Global Impact of the COVID-19 Pandemic on Stroke Volumes and Cerebrovascular Events: A 1-Year Follow-up

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Source / Izvornik: **Neurology, 2023, 100, 408 - 421**

Journal article, Published version
Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

https://doi.org/10.1212/WNL.0000000000201426

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:220:554797

RESEARCH ARTICLE

Global Effect of the COVID-19 Pandemic on Stroke Volumes and Cerebrovascular Events

A 1-Year Follow-up

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Neurology® 2023;100:e408-e421. doi:10.1212/WNL.0000000000201426

Abstract

Background and Objectives

Declines in stroke admission, IV thrombolysis (IVT), and mechanical thrombectomy volumes were reported during the first wave of the COVID-19 pandemic. There is a paucity of data on the longer-term effect of the pandemic on stroke volumes over the course of a year and through the second wave of the pandemic. We sought to measure the effect of the COVID-19 pandemic on the volumes of stroke admissions, intracranial hemorrhage (ICH), IVT, and mechanical thrombectomy over a 1-year period at the onset of the pandemic (March 1, 2020, to February 28, 2021) compared with the immediately preceding year (March 1, 2019, to February 29, 2020).

Methods

We conducted a longitudinal retrospective study across 6 continents, 56 countries, and 275 stroke centers. We collected volume data for COVID-19 admissions and 4 stroke metrics: ischemic stroke admissions, ICH admissions, IVT treatments, and mechanical thrombectomy procedures. Diagnoses were identified by their *ICD-10* codes or classifications in stroke databases.

Results

There were 148,895 stroke admissions in the 1 year immediately before compared with 138,453 admissions during the 1-year pandemic, representing a 7% decline (95% CI [95% CI 7.1–6.9]; $p < 0.0001$). ICH volumes declined from 29,585 to 28,156 (4.8% [5.1–4.6]; $p < 0.0001$) and IVT volume from 24,584 to 23,077 (6.1% [6.4–5.8]; $p < 0.0001$). Larger declines were observed at high-volume compared with low-volume centers (all $p < 0.0001$). There was no significant change in mechanical thrombectomy volumes (0.7% [0.6–0.9]; $p = 0.49$). Stroke was diagnosed in 1.3% [1.31–1.38] of 406,792 COVID-19 hospitalizations. SARS-CoV-2 infection was present in 2.9% ([2.82–2.97], 5,656/195,539) of all stroke hospitalizations.

Discussion

There was a global decline and shift to lower-volume centers of stroke admission volumes, ICH volumes, and IVT volumes during the 1st year of the COVID-19 pandemic compared with the prior year. Mechanical thrombectomy volumes were preserved. These results suggest preservation in the stroke care of higher severity of disease through the first pandemic year.

Trial Registration Information

This study is registered under NCT04934020.

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Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Glossary

ICH = intracranial hemorrhage; **IVT** = IV thrombolysis; **PSC** = primary stroke center.

More than 2 years after the COVID-19 pandemic was declared in early 2020, over 500 million confirmed cases and 6 million deaths have been reported worldwide. Although pulmonary dysfunction is the most common symptom of COVID-19, infection also yields significant disruption of the coagulation system and is a potential trigger for ischemic stroke.[1-3]

Stroke represents an important complication in an estimated 1.1%–1.5% of COVID-19–admitted patients.[4-8] As a result of the early surge in COVID-19 admissions, the allocation of health care resources and the delivery of stroke care have been affected.[9-13] During the first wave of the COVID-19 pandemic in 2020, declines in stroke admission volumes, IV thrombolysis (IVT), and mechanical thrombectomy have been reported across regional,[14-17] national,[18-23] and global[6,24-29] studies. In our initial report covering the first 4 months of the COVID-19 pandemic, we observed a greater than 10% decrease in global stroke admissions, IVT treatments, and IVT transfers, followed by recovery of stroke volume in later months. This report demonstrated the substantial effect of the first wave of the COVID-19 pandemic on global stroke volumes. In the later part of 2020, a second wave of the pandemic caused surges in COVID-19 cases throughout the globe. The effects of changes in governmental responses to this second wave, including increased public education efforts and intermittent lockdowns during the 1st year, are scarce. Here, we report the effect of COVID-19 on global stroke volumes over the 1st year of the pandemic.

Study Objective and Hypothesis

The primary objective of this study was to evaluate the 1-year volumes of the following stroke metrics: (1) ischemic stroke admissions, (2) intracranial hemorrhage (ICH) admissions, (3) IVT, and (4) mechanical thrombectomy (MT) during the pandemic (March 1, 2020, to February 28, 2021) and compare these metrics with the same 1-year period immediately prior (March 1, 2019, to February 29, 2020). Our primary prespecified hypotheses were that, in the setting of the pandemic's continued strain on health care resources, (1) there would be a reduction in all the aforementioned stroke metrics and (2) centers with more COVID-19 volumes would report greater decreases in stroke admissions.

Methods

Study Design

This was a cross-sectional, observational, retrospective follow-up study evaluating monthly aggregate volumes of consecutive patients hospitalized with a diagnosis of ischemic stroke, ICH, or COVID-19 and acute reperfusion therapies including IVT and mechanical thrombectomy. The diagnosis was identified by stroke databases or related *ICD-10* codes (primary, secondary, or tertiary discharge codes).

This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline (eTable 1, links.lww.com/WNL/C442). The study is registered under NCT04934020 (clinicaltrials.gov).

Setting and Participants

Data were collected from collaborators of a prior global study during the first wave of the pandemic, which consisted of 457 stroke centers across 70 countries.[7] These sites were selected by contact with stroke leaders of national and international stroke societies, who invited sites within their network to participate in this study. These societies included the Society of Vascular and Interventional Neurology, the European Stroke Organization, the Middle East North Africa Stroke and Interventional Neurotherapies Organization, the Japanese Society of Vascular and Interventional Neurology, and the Latin America Stroke Group. An additional 23 sites were invited by publicly available information via institution email addresses.

A comprehensive stroke center was defined as a center that offered mechanical thrombectomy; a primary stroke center (PSC) was defined as a center that did not. Centers with no thrombectomy service at the beginning of the study period that later became thrombectomy capable during the study period were classified as PSC; these centers were excluded from the mechanical thrombectomy analysis. Of the 480 centers invited to contribute to this follow-up 1-year study, we received data from 275 stroke centers across 56 countries and 6 continents. Each center was verified for profound drops in volume (i.e., > 50%) that may have biased the analysis. Potential confounders including rerouting or diversion of cases to another hospital were inquired to centers where profound drops in volume were noted. Centers were excluded due to incomplete data during the study period for ischemic stroke (30 centers), ICH (36 centers), IVT (36 centers), and mechanical thrombectomy (76 centers).

We defined the beginning of the pandemic in each country based on the date of the first reported case[30] (eTable 2, links.lww.com/WNL/C442). We defined the second wave with 2 definitions. Our primary definition was that the number of COVID-19 cases must decline by greater than 50% from the previous wave's peak and more than double at the next peak. The start date for this occurrence was chosen as the minimum closest to the second wave. Secondarily, we defined the second wave as the first definition, with the addition of 2 or more months apart between the peak of the first wave and the start of the second wave[31] (eTable 2).

Data were collected between May 1, 2021, and September 15, 2021, via electronic medical record to capture completely coded data through the end of the study period, May 31, 2021. Data were submitted to the coordinating sites, Boston Medical Center and Emory University School of Medicine, via excel sheet. Data verification was conducted with the receipt of data from each site by the lead author (T.N.N.), with additional queries related to incomplete data entry returned to submitting authors, with deadline extension to October 30, 2021. The Principal Investigator (T.N.N.) and the lead statistician had access to all data. Investigators at the coordinating sites had access to site-level data for the purposes of data merging, data verification, and statistical analysis.

Study Variables and Outcome Measures

Study variables were collected as monthly aggregate volumes. Ischemic stroke admission was defined as admission to a hospital with a TIA or ischemic stroke as the primary diagnosis. IVT was defined as acute ischemic stroke treatment with IVT. *ICD-10* codes for ischemic stroke used were as follows: I63.0 (Cerebral infarction), I63.1 (Cerebral infarction due to embolism of precerebral arteries), I63.2 (Cerebral infarction due to unspecified occlusion or stenosis of precerebral arteries), I63.3 (Cerebral infarction due to thrombosis of cerebral arteries), I63.4 (Cerebral infarction due to embolism of cerebral arteries), I63.5 (Cerebral infarction due to unspecified occlusion or stenosis of cerebral arteries), I63.8 (Other cerebral infarction), and I63.9 (Cerebral infarction, unspecified). A physician, stroke, or research coordinator verified case ascertainment by existing stroke databases, including the Get with the Guidelines Stroke Database, the Czech Republic National Stroke Database, and the Japan National Stroke Database.

ICH was defined as admission to a hospital with an intracranial or intracerebral hemorrhage as the primary diagnosis. *ICD-10* codes for ICH used were as follows: I61 (Nontraumatic ICH), I61.0 (Nontraumatic ICH in hemisphere, subcortical), I61.1 (Nontraumatic ICH in hemisphere, cortical), I61.2 (Nontraumatic ICH in hemisphere, unspecified), I61.3 (Non-traumatic ICH in the brain stem), I61.4 (Nontraumatic ICH in the cerebellum), I61.5 (Nontraumatic ICH, intraventricular), I61.6 (Nontraumatic ICH, multiple localized), I61.8 (Other non-traumatic ICH), and I61.9 (Nontraumatic ICH, unspecified).

COVID-19 admission was defined as any patient admitted with a COVID-19 diagnosis to the hospital, encompassing a non-neurologic diagnosis. The *ICD-10* code for COVID-19 diagnosis used was UO7.1.

Bias

Centers were screened for potential duplicate data. To avoid data reporting lag bias, we did not include centers with incomplete data for the variable of interest. Centers submitting data from a stroke network were asked not to duplicate IVT or large vessel occlusion patients transferred from a PSC to a comprehensive stroke center. PSCs were excluded from the MT analysis. In certain nations, COVID-19 case volumes did not demonstrate distinct peaks, either due to consistently high volumes (e.g., Guatemala) or extremely low volumes (e.g., New Zealand), obscuring pandemic waves.

Statistical Analysis

First, we compared percentage change in the absolute number of ischemic stroke, ICH, IVT, and MT admissions before and during the COVID-19 pandemic. The 95% CIs for percentage change were calculated using the Wilson procedure without correction for continuity.[32] The method is computationally simpler with good coverage properties. The differences in admissions across the 2 periods were assessed for significance using the Poisson Means test. The analysis was repeated by hospital volume (low, intermediate, or high), stroke center (primary or comprehensive), and hospital COVID-19 volume (low, intermediate, or high). The relative percentage decrease in volume between different categories (for example, low vs intermediate hospital volume) was tested using the z-test of proportion.

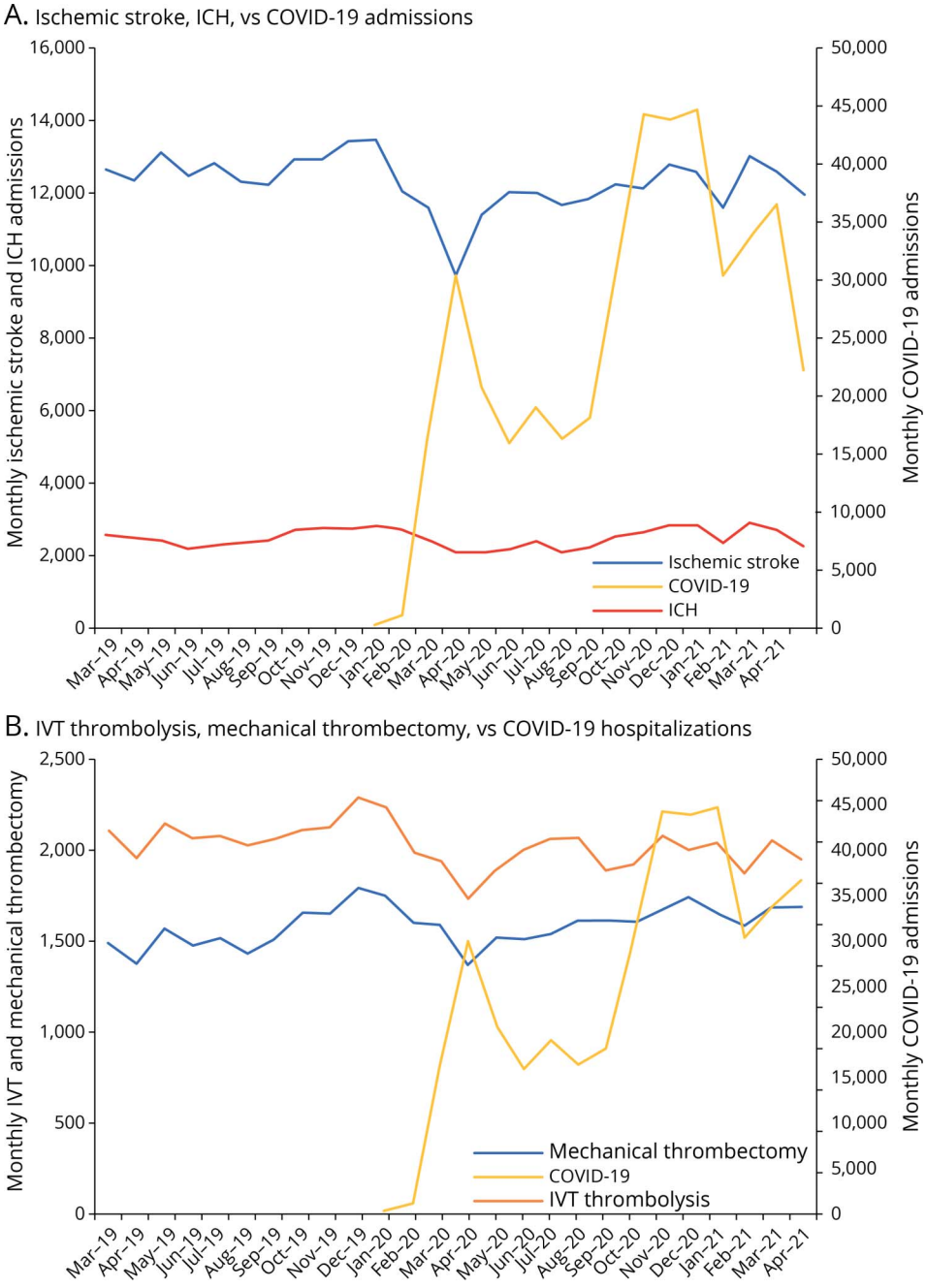
We then compared average monthly volumes (admissions/month) of ischemic stroke, ICH, IVT, and MT before and during the COVID-19 pandemic. The data were analyzed in a mixed design using a repeated-measures analysis of variance (PROC MIXED analysis in SAS) for accounting for the paired data structure and potential covariates. The autoregressive, compound symmetrical, and unstructured variance-covariance matrix structures were analyzed for the best model determined by the Akaike Information Criterion. The unstructured matrix was the best fit and was used for the analyses. The monthly hospital volume analysis was adjusted for the date of the peak COVID-19 volume for each country, the start date of the second wave, and the continent. Estimated marginal means were calculated using the LSMEANS statement in PROC MIXED. Similar to the overall volume analysis, monthly volume analysis was stratified by hospital volume, stroke center, and COVID-19 volume.

Finally, we performed a supplementary analysis comparing percentage change in absolute volume and monthly volume between before and during COVID-19 periods across different continents of the world. All data were analyzed using SAS version 9.4 (SAS Institute), and the significance level was set at a p value of < 0.05.

Standard Protocol Approvals, Registrations, and Patient Consents

This was an investigator-initiated study. As this was a continuation of our prior work, the institutional review boards from the coordinating sites (Emory University and Boston Medical Center) considered that the investigators did not have access to protected health information in this follow-up study, and thus, no IRB oversight was required because the study did not meet the US federal description of human

Figure 1 Monthly Volume for Ischemic Stroke Admissions, Intracranial Hemorrhage Admissions, IV Thrombolysis, Mechanical Thrombectomy, and COVID-19 Admissions



(A) Monthly admission volume for ischemic stroke (blue), intracranial hemorrhage (red), and COVID-19 (yellow). (B) Monthly volume for IV thrombolysis (orange), mechanical thrombectomy (blue), and COVID-19 (yellow).

subject research. Site-specific IRB approval was obtained where required by local regulations or institutional policy. There was no protective health information data included in this study. The study was funded by the Society of Vascular and Interventional Neurology research pilot grant. This study was registered under NCT04934020.

Data Availability

Data are available on reasonable request to the corresponding author.

Results

Overall, there were 345,089 ischemic stroke and ICH admissions across the 2 epochs 1 year prepandemic and the first year during the pandemic. There were 24,584, 23,077 IVT therapies (overall IVT, n = 47,661) and 18,375, 18,507 mechanical thrombectomy procedures (overall MT, n = 36,882) included across the prior-year pandemic, and 1-year pandemic period, respectively (Figure, A, B). Data contributions by continent and their relative changes across the

Table 1 Ischemic Stroke Admissions Overall and Monthly Volumes Before and During the COVID-19 Pandemic

	Overall volume					Monthly volume[a]			
							Before COVID-19	During COVID-19	
	N	n1	n2	Change, % (95% CI)	*p* Value	N	Adjusted mean (SE)		*p* Value
Overall	245	148,895	138,453	−7.0 (−7.1 to −6.9)	<0.0001	251	43.8 (4.0)	40.3 (3.9)	<0.0001
Hospital ischemic stroke volume[b]									
Low	83	19,437	18,440	−5.1 (−5.5 to −4.8)	<0.0001	84	18.5 (1.1)	17.6 (1.2)	0.081
Intermediate	82	41,789	39,145	−6.3 (−6.6 to −6.1)	<0.0001	84	40.6 (1.9)	38.2 (2.0)	0.0003
High	80	87,669	80,868	−7.8 (−7.9 to −7.6)	<0.0001	83	84.4 (6.3)	77.4 (6.4)	<0.0001
Primary vs comprehensive stroke center[c]									
Primary	68	26,141	24,007	−8.2 (−8.5 to −7.8)	<0.0001	70	28.7 (4.9)	26.5 (5.0)	0.058
Comprehensive	177	122,754	114,446	−6.8 (−6.9 to −6.6)	<0.0001	181	49.3 (6.7)	45.4 (6.6)	<0.0001
Hospital COVID-19 volume[d]									
Low	70	37,281	34,811	−6.6 (−6.9 to −6.4)	<0.0001	71	35.5 (6.1)	32.7 (6.0)	0.011
Intermediate	70	42,660	40,391	−5.3 (−5.5 to −5.1)	<0.0001	71	50.8 (7.2)	47.9 (7.1)	0.004
High	70	47,129	41,931	−11.0 (−11.3 to −10.8)	<0.0001	72	45.1 (6.7)	39.3 (6.5)	<0.0001

Abbreviations: N = number of hospitals; n1 = number of admissions during 12 months before the COVID-19 pandemic; n2 = number of admissions during 12 months of the COVID-19 pandemic; SE = standard error.
[a] The monthly volume analysis is adjusted for the date of peak COVID-19 volume for each country, the start date of the second wave, and the continent.
[b] *p*: low vs intermediate = <0.0001; low vs high = <0.0001; and intermediate vs high = <0.0001.
[c] *p*: primary vs comprehensive = <0.0001.
[d] *p*: low vs intermediate = <0.0001; low vs high = <0.0001; and intermediate vs high = <0.0001.

pandemic are presented in eTables 3–6 (links.lww.com/WNL/C442).

Ischemic Stroke Admissions

There were 148,895 admissions for ischemic stroke in the 1 year prepandemic, and 138,453 admissions during the 1-year pandemic, representing a 7% absolute decrease ([95% CI −7.1 to −6.9]; $p < 0.0001$, n = 245 sites) in ischemic stroke admissions; monthly mean (SE) volume decreased accordingly (43.8 [4.0] to 40.3 [3.9]; $p < 0.0001$, n = 251 sites). The observed relative decrease in volumes was larger at higher volume stroke admission centers (low vs intermediate vs high; $p < 0.0001$) and higher volume COVID-19 centers (low vs intermediate vs high; $p < 0.0001$). In the tertile of high-volume stroke centers, 32/71 (45%) of centers were high-tertile COVID-19 centers. The observed decrease in volumes was smaller at comprehensive stroke centers than PSCs (−6.8% vs −8.2%; $p < 0.0001$) (Table 1).

Geographic variation was noted in the change of ischemic stroke admissions over the 1-year period: Europe, −5.7% ([−5.9 to −5.5]; $p < 0.0001$); North America, −6.2% ([−6.5 to −6.0]; $p < 0.0001$); Asia, −10.6% ([−11.0 to −10.3]; $p < 0.0001$); South America, −13.3% ([−14.4 to −12.2]; $p < 0.0001$); Oceania, 4.7% ([4.0–5.4]; $p = 0.05$); and Africa, −15.3% ([−18.6 to −12.5]; $p = 0.008$) (eTable 3, links.lww.com/WNL/C442)

ICH Admissions

There were 29,585 admissions for ICH in the 1 year prepandemic, and 28,156 admissions during the 1-year pandemic, representing a 4.8% absolute decrease ([−5.1 to −4.6]; $p < 0.0001$, n = 239 sites); monthly mean (SE) volume decreased (9.7 (1.1) to 9.2 (1.1); $p = 0.015$, n = 246 sites). The observed decrease in volumes was greater at high-volume compared with intermediate-volume ($p < 0.0001$) centers and with a gradient of decrease in higher volume COVID-19 centers (low vs intermediate vs high; $p < 0.0001$). At low-volume ICH centers, there was a 14.6% ([13.2–16.1]; $p < 0.0001$) increase in ICH admissions. At low-volume COVID-19 centers, there was no difference (−1.7% [−2.0 to −1.4]; $p = 0.27$) in ICH admissions. In the tertile of high-volume ICH centers, 27/70 (39%) were high-tertile COVID-19 centers. There was no observed decrease in ICH admissions at PSCs (−3.2% [−3.8 to −2.7]; $p = 0.15$) but a 5.1% ([−5.4 to −4.8]; $p < 0.0001$) decrease at comprehensive stroke centers (Table 2), with continental variation noted (eTable 4, links.lww.com/WNL/C442).

IVT

There was a relative decline in IVT, with 24,584 therapies in the prepandemic year compared with 23,077 during the pandemic year, representing a 6.1% absolute decrease ([−6.4 to −5.8]; $p < 0.0001$ n = 239 sites); monthly mean

Table 2 Intracerebral Hemorrhage Admissions Overall and Monthly Volumes Before and During the COVID-19 Pandemic

	Overall volume					Monthly volume[a]			
							Before COVID-19	During COVID-19	
	N	n1	n2	Change, % (95% CI)	*p* Value	N	Adjusted mean (SE)		*p* Value
Overall	239	29,585	28,156	−4.8 (−5.1 to −4.6)	<0.0001	246	9.7 (1.1)	9.2 (1.1)	0.015
Hospital intracerebral hemorrhage volume[b]									
Low	80	2,319	2,657	14.6 (13.2 to 16.1)	<0.0001	82	2.5 (0.27)	2.9 (0.30)	0.017
Intermediate	80	7,235	6,865	−5.1 (−5.6 to −4.6)	0.002	82	7.4 (0.51)	7.0 (0.52)	0.011
High	79	20,031	18,634	−7.0 (−7.3 to −6.6)	<0.0001	82	21.4 (2.9)	20.0 (2.7)	0.013
Primary vs comprehensive stroke center[c]									
Primary	65	4,010	3,882	−3.2 (−3.8 to −2.7)	0.150	68	4.9 (0.99)	4.8 (0.98)	0.664
Comprehensive	174	25,575	24,274	−5.1 (−5.4 to 4.8)	<0.0001	178	11.0 (2.0)	10.3 (2.0)	0.014
Hospital COVID-19 volume[d]									
Low	68	8,434	8,292	−1.7 (−2.0 to −1.4)	0.272	69	8.5 (1.5)	8.3 (1.5)	0.478
Intermediate	70	7,229	6,939	−4.0 (−4.5 to −3.6)	0.015	71	7.4 (1.3)	7.1 (1.3)	0.184
High	69	10,772	9,727	−9.7 (−10.3 to −9.2)	<0.0001	71	12.1 (3.0)	10.8 (2.8)	0.044

Abbreviations: N = number of hospitals; n1 = number of admissions during 12 months before the COVID-19 pandemic; n2 = number of admissions during 12 months of the COVID-19 pandemic; SE = standard error.
[a] The monthly volume analysis is adjusted for the date of peak COVID-19 volume for each country, the start date of the second wave, and the continent.
[b] *p*: low vs intermediate = N/A; low vs high = N/A; and intermediate vs high = <0.0001.
[c] *p*: primary vs comprehensive = <0.0001.
[d] *p*: low vs intermediate = <0.0001; low vs high = <0.0001; and intermediate vs high = <0.0001.

(SE) volume decreased (7.5 [1.1] to 7.0 [1.1]; $p = 0.006$, n = 244 sites) (Figure B). There was a 7.1% ([6.8–8.2]; $p = 0.02$) increase in IVT at low-volume IVT centers. For intermediate-volume centers, there was no significant change (−3.1% [−3.5 to −2.7]; $p = 0.07$), and for high-volume centers, there was a 9.4% ([−9.8 to −8.9]; $p < 0.0001$) relative decrease in IVT volume. The observed volume decrease was greater at higher-volume COVID-19 centers (low vs intermediate vs high; $p < 0.0001$). In the tertile of high-volume IVT centers, 33/72 (46%) were high-tertile COVID-19 centers. There was a larger relative decrease in IVT volumes at PSCs than comprehensive stroke centers (−11.4% vs −4.9%; $p < 0.0001$) (Table 3) with continental variation (eTable 5, links.lww.com/WNL/C442).

Mechanical Thrombectomy

There was no change in MT volume from the prepandemic to pandemic year (18,375 vs 18,507, 0.7 ([0.6–0.9]; $p = 0.49$, n = 199 sites); monthly volume was also similar between the 2 epochs (6.2 (1.1) vs 6.3 (1.1); $p = 0.72$, n = 205 sites) (Table 4, Figure, B). Among all subgroups, the only difference was a 13.6% ([11.9–15.4]; $p = 0.001$) relative increase at low MT volume centers (Table 4), with continental variation (eTable 6, links.lww.com/WNL/C442).

Rates of Concomitant Stroke With COVID-19 Admissions

Concomitant stroke diagnosis with COVID-19 admissions was reported by 218 centers. Overall, stroke diagnosis (any type) was present in 1.3% ([95% CI 1.31–1.38], 5,453/406,792) of COVID-19 admissions. There was continental variation: Africa 0.8% ([0.68–1.04], 87/10,321), Asia 1.6% ([1.52–1.75], 727/44,664), Oceania 0% ([0–1.11], 0/345), Europe 1.6% ([1.55–1.67], 2,689/166,692), North America 1.1% ([1.06–1.16], 1,688/152,654), and South America 0.8% ([0.73–0.93], 262/32,116; Table 5).

Concomitant SARS-CoV-2 infection with stroke admission was present in 2.9% ([95% CI, 2.82–2.97], 5,656/195,539) overall, with geographic variation: Africa 4.8% ([3.9–5.9], 87/1,802), Asia 1.5% ([1.37–1.58], 782/53,109), Oceania 0% ([0–0.08], 0/5,032), Europe 3.7% ([3.57–3.84], 2,811/75,993), North America 3.2% ([3.04–3.34], 1,714/53,730), and South America 4.5% ([3.96–5.02], 262/5,873; Table 6).

Discussion

In this cross-sectional study, after the onset of the COVID-19 pandemic, there were substantial decreases in ischemic stroke

Table 3 IV Thrombolysis Overall and Monthly Volumes Before and During the COVID-19 Pandemic

	Overall volume					Monthly volume[a]			
							Before COVID-19	During COVID-19	
	N	n1	n2	Change, % (95% CI)	*p* Value	N	Adjusted mean (SE)		*p* Value
Overall	239	24,584	23,077	−6.1 (−6.4 to −5.8)	<0.0001	244	7.5 (1.1)	7.0 (1.1)	0.006
Hospital IV thrombolysis volume[b]									
Low	80	2,222	2,379	7.1 (6.8 to 8.2)	0.021	81	1.9 (0.33)	2.1 (0.35)	0.157
Intermediate	80	6,804	6,596	−3.1 (−3.5 to −2.7)	0.072	82	7.0 (0.23)	6.8 (0.32)	0.425
High	79	15,558	14,102	−9.4 (−9.8 to −8.9)	<0.0001	81	16.3 (1.3)	14.9 (1.3)	0.001
Primary vs comprehensive stroke center[c]									
Primary	62	4,621	4,092	−11.4 (−12.4 to −10.6)	<0.0001	64	7.0 (1.4)	6.4 (1.3)	0.092
Comprehensive	177	19,963	18,985	−4.9 (−5.2 to −4.6)	<0.0001	180	7.8 (1.2)	7.4 (1.1)	0.030
Hospital COVID-19 volume[d]									
Low	68	5,710	5,651	−1.0 (−1.3 to −0.80)	0.580	69	5.0 (1.2)	5.0 (1.2)	0.810
Intermediate	70	7,347	6,897	−6.1 (−6.7 to −5.6)	0.0002	71	7.6 (1.3)	7.2 (1.3)	0.122
High	67	8,470	7,426	−12.3 (−13.1 to −11.7)	<0.0001	69	9.6 (0.95)	8.5 (0.85)	0.003

Abbreviations: N = number of hospitals; n1 = number of admissions during 12 months before the COVID-19 pandemic; n2 = number of admissions during 12 months of the COVID-19 pandemic; SE = standard error.
[a] The monthly volume analysis is adjusted for the date of peak COVID-19 volume for each country, the start date of the second wave, and the continent.
[b] *p*: low vs intermediate = N/A; low vs high = N/A; and intermediate vs high = <0.0001.
[c] *p*: primary vs comprehensive = <0.0001.
[d] *p*: low vs intermediate = <0.0001; low vs high = <0.0001; and intermediate vs high = <0.0001.

admissions (7.0% [95% CI: 7.1–6.9]), ICH admissions (4.8% [5.1–4.6]), and IVT use (6.1% [6.4–5.8]) in the 1 year of the pandemic compared with the year prior. However, there was no significant difference in the volume of MT between the pandemic and prepandemic year. As noted in our prior work with the first wave, among centers with high COVID-19 admission volumes, there was a greater decrease in stroke admission volumes compared with those with low COVID-19 admission volumes (6.6% vs 11.0%; $p < 0.0001$). These findings are consistent with recent national studies evaluating the effect of COVID-19 on stroke admissions during the second wave of the pandemic.[33]

We observed an overall relative decrease in ischemic stroke admission volume across 245 primary and comprehensive stroke centers worldwide. This trend was consistent across all prespecified subgroups. As hypothesized, centers with high COVID-19 volumes had greater decreases in stroke admission volume than those with low COVID-19 volumes. This may reflect a lack of capacity to accommodate stroke admissions at centers with high COVID-19 admissions or different stroke triage patterns during the COVID-19 pandemic. Comprehensive stroke centers experienced a smaller relative decrease in stroke admission volume than PSCs (−6.8% vs −8.2%).

Overall, ICH admission volumes decreased by 4.8% (5.1–4.6). Of note, there was a 14.6% (13.2–16.1) increase in ICH volumes at low-volume ICH centers. These results may indicate a partial shift in the volume of patients with ICH from intermediate- and high-volume centers to low-volume centers, perhaps due to capacity limitations imposed by the high volume of patients with COVID-19 at tertiary care centers.

The overall volume of IVT admissions decreased by 6.1% (6.4–5.8) during the pandemic year compared with the prior year, in line with our prior findings of decline in IVT volumes during the first wave of the pandemic.[7] This difference was driven by a large decrease in IVT at high-volume centers (9.4%) while there was no significant difference at intermediate-volume centers and a 7.1% (6.8–8.2%) increase in IVT at low-volume centers.

No difference in overall mechanical thrombectomy volumes was observed in this study. The maintenance of mechanical thrombectomy volumes despite large decreases in overall stroke admission volumes suggests that the population of patients with large vessel occlusion was not significantly reduced through the pandemic year, concordant with early findings from the US Get With the Guidelines Stroke Registry.[21] Alternatively, any decline in mechanical thrombectomy volume related to the COVID-19 pandemic may have been offset by expanded indications for mechanical thrombectomy[34-41] or increased recruitment of cases by low-volume centers.

Table 4 Mechanical Thrombectomy Overall and Monthly Volumes Before and During the COVID-19 Pandemic

	Overall volume					Monthly volume[a]			
							Before COVID-19	During COVID-19	
	N	n1	n2	Change, % (95% CI)	*p* Value	N	Adjusted mean (SE)		*p* Value
Overall	199	18,375	18,507	0.7 (0.6 to 0.9)	0.492	205	6.2 (1.1)	6.3 (1.1)	0.715
Hospital mechanical thrombectomy volume[b]									
Low	66	1,423	1,616	13.6 (11.9 to 15.4)	0.001	69	1.6 (0.24)	1.8 (0.28)	0.101
Intermediate	67	5,221	5,426	3.9 (3.4 to 4.5)	0.047	69	6.6 (0.27)	6.8 (0.32)	0.312
High	66	11,731	11,465	−2.3 (−2.6 to −2.0)	0.081	67	14.6 (1.2)	14.2 (1.2)	0.260
Primary vs comprehensive stroke center[c]									
Primary	19	826	883	6.9 (5.4 to 8.8)	0.168	21	3.0 (1.0)	3.2 (1.1)	0.605
Comprehensive	180	17,549	17,624	0.4 (0.3 to 0.5)	0.689	184	6.5 (1.2)	6.6 (1.2)	0.844
Hospital COVID-19 volume[d]									
Low	56	4,076	4,043	−0.8 (−1.1 to −0.6)	0.714	57	5.3 (1.2)	5.2 (1.2)	0.830
Intermediate	51	4,705	4,817	2.4 (2.0 to 2.9)	0.251	54	6.9 (1.6)	7.1 (1.7)	0.601
High	63	6,771	6,720	−0.8 (−1.0 to −0.6)	0.661	64	5.6 (1.2)	5.6 (1.2)	0.770

Abbreviations: N = number of hospitals; n1 = number of admissions during 12 months before the COVID-19 pandemic; n2 = number of admissions during 12 months of the COVID-19 pandemic; SE = standard error.
[a] The monthly volume analysis is adjusted for the date of peak COVID-19 volume for each country, the start date of the second wave, and the continent.
[b] *p*: low vs intermediate = <0.0001; low vs high = <N/A; and intermediate vs high = N/A.
[c] *p*: primary vs comprehensive = <0.0001.
[d] *p*: low vs intermediate = N/A; low vs high = 1.0; and intermediate vs high = N/A.

Stroke represents an important complication in COVID-19 infection in an estimated 1.1%–1.5% of COVID-19–admitted patients.[4,5,8] In our study, stroke was present in 1.3% of COVID-19–admitted patients, in alignment with previous studies. There were 2.9% of all hospitalized patients with stroke with concomitant SARS-CoV-2 infection. Although we cannot ascertain whether these cases were a direct complication of COVID-19 or an overlap of 2 conditions that are now relatively common, we would favor the latter as it has become evident that stroke is a relatively rare complication of COVID-19.

Altogether, these results indicate a decrease in multiple measures of stroke volume and a shift of volumes toward previously lower volume centers but with the maintenance of mechanical thrombectomy volumes. The reduced volumes may suggest the reduced presentation of patients with mild stroke and TIA or changes in clinician decision-making, resulting in fewer admissions.[42,43] Alternatively, it is also possible that patients with mild stroke were being triaged to the outpatient setting. Notably, mild strokes accounted for as many as 40% of all IVT cases and 10.7% of all EVT cases across 179,710 patients with AIS in a US-based study.[44] This might explain the discrepancy in the relative declines among IVT and EVT observed in the current report. Although the maintenance of mechanical thrombectomy volumes is reassuring as to the appropriate treatment of patients with large

Table 5 Proportion of Patients Hospitalized With COVID-19 With Concomitant Diagnosis of Stroke

	Number of centers	COVID-19 with any stroke	COVID-19 hospitalization	%	95% CI	
Overall	218	5,453	406,792	1.34	1.31	1.38
Asia	51	727	44,664	1.63	1.52	1.75
North America	55	1,688	152,654	1.11	1.06	1.16
Europe	90	2,689	166,692	1.61	1.55	1.67
South America	11	262	32,116	0.82	0.73	0.93
Oceania	6	0	345	0	0	1.11
Africa	5	87	10,321	0.84	0.68	1.04

Table 6 Rates of Concomitant COVID-19 With Stroke Hospitalizations

	Number of centers	COVID-19 with any stroke	Stroke hospitalization	%	95% CI	
Overall	225	5,656	195,539	2.89	2.82	2.97
Asia	54	782	53,109	1.47	1.37	1.58
North America	57	1,714	53,730	3.19	3.04	3.34
Europe	93	2,811	75,993	3.7	3.57	3.84
South America	11	262	5,873	4.46	3.96	5.02
Oceania	5	0	5,032	0	0	0.08
Africa	5	87	1,802	4.8	3.93	5.92

vessel occlusion, the shift seen in other volume measures toward lower volume centers is a trend to be noted. Previous studies have indicated that treatment at high-volume centers is associated with better outcomes following stroke, ICH,[45] and mechanical thrombectomy.[46] In the Oceania region, where COVID-19 has been highly controlled, no differences were seen in stroke or ICH admission volumes, and increases were seen in both IVT and thrombectomy volumes (eTables 5, 6, links.lww.com/WNL/C442), further highlighting the effects of the pandemic. In addition, COVID-19 was associated with 2.9% of stroke admissions in this study. Taken with recent studies suggesting that SARS-CoV-2 is likely to become endemic across the globe, this raises concern that SARS-CoV-2 may become an addition to other respiratory infections (influenza and mycoplasma pneumonia) known to trigger and present as a risk factor for stroke. Long-term stroke metric and outcome data are important to evaluate whether these changes persist beyond the pandemic. Some clinical practices for stroke diagnostic evaluation and management may be updated based on reorganization of stroke care during the pandemic.[47]

Although we have robustly shown differences in population-level trends, our study is limited by the inability to characterize the reason for the changes in volumes over the subsequent waves of the pandemic. Inherent to our cross-sectional study design, we could not track changes on the patient level, and the observed population-level changes may be due to confounding factors. Future studies are important to understand patient-level factors influencing the observed trends in stroke volumes. In addition, we had limited ability to study the effects of governmental policies (e.g., lockdowns) on stroke volumes because the COVID-19 pandemic has affected every nation differently by timing and severity.

During the first year of the COVID-19 pandemic, worldwide ischemic stroke admission, ICH admission, and IVT volumes were relatively decreased while there was no relative change in mechanical thrombectomy volumes. Furthermore, shifts were seen in volumes toward lower-volume centers. A slight recovery in volumes was seen over the year compared with the initial months of the pandemic, but persistently low volumes raise concern that milder forms of a stroke may be untreated or are being redirected to the outpatient setting. Ongoing surveillance and additional future research are warranted to monitor stroke metrics[48-50] and long-term patient outcomes, ensure that public education measures are continued, and ensure that patients continue to seek timely care for stroke.

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Acknowledgment

The authors acknowledge the following contributors for participating in data collection: Megan Brady, MPH, MSW (Henry Ford); Dawn Scozzari, RHIT (Henry Ford); Elisabeth Dirren, MD (Geneva University Hospitals, Geneva, Switzerland); Claudio Rodríguez Fernández (Hospital Universitario Rey Juan Carlos); Jorge Escartín López (Hospital Universitario Rey Juan Carlos); José Fernández-Ferro (Hospital Universitario Rey Juan Carlos); Beatriz de la Cruz Fernández (Hospital Universitario Rey Juan Carlos); Niloofar Mohammadzadeh as data entry staff in Neurosciences Research Center, Tabriz University of Medical Sciences, Tabriz, Iran; Filipe Bessa, MD (Hospital de Santa Maria–Centro Hospitalar Lisboa Norte, Portugal); Nina Jancar, MD (Hospital de Santa Maria–Centro Hospitalar Lisboa Norte, Portugal); and Neil C. Suryadevara, MD (SUNY Upstate, NY).

Study Funding

The study was funded by the Society of Vascular and Interventional Neurology pilot grant.

Disclosure

D. Aguiar de Sousa reported speaker fees from Bayer, travel support from Boehringer Ingelheim, participating in an advisory board for AstraZeneca, and DSMB participation for the SECRET trial, outside the submitted work. K. Alpay reported a research grant from The Radiological Society of Finland. D. Altschul reported consulting fees from Stryker, MicroVention, and Siemens and stocks in NTI. J. Blasco reported speaker and

CEC fees from Stryker and Medtronic, respectively. H. Budinvevic reported speaker fees from Boehringer Ingelheim, Bayer, Pfizer, Berlin, and Chemie Menarini and participation in an advisory board for Boehringer Ingelheim, outside the submitted work. M. Bolognese reported participation in the advisory board (AstraZeneca) and speaker fee (Roche), outside the submitted work. L. Catanese reported research grants from Servier Canada Inc., CIHR, and the Canadian Stroke Consortium and adjudication fees for Ischemia Care. J. Coutinho has received grants paid to his institution from Boehringer Ingelheim, Bayer, and Medtronic. A. Cruz-Culebras reported travel support from Daiichi Sankyo and fees for participating in an advisory board for Alexion, outside the submitted work. C. Falup-Pecurariu reported royalties from Springer Nature Publishing Group and Elsevier, research grant from Transilvania University Brasov, and speaker fees and honoraria from the International Parkinson and Movement Disorders Society and AbbVie, outside the submitted work. M. Farhoudi reported a research grant (number: 700/1483) from the Research & Technology Deputy, Ministry of Health, Iran. U. Fischer reported research grants from Medtronic (BEYOND SWIFT and SWIFT DIRECT); serving as consultant for Medtronic, Stryker, and CSL Behring; and participating in an advisory board for Alexion/Portola, outside the submitted work. H. Imamura reported lecturer's fees from Medtronic and Stryker, outside the submitted work. H.K. Iversen reported fees as advisory board member or lecturer from Bayer, Bristol-Myers Squibb, Pfizer, and Boehringer Ingelheim. P.T. Kan reported consulting for Stryker Neurovascular and Imperative Care and stock ownership in InNeuroCo and Deinde. P.T. Kan received grant support from NIH U18EB029353-01 and Medtronic. E. Keller reported reported consulting fees for consultancy for Roche, Zoll Medical, and Bard Medical, outside the submitted work I. Linfante reported consulting fees from Penumbra, Medtronic, Stryker, MicroVention, InNeuroCo, and Three Rivers. P. Michel reported grants from the Swiss National Science Foundation and Swiss Heart Foundation, outside the submitted work. R. Mikulik was supported by project No. CA18118, IRENE COST Action funded by COST Association, by the IRIS-TEPUS Project No. LTC20051 from the INTER-EXCELLENCE INTER-COST Program of the Ministry of Education, Youth and Sports of the Czech Republic, and by STROCZECH within CZECRIN Large Research Infrastructure No. LM2018128 funded by the state budget of the Czech Republic. S. Nagel reported personal fees for consultancy for Brainomix and payment for lectures including speaker bureaus with Boehringer Ingelheim and Pfizer, outside the submitted work. T.N Nguyen reported research support from Medtronic and SVIN (related). C.H. Nolte reported consulting fees from Abbot, Alexion, Boehringer Ingelheim, Bayer Pharma, Bristol-Myers Squibb, Daiichi Sankyo, and Pfizer Pharma. R.G. Nogueira reported consulting fees for advisory roles with Anaconda, Biogen, Cerenovus, Genentech, Hybernia, Imperative Care, Medtronic, Phenox, Philips, Prolong Pharmaceuticals, Stryker Neurovascular, Shanghai Wallaby, and Synchron, stock options for advisory roles with Astrocyte, Brainomix, Cerebrotech, Ceretrieve, Corindus Vascular Robotics, Vesalio, Viz-AI, RapidPulse, and Perfuze, and investments in Viz-AI, Perfuze, Cerebrotech, Reist/Q'Apel Medical, Truvic, and Viseon. R. Ornello reported personal fees from Novartis, Teva, and Eli Lilly and nonfinancial support from Allergan/AbbVie, Novartis, and Teva, outside the submitted work. S. Ortega Gutierrez reports being a consultant for Medtronic and Stryker Neurovascular and receiving grants from Stryker, IschemiaView, Viz.ai, and Siemens. A. Pikula reported research grants from CIHR and the Canadian Stroke Consortium. A.S. Puri is a consultant for Cerenovus, CereVasc, Merit, and Medtronic and reported a research grant from Medtronic and stocks in InNeuroCo, Galaxy, Agile, Perfuze, and NTI. A. Ranta reported research funding support from the New Zealand Health Research Council and the New Zealand Ministry of Health. P. Ringleb reported personal fees from Boehringer Ingelheim, Bayer, Bristol-Myers Squibb, and Pfizer, outside the submitted work. N. Sakai reported research grants from Daiichi Sankyo, Medtronic, and Terumo and lecture fees from Asahi Intecc, Daiichi Sankyo, Medtronic, and Stryker, outside the submitted work. P. Sedova and R. Mikulik were supported by the project No. CA18118, IRENE COST Action–Implementation Research Network in Stroke Care Quality, by the project No. LQ1605 from the National Program of Sustainability II, and by the IRIS-TEPUS Project No. LTC20051 from the INTER-EXCELLENCE INTER-COST program of the Ministry of Education, Youth and Sports of the Czech Republic. Dr Sheth reported research grants from the NIH (grants U18EB029353 and R01NS121154) and American Academy of Neurology/the SVIN and consultancy fees from Penumbra and Cerenovus. Dr Siegler reported consulting fees from Ceribell and speakers' bureau involvement with AstraZeneca, outside the submitted work. M. Škorňa reported speaker fees from Pfizer, Medtronic, Boehringer Ingelheim, and Bayer. G. Thomalla reported fees as a consultant or lecturer from Acandis, Alexion, Amarin, Bayer, Bristol-MyersSquibb/Pfizer, Boehringer Ingelheim, Daiichi Sankyo, Portola, and Stryker. K. Toyoda received lecture honoraria from Daiichi Sankyo, Otsuka, Novartis, Abbott, Bayer Yakuhin, and Bristol-Myers Squibb, outside the submitted work. W. Asyraf Wan Zaidi reported consultant or lecturer fees from Allm inc, Boehringer Ingelheim, Bayer, EP Plus, Medtronic, Pfizer, and Stryker. H. Yamagami reported research grants from Bristol-Myers Squibb, lecturer fees from Bayer, Daiichi Sankyo, and Stryker, and membership of the advisory boards for Daiichi Sankyo, outside the submitted work. O.O. Zaidat reported consulting fees for Stryker, Medtronic, Cerenovus, and Penumbra and research grants from Stryker, Medtronic, Cerenovus, Penumbra, and Genentech; O.O. Zaidat had a patent for Ischemic Stroke issued. R. Herzig was supported by the Ministry of Health of the Czech Republic (grant No. DRO - UHHK 00179906) and Charles University, Czech Republic (Cooperatio Program, research area NEUR). M.A. Khan reported research funding from MSU-Spectrum Alliance, Genentech, and the NIH unrelated to this manuscript. The other authors report no relevant disclosures. Go to Neurology.org/N for full disclosures.

Publication History

Received by *Neurology* December 14, 2021. Accepted in final form September 2, 2022. Submitted and externally peer reviewed. The handling editor was José Merino, MD, MPhil, FAAN.

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Authors, their locations, and their contributions are listed at links.lww.com/WNL/C443

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