



# Ischemic Stroke and Coronavirus Infection: Complications of Endovascular Thrombectomy

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## Abstract

The objective of our study was to compare complications of endovascular thrombectomy (EVT), in ischemic stroke (IS) patients admitted with or without COVID-19 to hospitals converted to deliver COVID-19-specific care.

**Materials and methods.** A retrospective analysis of 817 clinical cases of IS patients aged 25–99 years treated in regional vascular centers of Saint Petersburg from 1 January to 31 December 2021, with confirmed thrombotic occlusion of cerebral vessels and subsequent EVT intervention.

**Results.** The EVT number per bed was significantly higher (1.6) in the non-converted hospitals compared to the COVID-19-converted hospitals (0.49;  $p < 0.001$ ). At the same time, more intraoperative complications (12% vs. 7.1%;  $p = 0.03$ ) were reported in non-converted hospitals compared to COVID-19 converted hospitals. The likelihood of a favorable functional outcome was higher in younger patients with less severe neurological deficits on admission and without concomitant COVID-19 or post-operative complications.

**Conclusion.** COVID-19 is a limiting factor for the effectiveness of an IS treatment in patients who underwent EVT, affecting thereby functional outcomes in this cohort of patients. The impact of the COVID-19 pandemic on intra-operative EVT complication rate was associated with disrupted triage of IS patients and an uneven distribution of the workload among surgical teams in the city hospitals.

**Keywords:** ischemic stroke; endovascular thrombectomy; cerebral artery thrombosis; novel coronavirus infection; complications

**Ethics approval.** The study was conducted with the voluntary informed consent of the patients. The research protocol was approved by the Ethics Committee of the Pavlov First Saint Petersburg State Medical University (protocol No. 2, dated November 18, 2022).

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# Ишемический инсульт и коронавирусная инфекция: анализ осложнений внутрисосудистой тромбэкстракции

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## Аннотация

**Цель исследования:** сравнительный анализ осложнений внутрисосудистой тромбэкстракции (ВСТЭ) при ишемическом инсульте (ИИ) у пациентов при сочетании с COVID-19 и без него в условиях перепрофилирования стационаров под лечение COVID-19.

**Материалы и методы.** Проведён ретроспективный анализ 817 историй болезни пациентов с ИИ в возрасте 25–99 лет, проходивших лечение в региональных сосудистых центрах Санкт-Петербурга с 1 января по 31 декабря 2021 г., с подтверждённой тромботической окклюзией церебральных сосудов и последующим выполнением ВСТЭ.

**Результаты.** Количество процедур ВСТЭ в расчёте на 1 койку в группе неперепрофилированных стационаров значительно выше (1,6) по сравнению с группой перепрофилированных стационаров (0,49;  $p < 0,001$ ). При этом в неперепрофилированных стационарах зарегистрировано большее количество интраоперационных осложнений (12% против 7,1%;  $p = 0,03$ ), чем в перепрофилированных. Вероятность благоприятного функционального исхода была выше у пациентов молодого возраста, без сопутствующего COVID-19, с небольшим неврологическим дефицитом при поступлении и при отсутствии послеоперационных осложнений.

**Заключение.** COVID-19 представляет собой фактор, лимитирующий эффективность лечения ИИ у пациентов с выполненной ВСТЭ, и влияет на функциональные исходы данной когорты пациентов. Влияние пандемии COVID-19 на развитие интраоперационных осложнений ВСТЭ было опосредовано нарушением общей логистики пациентов с ИИ и неравномерным распределением нагрузки на хирургические бригады стационаров.

**Ключевые слова:** ишемический инсульт; внутрисосудистая тромбэкстракция; тромбоз церебральных артерий; новая коронавирусная инфекция; осложнения

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## Introduction

Endovascular therapy has significantly expanded pathogenetic treatment options and time window for patients with acute ischemic stroke (IS) caused by large vessel occlusion (LVO) [1–3]. In regional vascular centers of Saint Petersburg, the number of endovascular thrombectomy (EVT) interventions for acute stroke increased annually from 2014 to 2020. While in 2014 only 8 EVTs were performed in Saint Petersburg (with the total number of 19,340 stroke patients admitted to regional vascular centers), in 2020 there were 624 interventions (with a total number of 17,832 stroke patients admitted to regional vascular centers) [4]. With the establishment of network of vascular centers in St. Petersburg, the hospital mortality was steadily decreasing from 26% and reached 15.8% in 2019, and stroke mortality has decreased 1.5-fold over the past 12 years, which is probably partly due to the increased availability of high-tech care<sup>1</sup>.

The COVID-19 pandemic resulted in limited triage opportunities affecting availability of medical interventions, especially those where the time is critical [5]. For patients with cardiovascular diseases, this factor has complicated diagnostic, treatment and triage algorithms, hence increasing the risk for unfavorable outcomes [6–8]. Moreover, since the beginning of the pandemic, an increasing number of acute cerebrovascular accidents in patients with COVID-19 have been reported. Stroke may be the first clinical manifestation of this infection, which made the triage procedure more challenging due to the need of emergency screening for SARS-CoV-2. A large pool of evidence suggests that SARS-CoV-2 infection exacerbates both the IS course and a triage procedure, leading to unfavorable functional outcomes in these patients [9–12]. Growing number of unfavorable outcomes could also be caused by delays in health care-seeking behavior. For example, an article on a retrospective analysis of LVO stroke described a clinical case of a late call for emergency medical care due to the fear of SARS-CoV-2 infection [13, 14].

World experience shows that even despite the challenging triage and the need to follow additional protocols of service interaction, the number of EVT interventions in IS patients during the pandemic could remain at a fairly high level. In a retrospective review of the treatment of 126 IS patients with COVID-19 in vascular centers in the United States, Canada, and Iran, EVT was performed in 15 patients (12.1%) [15]; a review of the treatment of 202 patients in the same category from December 2019 to October 2020 reported EVT in 19 patients (9.4%), which seems rather modest; however, the combination of thrombolytic therapy and EVT was reported in 47 patients (23.3%), which together represents a significant proportion of 30% (66 patients) [16]. According to the

<sup>1</sup> Official website of the Health Committee of St. Petersburg. In Saint Petersburg, the stroke mortality decreased one and a half times over the last 12 years.  
URL: <http://zdrav.spb.ru/ru/news/1970> (accessed on: 21.04.2024).

Danish registry [18], of 23,688 stroke patients in Denmark, 552 patients underwent EVT between 1 January 2019 and 28 February 2021. The study revealed a decrease in the total number of IS patients admitted within 1 week after the implementation of quarantine measures, but the mean number of intravascular interventions remained constant throughout the study [9, 17].

The **objective** of this study was to compare EVT complication rates and outcomes in IS patients with and without COVID-19 treated in regional vascular centers of St. Petersburg, some of which were converted to deliver COVID-19 specific care.

## Materials and methods

We retrospectively analyzed 817 medical records of all IS patients (365 males and 452 females) aged 25–99 years who underwent EVT from 1 January 2021 to 31 December 2021 in 11 vascular centers of Saint Petersburg (Pokrovsky City Hospital No. 1, Hospital for War Veterans, Mariinsky City Hospital No. 16, Nikiforov's All-Russian Center for Emergency and Radiation Medicine, Almazov National Medical Research Center, Alexandrovsky City Hospital No. 17, City Hospital No. 40, City Multidisciplinary Hospital No. 2, Dzhanelidze Research Institute of Emergency Medicine, City Hospital No. 26, St. Elizabeth City Hospital).

The inclusion criteria were:

- ischemic stroke confirmed by neuroimaging, i.e. computed tomography (CT) or magnetic resonance imaging (MRI);
  - confirmed thrombotic occlusion of proximal cerebral arteries followed by EVT intervention;
  - no history of thrombolytic therapy within the comprehensive treatment plan.
- The exclusion criteria were:
- no polymerase chain reaction test for SARS-CoV-2;
  - no indications for EVT;
  - no control CT performed 24 hours post-surgery.

Demographic and clinical data, the nature of the stroke lesion, angiographic reperfusion assessment results, EVT complication rate, intracranial hemorrhage rate, and treatment outcomes were recorded. Surgical interventions were performed according to routine clinical indications<sup>2</sup>. All patients underwent standard clinical and neurological examination, and the clinical diagnosis of IS was established according to ICD-10 and TOAST criteria. Neurological deficit was assessed using the National Institutes of Health Stroke Scale (NIHSS). EVT success was determined by control angiography; result was considered as success if the lumen of the cerebral artery was restored with mTICI score of 2b to 3 and as failure if mTICI score was 0 to 2a. Complications were evaluated by control

<sup>2</sup> Ischemic Stroke and Transient Ischemic Attack in Adults: National Clinical Guidelines, 2021.  
URL: [https://cr.minzdrav.gov.ru/schema/171\\_2](https://cr.minzdrav.gov.ru/schema/171_2)  
(accessed on: 21.04.2024).

CT scans according to The Heidelberg Bleeding Classification [18]. The intraoperative complications to study were selected based on the practice of multicenter studies [19].

Functional outcome was considered favorable if modified Rankin score (mRS) was 0 to 2 and unfavorable if mRS was 3 to 5; death corresponded to mRS of 6. We also assessed mortality on day 90 after the stroke onset in a cohort of discharged patients based on cases registered in the Saint Petersburg State Information System. Death causes were reported based on autopsy results (for in-hospital deaths).

Quantitative data were presented as medians, Q1 (25%) and Q3 (75%) quartiles; categorical (qualitative) data were presented as rates and percentages; 95% confidence intervals (CI) were calculated for proportions. For all numerical data, preliminary testing for normality of distribution was performed using Shapiro-Wilk test, as well as skewness-kurtosis test by calculating  $p$ -value when testing the null hypothesis about normal distribution of the variable. Student's  $t$ -test for independent samples was used for statistical analysis of data with normal distribution. Non-parametric Wilcoxon and Mann-Whitney tests were used for data significantly deviating from normal distribution. The association between categorical variables was evaluated using Fisher's exact test and Pearson's  $\chi^2$  test. Multivariate analysis by binary logistic regression was used to assess correlation between clinically relevant factors and favorable outcomes. All reported  $p$  values were based on two-sided tests of significance. Differences were considered significant at  $p < 0.05$ . All calculations were performed using R package version 4.3.1.

## Results

Distribution of patients to vascular centers of Saint Petersburg during the COVID-19 pandemic is presented in Table 1. The triage of stroke patients during this period was based on the presence or absence of COVID-19. Hence, in Saint Petersburg, only three (Dzhanelidze Research Institute of Emergency Medicine, City Hospital No 26, St. Elizabeth City Hospital) of 11 regional vascular centers were not converted to COVID-19 care, but the total number of

patients who underwent EVT in these hospitals was higher (479 vs 338).

There were no significant differences in age, gender, NIHSS score, 90-day mortality, and functional outcomes in patients treated in both types of hospitals (Table 2). At the same time, statistically significant differences by the same parameters were found between patients with and without COVID-19 regardless of treatment site (Table 3). Thus, the NIHSS score at admission and mortality were higher in the COVID-19 patients, whereas the functional outcomes in COVID-19-free patients were significantly more favorable (mRS of 4 vs 3, respectively;  $p < 0.001$ ).

The data on EVT complications in the patients treated in COVID-19 converted and non-converted hospitals are presented in Table 4. There is a trend for an increased incidence of the new emboli in the same territory in the patients treated in non-converted hospitals. However, in general, the rate of these complications was low, and the correction for multiple comparisons was not performed in the statistical analysis, so, it cannot be excluded that this difference is random.

No statistically significant differences were revealed by control CT scans 24 h after EVT (Table 2). We noted a trend for an increased incidence of intracerebral hematomas type 1 in the patients treated in COVID-19-converted hospitals, as well as in the COVID-19 patients (Table 3); however, this difference was below statistical significance threshold in both groups.

There was a trend for an increased incidence of arterial perforation in the patients with concomitant COVID-19 (Table 3), but due to extremely low incidence of this complication the statistical significance of this intergroup difference could not be evaluated. The incidence of subarachnoid hemorrhages in the patients with concomitant COVID-19 also tended to increase, but the inter-group difference was below statistical significance threshold, as in the case of arterial perforations.

Cumulatively, we found a statistically significant increase in intraoperative complication rate in the patients treated in non-converted hospitals (Table 2).

**Table 1. Distribution of patients to regional vascular centers based on an adjusted triage procedure**

Parameter	COVID-19 converted hospitals	Non-converted hospitals	$p$
Beds, $n$	693	300	
EVT interventions, $n$	338	479	
EVTs/bed, $n$	0,49	1,6	
EVT proportion in total number of IS cases, %	4,1	5,3	< 0,001
Treated IS cases, $n$	8165	8973	
Treated IS cases/bed, $n$	11,7	29,9	

**Table 2. Main clinical characteristics and outcomes in IS patients who underwent EVT in COVID-19-converted and non-converted hospitals**

Parameter	COVID-19-converted hospitals (n = 338)	Non-converted hospitals (n = 479)	p
Age	73 (63; 82)	74 (65; 83)	0,2
Males	155 (46% [40%; 51%])	210 (44% [39%; 48%])	0,6
COVID-19	80 (24% [19%; 29%])	139 (29% [25%; 33%])	0,089
NIHSS score at admission	15 (10; 18)	16 (12; 19)	0,011
In-hospital mortality	112 (33% [28%; 38%])	182 (38% [34%; 43%])	0,2
90 days post-stroke mortality	108 (36% [30%; 41%])	167 (39% [35%; 44%])	0,3
<b>Intraoperative complications</b>			
new emboli in the same territory	16 (4,7% [2,8%; 7,7%])	44 (9,2% [6,8%; 12,0%])	0,016
arterial dissection	7 (2,1% [0,91%; 4,4%])	9 (1,9% [0,92%; 3,7%])	0,8
arterial perforation	1 (0,3% [0,02%; 1,9%])	3 (0,6% [0,16%; 2,0%])	0,6
vasospasm requiring treatment	4 (1,2% [0,38%; 3,2%])	5 (1,0% [0,38%; 2,6%])	> 0,9
emboli in a new territory	1 (0,3% [0,02%; 1,9%])	1 (0,2% [0,01%; 1,3%])	> 0,9
<b>Post-operative complications</b>			
hemorrhagic infarction type 1	6 (1,8% [0,72%; 4,0%])	14 (2,9% [0,72%; 4,0%])	0,3
hemorrhagic infarction type 2	28 (8,3% [5,7%; 12,0%])	34 (7,1% [5,0%; 9,9%])	0,5
parenchymal hematoma type 1	23 (6,8% [4,5%; 10,0%])	19 (4,0% [2,5%; 6,2%])	0,072
parenchymal hematoma type 2	26 (7,7% [5,2%; 11,0%])	25 (5,2% [3,5%; 7,7%])	0,2
intraventricular hemorrhage	1 (0,3% [0,02%; 1,90%])	2 (0,4% [0,07%; 1,7%])	> 0,9
subarachnoid hemorrhage	11 (3,3% [1,7%; 5,9%])	23 (4,8% [3,10%; 7,20%])	0,3
<b>Total complication rate</b>			
intraoperative complications	24 (7,1% [4,7%; 11,0%])	56 (12,0% [9,0%; 15,0%])	0,030
post-operative complications	83 (25,0% [20,0%; 30,0%])	92 (19,0% [16,0%; 23,0%])	0,066
intra- and post-operative complications	5 (2,3% [0,84%; 5,5%])	18 (3,0% [1,8%; 4,8%])	0,6
<b>Functional outcome</b>			
Parameter	COVID-19 converted hospitals (n = 226)	Non-converted hospitals (n = 297)	p
Functional outcome at discharge, mRS excluding in-hospital mortality	3 (2; 4)	3 (2; 4)	0,8

Table 3. Main clinical characteristics and outcomes in groups of IS patients with or without COVID-19

Parameter	COVID-19 patients (n = 219)	COVID-19-free patients (n = 598)	p
Age	75 (67; 84)	73 (63; 82)	0,023
Males	103 (47% [40%; 54%])	262 (44% [40%; 48%])	0,4
NIHSS score at admission	17 (13; 20)	15 (10; 18)	< 0,001
In-hospital mortality	114 (52% [45%; 59%])	180 (30%; [26%; 34%])	< 0,001
90 days post-stroke mortality	98 (51% [44%; 59%])	177 (33% [29%; 37%])	< 0,001
<b>Intraoperative complications</b>			
new emboli in the same territory	16 (7,3% [4,4%; 12%])	44 (7,4% [5,5%; 9,8%])	> 0,9
arterial dissection	3 (1,4% [0,35%; 4,3%])	13 (2,2% [1,2%; 3,8%])	0,6
arterial perforation	3 (1,4% [0,35%; 4,3%])	1 (0,2% [0,01%; 1,1%])	0,061
vasospasm requiring treatment	2 (0,9% [0,16%; 3,6%])	7 (1,2% [0,51%; 2,5%])	> 0,9
emboli in a new territory	0 (0,0% [0,00%; 2,1%])	2 (0,3% [0,06%; 1,3%])	> 0,9
<b>Post-operative complications</b>			
hemorrhagic infarction type 1	4 (1,8% [0,59%; 4,9%])	16 (2,7% [1,6%; 4,4%])	0,5
hemorrhagic infarction type 2	19 (8,7% [5,4%; 13,0%])	43 (7,2% [5,3%; 9,7%])	0,5
parenchymal hematoma type 1	16 (7,3% [4,4%; 12,0%])	26 (4,4% [2,9%; 6,4%])	0,091
parenchymal hematoma type 2	14 (6,4% [3,7%; 11,0%])	37 (6,2% [4,5%; 8,5%])	> 0,9
intraventricular hemorrhage	0 (0,0% [0,00%; 2,1%])	3 (0,5% [0,13%; 1,6%])	0,6
subarachnoid hemorrhage	14 (6,4% [3,7%; 11,0%])	20 (3,4% [2,1%; 5,2%])	0,054
<b>Total complication rate</b>			
intraoperative complications	22 (10% [6,5%; 15,0%])	58 (9,7% [7,5%; 12,0%])	0,9
post-operative complications	53 (24,0% [19,0%; 31,0%])	122 (20,0% [17,0%; 24,0%])	0,2
intra- and post-operative complications	10 (3,0% [1,5%; 5,5%])	13 (2,7% [1,5%; 4,7%])	0,8
<b>Functional outcome</b>			
Parameter	COVID-19 patients (n = 105)	COVID-19-free patients (n = 418)	p
Functional outcome at discharge, mRS excluding in-hospital mortality	4 (3; 5)	3 (2; 4)	< 0,001

Table 4. Multiple correlation coefficients between the rates of favorable functional outcomes (mRS 0–2) and clinically significant variables in the study group

Parameter	Odds ratio	95% CI	p
Age	0,97	0,96–0,98	< 0,001
Treated in non-converted hospital	1,22	0,84–1,78	0,300
COVID-19-free patients	7,39	4,13–14,3	< 0,001
NIHSS score at admission	0,89	0,86–0,92	< 0,001
Absence of intraoperative complications	1,08	0,58–2,07	0,800
Absence of postoperative complications	2,20	1,31–3,84	0,004

The analysis of the factors associated with favorable functional outcomes showed no significant influence of treatment site or intraoperative complication rate (Table 4). Thus, the factors associated with favorable functional outcomes include younger age, milder neurological deficits on admission, and the absence of post-operative complications or COVID-19.

## Discussion

We studied a population representative for the extended COVID-19 pandemic: a continuous sampling of IS patients underwent EVT in metropolitan vascular centers during 2021. We found that concomitant COVID-19 had no significant effect on the intraoperative or postoperative complication rate. However, when comparing the groups of patients treated in COVID-19-converted and non-converted hospitals, there was a statistically significant increase in the overall intra-operative complication rate in patients treated in non-converted hospitals.

This may be caused by organizational factors (i.e. suboptimal pre-hospital and in-hospital logistics for IS patients) limiting the success of specialized treatment techniques. On a per-bed basis, three times more IS patients were treated in non-converted hospitals and three times more EVT interventions were performed compared to per-bed load in the COVID-19-converted hospitals. The in-flow of patients during the pandemic increased while hospital staffing remained unchanged, which possibly led to an excessive staff workload, especially for surgical teams resulted in the higher rates of intraoperative complications.

The negative impact of organizational challenges is consistent with a worldwide trend; for example, less favorable outcomes in stroke patients treated during the COVID-19 pandemic have been reported in most cohort studies [20, 21].

We would like to emphasize that this study was not designed to evaluate the effectiveness of EVT compared to other treatment options, as this analysis does not include data on IS patients who did not undergo any surgery. Noteworthy, there was no significant difference in the proportion of COVID-19 patients in both COVID-19-converted and non-converted hospitals. Thus, the COVID-19 diagnosis and the treatment site could not directly influence the decision to choose surgery as a treatment option.

In IS patients with concomitant COVID-19, no statistically significant increase in both intraoperative and postoperative complication rates was reported despite the specific anticoagulant prophylaxis (according to COVID-19 management protocols).

Nevertheless, according to multivariate analysis data, concomitant COVID-19 turned out to be a predictor of unfavorable outcomes, regardless of the patient's age, stroke severity, and intra- and post-operative complications. At the same time, the hospital profile (converted or non-converted) had no effect on the disease outcomes. These findings confirm that COVID-19 worsens the IS outcome not only by indirectly affecting the organization of health care and logistics, but also by directly complicating the course of the disease.

## Limitations of the study

Our study was based on a retrospective analysis of case records; it was observational and did not consider treatment outcomes of patients who did not undergo EVT due to extreme severity of their respiratory syndrome or multiple organ damage that complicated COVID-19 course. It is also known that COVID-19 itself can contribute to an overall increase in NIHSS score [22], therefore, it cannot be excluded that in some COVID-19 patients, NIHSS scores above optimal cut-offs precluded EVT, while patients with an equivalent volume of brain lesion but without COVID-19 underwent the intervention, and thus the brain damage in patients without COVID-19 was initially more extensive. We did not consider cases with reduced EVT availability due to organizational challenges, including administrative issues and delays due to inter-hospital transfers.

## Conclusions

In patients who underwent EVT in regional vascular centers of Saint Petersburg in 2021, concomitant COVID-19 did not affect the complication rates during interventional treatment of patients with hyperacute ischemic stroke. Nevertheless, the COVID-19 pandemic had an indirect negative impact on the IS course after EVT due to logistical disruption, uneven patient-bed allocation, triage challenges and, as a consequence, increased medical staff workload (especially in surgical teams). This factor may contribute to an increase in intra-operative complication rate in the hospitals with a large number of patients allocated to a smaller number of beds (non-converted hospitals in our study).

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