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ORIGINAL ARTICLE

Association of the COVID-19 outbreak with acute stroke care in Switzerland

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Abstract

Background and purpose: In Switzerland, the COVID-19 incidence during the first pandemic wave was high. Our aim was to assess the association of the outbreak with acute stroke care in Switzerland in spring 2020.

Methods: This was a retrospective analysis based on the Swiss Stroke Registry, which includes consecutive patients with acute cerebrovascular events admitted to Swiss Stroke Units and Stroke Centers. A linear model was fitted to the weekly admission from 2018 and 2019 and was used to quantify deviations from the expected weekly admissions from 13 March to 26 April 2020 (the "lockdown period"). Characteristics and 3-month outcome of patients admitted during the lockdown period were compared with patients admitted during the same calendar period of 2018 and 2019.

Results: In all, 28,310 patients admitted between 1 January 2018 and 26 April 2020 were included. Of these, 4491 (15.9%) were admitted in the periods March 13–April 26 of the years 2018–2020. During the lockdown in 2020, the weekly admissions dropped by up to 22% compared to rates expected from 2018 and 2019. During three consecutive weeks, weekly admissions fell below the 5% quantile (likelihood 0.38%). The proportion of intracerebral hemorrhage amongst all registered admissions increased from 7.1% to 9.3% ($p = 0.006$), and numerically less severe strokes were observed (median National Institutes of Health Stroke Scale from 3 to 2, $p = 0.07$).

Conclusions: Admissions and clinical severity of acute cerebrovascular events decreased substantially during the lockdown in Switzerland. Delivery and quality of acute stroke care were maintained.

KEYWORDS
COVID-19, epidemiology, stroke

INTRODUCTION

In Switzerland, the incidence of SARS-CoV-2 infections during the first wave of the COVID-19 pandemic wave was high (342/100,000) [1]. To curb the pandemic, the Swiss Federal Council declared a national lockdown from 13 March 2020 to 26 April 2020, with a major impact on all domains of daily life. Schools and non-essential shops were closed nationwide, and all gatherings of more than five people in public spaces were banned. Unlike in many other countries, no strict confinement was imposed. These unprecedented circumstances raised concern about potential restrictions in medical care of acute cardiovascular diseases. Many stroke physicians perceived a decrease in the number of admitted patients with ischaemic stroke and intracerebral hemorrhage (ICH), similar to what has been reported in other countries [2–10]. The aim of this work was to investigate changes in weekly admissions, clinical patient characteristics, delivery of acute therapy and functional 3-month outcome amongst patients with acute cerebrovascular events during the lockdown period compared to rates from 2018 and 2019 based on the prospective Swiss Stroke Registry.

METHODS

This is a retrospective analysis of prospectively collected data from the Swiss Stroke Registry, an institutional review board approved national web-based registry designed for quality assurance and multi-centric research in acute stroke care in Switzerland. Registry details have been given previously [11]. Briefly, the registry collects a standardized dataset of all patients with acute cerebrovascular events including a follow-up assessment after 3 months and is compulsory for all hospitals certified as Stroke Units or Stroke Centers, in line with European Stroke Organization criteria [12]. The registry includes 10 Stroke Centers and 12 Stroke Units, which—in contrast to Stroke Centers—do not perform acute endovascular treatments. The registry was implemented in the clinical data management system secuTrial and data processing is aided by the software package secuTrial [13]. The de-identified data that support the findings of this study are available from the corresponding author upon reasonable request.

For this analysis, consecutive patients with an acute ischaemic stroke, ICH or transient ischaemic attack (TIA) admitted to a certified Stroke Center or Stroke Unit between 1 January 2018 and 8 June 2020 were included to investigate any deviation in the observed from the expected admission rates during the first lockdown period, which was defined from 13 March 2020 to 26 April 2020. In addition, patient characteristics, acute therapy and functional outcome of patients admitted during the lockdown period were compared to those admitted in the same period in the years 2018 and 2019.

The weekly admissions for acute ischaemic stroke, TIA and ICH were compared between the two periods. Also compared was the time from symptom onset or last seen well to hospital admission; patient referral (e.g., ambulance or self-referral); severity of symptoms on admission (measured by the National Institutes of Health Stroke Scale [NIHSS]); rate of acute stroke treatments delivered (including intravenous thrombolysis [IVT] and endovascular therapy [EVT]); in-hospital performance measures defined as the time from hospital admission to start of IVT ("door-to-needle time") or EVT ("door-to-groin-puncture time"); rate of patients with wake-up stroke treated by IVT or EVT (defined as a stroke with symptoms that were present when the patient awoke but not prior to falling asleep); stroke etiology defined by the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria [14] (cardiac embolism, small vessel disease, large artery atherosclerosis, other defined cause, multiple causes, no identified cause); in-hospital outcome including symptomatic intracerebral hemorrhage, all-cause mortality; level of disability at 3 months (measured by the modified Rankin Scale [15]); and all-cause mortality at 3 months. At 3 months, information on functional outcomes and mortality was available for 80% of patients.

Geographical comparison

Across geographical regions within Switzerland, the COVID-19 incidence rates differed during the first pandemic wave. "High-incidence" regions were defined as having more than 700 COVID-19 cases/100,000 people by 27 April 2020 according to the statistics of the Federal Office of Public Health; high-incidence cantons were Ticino, Geneva, Vaud, Vallis. Weekly admissions for high-incidence regions were compared to the rest of the country [1].

Statistical analysis

As over the years 2015–2019 the number of weekly stroke admissions had been increasing following a linear trend, it was assumed that this trend would have continued in 2020 if the COVID-19 pandemic had not occurred. Hence, a linear model was fitted to the data from the years prior to 2020 and this model was used to quantify deviations from the expectation. Fitting this linear model simply to the total number of across-center hospital admissions would be problematic, however. Not all centers contributed their numbers to the study dataset from 2015 onward, but instead started contributing in later years. Each addition of a center leads to a jump in the total number of admissions in the year of its addition. To make sure that these jumps do not influence the estimate of our linear model of the steady increase of admissions over time, our analysis was repeated using three subsets of the study data: one containing all centers contributing since 2015 with years 2015–2020, one with all centers contributing since 2016 with years 2016–2020, and one with all centers contributing since 2018 with years 2018–2020 (which are all centers). Since the analysis described above revealed a clear decline of stroke admissions in the 2020 Swiss lockdown period, the question of whether the population of admitted cases had in some way changed was posed. Due to known, pandemic independent, temporal trends in certain variables a comparison of, for example, 2020 to 2015 was considered inappropriate. It was decided to compare the patient population of weeks 11–17 in 2020 to the patient population of weeks 11–17 in 2018 and 2019. The analysis period spanned from 1 January 2018 to 8 June 2020.

Categorical variables were summarized as counts and percentages, continuous ones as median and interquartile ranges. Categorical variables were compared with the Fisher's exact test, continuous variables with the Wilcoxon rank-sum test. *p* values are two-tailed. *p* values <0.05 were considered statistically significant. Statistical analysis was performed by P.W. and G.D. using R (R Core Team 2019 [16]).

RESULTS

Overall, 28,310 patients were admitted between 1 January 2018 and 8 June 2020. Of these, 4491 (15.9%) were admitted during the lockdown period 2020 ($n = 1487$) and the same calendar period of 2018 and 2019 ($n = 3004$). The weekly admissions during the lockdown period decreased up to 22% compared to expectations from admission trends since 2018 (Figure 1). During three consecutive lockdown weeks, the admission rate was lower than the 5% quantile of expectations (probability of observing at least that many extreme values without the lockdown: 0.38%). In a sensitivity analysis excluding patients with TIA, the drop in admission was even more pronounced, with four consecutive lockdown weeks falling under the 5% quantile of expectations (probability of 0.02% without the lockdown) (Figure 1). A comparison to the years 2015–2019 did not change these findings (Figure S1). The geographical analysis revealed

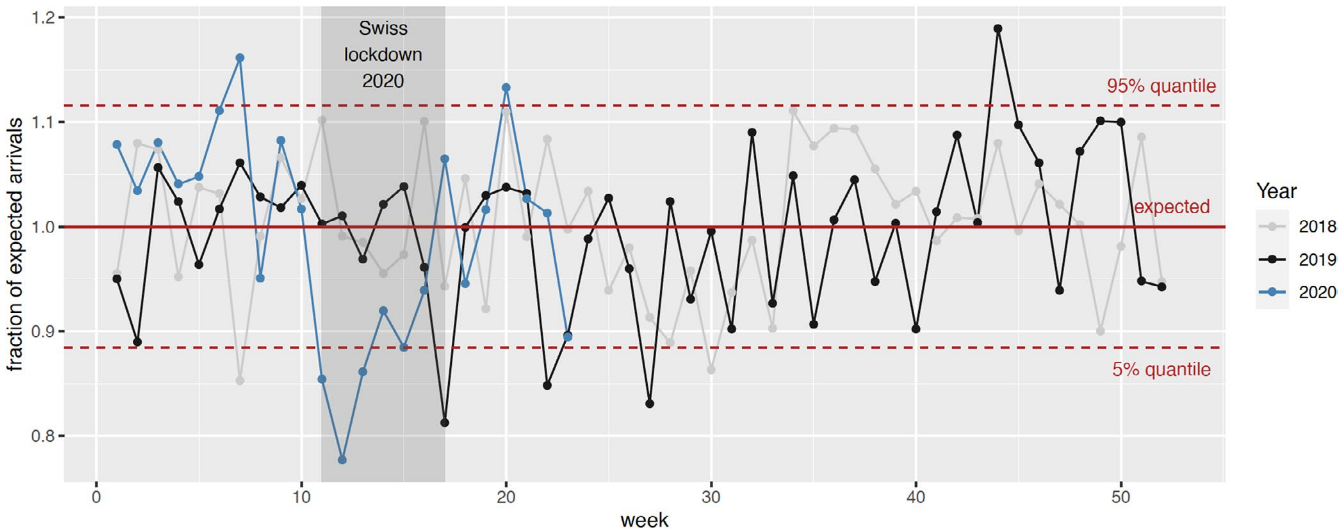

FIGURE 1 Weekly admissions registered in the Swiss Stroke Registry from 1 January 2018 to 8 June 2020 (top). The linear regression is based on the data from 2018–2019. Week 53 has been removed for all years. Fractions compared to the expected number of arrivals (bottom) [Colour figure can be viewed at wileyonlinelibrary.com]

that the admission drop was more pronounced in regions with an average COVID-19 incidence than in regions with a high COVID-19 incidence (Figure 2a,b).

Table 1 summarizes the characteristics of patients admitted during the lockdown period (2020) versus during the same calendar period in 2018 and 2019. The distribution of cerebrovascular events was significantly different ($p = 0.006$) with higher proportions of ICH (9.3% vs. 7.1%) and TIA (19% vs. 17%) and a lower proportion of ischaemic strokes (72% vs. 76%) during the lockdown. Referral modes were significantly different ($p < 0.001$) during the lockdown, with more patients admitted through emergency medical services (48% vs. 42%).

Etiologies of stroke were significantly different ($p = 0.006$) during the lockdown, with fewer proportion of cardioembolic strokes (20% vs. 26%). There were no statistically significant differences for onset-to-door time. On admission, stroke severity (median NIHSS) was 2 (interquartile range 1–6) during the lockdown period versus 3 (interquartile range 1–7) in 2018–2019 ($p = 0.07$). There was no statistically significant difference in the proportion of patients treated with recanalization therapies, in the door-to-needle or door-to-groin times, nor in the disability and mortality rates between the lockdown period and the previous 2 years (Table 2).

DISCUSSION

The main finding of this nationwide observational study is that weekly rates of cerebrovascular events fell by up to 22% during the Swiss national lockdown compared to expectations from admission trends from the years 2018–2019. It is very unlikely that this is explained by chance alone. No evidence was found supporting assumptions that patients with milder strokes have not been admitted, since—during the lockdown—median NIHSS was lower compared to the previous 2 years. There were differences in the types and etiology of strokes with more ICH and fewer cardioembolic strokes during the lockdown.

According to a meta-analysis of 18 cohort studies including 67,845 patients, SARS-CoV-2 infection was associated with an increased odds of ischaemic stroke (odds ratio 3.58, 95% confidence interval 1.43–8.92) [17]. Yet, this did not translate into an observable increase of stroke admissions during the first peak of the pandemic. Instead, a reduction was observed in admissions for stroke, in line with what was reported for several other countries. For instance, in China, across 280 hospitals, there were fewer hospital admissions during the COVID-19 outbreak (−40%) [9]. In the USA, in the Get with the Guidelines—Stroke National Registry, stroke presentations decreased by an average of 15.3% per week between 4 February 2020 and 29 June 2020 compared with similar months in 2019 [18]. In Joinville, Brazil, there were 36.4% fewer stroke admissions during the COVID-19 restrictions in the city compared to the same period in 2019, with no difference in admissions for severe stroke and ICH [8]. In southern Spain, the number of hospital admissions was 25% lower compared to the previous months [5]. At the Hospital Clinic of Barcelona, Spain, there was a 23% decline of stroke admissions compared to March 2019 [19]. In two German academic centers, stroke admission rates decreased by 40% and 46% in the temporal context of the implementation of public health measures compared to 2019 [7].

As COVID-19 represents a risk factor for ischaemic stroke, as seen in a large study from Sweden, the reduction in stroke admission during the lockdown is intriguing [20]. Possible reasons for fewer stroke admissions include [21] that strict “stay at home” orders and fear of infection may have led patients with milder strokes not to seek care. However, no supporting evidence for this assumption was found: during the lockdown period, symptom severity was lower compared to the previous years. The underlying mechanisms for fewer admissions can only be hypothesized. Social

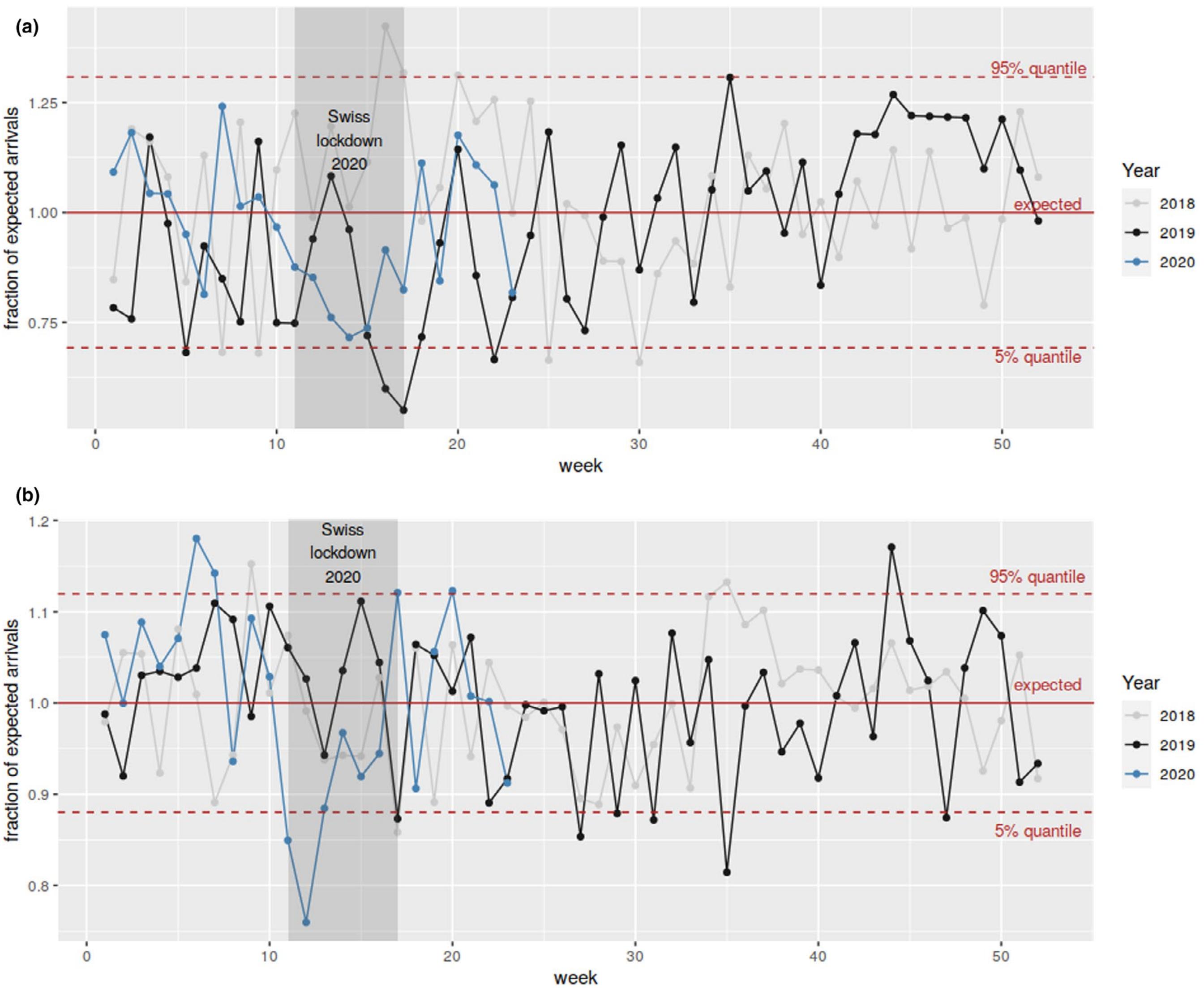

FIGURE 2 (a) High COVID-19 incidence regions (>700 COVID-19 cases/100,000 inhabitants; all regions located in the Italian and French speaking parts of Switzerland). (b) Average COVID-19 incidence regions. Weekly arrivals registered in the Swiss Stroke Registry from 1 January 2018 to 8 June 2020 (top). The linear regression is based on the data from 2018–2019. Week 53 has been removed for all years. Fractions compared to the expected number of arrivals (bottom) [Colour figure can be viewed at wileyonlinelibrary.com]

isolation, especially amongst the elderly, may have contributed to under-detection of stroke by proxies or delayed detections without admission to a stroke unit or stroke center. It is possible that stroke incidence itself has declined, for instance due to behavioral and environmental changes during the lockdown. Indeed, long working hours are associated with a 33% relative risk increase of incident stroke [22]. Air pollutants have a marked and close temporal association with admissions to hospital for stroke or mortality from stroke, as seen in a meta-analysis of observational studies [23]. Behavioral changes may have reduced the incidence of other respiratory tract infections known to be associated with stroke [24].

Despite the increase of referrals with emergency services, a lack of capacity in general or restrictions in acute stroke pathways are unlikely contributors to the observed decrease in admissions. In Switzerland, emergency services did not reach saturation although some patients had to be transferred to other hospitals. Moreover, all participating centers were reminded of the importance of completion of data entry during and after the first pandemic wave. It was deemed unlikely that stroke underdiagnosis or reduced case ascertainment in the Swiss Stroke Registry can explain the reported admission drop compared to pre-pandemic years.

The rate of recanalization therapies remained constant during the pandemic, in line with international observations [17]. Door-to-needle and door-to-groin times did not change significantly during the lockdown period, similarly to what has been found in a recent international multicenter cohort study across 20 stroke centers in Europe and Israel [25]. In China, however, stroke care was temporarily reduced in the majority of hospitals; accordingly, thrombolysis and thrombectomy rates dropped by about 25% compared to the same period in 2019 [9].

In regions with a high COVID-19 incidence a more pronounced drop in stroke admission rates was expected due to stricter

TABLE 1 Characteristics of patients admitted during the Swiss lockdown period[a] 2020 versus the same calendar period in 2018 and 2019

	2018–2019 (*n* = 3004)	2020 (*n* = 1487)	*p*
Women, *n* (%)	1293 (43)	611 (41)	0.2
Age, median (IQR)	75 (64–83)	75 (63–83)	0.3
NIHSS on admission, median (IQR)	3 (1, 7)	2 (1, 6)	0.07
Hypertension, *n* (%)	2105 (74)	1073 (74)	0.9
Hyperlipidemia, *n* (%)	1741 (61)	904 (62)	0.6
Diabetes mellitus, *n* (%)	593 (21)	307 (21)	0.6
Atrial fibrillation, *n* (%)	663 (23)	303 (21)	0.06
History of stroke, *n* (%)	518 (18)	273 (19)	0.6
Event type, *n* (%)			
Ischaemic stroke	2274 (76)	1065(72)	0.006
Intracerebral hemorrhage	213 (7.1)	138 (9.3)	
Transient ischaemic attack	517 (17)	284 (19)	
Referral mode, *n* (%)			
Emergency service	1223 (42)	710 (48)	<0.001
Self-referral	635 (22)	273 (19)	
Family physician	344 (12)	194 (13)	
Other hospital	581 (20.5)	254 (17)	
In-hospital event	119 (4)	44 (3)	
Etiology of ischaemic stroke, *n* (%)			
Cardioembolic	679 (26)	268 (20)	0.001
Large artery atherosclerosis	405 (16)	188 (14)	
More than one possible etiology	192 (7)	112 (9)	
Small vessel disease	286 (11)	150 (11)	
Other etiology	155 (6)	88 (7)	
Unknown	891 (34)	510 (39)	
Onset time, *n* (%)			
Known	1972 (66)	933 (63)	0.07
Unknown	629 (21)	355 (24)	
Wake-up stroke	390 (13)	196 (13)	
mRS pre-hospital, *n* (%)			
0–2	2005 (90)	962 (90)	0.8
3–5	228 (10)	105 (9.8)	

Note: Statistics presented: median (interquartile range); n (%). Statistical tests performed: chi-squared test of independence; Wilcoxon rank-sum test.

Abbreviations: IQR, interquartile range; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.

[a]From 13 March to 26 April.

adherence to stay-at-home instructions. The opposite was the case—regions with an average COVID-19 incidence experienced a more pronounced drop. Possible reasons can only be hypothesized: in the high COVID-19 incidence regions, the incidence of acute cerebrovascular events may have been higher or the threshold to seek medical attention for stroke symptoms lower.

An increase in the ICH proportion amongst hospitalized neurological patients was observed in the main hospital in Sarajevo (Bosnia-Herzegovinia) during the war from 1992 to 1995. However, also the proportion of patients with ischaemic stroke increased, albeit less markedly [26,27]. Proposed reasons include severe shortages of cardiovascular drugs and increased level of stress amongst the population [26]26. During the Swiss lockdown, hints about a reduced supply of cardiovascular drugs are not available, so that the reasons for the relative increase in ICH remain unknown.

The main strength of this study is the national scope and prospective design of the Swiss Stroke Registry, which had been established years before the COVID-19 outbreak. This enabled us to examine the effect of the lockdown using data defined a priori from all certified Stroke Centers and Stroke Units in Switzerland. Data in the 2 years prior to the pandemic were used to model fluctuations of admission rates and demonstrated that the observed decrease during the lockdown is very unlikely to be explained by chance. Moreover, the Swiss Stroke Registry includes patients treated with and without acute recanalization therapies, allowing for inclusions of a broader study population and examination of the proportion of patients receiving acute therapy.

There are several important limitations. First, the Swiss Stroke Registry captures only those patients admitted to certified Stroke Units and Stroke Centers—an estimated two-thirds of all Swiss stroke patients. It remains unclear how our findings can be generalized to hospitals not certified for acute stroke care. Secondly, statistical power is limited to understand why the drop in stroke admission was more pronounced in regions with an average COVID-19 incidence. Finally, despite the fact that our national criteria for Stroke Centers and Stroke Units are in line with European Stroke Organization guidelines, differences in the type and severity of lockdown measures and pre-hospital services limit the generalizability of our findings outside Switzerland.

In conclusion, fewer patients than expected were admitted for cerebrovascular events in Switzerland during the lockdown period in 2020. Stroke severity was lower during the lockdown. Importantly, the Swiss healthcare system was able to ensure the same high standard of stroke care with the same availability, speed of delivery and short-term outcome as in the years before without a pandemic crisis. The population should be informed to seek urgent medical care in the case of acute neurological symptoms, irrespective of the pandemic situation.

CONFLICT OF INTERESTS

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TABLE 2 Performance measures and 3-month outcomes of patients admitted during the lockdown period[a] 2020 versus the same calendar period in 2018 and 2019

	2018–2019 ($n = 3004$)	2020 ($n = 1487$)	p
Onset-to-door time (min), median (IQR)	276 (106–934)	311 (105–1039)	0.3
Intravenous thrombolysis, median (IQR)	481 (22%)	234 (22.1)	0.6
Door-to-IVT time (min), median (IQR)	40 (30–61)	38 (29–55)	0.5
Endovascular treatment, median (IQR)	372 (17%)	159 (15%)	0.14
Door-to-groin time (min), median (IQR)	84 (55–114)	80 (51–103)	0.3
mRS 90 days, *n* (%)			
Available mRS information (*n*, %)[b]	2270 (76%)	1241 (83%)	>0.9
0–2	1512 (67%)	829 (67%)	
3–5	447 (20%)	247 (20%)	
6	311 (13%)	165 (13%)	

Note: Statistical tests performed: chi-squared test of independence; Wilcoxon rank-sum test.
Abbreviations: IQR, interquartile range; IVT, intravenous thrombolysis; mRS modified Rankin Scale.
[a]From 13 March to 26 April.
[b]Percentage refers to people with available mRS at 90 days.

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AUTHOR CONTRIBUTIONS

Gian Marco De Marchis: Conceptualization (equal); data curation (equal); funding acquisition (equal); investigation (equal); validation (equal); writing—original draft (equal); writing—review and editing (equal). Patrick Wright: Data curation (equal); formal analysis (equal); investigation (equal); validation (equal); writing—review and editing (equal). Patrik Michel: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Davide Strambo: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Emmanuel Carrera: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Elisabeth Dirren: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Andreas R Luft: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Susanne Wegener: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Carlo Cereda: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Georg Kägi: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Jochen Vehoff: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Henrik Gensicke: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Philippe A Lyrer: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Krassen Nedeltchev: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Timo Kahles: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Manuel Bolognese: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Stephan Salmen: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Rolf Sturzenegger: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Christophe Bonvin: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Christian Berger: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Ludwig Schelosky: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Marie-Luise Mono: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Biljana Rodic: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Andrea von Reding: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Guido Schwegler: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Alexander Tarnutzer: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Friedrich Medlin: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Andrea M Humm: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Nils Peters: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Morin Beyeler: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Javier Fandino: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Lilian Kriemler: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). David Bervini: Data curation (equal); investigation (equal); validation (equal); writing—original draft (equal). Lars Hemkens: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Pasquale Mordasini: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Marcel Arnold: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Urs Fischer: Data curation (equal); investigation (equal); validation (equal); writing—review and editing (equal). Leo H Bonati: Data curation (equal); investigation (equal); validation (equal); writing—original draft (equal).

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DATA AVAILABILITY STATEMENT

The de-identified data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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