We included 2147 patients with COVID-19, of whom 586 (27.3%) needed treatment at an intensive care unit. Thirty-eight patients (1.8%) had an ischemic stroke. Patients with stroke were older but did not differ in sex or cardiovascular risk factors. Median time between the onset of COVID-19 symptoms and diagnosis of stroke was 2 weeks. The incidence of ischemic stroke was higher among patients who were treated at an intensive care unit (16/586; 2.7% versus nonintensive care unit, 22/1561; 1.4%; $P=0.039$). Pulmonary embolism was more common in patients with (8/38; 21.1%) than in those without stroke (160/2109; 7.6%; adjusted risk ratio, 2.08 [95% CI, 1.52–2.84]). Twenty-seven patients with ischemic stroke (71.1%) died during admission or were functionally dependent at discharge. Patients with ischemic stroke were at a higher risk of in-hospital mortality (adjusted risk ratio, 1.56 [95% CI, 1.13–2.15]) than patients without stroke.

CONCLUSIONS: In this multicenter cohort study, the cumulative incidence of acute ischemic stroke in hospitalized patients with COVID-19 was ≈2%, with a higher risk in patients treated at an intensive care unit. The majority of stroke patients had a poor outcome. The association between ischemic stroke and pulmonary embolism warrants further investigation.

GRAPHIC ABSTRACT: An online graphic abstract is available for this article.

Key Words: COVID-19 ■ hospital mortality ■ incidence ■ intensive care units ■ patient discharge ■ pulmonary embolism

Nonstandard Abbreviations and Acronyms

COVID-19	coronavirus disease 2019
ICU	intensive care unit
IQR	interquartile range
PE	pulmonary embolism
TOAST	Trial of ORG 10172 in Acute Stroke Treatment

Coronavirus disease 2019 (COVID-19) has affected millions of people worldwide. The clinical course of COVID-19 may be complicated by venous and arterial thromboembolic events.[1,2] Pulmonary embolism (PE) accounts for the majority of these events, but other cardiovascular complications, including ischemic stroke, have also been reported. In contrast to early reports suggesting an increased risk of ischemic stroke among patients hospitalized with COVID-19, results from later reports are less consistent.[3–17] The occurrence of ischemic stroke varied, ranging from 0.01% to 6.9%. This may be explained, in part, by differences in study design, sample size, case-findings methods, and settings. Studies that reported clinical details have suggested an increased severity of stroke symptoms, more cryptogenic strokes, and a worse outcome,[3,4,18] including higher in-hospital mortality rates,[3–5] in patients with COVID-19 than in those without. Nevertheless, large cohort studies reporting data on stroke details are limited, as ischemic strokes were often not assessed by neurologists. In addition, little data are available on the relationship between ischemic stroke and other cardiovascular complications in patients with COVID-19. To improve our understanding of the relationship between COVID-19 and ischemic stroke, we assessed risk factors, time course, hospital setting, the relationship with other cardiovascular complications, stroke severity, and outcomes of ischemic stroke in patients hospitalized with COVID-19 during the first wave of the pandemic across 16 centers in the Netherlands.

See related article, p 3987

METHODS

Study Design

This study was conducted within the CAPACITY-COVID international patient registry (www.capacity-covid.eu; https://www.clinicaltrials.gov; unique identifier: NCT04325412). Details regarding CAPACITY-COVID have been outlined elsewhere.[19] In short, the case report form of the International Severe Acute Respiratory and Emerging Infection Consortium was extended within CAPACITY-COVID to collect in-depth information on cardiovascular history, medication, and cardiac and thromboembolic events in patients hospitalized with COVID-19. STROCORONA (Stroke in Corona Patients) was incorporated as a substudy within CAPACITY-COVID, to obtain additional information on neurovascular history and the occurrence of ischemic stroke during hospitalization, including data on vascular risk factors, etiology, severity, and outcome. Sixteen Dutch hospitals participated in STROCORONA. Ethical approval was obtained in all participating hospitals, and the necessity of a consent procedure was determined to conform local regulations. The majority of participating sites had an opt-out approach.[20] The data of this study can be made available upon reasonable request to the data access committee of CAPACITY-COVID.

Study Population and Data Collection

We included adult patients with a laboratory-confirmed SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2) infection (determined by a positive polymerase chain reaction test result from a nasopharyngeal swab) who were admitted to a hospital during the first wave of the pandemic in the Netherlands (March 1 to August 1, 2020). Patients who were strongly suspected of COVID-19 were retested. If their tests remained negative, they were excluded from the current study. We retrieved data on demographics, comorbidities, prehospital medication, the need of mechanical ventilation, treatment at a high-dependency or intensive care unit (ICU) during admission, in-hospital mortality, and the occurrence of cardiac or thromboembolic complications: deep vein thrombosis, PE, acute coronary syndrome, endocarditis, and new-onset atrial fibrillation. Outcome definitions of cardiac and thromboembolic complications have been reported previously.[20] For STROCORONA, patient files of all cases were systematically screened and scored by neurologists or other physicians with experience in stroke research per hospital to identify ischemic stroke during hospitalization. In addition, data on prior transient ischemic attack, ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, or vascular dementia were collected. Ischemic stroke was defined as a sudden onset of focal neurological signs originating from the brain or retina that persisted for >24 hours or until death, confirmed with neuroimaging demonstrating either infarction in the corresponding vascular territory or absence of another apparent cause.[21] We recorded whether patients had been examined by or under supervision of a neurologist. We graded stroke severity at the time of diagnosis with the National Institutes of Health Stroke Scale and collected data on acute stroke treatment (intravenous thrombolysis, endovascular treatment, and antithrombotic treatment), timing (median time between onset of COVID-19 symptoms and stroke diagnosis), and imaging findings (vascular territory, intracranial large vessel occlusion). We classified stroke etiology with the TOAST (Trial of ORG 10172 in Acute Stroke Treatment) criteria and scored stroke outcome at discharge with the modified Rankin Scale.[22]

Statistical Analysis

Baseline characteristics are summarized with descriptive statistics as median (interquartile range [IQR]), mean (SD), or frequencies (proportions) where appropriate. We performed a quality check of the data set and recoded entry errors as missing data. We did not impute missing values (Table I in the Data Supplement). We calculated the cumulative incidence of ischemic stroke with corresponding 95% CIs and stratified results according to age and

sex. Since 3 participating hospitals only included patients with cardiovascular risk factors or patients for whom a cardiologist was consulted during admission, a sensitivity analysis excluding these three centers was performed. We compared the occurrence of other cardiovascular complications and in-hospital mortality between patients with and without ischemic stroke with χ^2 or Student t tests as appropriate and calculated risk ratios with Poisson regression.[23] We adjusted risk ratios for age, sex, and treatment on an ICU. For stroke outcome, we calculated the proportion of ischemic stroke patients with an unfavorable outcome (death or dependency [modified Rankin Scale score of ≥3]) at discharge. We report our findings in accordance with the RECORD guidelines (Reporting of Studies Conducted Using Observational Routinely-Collected Data; Table II in the Data Supplement).

RESULTS

We included a total of 2147 patients in STROCORONA (Figure I in the Data Supplement). Table 1 shows the baseline characteristics. The median age was 70.0 years (IQR, 59.0–77.0); about one-third of the patients were female (769; 35.8%), and cardiovascular comorbidities were common. Of all patients, 586 (27.3%) received treatment at an ICU. In general, patients treated at an ICU were younger and had fewer comorbidities than patients treated on a general ward only (Table III in the Data Supplement). Ischemic stroke occurred in 38 of 2147 (1.8% [95% CI, 1.3%–2.4%]) patients (Table 2). All ischemic strokes were diagnosed by a neurologist. These patients were older than patients without ischemic stroke, had a lower BMI, and had higher platelet counts at baseline but did not differ in terms of sex, cardiovascular comorbidities, and prehospital medication (Table 1; Table IV in the Data Supplement). After stratification by age, no differences in cardiovascular risk factors between patients with and without ischemic stroke were found (Table V in the Data Supplement). In a sensitivity analysis excluding 3 hospitals that excluded patients without cardiovascular risk factors or cardiologist consultation, baseline characteristics and cumulative stroke incidence were similar (Table VI in the Data Supplement). The median time between the onset of COVID-19 symptoms and stroke diagnosis was 14 days (IQR, 9–25 days) for all patients, 23 days (IQR, 13–29) for patients who received ICU treatment, and 10 days (IQR, 3–18) for patients treated on a general ward only (P=0.031; Figure 1; Table 3). The cumulative incidence of ischemic stroke was 2.7% in patients who were treated at an ICU (16/586 [95% CI, 1.7%–4.4%]) and 1.4% in patients who only received treatment on a general ward (22/1561 [95% CI, 0.9%–2.1%]; P=0.039). Age- and sex-stratified cumulative incidence is given in Table 2 and details about stroke severity, subtype, imaging, treatment, and outcome in Table 3. Stroke patients treated at an ICU were younger than those treated at a general ward only (ICU, 63.4 years [SD, 15.2]; general ward, 79.2 [SD, 8.1]; P<0.001), frequently had other thromboembolic events (ICU, 8/16 [50%]; general ward,

2/22 [9.1%]; P=0.020), and had more severe strokes (ICU: median National Institutes of Health Stroke Scale score, 22.0; IQR, 3.8–30.0; general ward, 5.0; IQR, 2.8–17.5; P=0.050; Table 3). Eighteen patients (47.4%) had a stroke of undetermined etiology; however, in 6 (33.3%), the diagnostic workup was incomplete because they were moribund. Differences between patients with and without cryptogenic stroke are summarized in Table VII in the Data Supplement and an overview of the available laboratory, imaging, telemetry, and other investigations in each patient is provided in Table VIII in the Data Supplement. The occurrence of other cardiovascular complications in patients with and without ischemic stroke is given in Table IX in the Data Supplement. PE was more common in patients with ischemic stroke (8/38 [21.1%] versus 160/2109 [7.6%]; P=0.002), also after adjustment for age, sex, and treatment on an ICU (adjusted risk ratio, 2.08 [95% CI, 1.52–2.84]). Patients with PE and ischemic stroke had higher median platelet counts at baseline (285×10⁹/L; IQR, 223–556) than patients with PE without ischemic stroke (230×10⁹/L; IQR, 180–306; P=0.026). The median time between onset of COVID-19 symptoms and PE diagnosis was 18 days (IQR, 12–25 days) for all patients, 19 days (IQR, 12–26) for patients who received ICU treatment, and 14 days (IQR, 8–21) for patients treated on a general ward only (P=0.04). In 5 of 8 (62.5%) patients with PE and ischemic stroke, PE was diagnosed before ischemic stroke. Three-quarters of the patients with ischemic stroke (27/38 [71.1%]) had a modified Rankin Scale score of ≥3 at discharge (Figure 2). Patients with ischemic stroke were at a higher risk of in-hospital mortality (adjusted risk ratio, 1.56 [95% CI, 1.13–2.15]) than patients without ischemic stroke. Age- and sex-stratified cumulative in-hospital mortality is shown in Table X in the Data Supplement. A timeline of admissions and in-hospital mortality during the first wave is given for the participating centers in the Netherlands in Figure II in the Data Supplement.

DISCUSSION

In this Dutch multicenter study, the overall cumulative incidence of ischemic stroke was 1.8% in patients hospitalized with COVID-19, with a higher rate of ischemic stroke in patients who needed treatment at an ICU (2.7%). Patients with ischemic stroke were older but did not have more cardiovascular risk factors when compared with patients without ischemic stroke. In addition, patients with ischemic stroke were twice as likely to have PE and were at higher risk of in-hospital mortality.

The overall incidence of ischemic stroke of 1.8% in hospitalized patients with COVID-19 is in line with previous hospital-based COVID-19 cohorts, which reported cumulative incidences ranging between 1.0% and 2.4%.[3–5] Lower stroke rates have been found in studies

Table 1. Baseline Characteristics of Hospitalized Patients With COVID-19, Stratified by Diagnosis of Ischemic Stroke

Characteristics*	Total cohort	No ischemic stroke (n=2109)	Ischemic stroke (n=38)	P value
Age, y; median (IQR)	70.0 (59.0–77.0)	70.0 (59.0–77.0)	74.5 (66.8–82.0)	P=0.013†
Sex (female)	769 (35.8)	753 (35.7)	16 (42.1)	P=0.415
BMI, kg/m²; mean (SD)	27.9 (5.0)	28.0 (5.0)	26.0 (4.4)	P=0.020†
Platelets, median (IQR)	202.0 (156.0–262.0)	201.0 (155.0–261.5)	245.5 (207.8–277.3)	P=0.013†
Medical history				
Hypertension	1034 (48.2)	1020 (48.4)	14 (36.8)	P=0.370
Diabetes	568 (26.5)	560 (26.6)	8 (21.1)	P=0.633
Hyperlipidemia	862 (40.1)	847 (40.2)	15 (39.5)	P=0.986
Peripheral artery disease	132 (6.7)	127 (6.6)	5 (14.7)	P=0.060
Coronary artery disease	448 (20.9)	443 (21.0)	5 (13.2)	P=0.238
Valvular heart disease	138 (6.4)	136 (6.4)	2 (5.3)	P=0.768
Heart failure	154 (7.2)	153 (7.3)	1 (2.6)	P=0.274
Atrial fibrillation	282 (13.1)	278 (13.2)	4 (10.5)	P=0.631
Venous thromboembolism	91 (4.2)	88 (4.5)	3 (7.9)	P=0.527
Chronic kidney disease	280 (13.0)	277 (13.1)	3 (7.9)	P=0.599
Inflammatory disease	258 (12.0)	254 (12.0)	4 (10.5)	P=0.916
COPD	251 (11.7)	245 (11.6)	6 (15.8)	P=0.706
TIA or ischemic stroke	277 (12.9)	271 (12.8)	6 (15.8)	P=0.592
Intracerebral hemorrhage	17 (0.8)	17 (0.8)	0	P=0.849
Subarachnoid hemorrhage	6 (0.3)	6 (0.3)	0	P=0.939
Vascular dementia	21 (1.0)	21 (1.0)	0	P=0.936

BMI indicates body mass index; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; IQR, interquartile range; and TIA, transient ischemic attack.

*All numbers are n (%) unless stated otherwise.

†$P \leq 0.05$.

that reported on a combination of hospitalized and non-hospitalized patients.[6,24] Higher rates of up to 6.9% have been reported in ICU populations or other selective populations.[5,25,26] In addition, the variation in ischemic stroke incidence may also be explained by other factors. First, most studies were performed in Asia and North America, with only a few European cohorts.[3–5,7] Geographic variation may explain some of the heterogeneity, with a higher incidence reported in Asia.[3] Second, regional differences in COVID-19 surges may have resulted in a higher threshold for seeking medical attention in pandemic areas, especially for patients with mild stroke symptoms. Third, in most studies, ischemic stroke was recorded as one of the various cardiovascular events, with case ascertainment often not performed by neurologists or stroke physicians.[6–8,27] This may have resulted in a systematic bias in the estimation of the cumulative stroke incidence among hospitalized patients with COVID-19 in these studies.

In contrast to some of the previous cohorts,[25,28] our findings suggest that patients with COVID-19 and

Table 2. Cumulative Incidence of Ischemic Stroke in Patients With and Without Treatment at an ICU, Stratified by Age and Sex

|	Total cohort, % (95% CI)	ICU treatment, % (95% CI)	General ward, % (95% CI)
All ischemic stroke patients	38/2147 (1.8 [95% CI, 1.3–2.4])	16/586 (2.7 [95% CI, 1.7–4.4])	22/1561 (1.4 [95% CI, 0.9–2.1])
Stratified by age			
<50 y	2/204 (1.0 [95% CI, 0.3–3.5])	2/49 (4.1 [95% CI, 1.1–13.7])	0/155 (0.0 [95% CI, 0–2.4])
50–69 y	11/816 (1.3 [95% CI, 0.8–3.5])	9/318 (2.8 [95% CI, 1.5–5.3])	2/498 (0.4 [95% CI, 0.1–1.5])
≥70 y	25/1127 (2.2 [95% CI, 1.5–3.3])	5/219 (2.3 [95% CI, 1.0–5.2])	20/908 (2.2 [95% CI, 1.4–3.4])
Stratified by sex			
Female	16/769 (2.1 [95% CI, 1.3–3.4])	6/157 (3.8 [95% CI, 1.8–8.1])	10/612 (1.6 [95% CI, 0.9–3.0])
Male	22/1378 (1.6 [95% CI, 1.1–2.5])	10/429 (2.3 [95% CI, 1.3–4.2])	12/949 (1.3 [95% CI, 0.7–2.2])

ICU indicates intensive care unit.
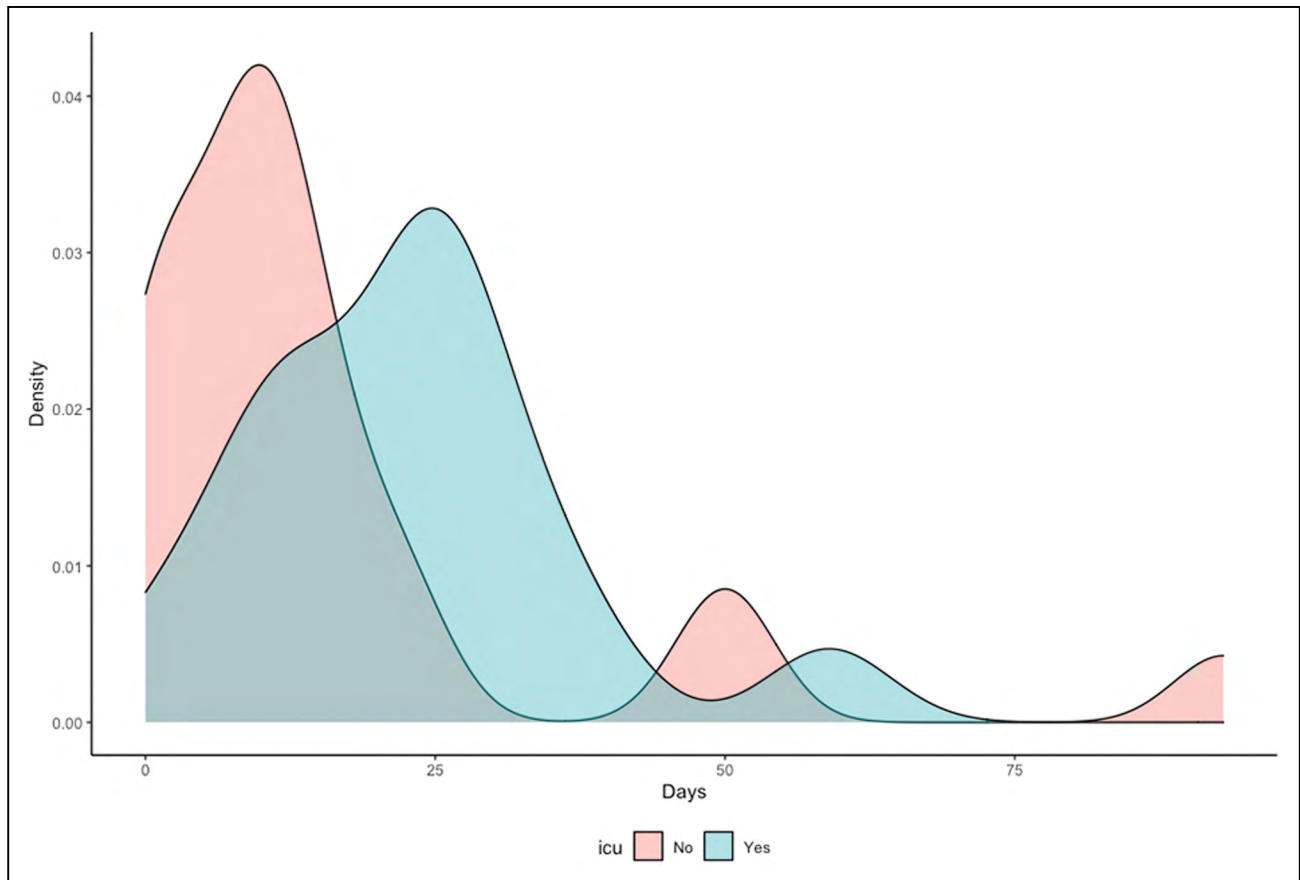
Figure 1. Median time between the onset of coronavirus disease 2019 (COVID-19) symptoms and diagnosis of ischemic stroke in patients treated at an intensive care unit (ICU) or on a general ward.

ischemic stroke did not have more cardiovascular risk factors than patients without a stroke. One explanation for this discrepancy may be that older patients with more vascular risk factors may not have been hospitalized or admitted to an ICU, because of treatment restrictions or patient preferences, which may have led to reduced survival rates in this group.[29] In addition, the greater severity of COVID-19 illness among hospitalized patients, especially those treated at an ICU, as well as the increased risk of medical complications during hospitalization, may, at least partially, have contributed to stroke risk in hospitalized COVID-19 patients without vascular risk factors.[30] To our knowledge, this is the first study to report on an association between PE and ischemic stroke in hospitalized patients with COVID-19.

Acute respiratory infections in general can act as a trigger for the short-term risk of ischemic stroke and myocardial infarction and are associated with a high risk of cardiovascular-related death.[31] Two recent studies have compared the occurrence of ischemic stroke in hospitalized patients with COVID-19 versus those with influenza. One study found that patients with COVID-19 appeared to have an increased stroke risk (COVID-19, 1.6%; influenza, 0.2%), whereas the other study found the risk of ischemic stroke to be similar in

patients with COVID-19 (1.2%) and influenza (1.2%).[9,28] In SARS-CoV and Middle-East Respiratory Syndrome, the occurrence of ischemic stroke has only been reported sporadically.[32] Pathophysiological mechanisms that could link COVID-19 to thromboembolic events include direct viral-induced endotheliitis, postinfectious immune-mediated responses, prothrombotic coagulopathy, and the occurrence of a hyperinflammatory state, with elevated D-dimer levels and antiphospholipid antibodies frequently found in patients with COVID-19 and thromboembolic complications.[2] Platelet counts varied across studies, but severe COVID-19 was often associated with thrombocytopenia.[2,25] Several studies have found that patients with COVID-19 who had ischemic stroke were more likely to die.[3–5] It remains unclear whether this association with an increased mortality is driven by disease severity and the prothrombotic state triggered by COVID-19. Other confounding factors, such as impeded functional recovery due to fever and infection and withdrawal of care in patients with COVID-19 and ischemic stroke, may also play a role.[33,34]

Our study has limitations. First, different forms of bias should be considered in observational research. Hospitalized patients with COVID-19, and in particular, those requiring treatment at an ICU, represent a selected group.

Table 3.   Characteristics of Ischemic Stroke in Patients With COVID-19 Treated at an ICU or on a General Ward

Characteristics*	Total cohort, % (n=38)	ICU treatment, % (n=16)	General ward, % (n=22)
Age, y; median (IQR)	74.5 (66.8–82.0)	66.5 (59.0–71.5)	80.5 (74.0–85.3)
Female sex	16 (42.1)	6 (37.5)	10 (45.5)
Prior antiplatelet use	10 (26.3)	3 (18.8)	7 (31.8)
Prior anticoagulant use	7 (18.4)	1 (6.3)	6 (27.3)
Time to diagnosis, d			
COVID-19 symptoms to stroke, median (IQR)	14.0 (8.5–24.8)	23.0 (13.3–28.5)	10.0 (2.8–17.5)
Stroke symptoms as presenting sign of COVID-19	4 (10.5)	1 (6.3)	3 (13.6)
NIHSS, median (IQR)	8.5 (3.0–23.8)	22.0 (3.8–30.0)	5.0 (2.8–17.5)
Hemisphere			
Left	17 (44.7)	7 (43.8)	10 (45.5)
Right	12 (31.6)	4 (25.0)	8 (36.4)
Both	6 (15.8)	5 (31.3)	1 (4.5)
Infratentorial	3 (7.9)	0	3 (13.6)
Large vessel occlusion			
Yes	10 (26.3)	3 (18.8)	7 (31.8)
No	11 (28.9)	7 (43.8)	4 (18.2)
No CTA†	17 (44.7)	6 (37.5)	11 (50.0)
Treatment			
IVT	2 (5.3)	1 (6.3)	1 (4.5)
EVT	5 (13.2)	2 (12.5)	3 (13.6)
Antiplatelet therapy	16 (42.1)	8 (50.0)	8 (36.4)
Anticoagulation	10 (26.3)	4 (25.0)	6 (27.3)
Etiology			
Large artery atherosclerosis	3 (7.9)	2 (12.5)	1 (4.5)
Cardioembolism	11 (28.9)	3 (18.8)	8 (50.0)
Small vessel occlusion	4 (10.5)	1 (6.3)	3 (13.6)
Other etiology	2 (5.3)	0	2 (9.1)
Undetermined etiology†	18 (47.4)	10 (62.5)	8 (50.0)
Occurrence of another cardiac or TE event‡	10 (26.3)	8 (50.0)	2 (9.1)
Outcome			
Unfavorable outcome§	27 (71.1)	11 (68.8)	16 (72.7)
In-hospital mortality	20 (52.6)	7 (43.8)	13 (59.0)

COVID-19 indicates coronavirus disease 2019; CTA, computed tomography angiogram; EVT, endovascular therapy; ICU, intensive care unit; IQR, interquartile range; IVT, intravenous therapy; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; PE, pulmonary embolism; and TE, thromboembolic.

*All numbers are n (%) unless stated otherwise.

†In 17 patients, no CTA was performed for the following reasons: 6 of 17 patients were moribund, 7 of 17 patients had no indication for CTA, and 4 of 17 patients had a carotid ultrasound instead. Large vessel occlusion was defined as an occlusion of the intracranial ICA with or without the terminal bifurcation, M1 and M2 segment of the middle cerebral artery, A1 or A2 segment of the anterior cerebral artery, vertebral artery, basilar artery, or P1 or P2 segment of the posterior cerebral artery.

‡Deep venous thromboembolism, PE, atrial fibrillation, cardiac ischemia, and endocarditis

§mRS score of ≥3 at discharge.

Numerous factors may have influenced whether patients sought emergency care, were admitted to a hospital, and received intensive treatment. Some patients with COVID-19 and ischemic stroke may have died before reaching the hospital, and milder affected patients or those with treatment restrictions may have stayed at home.[35] This may have underestimated the overall rate of ischemic stroke in patients hospitalized with COVID-19. In addition, we used data from a registry primarily set up to detect cardiac and thromboembolic complications in patients with COVID-19. To assure complete and systematic case ascertainment for ischemic stroke, medical records of all eligible patients were revisited by neurologists or other physicians with experience in stroke research. The high caseload of COVID-19 patients in some hospitals, in combination with contagion containment and sedation on an ICU, may
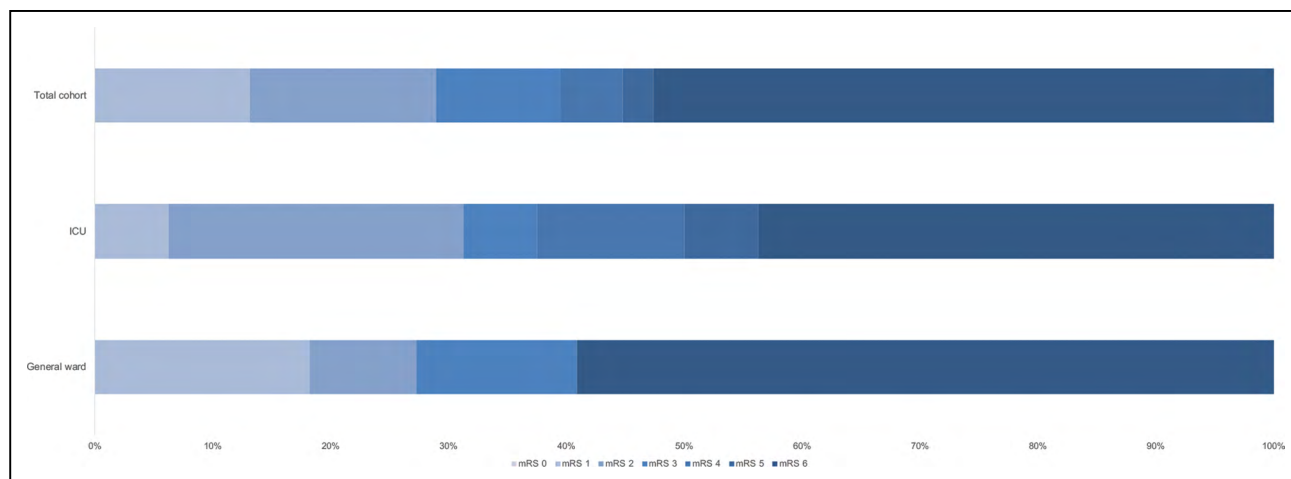
Figure 2. Outcome of ischemic stroke in patients with coronavirus disease 2019 (COVID-19) assessed with the modified Rankin Scale (mRS) at discharge in patients with and without treatment at an intensive care unit (ICU).

have impeded imaging investigations to diagnose ischemic strokes, especially among moribund patients. This may have resulted in an overestimation of the percentage of strokes with undetermined etiology. Among patients with PE and ischemic stroke, the diagnostic workup to rule out a patent foramen ovale was often not performed. In contrast, the relatively large proportion of patients with a cardioembolic etiology may reflect the accessibility of telemetry. In addition, laboratory findings should be interpreted with caution, as these were recorded in different stages of the disease and D-dimers were only selectively tested. Furthermore, as ischemic stroke was the primary outcome of this study, we did not report data on other neurological complications, such as intracerebral hemorrhage and cerebral venous thrombosis.[2] Finally, we only included patients with COVID-19 admitted during the first wave of the pandemic and were unable to adjust for changes in management and treatment strategies that occurred over time. This may hamper the generalizability of our results to later phases of the pandemic. A recent comparison between the second and first waves in the Netherlands has shown a decline in in-hospital mortality rates of patients with COVID-19.[7] Due to the novelty of this pandemic, comparisons with hospital populations from previous years and across different waves should, however, be interpreted with caution.[7,36] The main strength of the CAPACITY-COVID consortium is that it is a multidisciplinary collaborative effort to systematically record thromboembolic complications in patients with COVID-19 in a longitudinal fashion. By incorporating STROCORONA, we were able to extend this large registry with cerebrovascular expertise and detailed ischemic stroke data and to link various cardiovascular complications in hospitalized patients with COVID-19.

CONCLUSIONS

In conclusion, the overall cumulative incidence of ischemic stroke in hospitalized patients with COVID-19 was ≈2%, with a higher risk in patients treated at an ICU. The finding that patients with COVID-19 and ischemic stroke were twice as likely to have PE than patients without stroke warrants further investigation. Our findings underscore the importance of appropriate antithrombotic strategies and increased awareness of stroke symptoms in hospitalized patients with COVID-19.

Affiliations

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Disclosures

Supplemental Materials

Online Figures I and II
Online Tables I–XI
References [37,38]

APPENDIX

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