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Impact of COVID-19 pandemic on acute stroke care in a tertiary stroke centre

Máté Héja[1]✉, István Fekete[1], Sándor Márton[2], László Horváth[3] & Klára Fekete[1]

The aim of this study was to evaluate how COVID-19 affected acute stroke care and outcome in patients with acute ischemic or hemorrhagic stroke. We performed a retrospective analysis on patients who were admitted with acute ischemic (AIS) or hemorrhagic (ICH) stroke from September 2020 to May 2021 with and without COVID-19. We recorded demographic and clinical data, imaging parameters, functional outcome and mortality at one year. Beside descriptive statistics we performed χ^2-probe, Mann-Witney U-test, Student t-probe and multivariate testing. We found a 29%-reduction in the number of AIS cases during the pandemic. The number of the large vessel occlusions /LVOs/ ($N=83$, 41.7%), from them 37 (17.7%) had mechanical thrombectomy (MT), was higher than before the COVID-19 period ($p=0.02$ and $p=0.001$, respectively). From all patients needing acute revascularization therapy ($N=137$) 118 patients received it, among them 20 (16.9%) had COVID-19. Those positive for COVID-19 were more likely to have a higher median NIHSS score at baseline and at 24 h ($p=0.02$ and $p=0.03$, respectively). They also had a lower rate of favourable outcome at discharge (15% vs. 41.8%; $p=0.024$) and at three months (25% vs. 52%, $p=0.02$), longer median hospitalization ($p<0.0001$), and a higher mortality rate (52% vs. 25%; $p=0.03$). The incidence of symptomatic intracerebral hemorrhage (sICH) did not differ between the groups. Regarding the ICH patients, NIHSS score at 24 h ($p=0.036$), mortality at 3 months ($p=0.004$) and at one year ($p=0.00$) were higher in the COVID-19 group. We concluded that the pandemic resulted fewer admission due to AIS with an increased number of LVOs and MTs. AIS patients with concomitant SARS-CoV-2 infection have more severe strokes and unfavorable long term outcome. The risk of sICH was not increased in COVID-19 positive patients therefore reperfusion therapies appear to be safe and beneficial for some individuals. Patients with ICH and comorbid COVID-19 have a very poor prognosis.

Keywords ischemic stroke, hemorrhagic stroke, COVID-19, reperfusion therapy, outcome

The World Health Organization (WHO) declared coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) as a pandemic on 11 March 2020. By the end of May 2021, having reported 83 thousand cumulative COVID-19 cases per million people, Hungary was one of Europe's most severely affected countries. COVID-19 not only caused a dramatic surge of respiratory infections worldwide, but it also had an impact on acute stroke care.

Early observations in several countries reported a reduction in admissions for acute ischemic stroke by as much as 50% and, in some cases, even 88%[1-3]. Furthermore, international surveys conducted by the World Stroke Organization (WSO) highlighted that in the vast majority of stroke centers the number of revascularization treatments significantly decreased, and the time from stroke onset to reperfusion treatment increased[4]. Despite the fall in stroke admissions, it was suggested that COVID-19 infections could cause stroke, and stroke patients appeared to be more susceptible to severe infection[4]. Several studies showed that patients with acute ischemic stroke (AIS) occurring with concomitant SARS-CoV-2 infection had more severe strokes and unfavorable functional outcomes after three months of follow-up[5–7]. Moreover, patients with stroke-related vascular risk factors such as hypertension, diabetes mellitus, and previous cardiac or cerebrovascular disease were at an increased risk of mortality and morbidity by COVID-19 [8]. Relatively few studies provided safety and efficacy data on reperfusion therapies - intravenous thrombolysis (IVT) and endovascular treatment - in stroke patients

[1]Department of Neurology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary. [2]Faculty of Arts, Institute of Political Science and Sociology, University of Debrecen, Debrecen, Hungary. [3]Department of Pharmaceutical Surveillance and Economics, Faculty of Pharmacy, University of Debrecen, Debrecen, Hungary. ✉email: heja.mate@med.unideb.hu

with COVID-19. These data suggested that reperfusion therapies on AIS in patients with COVID-19 appeared to be safe; however, functional outcomes were significantly worse, and the three-month mortality was higher[9].

Spontaneous intracerebral hemorrhage (ICH) is a devastating disease with high mortality and morbidity. The clinical outcomes of ICH patients with COVID-19 infection are not fully known, but recent multicenter studies suggested that concomitant COVID-19 will prolong the hospital stay and further increase the mortality in this population[10–12].

In our study, we sought to evaluate the impact of the COVID-19 outbreak on acute care in our stroke center during two epidemic waves. We also compared the clinical characteristics and functional outcomes of AIS and ICH in patients with or without SARS-CoV-2 infection.

Methods

Study design

We performed a retrospective analysis of all acute stroke patients (ischemic or hemorrhagic) admitted to a tertiary stroke center, i.e. the Neurological Intensive Care Unit at the University of Debrecen, from 1 September 2020 to 31 May 2021. The first SARS-CoV-2 infection occurred in Hungary on 4 March 2020 (10th week of 2020) isolated. Based on the epidemic's dynamic in Hungary, the first wave of the epidemic can be attributed to the period between March 4 and July 17 (29th week of 2020). In terms of case numbers, in contrast to Western European countries, the first wave was characterized by a flat curve, most infections occurred in geographical hot spots (Budapest, Pest county) and the number of hospitalized patients did not increase, thanks to strict isolation rules. Practically, this was a very special period, without increase in patient number, this was a silent period. Therefore, in terms of acute stroke care, there was no significant difference compared to the COVID-free periods. The second wave of pandemic in Hungary occurred between August 10 (32th week of 2020) and December 20 (50th week of 2020). The first hotspots were in the capital, isolated, and in our region SARS COV2 infections occurred only in September, after people returning form their summer holidays. The second wave was different from the first wave, namely the number of SARS-CoV-2 infections and deaths were substantially higher and the pressure on the healthcare system was intense. The third wave of epidemic can be attributed to the period between February 17 (6th week of 2021) and May 31 (21th week of 2021) [13–14]. Based on the epidemic's dynamics, the study period represented the second and third waves of the COVID-19 pandemic in Hungary.

Our center receives patients from an area of approximately 90 km in diameter. The density of the population in the catchment area is 600,000 inhabitants and the annual hospitalization for acute stroke falls in the range of 600–700.

Regarding the AIS patients, we compared the number of cases, demographic data, the rate of intravenous and endovascular therapies, and logistic parameters of stroke with those of the patients admitted in the corresponding periods in the previous two years (from 1 September 2018 to 31 May 2019, and from 1 September 2019 to 31 May 2020). In addition, we assessed whether the vascular risk factors, stroke severity, functional outcome, and mortality in patients with acute ischemic stroke treated with intravenous thrombolysis and/or mechanical thrombectomy differed in the groups of patients with and without SARS-CoV-2 infection. From the 198 patients transferred to our centre with the referral diagnosis of stroke, 48 patients were excluded from the data analysis, because of insufficient or missing data. By them revascularization therapy was not an option (e.g. non-disabling symptoms, verified later as TIA, and/or other diseases). These patients were transferred to another hospital/department or discharged in accordance with current regulations after rapid imaging and laboratory testing. We had sufficient data from 150 patients, 118 patients were diagnosed with AIS and 32 with ICH.

The study was approved by the Regional and Institutional Ethics Committee of University of Debrecen Clinical Centre (protocol number: 5473 – 2020). All methods were performed in accordance with the relevant guidelines and regulations. Written informed consent was obtained from all participants and/or their legal guardians.

Database

The following variables were recorded for all patients: demographic data (age and sex), vascular risk factors (hypertension, diabetes mellitus, atrial fibrillation, hyperlipidemia, prior stroke, congestive heart failure), prior antithrombotic medication, stroke severity, stroke subtype, occurrence of large vessel occlusion (LVO), treatment modality, time parameters of stroke (onset-to-treatment time [OTT], door-to-needle time [DNT], door-to-groin time [DGT]), rate of symptomatic intracranial hemorrhage (sICH), functional outcome at discharge and at three months, and one year mortality. Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS) on admission and 24 h later. NIHSS scores were presented as medians (1.;3.quartile). The ischemic stroke subtype was classified according to the Trial of ORG 10,172 in Acute Stroke Treatment Criteria (TOAST)[15]. The modified Rankin scale (mRS) was used to evaluate the functional outcome at discharge and at three months. The outcome was considered favorable when the score was 0–2, unfavorable outcome was mRS 3–6. At one year, the outcome was labeled as "dead" or "alive".

Imaging

All patients underwent non-contrast CT on admission. Arterial occlusion (trunk or at least one branch of any large artery) was identified by CT-angiography. The Alberta Stroke Programme Early CT Score (ASPECTS) was determined on admission and at 24 h, unblinded to patient characteristics, and was stratified to <7; 7–9 and 10. To evaluate hemorrhagic transformation, CT was repeated 24 h after treatment and in case of clinical deterioration. Intracranial hemorrhage was defined as presence of any hemorrhage within the intracranial vault. Regarding the symptomatic intracranial hemorrhage we used three definitions: the SITS, the ECASS and the

RCT NINDS criteria [16]. In case of clinical suspicion, an additional chest computed tomography was also performed simultaneously with the neuroimaging to rule out COVID-19 pneumonia.

Treatment

IVT was performed in accordance with the ESO guidelines[17]. The total amount of rt-PA was 0.9 mg/kg body weight (maximum 90 mg), with 10% of the dose given as a bolus followed by an infusion over 60 min using a syringe pump. Continuous monitoring of neurological status, pulse, blood pressure, temperature and oxygen saturation was performed according to guideline recommendations[18]. In patients diagnosed with LVO, the treatment started intravenously and was followed by mechanical thrombectomy (MT) and in patients not otherwise candidates for IVT, MT was used alone. Stent retriever thrombectomy was the first-line approach by using 3 × 20 mm or 4 × 30 mm TREVO retriever devices (Stryker Neurovascular). If the occluded blood vessel had a significant stenosis or other lesions after mechanical thrombectomy with stent retriever, the neurointerventionalist decided whether to perform aspiration thrombectomy, balloon dilatation, stent implantation or another rescue therapy based on the subject's clinical conditions. The procedure was performed by a qualified neurointerventional radiologist. Modified Thrombolysis in Cerebral Infarction (mTICI) classification was used to evaluate the rate of recanalization.

At our stroke centre, we aim to perform mechanical thrombectomy for patients with anterior circulation stroke under conscious sedation using short-acting anaesthetic drugs such as midazolam, fentanyl or propofol based on the choice of anaesthesiologist in the thrombectomy team having expertise in both (general/local) methods. In our cohort, only two patients with anterior circulation stroke underwent general anaesthesia due to severe agitation or vomiting during the procedure. On the other hand, in patient with posterior circulation stroke, especially in basilar artery occlusion, we usually apply general anaesthesia because of potential higher risk of aspiration due to the impairment of coughing reflex, and to fully immobilize the patient to reduce the risk of procedural complications and shortening the time to recanalization.

Regarding the ICH patients, all of them received conservative treatment. Mannitol has been used to reduce acutely elevated intracranial pressure. In patients with anticoagulant-associated hemorrhage reversal of anticoagulant effect has been made with specific antidote or prothrombrin complex concentrate. Patients underwent neurosurgical procedure (ventricular drain implantation, hematoma evacuation) were excluded.

COVID-19 screening and diagnosis

In our catchment area, all potential stroke patients who were candidates for revascularization treatment were referred by paramedics to the neurologist on-duty. The neurologist obtained information about the patient during the referral. Initial screening for SARS-CoV-2 infection was performed during this phone call and included evaluation for recent SARS-CoV-2 exposure, history of fever or respiratory symptoms and vaccination status. After the patients' arrival, nasopharyngeal swab specimens were obtained and tested for SARS-CoV-2 infection by reverse transcription polymerase chain reaction (rt-PCR). Until the results arrive, the patients were isolated in the so-called „gray zone" wards. According to the local regulations, if the PCR test was positive, patients were transferred to the hospital designated for the care of patients positive for COVID[19].

Statistical analysis

Statistical analysis was carried out using the SPSS for Windows 19.0 program suite (SPSS Inc. Chicago, USA). Means, medians and standard deviations were calculated using descriptive statistic methods. Continuous data were compared using the Student *t* test in normally distributed variables and the Mann–Whitney *U* test if the variables were not normally distributed. Categorical data were compared using contingency tables, however the $\chi 2$ test, or the Fisher exact test were chosen if one cell had an expected count of less than five. All tests were performed at a significance level of $p < 0.05$. Logistic regression models were used to identify the independent predictors of 3-month disability. The analysis was performed with the multivariate general linear model. In the models, disability at 3 months (mRS > 2 was the dependent variable, and the factors found to be associated with outcome by univariate analyses were entered as confounding variables. The variables were excluded from the analysis one by one, and the variable with $p > 0.05$ and closest to 1.0 was removed, until all features left in the model had $p > 0.05$[18].

Results

Clinical characteristics of AIS patients before and during the COVID-19 pandemic

While in the examined period of 2020/21 we treated 198 stroke patients, in the similar periods of the previous two years we treated 277 and 260 patients, respectively *(*Fig. 1*)*. Compared with the average of the previous two years, this represented a 29% decrease in the number of patients admitted due to AIS. From the 150 patients included in the data analysis 118 were suitable for revascularization therapy. Based on NIHSS score, there were no differences in age, sex and stroke severity between the groups of patients treated before and during the COVID-19 pandemic. The incidence of LVOs was significantly higher in the COVID-19 period compared with that of the previous years ($p = 0.043$ and $p = 0.042$, respectively). The ratio of IVTs did not differ significantly in the COVID-19 period. However, we observed a significant increase in the number of mechanical thrombectomies in the COVID-19 period ($p = 0.0004$ and $p = 0.0006$, respectively). No differences were found in the time parameters of AIS care, i.e. OTT, DNT and DGT. The detailed data are provided in Table 1.

Baseline characteristics of AIS patients positive or negative for COVID-19

The detailed bivariate analysis between AIS patients positive or negative for COVID-19 is shown in Table 2. A total of 118 patients with AIS underwent recanalization treatment in our department during the study period, of

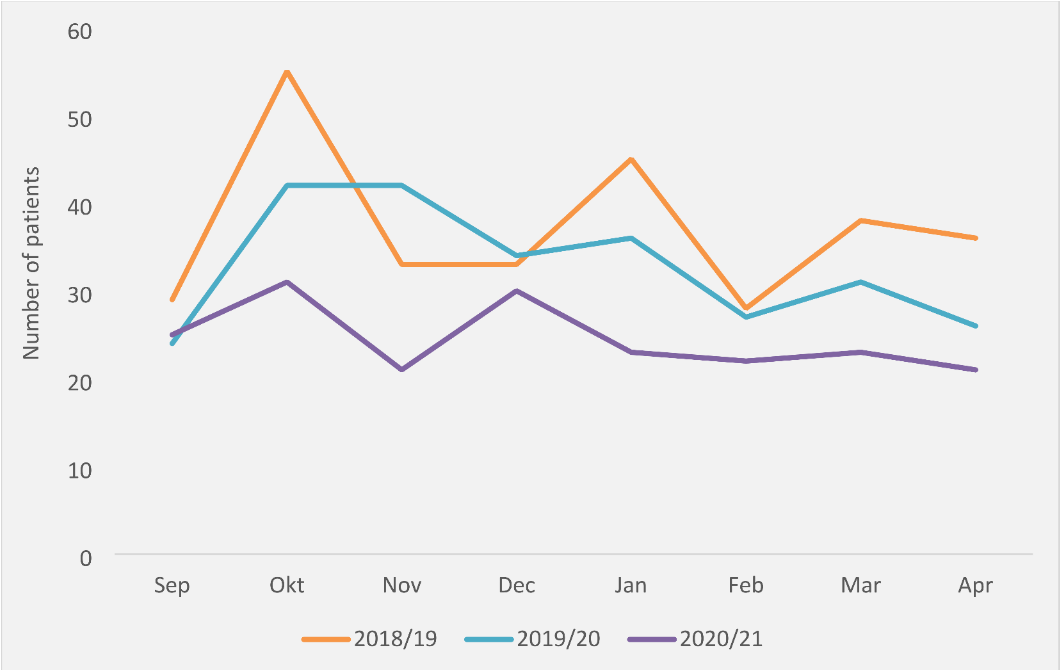


Fig. 1. Number of AIS patients admitted to our Stroke Center before and during the COVID-19 pandemic (AIS: Acute ischemic stroke; COVID-19: Coronavirus disease-19).

		Treatment period		*p*-value
Variable	**Sep 2018 – May 2019**	**Sep 2019 – May 2020**	**Sep 2020 – May 2021**	
Number of cases, n	277	260	198	-
Gender, male, n (%)	149 (53.7)	133 (51.2)	98 (49.5)	0.355[a] 0.725[b]
Age (years), mean ± SD	70.9 ± 11.7	68.5 ± 12.9	67.5 ± 13.3	0.262[a] 0.874[b]
NIHSS score on admission, median (1;3 quartile)	10 (5.25;14)	8 (5;13)	10 (5;15)	0.652[a] 0.280[b]
Mild stroke (NIHSS 1–4), n (%)	37 (13.4)	52(20)	39 (19.7)	0.063[a] 0.936[b]
Moderate stroke (NIHSS 5–15), n (%)	172 (62.1)	149 (57.3)	117 (55.6)	0.467[a] 0.749[b]
Moderate to severe stroke (NIHSS 16–20), n (%)	54 (19.5)	45 (17.3)	29 (14.6)	0,170[a] 0.443[b]
Severe stroke (NIHSS 21–42), n (%)	14 (5)	14 (5.4)	13 (6.6)	0.483[a] 0.594[b]
Large vessel occlusion, n (%)	***91 (32.8)***	***85 (32.6)***	***83 (41.7)***	***0.043***[a] ***0.042***[b]
Intravenous thrombolysis, n (%)	105 (37.9)	98 (37.8)	83 (41.7)	0.361[a] 0.359[b]
Mechanical thrombectomy, n (%)	***20 (7.2)***	***19 (7.3)***	***35 (17.7)***	***0.0004***[a] ***0.0006***[b]
Onset to needle time (min), median ± SD	165 ± 70.8	152 ± 63.6	153.5 ± 58.6	0.262[a] 0.983[b]
Door to needle time (min), median ± SD	54 ± 16.8	50 ± 15.7	47 ± 20.2	0.113[a] 0.465[b]
Door to groin time (min), median ± SD	115 ± 73.6	108 ± 69.6	112 ± 91.2	0.152[a] 0.114[b]
Onset to recanalization time (min), median ± SD	273 ± 82.1	255 ± 79.3	257 ± 85.1	0.425[a] 0.963[b]

Table 1. Clinical characteristics before and during the COVID-19 pandemic. Correlation shown between parameters in Sep 2018-May 2019 and Sep 2020-May 2021[a], and Sep 2019-May 2020 and Sep 2020-May 2021[b]. Significant values are in bold and italics.

		Patient groups		
Variable	All patients ($n=118$)	negative for COVID-19 ($n=98$)	positive for COVID-19 ($n=20$)	p-value
Age (years), mean ± SD	67 ± 13.7	66.3 ± 14.1	69.9 ± 9.4	0.14
Gender, male, n (%)	63 (54)	51 (52)	12 (60)	0.51
Risk factors				
Hypertension, n (%)	82 (69.4)	68 (69.3)	14 (70)	0.956
Diabetes mellitus, n (%)	28 (23.7)	23 (23.4)	5 (25)	0.916
History of stroke, n (%)	25 (21.2)	19 (19.4)	6 (30)	0.366
Atrial fibrillation, n (%)	20 (16.9)	16 (16.3)	4 (20)	0.689
Congestive heart failure, n (%)	25 (21.2)	19 (19.4)	6 (30)	0.367
Hyperlipidemia, n (%)	37 (31.4)	31 (31.6)	6 (30)	0.886
≥ 2 risk factors, n (%)	68 (57.6)	56 (57.1)	12 (60)	0.813
Prior antithrombotic treatment				
Antiplatelets, n (%)	26 (22)	23 (23.5)	3 (15)	0.293
Anticoagulants, n (%)	19 (16.1)	15 (15.3)	4 (20)	0.602
Stroke subtype				
Atherothrombotic, n (%)	26 (22)	23 (23.5)	3 (15)	0.558
≥ 70% stenosis, n (%)	14 (11.9)	13 (13.3)	1 (5)	0.432
occlusion, n (%)	12 (10.2)	10 (10.2)	2 (10)	0.978
Cardioembolic, n (%)	45 (38.1)	37 (37.8)	8 (40)	0.850
Lacunar, n (%)	12 (10.2)	11 (11.2)	1 (5)	0.688
Other specific cause, n (%)	4 (3.4)	3 (3.1)	1 (5)	0.529
Cryptogenic, n (%)	28 (23.7)	22 (22.4)	6 (30)	0.469
Treatment modality, n (%)				
Intravenous thrombolysis, n (%)	83 (70.3)	67 (68.3)	16 (80)	0.357
Mechanical thrombectomy, n (%)	35 (29.7)	33 (33.7)	2 (10)	0.134
NIHSS score on admission, median (1;3 quartile)	***10 (5;14.5)***	***9 (5;14)***	***12 (9;17)***	***0.02****
Onset to needle time (min), median ± SD	146 ± 59.3	150 ± 60.8	132 ± 51	0.13
Door to needle time (min), median ± SD	44 ± 21.7	45 ± 17.8	42 ± 19	0.29
Door to groin time (min), median ± SD	110 ± 80.9	110 ± 86.5	112 ± 27.6	0.34
Onset to recanalisation (min), median ± SD	257.9 ± 85.1	251.6 ± 76.5	307.5 ± 173.24	0.19

Table 2. Baseline characteristics of patients negative or positive for COVID-19 in the AIS group. (AIS: Acute ischemic stroke; COVID-19: Coronavirus disease 19; NIHSS: National Institutes of Health Stroke Scale)

which 20 (16.9%) were COVID-19 positive. However, 19 patients had to be excluded from recanalization therapy due to exceeding the time window or extensive ischemic lesion visible in the CT on admission. Overall, the patients had a mean (± standard deviation) age of 67 ± 12 years on diagnosis, and more than half of them were males (63/118; 54%). There were no significant differences in age and sex between the groups of patients positive or negative for COVID-19. Hypertension was the most remarkable risk factor in our cohort (69.4%) followed by hyperlipidemia (31.4%) and diabetes (23.7%). The majority of patients had multiple (≥ 2) coexisting risk factors (57.6%), with a minority having one risk factor only (23.7%) or no risk factors at all (18.6%). The two groups had similar risk factor profiles, except that the patients positive for COVID-19 were more likely to have prior strokes and congestive heart failure, but the differences were not statistically significant. Prior antithrombotic treatments were similar in both groups. As for the etiology of strokes, cardioembolic strokes accounted for most of the cases (38.1%), followed by cryptogenic (23.7%) and atherothrombotic causes (22%). Among the cardioembolic stroke patients with COVID-19, five (25%) had novel atrial fibrillation. In two patients, the chest CT revealed a thrombus in the left atrial appendage. Transthoracal echocardiography revealed a ventricular thrombus in one patient, and mitral valve vegetation in another patient. There were no significant differences between the two groups regarding the etiology of strokes. Figure 2 presents the distribution of strokes based on etiology in our cohort. Regarding the treatment modality, most of the patients (70.3%) received IVT. Out of the 56 patients with large artery occlusion, 35 underwent mechanical thrombectomy, which constitutes 29.7% of the entire patient population and 62.5% of all patients with large vessel occlusion. Out of the 56 patients with large artery occlusion, 35 underwent mechanical thrombectomy, which constitutes 29.7% of the entire patient population and 62.5% of all patients with large vessel occlusion. Among them, complete or near-complete (mTICI3 or mTICI2c) recanalization was achieved in 24 patients (68%): from them 2 patients were COVID-19 positive (8.3% within the group) and 22 were COVID-19 negative (91.7% within the group). While partial reperfusion (mTICI2a, 2b or 1) was achieved in 10 patients (29%), all of them were COVID-19 negative. No reperfusion was noted only in one patient. In some cases, we noticed that after a while, despite successful thrombectomy, rapid thrombus formation was observed in the distal small vessels, similar to ice flower formation in the COVID-19 group.

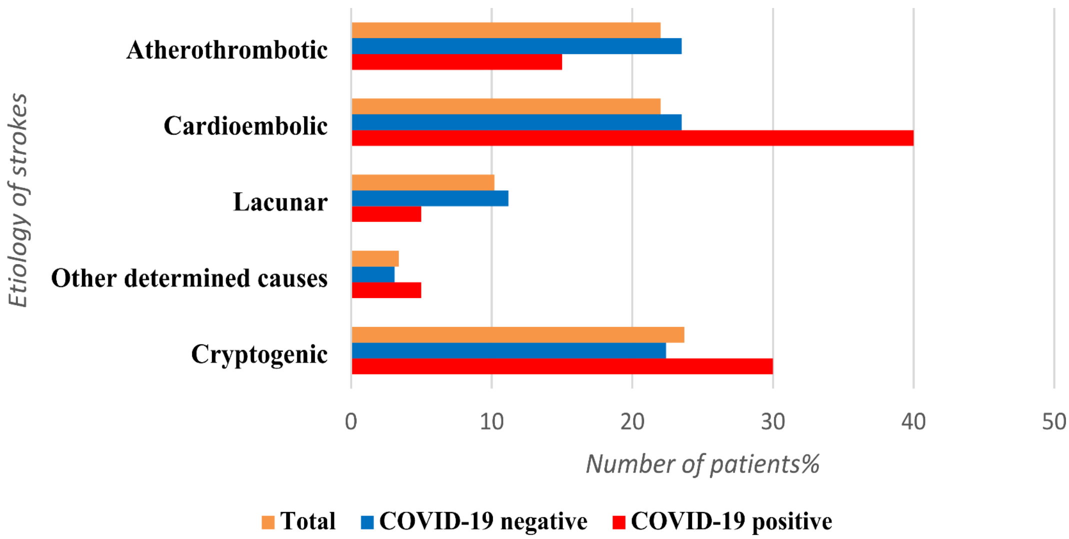


Fig. 2. Distribution of AIS based on the etiology (AIS: Acute ischemic stroke; COVID-19: Coronavirus disease 19).

The indication for mechanical thrombectomy was a joint decision with the interventional neuroradiologist in every case. In cases where mechanical thrombectomy was not indicated the main reasons were low ASPECT score, mild stroke symptoms (NIHSS score < 6) or technical considerations (occlusion of a distal artery branch, extensive thrombosis of the vessels). There were no significant differencies in the treatment modalities between the two groups. In terms of severity, patients positive for COVID-19 were more likely to have a higher median [1;3 quartile] NIHSS score (12 [9;7]), compared to the negative ones (9 [5;14]). The difference was statistically significant ($p = 0.02$). No significant differences were seen between the two groups regarding the time from symptom onset to treatment or the length of hospitalization.

Among the patients with confirmed SARS-CoV-2 infection, seven subjects (35%) presented with respiratory insufficiency ($pO2 < 60$ mmHg) requiring oxygen therapy during hospitalization. COVID-19 symptoms affecting our cohort included dyspnea (60%), fever (45%), fatigue (5%) and joint pain (5%). Six patients (30%) showed no symptoms of COVID-infection.

CT characteristics of AIS patients positive or negative for COVID-19

CT characteristics on admission and at 24 h are summarized in Table 3. Most strokes were located in the anterior circulation in both groups. In our cohort, 56 patients (47.5%) had LVO, among them 23.2% had multiple vascular territory LVO. Regarding the etiology, 22 patients (39,3%) had atrial fibrillation, while 5 patients (8,9%) had other cardioembolic source (valvular vegetation, heart thrombus). Atherothrombotic origin could be found in 12 patients (21,4%), while 2 patients (3,6%) had extracranial carotid artery dissection. In 14 patients (0,25%), no clear cause for the large vessel occlusion was identified, and therefore it was classified as cryptogenic. Among them 5 patient had COVID-19. There was no significant difference between the two groups regarding the occurrence of LVO. Most of the patients had ASPECT scores ≥ 7 on admission in both groups. At 24 h, more than half (57.1%) of the patients with COVID-19 had < 7 ASPECTS scores, while the corresponding figure in the other group was only 40.2%, the difference being statistically not significant. Regarding the hemorrhagic complications after revascularization treatment, ICH occurred in seven patients (5.9%), while sICH was detected in two patients (1.7%). Neither total ICH, nor sICH was significantly different between the two groups. Chest CT was performed in 78 patients on admission or within 24 h. Among them, pneumonia was detected in 15 patients (23%), of which six patients (40%) were confirmed to be positive for COVID-19. Other chest abnormalities found on the CT were as follows: pulmonary edema and/or hydrothorax in 19 patients (24.4%), cardiomegaly in 14 patients (17.9%), pulmonary emphysema in five patients (6.4%), lung tumor in two patients (2.5%) and concomitant pulmonary embolism in one patient (1.3%). Figure 3 presents the findings of the chest CT examinations.

Outcome of AIS patients

Table 4; Figs. 4 and 5 summarize the data of clinical outcomes. At 24 h, the patients with COVID-19 had higher median (1;3 quartile) NIHSS scores than the ones free from the disease the scores being 11 (8,75;15) and 7 (3;14), respectively. The difference was also statistically significant ($p = 0.03$). Based on the mRS score at discharge, significantly fewer patients ($p = 0.024$) had favorable outcomes (mRS: 0–2) in the group positive for COVID-19 compared to the group free from COVID-19. The median hospital stay was also significantly longer ($p < 0.0001$) in patients with the COVID-19 infection. Based on the 3-month follow-up, only 25% of patients in the group positive for COVID-19 had favorable outcomes, which was significantly worse ($p = 0.03$) compared to the group negative for COVID-19 (52%). In our cohort, we had an overall one-year mortality rate of 27.11% (32/118). The mortality rate in the group positive for COVID-19 was 50% (10/20), while the in the other group 22.45% (22/98),

		Patient groups		
Variable	All patients (n = 118)	negative for COVID-19 (n = 98)	positive for COVID-19 (n = 20)	p-value
Location of stroke				
Anterior circulation, n (%)	103 (87.3)	85 (86.7)	18 (90)	0.965
Posterior circulation, n (%)	15 (12.7)	13 (8.2)	2 (10)	0.975
Large vessel occlusion, n (%)	56 (47.5)	48 (49)	8 (40)	0.626
Cardioembolic, n (%)	27 (48.2)	24 (50)	3 (37.5)	0.701
Atherothrombotic, n (%)	13 (23.2)	12 (25)	0 (0)	-
Other specific cause, n (%)	2 (3.6)	2 (4.2)	0 (0)	-
Cryptogenic, n (%)	14 (25)	9 (18.8)	5 (62.5)	0.008
ASPECT score on admission, n (%)				
10	72 (70)	60 (70.6)	12 (60)	0.741
7–9	19 (20.3)	17 (20)	2 (20)	0.514
<7	102 (9.7)	8 (9.4)	4 (10)	0.216
ASPECT score at 24 h, n (%)				
10	30 (33)	27 (35.1)	3 (21.4)	0.373
7–9	22 (24)	16 (24.7)	3 (21.4)	1.0
<7	42 (43)	34 (40.2)	8 (57.1)	0.37
missing data	12 (11.6)	8 (9.4)	4 (20)	
Intracranial hemorrhage, n (%) sICH, n (%)	7 (5.9) 2 (1.7)	4 (4.1) 1 (1)	3 (15) 1 (5)	**0.06**

Table 3. CT parameters of patients negative or positive for COVID-19 in the AIS group (AIS: Acute ischemic stroke; ASPECTS: Alberta Stroke Program Early CT Score; COVID-19: Coronavirus disease 19; sICH: symptomatic intracranial hemorrhage).

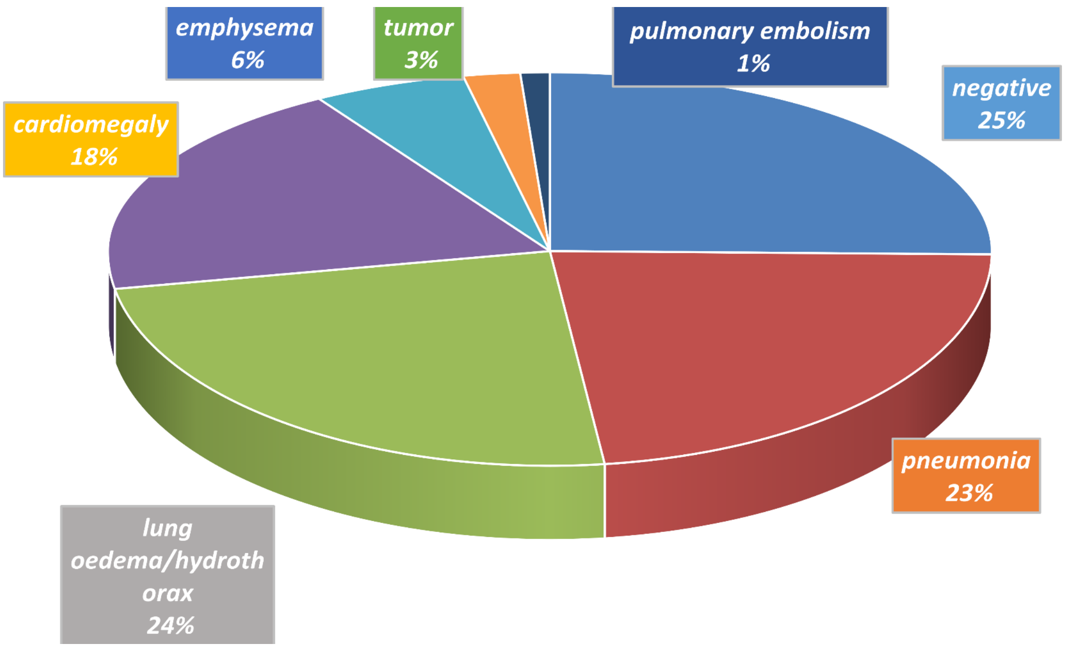


Fig. 3. Findings of the chest CT examinations in the whole cohort.

the difference being statistically significant (p = 0.024). Of the ten patients, six (60%) died from COVID-19 complications, and four patients (40%) died due to stroke complications. Of the aforementioned six patients, four died from severe pneumonia and multiorgan failure, one patient deceased due to pulmonary embolism, and one patient passed away because of disseminated intravascular coagulation with multiple thromboembolic events.

We compared the clinical outcomes and mortality rates based on the treatment status. Almost half of the patients (47.4%) without recanalization treatment were dead at three months, while the corresponding figure among patients with recanalization was 26.3% (p = 0.1). At one year, significantly fewer patients were alive

Patient groups				
Variable	All patients (n = 118)	negative for COVID-19 (n = 98)	positive for COVID-19 (n = 20)	p-value
NIHSS score at 24 h, median (1;3 quartile)	9 (3,5; 15)	7 (3;14)	11 (8,75;15)	***0.03***
mRS score at discharge				
Favorable outcome (mRS: 0–2), n (%)	44 (37.3)	41 (41.8)	3 (15)	***0.024***
Moderate/severe disability (mRS: 3–5), n (%)	50 (42.4)	39 (39.8)	11 (55)	*0.23*
Death (mRS = 6), n (%)	24 (20.3)	18 (18.4)	6 (30)	*0.24*
Hospital stay (day), median (1;3 quartile)	9 (5;17.5)	7(5;13)	26 (18;36)	**< *0.0001***
mRS score at 3 months				
Favorable outcome (mRS: 0–2), n (%)	56 (47.4)	51 (52)	5 (25)	***0.03***
Moderate/severe disability (mRS: 3–5), n (%)	25 (21.2)	20 (20.4)	5 (25)	0.76
Death (mRS = 6), n (%)	31 (26.3)	23 (23.5)	8 (40)	0.16
missing data, n (%)	6 (5.1)	4 (4.1)	2 (10)	
Mortality at one year	32 (27.1)	22 (22.4)	10 (50)	***0.024***
missing data	9 (7.6)	7 (7.1)	2 (10)	

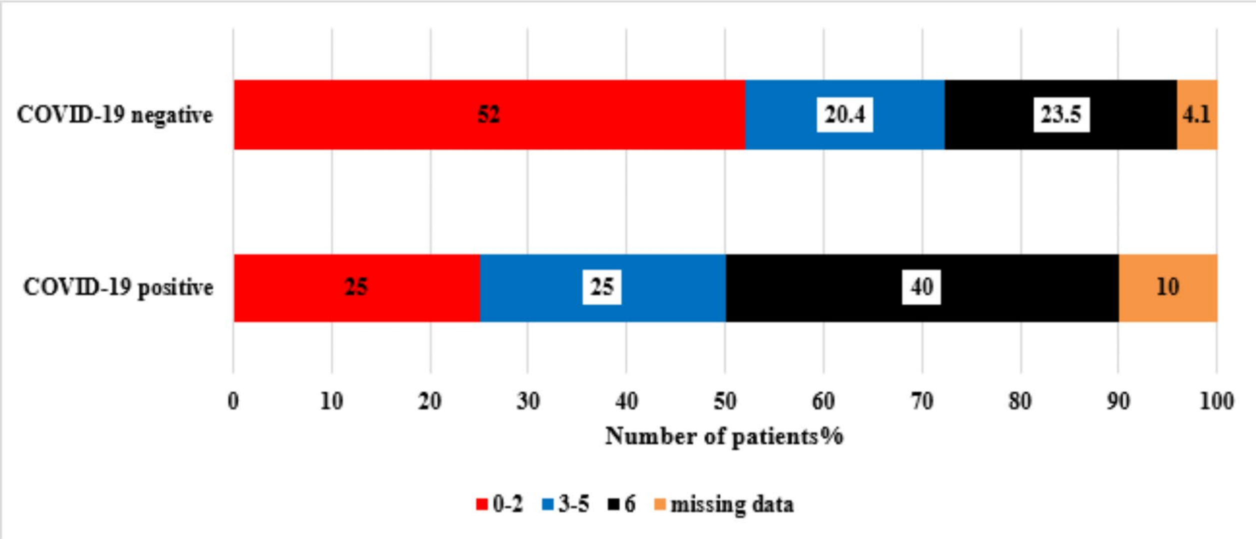
Table 4. Hospital stay, functional outcome and one year mortality of patients negative or positive for COVID-19 in the AIS group. *p values* counted between COVID 19 positive and negative groups. (AIS: Acute ischemic stroke; COVID-19: Coronavirus disease 19; mRS: modified Rankin scale; NIHSS: National Institutes of Health Stroke Scale)

among ones without recanalization ($p = 0.59$). Table 5; Figs. 6 and 7 summarize the functional outcome and mortality based on the treatment status.

In a logistic regression model, older age and heart failure were significant independent risk factors for worse outcomes at three months but, due to the small sample size, especially in the group with COVID-19, the results should be interpreted with caution *(*Table 6.*).* If mRS 6 was given as the outcome of the model no significant factors could be identified, but this should be interpreted with even more cautiously, because of small sample sizes within the subgroups of mRS 6.

Clinical characteristics and outcome of ICH patients
The detailed bivariate analysis of clinical characteristics and outcome between ICH patients positive or negative for COVID-19 is shown in Tables 7 and 8*and* Figs. 4 and 5. A total of 32 patients with hemorrhagic stroke were observed during the COVID-19 period, among them 12 (38.7%) were positive for SARS-CoV2. 75% of COVID-19 positive ICH patients were male. The mean age of COVID-19 positive patients was higher compared to unaffected ICH patients. Hypertension was the most remarkable risk factor for ICH in both group, and the mean systolic blood pressure did not differ significantly between the positive and negative patients. COVID-19 positive patients were more likely to have previous stroke and hyperlipidemia ($p = 0.042$). Noteworthy, almost half of the individuals (48.4%) received antithrombotic treatment prior to the onset of hemorrhage, with a higher ICH rate among COVID-positive patients receiving anticoagulation. Most hemorrhages (61.3%) affected the basal ganglia or thalamic region, followed by lobar (22.6%) and cerebellar (9.7%) bleedings. With CT-angiography, none of the patients had vascular abnormality in the background of ICH. There was a trend in the severity of neurological symptoms on admission with a higher mean NIHSS score in the COVID-19 group, but the difference was not statistically significant ($p = 0.08$). However, the mean NIHSS score at 24 h was significantly higher in ICH patients with COVID-19 ($p = 0.036$). Regarding the long term outcome, 3 months (75 vs. 20, $p = 0.004$) and one year mortality (75 vs. 25, respectively, $p = 0.01$). were higher in COVID-positive patients compared to negative ones.

Discussion
The COVID-19 pandemic has affected the entire world and has had a great impact on healthcare, influencing the treatment of patients with acute stroke. In this single-center retrospective study, we evaluated experience with patients presenting with acute stroke (ischemic or hemorrhagic) at our department during the first two waves of the COVID-19 pandemic. A multicenter study conducted in 275 stroke centers examined the numbers of ischemic stroke admissions, ICH admissions, intravenous thrombolysis treatments, and mechanical thrombectomy procedures were examined in this large study. According to their findings, there was a decrease of stroke admission, ICH incidence, and IVT treatment during the 1st year of the COVID-19 pandemic compared with the prior year. The rate of mechanical thrombectomy did not change significantly. This study summarized the important changes in the number of treated stoke patients calling attention to the fact that we should not overlook stoke patients even during the pandemic[20]. In line with other studies[21–22], we found a decreased number of AIS cases in 2020/21 compared to the previous periods free from COVID-19. This change in stroke presentation due to COVID-19 may be the result of several factors. Patients with milder stroke or transient ischemic attacks were likely to avoid the healthcare system because they were terrified of being exposed to and infected by the virus, which could be dangerous since these patients are at increased risk of a recurrent ischemic stroke and it would warrant secondary prevention[23]. In addition, due to restrictions in public gatherings and



B/ ICH group (N=32)

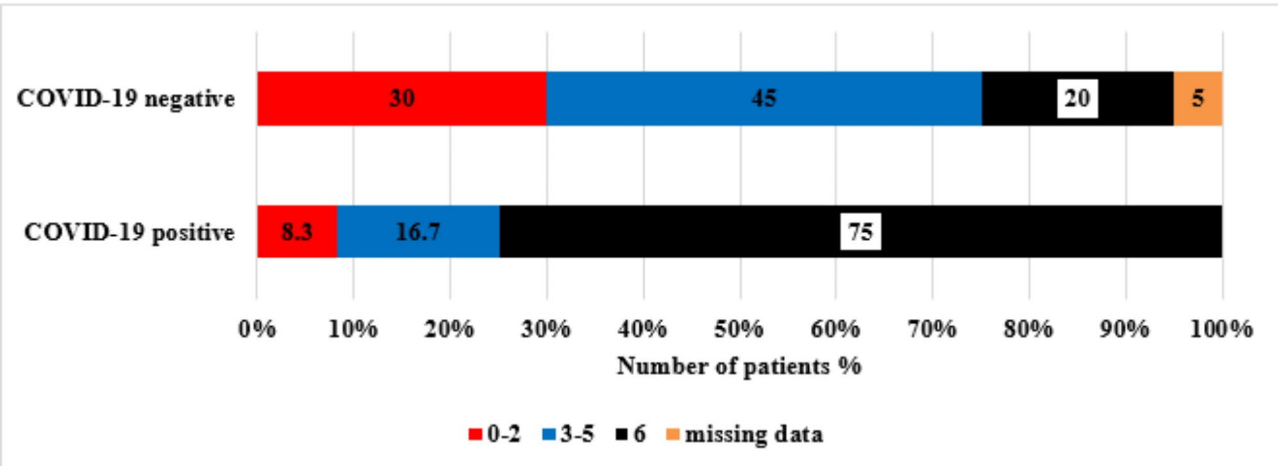
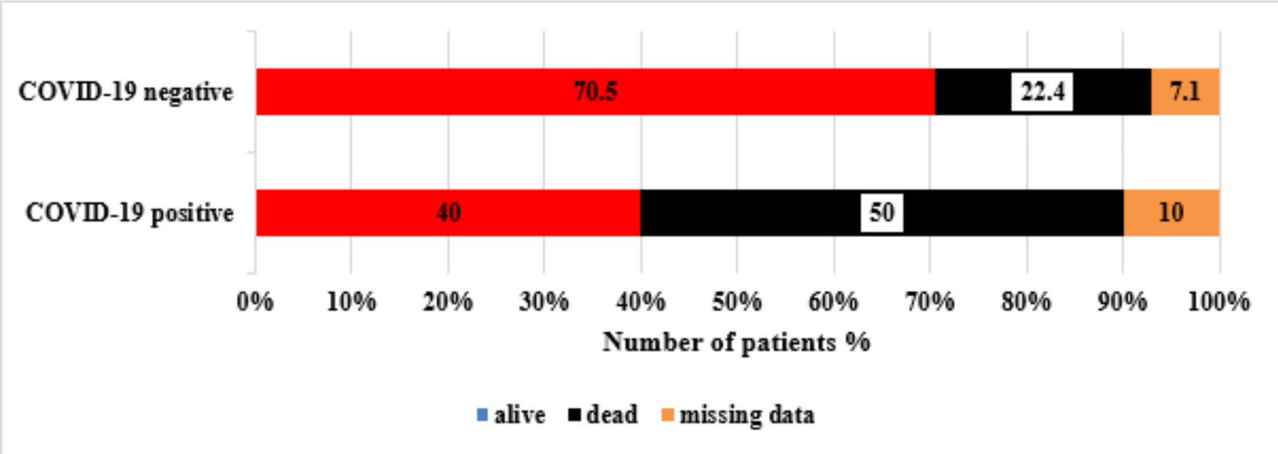


Fig. 4. Outcome at three months based on COVID-19 status (AIS: Acute ischemic stroke; COVID-19: Coronavirus disease 19).

social distancing measures, patients with an acute stroke were sometimes found by others in a delayed fashion[21]. Delays in presentation prevented patients from time-sensitive recanalization therapies and possibly caused increased morbidity and mortality. We observed no significant differences in age and gender between the groups of patients in the periods before and during COVID-19, while other studies were inconclusive[24,25]. In contrast with other studies[22,26]. We found no reduction in the number of IVTs performed in our center. However, similarly to a large multicenter cohort study[27] reported by Khandelwal et al., we found a significant increase in the number of LVOs in the COVID-period. Endovascular treatment had been (and is still) the standard procedure in the case of LVOs therefore, compared to the previous years, more patients underwent thrombectomy. A number of studies reported that during the pandemic AIS patients were treated with delay due to longer time from symptom onset to treatment and longer door-to-needle time[28–30]. However, we did not find significant delays in onset-to-needle and door-to-needle time before and during COVID-19 pandemic. It is important to note that – during the COVID-period – our department followed the same protocol for AIS care as in the control periods with safe COVID and non-COVID patient pathways. During the pandemic, the multidisciplinary collaboration process was excellent. The ambulance service informed the stroke centre that a patient with the suspicion of COVID-19 and stroke is arriving. The patient arrived to the CT laboratory, where the stroke team was waiting for the patient. The onset of the endovascular intervention needed also less time possible, because there was no scheduled and elective examination at that time due to the pandemic. The importance of multidisciplinary collaboration has also been emphasized by several studies, which reported shortening door-to-needle times during the COVID period[31,32]. In addition, the national guidelines clearly stated that revascularization treatments were urgent procedures, so they had to be performed regardless of the epidemic situation then. Despite the additional steps introduced during AIS care (e.g. use of personal protective equipment, COVID-19 screening), OTT and DNT



B/ICH group (N=32)

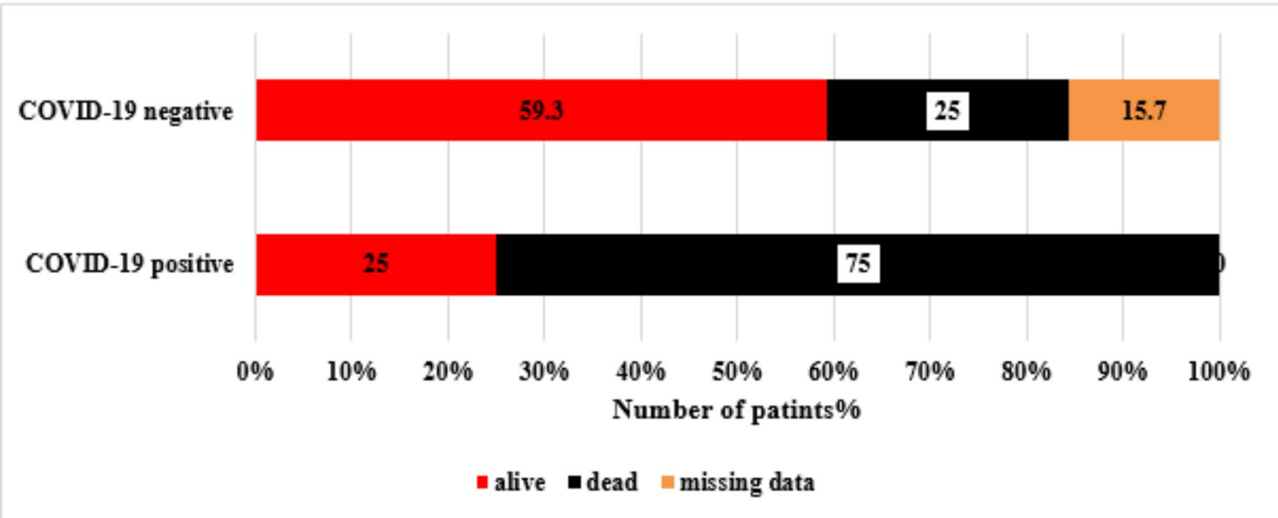


Fig. 5. Outcome at one year based on COVID-19 status (AIS: Acute ischemic stroke; ICH: Intracerebral hemorrhage; COVID-19: Coronavirus disease 19).

Patient groups			
Variable	Patients with recanalization ($n=118$)	Patients without recanalization ($n=19$)	p-value
NIHSS score at 24 h, median (1;3 quartile)	9 (3,5; 15)	17 (7;21)	***0.017***
Hospital stay (day), median (1;3 quartile)	9 (5;17.5)	11(5.75;23.5)	0.400
mRS score at 3 months			
Favorable outcome (mRS: 0–2), n (%)	56 (47.4)	5 (26.3)	0.13
Moderate/severe disability (mRS: 3–5), n (%)	25 (21.2)	5 (26.3)	0.57
Death (mRS = 6), n (%)	31 (26.3)	9 (47.4)	***0.1***
missing data, n (%)	6 (5.1)	0 (0)	
Mortality at one year	30 (25.4)	9 (47.4)	***0.59***
missing data	9 (7.6)	0 (0)	

Table 5. Clinical outcomes and one-year mortality of patients based on treatment status in the AIS group (AIS: Acute ischemic stroke; mRS: modified Rankin scale; NIHSS: National Institutes of Health Stroke Scale).

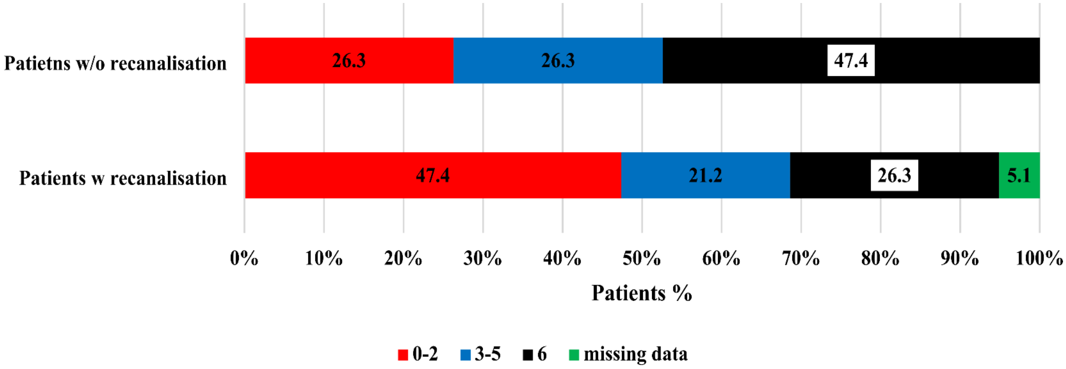


Fig. 6. Outcome at three months, based on treatment status in AIS patients (AIS: Acute ischemic stroke; mRS: modified Rankin scale).

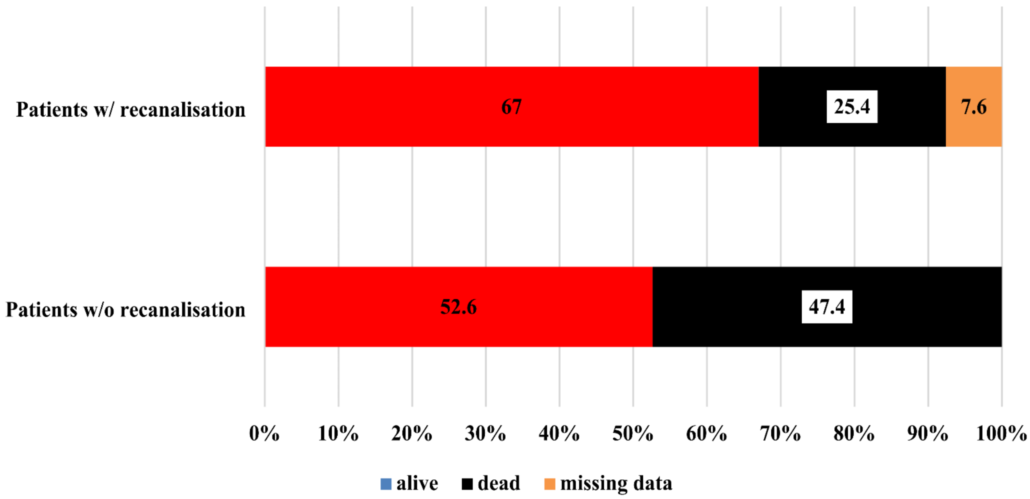


Fig. 7. Outcome at one year, based on treatment status in AIS (AIS: Acute ischemic stroke).

	Exp(B)(95%CI)	*p*
age	1.308 (1.033–1.658)	**0.026**
heart failure	0.005 (0.00-1.125)	**0.055**
diabetes mellitus	0.075 (0.001–3.867)	0.198
atrial fibrillation	8.054 (0.033-1973.106)	0.457
hyperlipidemia	1.816 (0.121–27.178)	0.666
previous stroke	9.080 (0.171–483.460)	0.277
systolic blood pressure on admission	1.075 (0.997–1.158)	0.060
hospital stay in days	1.086 (0.887–1.329)	0.425
large vessel occlusion	0.044 (0.001–3.227)	0.154

Table 6. Predictors of outcome with logistic regression model.

		Patient groups		
Variable	All patients with ICH ($n=32$)	negative for COVID-19 ($n=20$)	positive for COVID-19 ($n=12$)	p-value
Age (years), mean ± SD	65.2 ± 14.8	62.8 ± 16.1	69.1 ± 11.9	0.11
Gender, male, n (%)	17 (54.8)	8 (42.1)	9 (75)	0.07
Risk factors				
Hypertension, n (%)	22 (70.9)	12 (63.2)	10 (83.3)	0.13
Diabetes mellitus, n (%)	8 (25.8)	4 (21.1)	4 (33.3)	0.481
History of stroke, n (%)	7 (22.6)	2 (10.5)	5 (41.7)	***0.042***
Hyperlipidemia, n (%)	7 (22.6)	2 (10.5)	5 (41.7)	***0.042***
≥ 2 risk factors, n (%)	13 (41.9)	6 (31.6)	7 (58.3)	0.141
Prior antithrombotic treatment				
Antiplatelets, n (%)	10 (32.3)	6 (31.6)	4 (33.3)	0.918
Anticoagulants, n (%)	5 (16.1)	1 (5.2)	4 (20)	***0.038***
Systolic blood pressure on admission (Hgmm), mean ± SD	180.5 ± 37.65	179.3 ± 32.4	182.5 ± 46.3	0.411
Bleeding location				
Basal ganglia/thalamus, n (%)	19 (61.3)	11 (57.9)	8 (66.6)	0.625
Lobar, n (%)	7 (22.6)	4 (21.1)	3 (25)	0.797
Cerebellar, n (%)	3 (9.7)	3 (15.8)	0 (0)	-
Subarachnoideal/subdural, n (%)	2 (6.5)	0 (0)	2 (16.7)	-
NIHSS score on admission, median (1;3 quartile)	8 (4;14)	7 (3;14)	10.5 (5.75;19.25)	0.08
NIHSS score at 24 h, median (1;3 quartile)	8 (5;15)	8 (2;14)	13 (5.25;21)	***0.036***

Table 7. Demographic data, risk factors and clinical characteristics of ICH patients negative or positive for COVID-19 (ICH: Intracerebral hemorrhage; COVID-19: Coronavirus disease 19; NIHSS: National Institutes of Health Stroke Scale).

		Patient groups		
Variable	All patients with ICH ($n=32$)	negative for COVID-19 ($n=20$)	positive for COVID-19 ($n=12$)	p-value
mRS score at discharge				
Favorable outcome (mRS: 0–2), n (%)	5 (15.6)	4 (20)	1 (8.3)	0.63
Unfavourable outcome (mRS: 3–5), n (%)	23 (71.9)	13 (65)	10 (83.4)	0.42
Death (mRS 6), n(%)	4 (12.5)	3 (15)	1 (8.3)	1.0
Hospital stay (day), median (1;3 quartile)	19 (13;30)	17 (13;23)	23 (12.5;37.25)	0.190
mRS score at 3 months				
Favorable outcome (mRS: 0–2), n (%)	7 (21.9)	6 (30)	1 (8.3)	0.21
Unfavourable outcome (mRS: 3–5), n (%)	11 (34.4)	9 (45)	2 (16.7)	0.14
Death (mRS 6), n (%)	13 (40.6)	4 (20)	9 (75)	***0.004***
missing data, n (%)	1 (3.1)	1 (5)	0 (0)	-
Mortality at one year	14 (43.8)	5 (25)	9 (75)	***0.01***
missing data	3 (9.6)	3 (15.7)	0 (0)	

Table 8. Hospital stay, functional outcome and one-year mortality of ICH patients negative or positive for COVID-19.). *p values* counted between COVID 19 positive and negative groups (COVID-19: Coronavirus disease 19; ICH: Intracerebral hemorrhage; mRS: modified Rankin scale; NIHSS: National Institutes of Health Stroke Scale).

were similar to pre-COVID-19 period emphasizing the importance of continuously complying with the safety regulations by the pre-hospital and hospital staff as well, during patient care.

In the literature, patients with AIS, who also tested positive for COVID-19, were younger and predominantly males[33,34]. The results in our study also suggested that, compared to women, men were much more affected, but we did not find significant differences as far as age was considered. The vast majority of AIS patients affected by COVID-19 in our study had common vascular risk factors such as hypertension, hyperlipidemia, and diabetes. This finding may differ from observations suggesting that patients with SARS-CoV-2 infection and developing AIS were without pre-existing cardiovascular risk factors[7,35]. Other studies suggested that, even if SARS-CoV-2 infection was a predisposing factor, the risk was mainly found in individuals who were already at risk for AIS due to other vascular risk factors[36,37]. In agreement with this assumption, the patients in our study were typical of a stroke cohort, with a mean age of 69.9 years, predominance of males (60%), and a high proportion of patients (60%) with at least two vascular risk factors.

In our cohort, cardioembolic stroke was the most prominent subtype, which was also reported in other single-center studies [38,39]. Some studies showed that patients with COVID-19 were likely to be at risk of cardiac arrhythmia due to stress cardiomyopathy, direct myocardial injury, hypoxia and electrolyte disturbances with a potentially increased risk of ischemic stroke[40,41]. As we showed, in the group positive for COVID-19, embolic strokes developed in five patients who had newly detected atrial fibrillation. Interestingly, cryptogenic stroke affecting almost one-third (30%) of our patients was the second most common stroke subtype in this group. The higher proportion of strokes of cryptogenic nature observed in our study might be explained by the different stroke pathogeneses related to COVID-19, e.g. endothelial inflammation, hypercoagulable state and cytokine storm [42]. However, it is important to note that we did not have complete workups for some patients who died during hospitalization, and therefore they could have been classified as "cryptogenic" and might have passed away due to another undiagnosed mechanism. This could be an explanation for the increased prevalence of cryptogenic strokes in patients with SARS-CoV-2 infection in our study and should be interpreted with caution.

In our study, OTT and DNT did not differ significantly between AIS patients infected with COVID-19 and the control group. In our stroke center, all potential stroke patients arrive directly at the CT laboratory where the initial examination and imaging are performed. Depending on the signs and symptoms and the CT findings, the patients are transferred to the neurological intensive care unit after the CT examination, where trained nurses prepare the patients for revascularization therapy. If the information is available for the paramedical team, our center is pre-notified about COVID-19 positivity and the stroke unit team make safety preparations in advance. However, in most cases, we had no information about the patient's COVID-19 status on arrival. Treating stroke and providing reperfusion therapy were regarded as a priority and did not cause delays in logistics in out stroke center.

As for the CT parameters, we found that most strokes were located in the anterior circulation in both patient groups; this was consistent with previous findings[38,43]. The reported incidence of LVOs in AIS is estimated to be 20–38% of total strokes outside the context of COVID-19[44]. In our cohort, the LVO incidence was higher at 47.5% (46 out of 118 patients). Furthermore, the presence of simultaneous multiple LVOs of different vascular territories (23.2%, 13/56) was also more common than its presumed prevalence in the current literature[45] .There are several studies suggesting that LVOs are more common in strokes in association with COVID-19, presuming that COVID-19 induces a prothrombotic state [25,46]. In contrast, we did not observe any significant differences regarding the incidence of large vessel occlusion between the two groups. It was probably due to the limited number of patients positive for COVID-19 in our cohort. In our study, the majority of stroke patients with COVID-19 had a more severe stroke, although there were no differences in ASPECT scores between the groups on admission. These results are comparable to those in previous reports[6]. We found that the ASPECT score at 24 h was less favorable in patients with COVID-19, but the difference was not statistically significant. In a previous cohort study, Fuentes et al. also reported significantly lower ASPECT scores and higher infarct volumes in patients suffering simultaneously from COVID-19 and AIS [47]. In a multivariate analysis, however, they found no association between the initial or 24-hour ASPECT scores and the outcomes. The occurrence of ICH and sICH (5.9% and 1.7%, respectively) was comparable to our previous findings in patients who underwent IVT in our stroke center[48]. The incidence of total ICH and sICH was similar in AIS patients with and without COVID-19.

. Results from our study are comparable to the aforementioned studies and provide additional insight into the safety of reperfusion therapies for stroke patients with COVID-19.

As we showed, 30% of COVID-19 positive patients had pneumonia on initial chest CT-examination. CT chest abnormalities (consolidation, ground glass opacity and reticular opacity in the presence of architectural distortion) may be seen in up to 82% of patients with COVID-19 infection on admission. The extent of pulmonary involvement may impact the therapeutic decisions in acute stroke management, including the need for intubation. According to a recommendation by the WSO on the management of AIS in patients with COVID-19 infection, concurrent pulmonary imaging using chest CT scans may be incorporated as part of the initial imaging in patients with acute stroke unless the addition of chest CTs causes delay for five minutes or longer before recanalization treatment[54]. Occasionally, additional chest CT scans can also reveal abnormalities that may be the underlying cause of stroke, as we saw it in two of our patients. However, it is important to note that chest imaging is not indicated as a screening test for COVID-19 in asymptomatic patients[55].

We hypothesized that patients with AIS and COVID-19 infection would have worse prognoses. Despite presenting similar demographic, risk factor profile and time parameters, our cohort of AIS patients with concurrent COVID-19 infection had significantly higher median NIHSS scores. Moreover, those scores remained significantly higher at 24 h, reflecting the persistence of a worse neurological deficit. This correlated with the literature reporting that patients with AIS and COVID-19 had more severe strokes compared to cohorts free from COVID-19[5,6,24,31]. When compared with AIS patients without COVID-19 in our study, the co-diagnosis of AIS and COVID-19 resulted in significantly longer hospitalization and a higher proportion of unfavorable functional outcomes, based on the mRS at discharge from the hospital. These results were not surprising given that patients with AIS and COVID-19 had more complications and required higher levels of support. As for the long-term outcome, the proportion of patients with favorable outcomes at three months was significantly lower in the group positive for COVID-19. This result is consistent with most of the recent studies showing lower rates of favorable outcomes at day 90 among patients with AIS and COVID-19[34,56]. It is difficult to determine if these differences in outcome are due to worse stroke severity in COVID-19 settings or due to difficulties in stroke care and rehabilitation in patients diagnosed with the SARS-CoV-2 infection. We believe that both scenarios are worth considering. Regarding mortality, our results are in agreement with previously published studies reporting that in patients with stroke, infection with COVID-19 has been associated with higher mortality rates[6,54]. In our study, in-hospital mortality was 30% among patients with simultaneous AIS and COVID-19, which is in line with the mortality rates in the range of 20-63.6% documented in the literature, but it is higher compared to the reported overall mean in-hospital mortality due to AIS ranging from 8 to 14% [6,7,58]. Several aspects related to the SARS-CoV-2 infection may explain our findings. These include respiratory distress and multiorgan failure observed in some patients. The aforementioned conditions have been shown to increase mortality and morbidity rates in patients with AIS[7,36,37].

In the literature, there are several potential mechanisms were described in the background of increased risk of hemorrhagic stroke in patients with COVID-19. Certain authors suggest that COVID-19 infection may disrupt the blood–brain barrier in numerous ways (e.g., by destabilizing tight junction proteins) resulting in endothelial dysfunction and ICH[59]. Moreover, recent studies strongly suggest the involvement of the renin–angiotensin system in the pathogenesis of both ICH and COVID-19. The downregulation of angiotensin converting enzyme 2 expression during SARS-CoV-2 infection may increase the level of angiotensin 2 in the serum, which can impair endothelial function and contribute to dysregulation of blood pressure, thus increasing the risk of hemorrhagic stroke[60]. Regarding the ICH patients in our cohort, we have demonstrated that concomitant COVID-19 infection significantly impacts the outcome in those patients. Mortality was higher at 3 months and at one year compared to COVID 19 negative subgroup. We found that early worsening of neurological symptoms expressed in NIHSS score at 24 h was more frequent among COVID-19 positive ICH patients. Similar finding was reported by Topcuoglu et al. in a prospective case cohort study of 46 patients[61]. An analysis from the COVID-19 Cardiovascular Registry conducted by Leasure et al. reported that ICH patients with COVID-19 infection had higher mortality rate than those without. In addition, their results indicated higher ICH rates among COVID-positive patients receiving anticoagulation compared to COVID-negative subjects[11]. Our findings are in line with these studies and warrants further investigation to improve outcomes for these high-risk cerebrovascular patients.

Our results on lack of follow-up show how difficult it was to follow patients in our stroke unit long-term, compared to our previous studies, and show how real-life studies highlight the difficulties of stroke care[18,48]. This might be due to the fact that our centre functioned in the region only as stroke centre actively, where regardless whether infected or not with the virus, dedicated stroke-care professionals were handling the patients. Sometimes COVID-19 positive patients were taken far from their home to dedicated centres in the country, which made the follow up difficult. But the patients were transferred to different centres later, and were lost follow-up. This draws attention to the difficulties of secondary stroke care during the COVID-19 pandemic, not only to the problems needed to solve acute care.

Of course, we are aware of the limitations of our study: Because of the retrospective single-center nature and the relatively small number of patients (especially in the group positive for COVID-19) selection and sampling might have been biased. As mentioned previously, it is possible that patients with less-disabling strokes were less likely to seek medical attention during the pandemic, which may have skewed the data in favor of LVO strokes. Due to the small sample size, especially in the group with COVID-19, the results of the logistic regression model should be interpreted with caution as far as the predictors of poor outcome are regarded. Despite these limitations, we believe that this study provides valuable data on the characteristics and functional outcome of acute stroke patients with concomitant SARS-CoV-2 infection and will help improve the care of this specific population of patients. Our study can show more aspects of stroke outcome in COVID-19 in a smaller cohort where the patients were treated with dedicated stroke team (nurses, anesthesiologists, interventionists, and neurologists), leading to a homogenous group and the bias from learning curve could be excluded, as well. We studied a real-life scenario, which findings could implemented immediately in case of a newer pandemic.

In conclusion, our study demonstrates how the COVID-19 pandemic affected the management of acute stroke patients at our tertiary stroke center. In particular, the evolving pandemic resulted in fewer admissions due to AIS, still an increased number of hospitalization for LVOs and MTs among them, but no delay in treatment. According to our results, AIS patients with concomitant SARS-CoV-2 infections had more severe strokes. Despite successful and timely reperfusion treatments, the functional outcomes were unfavorable due to the rise in mortality rates after the three-month follow-up period. However, the risk of sICH did not increase therefore reperfusion therapies appear to be safe and beneficial for certain patients. Regarding the ICH patients, our finding suggest that early deterioration of neurological condition is more likely among COVID-19 patients. While the mortality in ICH is typically high, it may be higher than expected in ICH patients with COVID-19.

Data availability

All data generated or analysed during this study are included in this published article.

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F.K. and H.M. led the initiative and revised the drafted document. F.K. and H.M. selected abstract, extracted data and drafted the manuscript. H.M., F.K. and H.L. were involved in the creation of the database. F.K. and H.M. is involved in investigation. H.M., M.S., H.L., F.K. and F.I. data curation, data analysis, and writing the original draft. F.I., F.K. were involved in supervision. All authors are involved in the conceptualization, methodology, review, and editing. All authors approved the final version.

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Competing interests
The authors declare no competing interests.

Additional information

Correspondence and requests for materials should be addressed to M.H.