Title page

Risk, clinical course and outcome of ischemic stroke in patients hospitalized with COVID-19: a multicenter cohort study

Cover title: Risk and outcome of ischemic stroke in hospitalized COVID-19 patients

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Abstract

Background and purpose

The frequency of ischemic stroke in patients with 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 infection admitted in 16 Dutch hospitals participating in the international CAPACITY-COVID registry between March 1st and August 1st, 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 (ICU). 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 onset of COVID-19 symptoms and diagnosis of stroke was two weeks. The incidence of ischemic stroke was higher among patients who were treated at an ICU (16/586; 2.7% versus non-ICU: 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 RR: 2.08; 95%CI:1.52-2.84). Twenty-seven patients with ischemic stroke (71.1%) died during admission or were functional dependent at discharge. Patients with ischemic stroke were at a

higher risk of in-hospital mortality (adjusted RR 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 approximately 2%, with a higher risk in patients treated at an ICU. The majority of stroke patients had a poor outcome. The association between ischemic stroke and pulmonary embolism warrants further investigation.

Non standard Abbreviations and Acronyms

COVID-19: Coronavirus disease 2019

ICU: Intensive Care Unit

PE: Pulmonary embolism

AF: Atrial fibrillation

NIHSS: National Institutes of Health Stroke Scale

IVT: Intravenous thrombolysis

EVT: Endovascular therapy

TOAST: Trial of Org 10172 in Acute Stroke Treatment

mRS: modified Rankin Scale

IQR: Interquartile range

SD: Standard deviation

CI: Confidence interval

RR: Risk ratio

Introduction

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 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.

Methods

Study design

This study was conducted within the CAPACITY-COVID international patient registry (www.capacity-covid-eu; 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 (ISARIC) 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 was incorporated as a substudy within CAPACITY-COVID, to obtain additional information on neurovascular history and the occurrence of ischemic stroke during hospitalisation, 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 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 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 1st to August 1st, 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, pre-hospital 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 (DVT), pulmonary embolism (PE), acute coronary syndrome (ACS), endocarditis, and new-onset atrial fibrillation (AF). 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 hospitalisation. 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 more than 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 if 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 (NIHSS) and collected data on acute stroke treatment (intravenous thrombolysis (IVT), endovascular treatment (EVT) 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 Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria and scored stroke outcome at discharge with the modified Rankin Scale (mRS).[22]

Statistical analysis

Baseline characteristics are summarized with descriptive statistics as median (interquartile range; IQR), mean (standard deviation; SD), or frequencies (proportions) where appropriate. We performed a quality check of the dataset and recoded entry errors as missing data. We did not impute missing values (Supplementary Table I). We calculated the cumulative incidence of ischemic stroke with corresponding 95% confidence intervals (95% CI) and stratified

results according to age and sex. Since three 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's t-tests as appropriate and calculated risk ratios (RR) with Poisson regression.[23] We adjusted RRs 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 (mRS of ≥3)) at discharge. We report our findings in accordance with the RECORD guidelines (Supplement, Table II).

Results

We included a total of 2147 patients in STROCORONA (Supplementary Figure I). Table 1 shows the baseline characteristics. The median age was 70.0 years (IQR: 59.0-77.0), about one-third of the patients was 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 (Supplementary Table III). 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 pre-hospital medication (Table 1 and Supplementary Table IV). After stratification by age no differences in cardiovascular risk factors between patients with and without ischemic stroke were found (Supplementary Table V). In a sensitivity analysis excluding three hospitals that excluded patients without cardiovascular risk factors or cardiologist consultation, baseline characteristics and cumulative stroke incidence were similar (Supplementary Table VI). The median time between 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 and 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 are 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 NIHSS 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 Supplementary Table VII and an overview of the available laboratory, imaging, telemetry, and other investigations in each patient is provided in Table VIII of the Supplement. The occurrence of other cardiovascular complications in patients with and without ischemic stroke is given in the Supplement (Table IX). Pulmonary embolism was more common in patients with ischemic stroke (8/38 (21.1%) vs 160/2109 (7.6%); p=0.002), also after adjustment for age, sex, and treatment on an ICU (aRR 2.08; 95% CI: 1.52-2.84). Patients with PE and ischemic stroke had higher median platelet counts at baseline ($285x10^9$/L; IQR: 223-556) than patients with PE without ischemic stroke ($230x10^9$/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 5/8 (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 mRS of ≥3 or more at discharge (Figure 2). Patients with ischemic stroke were at a higher risk of in-hospital mortality (adjusted RR 1.56; 95% CI: 1.13-2.15) than patients without ischemic stroke. Age- and sex-stratified cumulative in-hospital mortality is shown in Supplementary Table X. A timeline of admissions and in-hospital mortality during the first wave is given for the participating centers in The Netherlands in Supplementary Figure II.

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 to patients without ischemic stroke. In addition, patients with ischemic stroke were twice as likely to have pulmonary embolism 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 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] Geographical 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 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 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 the 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 pulmonary embolism 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. 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 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 pulmonary embolism and ischemic stroke, the diagnostic work-up 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 wave 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 extent this large registry with cerebrovascular expertise and detailed ischemic stroke data and to link various cardiovascular complications in hospitalized patients with COVID-19.

Conclusion

In conclusion, the overall cumulative incidence of ischemic stroke in hospitalized patients with COVID-19 was approximately 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 pulmonary embolism 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.

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Supplement

Figure I-II

Table I-XI

References 37-38

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Figure legends

Figure 1

Title: Median time between onset of COVID-19 symptoms and diagnosis of ischemic stroke in patients treated at an ICU or on a general ward

Figure 2

Title: Outcome of ischemic stroke in patients with COVID-19 assessed with the modified Rankin Scale at discharge in patients with and without treatment at an ICU

Abbreviations: ICU = Intensive Care Unit, mRS = modified Rankin Scale.

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, years (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/m^2 (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

*All numbers are n (%) unless stated otherwise

Abbreviations: IQR = interquartile range, SD = standard deviation, BMI = body mass index, COPD = chronic obstructive pulmonary disease, TIA = transient ischemic attack.

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; 1.3-2.4)	16/586 (2.7; 1.7-4.4)	22/1561 (1.4; 0.9-2.1)
Stratified by age			
<50 years	2/204 (1.0; 0.3-3.5)	2/49 (4.1; 1.1-13.7)	0/155 (0.0; 0-2.4)
50-69 years	11/816 (1.3; 0.8-3.5)	9/318 (2.8; 1.5-5.3)	2/498 (0.4; 0.1-1.5)
≥70 years	25/1127 (2.2; 1.5-3.3)	5/219 (2.3; 1.0-5.2)	20/908 (2.2; 1.4-3.4)
Stratified by sex			
Female	16/769 (2.1; 1.3-3.4)	6/157 (3.8; 1.8-8.1)	10/612 (1.6; 0.9-3.0)
Male	22/1378 (1.6; 1.1-2.5)	10/429 (2.3; 1.3-4.2)	12/949 (1.3; 0.7-2.2)

Abbreviations: CI = confidence interval.

Table 3. Characteristics of ischemic stroke in patients with COVID-19 treated at an ICU or on a general ward

Characteristics*	**Total cohort (%)**	**ICU treatment (%)**	**General ward (%)**
	n=38	**n=16**	**n=22**
Age, years (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 (days)			
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 CT angiography†	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)
Cardio-embolism	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)

Unfavorable outcome§	27 (71.1)	11 (68.8)	16 (72.7)
In-hospital mortality	20 (52.6)	7 (43.8)	13 (59.0)

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

† In 17 patients no CT angiogram was performed for the following reasons: 6/17 patients were moribund, 7/17 patients had no indication for CTA and 4/17 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/or M2 segment of the MCA, A1 and/or A2 segment of the ACA, VA, BA, or P1 and/or P2 segment of the PCA.

‡ Deep venous thromboembolism, pulmonary embolism, atrial fibrillation, cardiac ischemia and endocarditis

§ mRS of ≥3 at discharge.

Abbreviations: IQR = interquartile range, NIHSS = national institute of health stroke scale, IVT = intravenous therapy, EVT = endovascular therapy, TE = thromboembolic.

Appendix

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