

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

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(SVIN COVID-19 Global Stroke Registry) Nguyen, Thanh N.; ...; Roje Bedekovic, Marina; Bralic, Marina; Budincevic, Hrvoje

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

## A 1-Year Follow-up

Thanh N. Nguyen, MD, FRCPC, Muhammad M. Qureshi, MBBS, MPH, Piers Klein, MA, Hiroshi Yamagami, MD, PhD, Robert Mikulik, MD, PhD, Anna Czlonskowska, MD, PhD, Mohamad Abdalkader, MD, Petra Sedova, MD, PhD, Anvitha Sathya, Hannah C. Lo, BS, et al., and the SVIN COVID-19 Global Stroke Registry

### Correspondence

Dr. Nguyen,  
thanh.nguyen@bmc.org

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## 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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## 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.<sup>1-3</sup>

Stroke represents an important complication in an estimated 1.1%–1.5% of COVID-19–admitted patients.<sup>4-8</sup> 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.<sup>9-13</sup> 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,<sup>14-17</sup> national,<sup>18-23</sup> and global<sup>6,24-29</sup> 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](https://links.lww.com/WNL/C442)). The study is registered under NCT04934020 ([clinicaltrials.gov](https://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.<sup>7</sup> 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<sup>30</sup> (eTable 2, [links.lww.com/WNL/C442](https://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<sup>31</sup> (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 U07.1.

### 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.<sup>32</sup> 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.

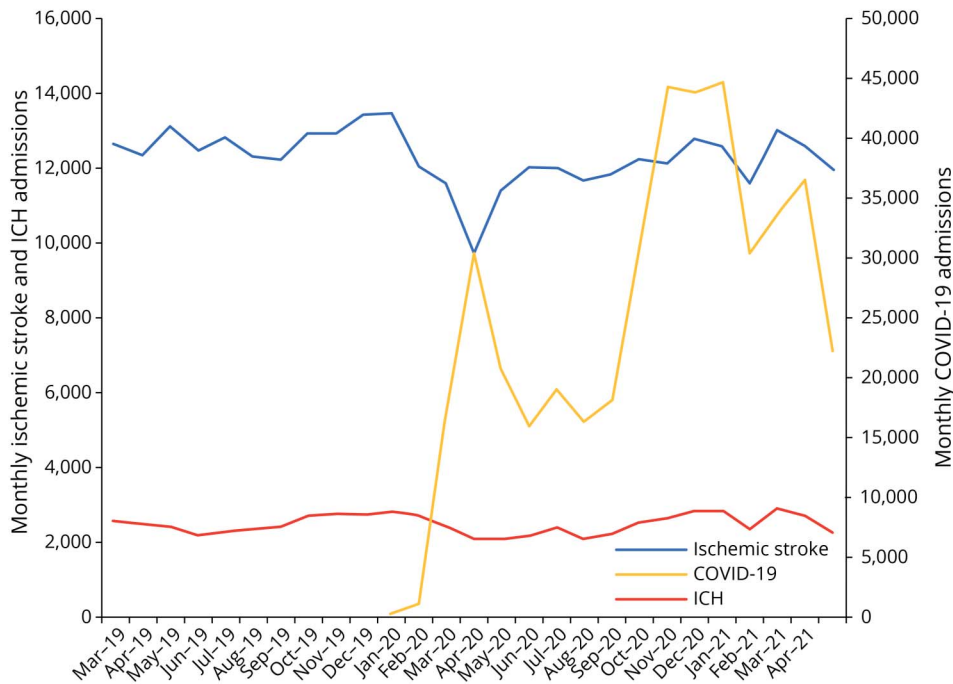
Finally, we performed a supplementary analysis comparing percentage change in absolute volume and monthly volume between before and during COVID-19 periods across different continents of the world. All data were analyzed using SAS version 9.4 (SAS Institute), and the significance level was set at a *p*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

### Standard Protocol Approvals, Registrations, and Patient Consents

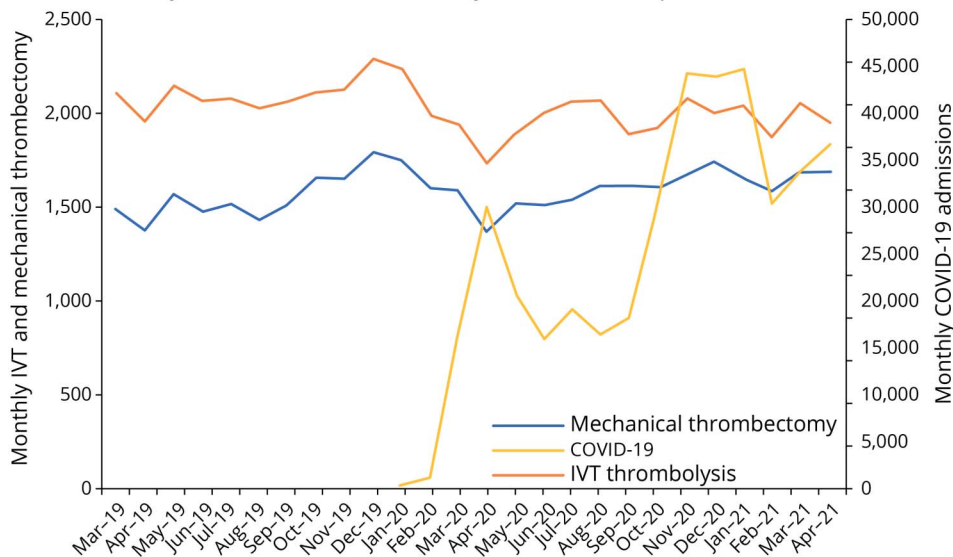
This was an investigator-initiated study. As this was a continuation of our prior work, the institutional review boards from the coordinating sites (Emory University and Boston Medical Center) considered that the investigators did not have access to protected health information in this follow-up study, 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.** Ischemic stroke, ICH, vs COVID-19 admissions



**B.** IVT thrombolysis, mechanical thrombectomy, vs COVID-19 hospitalizations



(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 <sup>a</sup>			
	N	n1	n2	Change, % (95% CI)	p Value	Before COVID-19		During COVID-19	
						N	Adjusted mean (SE)	N	Adjusted mean (SE)
<b>Overall</b>	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
<b>Hospital ischemic stroke volume<sup>b</sup></b>									
<b>Low</b>	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
<b>Intermediate</b>	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
<b>High</b>	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
<b>Primary vs comprehensive stroke center<sup>c</sup></b>									
<b>Primary</b>	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
<b>Comprehensive</b>	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
<b>Hospital COVID-19 volume<sup>d</sup></b>									
<b>Low</b>	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
<b>Intermediate</b>	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
<b>High</b>	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.

<sup>a</sup> 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.

<sup>b</sup> p: low vs intermediate = <0.0001; low vs high = <0.0001; and intermediate vs high = <0.0001.

<sup>c</sup> p: primary vs comprehensive = <0.0001.

<sup>d</sup> 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](https://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](https://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](https://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				p Value	Monthly volume <sup>a</sup>			p Value
	N	n1	n2	Change, % (95% CI)		N	Before COVID-19 Adjusted mean (SE)	During COVID-19	
<b>Overall</b>	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
<b>Hospital intracerebral hemorrhage volume<sup>b</sup></b>									
<b>Low</b>	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
<b>Intermediate</b>	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
<b>High</b>	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
<b>Primary vs comprehensive stroke center<sup>c</sup></b>									
<b>Primary</b>	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
<b>Comprehensive</b>	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
<b>Hospital COVID-19 volume<sup>d</sup></b>									
<b>Low</b>	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
<b>Intermediate</b>	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
<b>High</b>	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.

<sup>a</sup> 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.

<sup>b</sup> p: low vs intermediate = N/A; low vs high = N/A; and intermediate vs high = <0.0001.

<sup>c</sup> p: primary vs comprehensive = <0.0001.

<sup>d</sup> 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](https://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](https://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 <sup>a</sup>				
	N	n1	n2	Change, % (95% CI)	p Value	Before COVID-19		During COVID-19		
						N	Adjusted mean (SE)	N	Adjusted mean (SE)	p Value
<b>Overall</b>	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	
<b>Hospital IV thrombolysis volume<sup>b</sup></b>										
<b>Low</b>	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	
<b>Intermediate</b>	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	
<b>High</b>	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	
<b>Primary vs comprehensive stroke center<sup>c</sup></b>										
<b>Primary</b>	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	
<b>Comprehensive</b>	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	
<b>Hospital COVID-19 volume<sup>d</sup></b>										
<b>Low</b>	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	
<b>Intermediate</b>	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	
<b>High</b>	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.

<sup>a</sup> 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.

<sup>b</sup> p: low vs intermediate = N/A; low vs high = N/A; and intermediate vs high = <0.0001.

<sup>c</sup> p: primary vs comprehensive = <0.0001.

<sup>d</sup> 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.<sup>33</sup>

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.<sup>7</sup> 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.<sup>21</sup> Alternatively, any decline in mechanical thrombectomy volume related to the COVID-19 pandemic may have been offset by expanded indications for mechanical thrombectomy<sup>34–41</sup> 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 <sup>a</sup>			
	N	n1	n2	Change, % (95% CI)	p Value	Before COVID-19		During COVID-19	
						N	Adjusted mean (SE)	N	Adjusted mean (SE)
<b>Overall</b>	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
<b>Hospital mechanical thrombectomy volume<sup>b</sup></b>									
<b>Low</b>	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
<b>Intermediate</b>	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
<b>High</b>	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
<b>Primary vs comprehensive stroke center<sup>c</sup></b>									
<b>Primary</b>	19	826	883	6.9 (5.4 to 8.8)	0.168	21	3.0 (1.0)	3.2 (1.1)	0.605
<b>Comprehensive</b>	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
<b>Hospital COVID-19 volume<sup>d</sup></b>									
<b>Low</b>	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
<b>Intermediate</b>	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
<b>High</b>	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.

<sup>a</sup> 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.

<sup>b</sup> p: low vs intermediate = <0.0001; low vs high = <N/A; and intermediate vs high = N/A.

<sup>c</sup> p: primary vs comprehensive = <0.0001.

<sup>d</sup> 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.<sup>4,5,8</sup> 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.<sup>42,43</sup> 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.<sup>44</sup> 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	
<b>Overall</b>	218	5,453	406,792	1.34	1.31	1.38
<b>Asia</b>	51	727	44,664	1.63	1.52	1.75
<b>North America</b>	55	1,688	152,654	1.11	1.06	1.16
<b>Europe</b>	90	2,689	166,692	1.61	1.55	1.67
<b>South America</b>	11	262	32,116	0.82	0.73	0.93
<b>Oceania</b>	6	0	345	0	0	1.11
<b>Africa</b>	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	
<b>Overall</b>	225	5,656	195,539	2.89	2.82	2.97
<b>Asia</b>	54	782	53,109	1.47	1.37	1.58
<b>North America</b>	57	1,714	53,730	3.19	3.04	3.34
<b>Europe</b>	93	2,811	75,993	3.7	3.57	3.84
<b>South America</b>	11	262	5,873	4.46	3.96	5.02
<b>Oceania</b>	5	0	5,032	0	0	0.08
<b>Africa</b>	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,<sup>45</sup> and mechanical thrombectomy.<sup>46</sup> 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](https://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.<sup>47</sup>

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<sup>48-50</sup> and long-term patient outcomes, ensure that public education measures are continued, and ensure that patients continue to seek timely care for stroke.

### Author Byline (Continued)

Ossama Yassin Mansour, MD, PhD, Husitha Reddy Vanguru, MD, Emilie Lesaine, MD, Georgios Tsvigoulis, MD, PhD, Aaron I. Loochtan, DO, Jelle Demeestere, MD, Ken Uchino, MD, Violiza Inoa, MD, Nitin Goyal, MD, Andreas Charidimou, MD, PhD, James E. Siegler, Shadi Yaghi, MD, Diana Aguiar de Sousa, MD, PhD, Mahmoud H. Mohammaden, MD, Diogo C. Haussen, MD, Espen Saxhaug Kristoffersen, MD, PhD, Virginia Pujol Lereis, MD, Sergio Daniel Scollo, MD, Bruce C. V. Campbell, MBBS, PhD, Alice Ma, MD, James Orton Thomas, BMed, Mark W. Parsons, PhD, Shaloo Singhal, MBBS, Lee-Anne Slater, MBBS, FRANZCR, Mmed, Rodrigo Tomazini Martins, MD, PhD, Chris Enzinger, MD, Thomas Gattringer, MD, Aminur Rahman, MD, FCPS, Thomas Bonnet, MD, Noemie Ligot, MD, Sylvie De Raedt, MD, PhD, Robin Lemmens, MD, Peter Vanacker, MD, Fenne Vandervorst, MD, Adriana Bastos Conforto, MD, PhD, Raquel C.T. Hidalgo, MD, Luciana de Oliveira Neves, MD, Rodrigo Targa Martins, MD, Daissy Liliana Mora Cuervo, MD, Leticia C. Rebello, MD, Igor Bessa Santiago, MD, Isabelle Lameirinhas da Silva, MD, Teodora Sakelarova, MD, Rosen Kalpachki, MD, Filip Alexiev, MD, Luciana Catanese, MD, Elena Adela Cora, MD, PhD, Mayank Goyal, MD, PhD, FRCPC, Michael D. Hill, MD, MSc, FRCPC, Michael E. Kelly, MD, PhD, Houman Khosravani, MD, PhD, Pascale Lavoie, MD, Lissa Peeling, MD, Aleksandra Pikula, MD, Rodrigo Rivera, MD, Hui-Sheng Chen, MD, Yimin Chen, MD, Xiaochuan Huo, MD, PhD, Zhongrong Miao, MD, PhD, Shuiquan Yang, MD, Marina Roje Bedekovic, MD, Marina Bralic, MD, PhD, Hrvoje Budincevic, MD, PhD, Angel Basilio Corredor-Quintero, MD, Osvaldo E. Lara-Sarabia, MD, MSc, Martin Cabal, MD, Dusan Tenora, MD, Petr Fibrich, MD, Roman Herzig, MD, PhD, FESO, FEAN, Helena Hlaváčová, MD, Emanuela Hrabanovska, MD, David Hlinovsky, MD, Lubomir Jurak, MD, PhD, Jana Kadlcikova, MD, Igor Karpowicz, MD, Lukas Klecka, MD, Martin Kovar, MD, David Lauer, MD, Jiri Neumann, MD, FESO, Hana Palouskova, MD, Martin Reiser, MD, Petra Rekova, MD, Vladimir Rohan, MD, Ondrej Skoda, MD, PhD, Miroslav Škorňa, MD, Lenka Sobotková, MD, Martin Sramek, MD, Lenka Zakova, MD, Hanne Christensen, MD, PhD, Nicolas Drenck, MD,

Helle Klingenberg Iversen, MD, DMSci, Thomas Clement Truelsen, MD, Troels Wienecke, MD, Khalid Sobh, MD, Pauli Ylikotila, MD, MSc, Kemal Alpay, MD, Daniel Strbian, MD, PhD, MSc, Patricia Bernady, MD, Philippe Casenave, MD, Maria Dan, MD, Jean-Marc Faucheux, MD, Jean-Christophe Gentric, MD, Elsa Magro, MD, Candice Sabben, MD, Peggy Reiner, MD, Francois Rouanet, MD, Ferdinand O. Bohmann, MD, Stefan Boskamp, MD, Joshua Mbroh, MD, MSc, Simon Nagel, MD, Christian H. Nolte, Peter A. Ringleb, MD, Michael Rosenkranz, MD, Sven Poli, MD, MSc, Götz Thomalla, MD, Theodoros Karapanayiotides, MD, PhD, Ioanna Koutroulou, MD, PhD, Odysseas Kargiotis, MD, Lina Palaodimou, MD, Jose Dominguo Barrientos Guerra, MD, Vikram Huded, MD, Bindu Menon, MD, Shashank Nagendra, MD, Chintan Prajapati, MD, P.N. Sylaja, MBBS, MD, DM, Nyoman Angga Krishna Pramana, MD, Achmad Firdaus Sani, MD, Abdoreza Ghoreishi, MD, Mehdi Farhoudi, MD, Elyar Sadeghi Hokmabadi, MD, Tariq Abu Raya, MD, Shani Avnery Kalmanovich, MD, Levite Ronen, MD, Sergiu Ionut Sabetay, MD, Maurizio Acampa, MD, PhD, Alessandro Adami, MD, Lucio Castellani, MD, Marco Longoni, MD, Raffaele Ornello, MD, PhD, Leonardo Renieri, MD, Claudia Rolla Bigliani, MD, Michele Romoli, MD, PhD, Simona Sacco, MD, Andrea Salmaggi, MD, Davide Sangalli, MD, Andrea Zini, MD, Ryosuke Doijiri, MD, Hiroki Fukuda, MD, Toshiyuki Fujinaka, MD, Kyohei Fujita, MD, Hirotochi Imamura, MD, Nobuyuki Sakai, MD, Takuya Kanamaru, MD, Naoto Kimura, MD, Ryuhei Kono, MD, Kosuke Miyake, MD, Manabu Sakaguchi, MD, Kenichiro Sakai, MD, Kazutaka Sonoda, MD, Kenichi Todo, MD, PhD, Fumio Miyashita, MD, Naoki Tokuda, MD, Yuji Matsumaru, MD, Shoji Matsumoto, MD, Nobuyuki Ohara, MD, Seigo Shindo, MD, Yohei Takenobu, MD, Takeshi Yoshimoto, MD, Kazunori Toyoda, MD, PhD, Takeshi Uwatoko, MD, Yoshiki Yagita, MD, Takehiro Yamada, MD, Nobuaki Yamamoto, MD, Ryoo Yamamoto, MD, Yukako Yazawa, MD, Yuri Sugiura, MD, Peter Kuria Waweru, MBChB, MSc, Jang-Hyun Baek, MD, Si Baek Lee, MD, Kwon-Duk Seo, MD, Sung-Il Sohn, MD, Anita Ante Arsovska, MD, PhD, Yong Chieh Chan, MD, Wan Asyraf Wan Zaidi, MMed, Ainul Syahrilfazli Jaafar, MD, Fernando Gongora-Rivera, MD, PhD, Manuel Martinez-Marino, MD, MSc, Adrian Infante-Valenzuela, MD, Stanislav Groppa, MD, PhD, Pavel Leahu, MD, Jonathan M. Coutinho, MD, PhD, Leon A. Rinkel, MD, Diederik W.J. Dippel, MD, PhD, Dianne H.K. van Dam-Nolen, MD, Annemarei Ranta, MD, PhD, FRACP, Teddy Y. Wu, PhD, Tajudeen Temitayo Adebayo, MBBS, Abiodun H. Bello, Ernest Okwundu Nwazor, MBBS, Taofiki Ajao Sunmonu, MD, Kolawole Wasiu Wahab, MD, Ole Morten Ronning, MD, PhD, Else Charlotte Sandset, MD, PhD, Amal M. Al Hashmi, MD, Saima Ahmad, MBBS, Umair Rashid, MD, Liliana Rodriguez-Kadota, MD, Miguel Ángel Vences, MD, Patrick Matic Yalung, MD, Jon Stewart Hao Dy, MD, Maria Carissa Pineda-Franks, MD, Christian Oliver Co, MD, Waldemar Broda, MD, PhD, Aleksander Debiec, MD, Malgorzata Dorobek, MD, PhD, Michal Adam Karlinski, MD, PhD, Beata M. Labuz-Roszak, MD, PhD, Anetta Lasek-Bal, MD, PhD, Halina Sienkiewicz-Jarosz, MD, Jacek Staszewski, MD, PhD, Piotr Sobolewski, MD, Marcin Wiacek, MD, Justyna Zielinska-Turek, MD, Andre Pinho Araujo, MD, Mariana Rocha, MD, Pedro Castro, MD, PhD, Vitor Tedim Cruz, MD, PhD, Paulo Venancio Ferreira, MD, Patricia Ferreira, MD, Ana Paiva Nunes, MD, Luisa Fonseca, MD, João Pedro Marto, MD, Teresa Pinho e Melo, MD, Miguel Rodrigues, MD, M. Luis Silva, MD, Adela Dimitriade, MD, Cristian Falup-Pecurariu, MD, PhD, May Adel Hamid, MD, Narayanaswamy Venketasubramanian, FRCP, Georgi Krastev, MD, PhD, Miroslav Mako, MD, Oscar Ayo-Martin, MD, PhD, Francisco Hernández-Fernández, MD, PhD, Jordi Blasco, MD, PhD, Alejandro Rodríguez-Vázquez, MD, Antonio Cruz-Culebras, MD, Francisco Moniche, MD, PhD, Joan Montaner, MD, PhD, Soledad Perez-Sanchez, MD, María Jesús García Sánchez, MD, Marta Guillán Rodríguez, MD, Katarina Jood, MD, PhD, Annika Nordanstig, MD, PhD, Michael V. Mazya, MD, PhD, Tiago T.P. Moreira, MD, PhD, Gianmarco Bernava, MD, Morin Beyeler, MD, Manuel Bolognese, MD, Emmanuel Carrera, MD, Tomas Dobrocky, MD, Grzegorz Marek Karwacki, MD, Emanuela Keller, MD, Chang Yang Hsieh, MD, Surawan Boonyakarnkul, MD, Anchalee Churojana, MD, Ozlem Aykac, MD, Atilla A-zcan Ozdemir, M.D., Arsida Bajrami, MD, Songul Senadim, MD, Syed Irteza Hussain, MD, Seby John, MD, Soma Banerjee, MD, Joseph Kwan, MD, Kailash Krishnan, PhD, Robert Lenthall, MBBS, MSc, FRCP, FRCP, Ashok Matthews, MD, Ken Wong, MD, Liqun Zhang, MD, PhD, Dorothea Altschul, MD, Kaiz S. Asif, MD, Zeelalem Bahiru, NP, Kristine Below, BS, José Biller, MD, FACP, FAAN, FANA, FAHA, Sean Ruland, DO, Saqib A. Chaudry, MD, Michael Chen, MD, Alex Chebl, MD, Jackie Cibulka, RN, Leon Cistrunk, Judith Clark, RN, Marco Colasurdo, MD, Alexandra Czup, MD, Adam de Havenon, MD, Salvatore D'Amato, MD, Sushrut Dharmadhikari, MD, Kasey B. Grimmett, BSN, RN, Adam A. Dmytriw, MD, MPH, Mark R. Etherton, MD, PhD, Chizoba Ezepue, MD, Mudassir Farooqui, MD, MPH, Steven K. Feske, MD, Lauren Fink, BSN, RN, Ulviyya Gasimova, MD, Amy K. Guzik, MD, Maryam Hakemi, BSN, MS, AGNP, Majesta Hovingh, MS, Muhib Khan, MD, Dinesh Jillela, MD, Peter T. Kan, MD, MPH, Rakesh Khatri, MD, Ayaz M. Khawaja, MD, Naim N. Khoury, MD, Nicole L. Kiley, PA-C, Benny S. Kim, MD, Murali K. Kolikonda, MD, Anna Luisa Kuhn, MD, PhD, Stephanie Lara, RN, MS-HCA, SCRNP, Guillermo Linares, MD, Italo Linfante, MD, Timothy G. Lukovits, MD, Sarah Lyan, NP, Shailesh S. Male, MD, Laith Maali, MD, John Mancin, DO, Hesham Masoud, MD, Ghada A. Mohamed, MD, MSc, Andre Monteiro, MD, Fadi Nahab, MD, Krishna Nalleballe, MD, Santiago Ortega-Gutierrez, MD MS, Ajit S. Puri, MD, Yazan Radaideh, MD, Rahul H. Rahangdale, MD, Ansaar Rai, MD, Pankajavalli Ramakrishnan, MD, PhD, Aravind B. Reddy, MD, Diana M. Rojas-Soto, MD, Jose Rafael Romero, MD, Natalia S. Rost, MD, MPH, Aaron Rothstein, MD, Setareh Salehi Omran, MD, Sunil A. Sheth, MD, Adnan H. Siddiqui, MD, PhD, Amy K. Starosciak, PhD, Nicholas E. Tarlov, MD, Robert A. Taylor, MD, Michael J. Wang, MD, Jared Wolfe, BA, Ka-Ho Wong, MBA, Huynh Vu Le, MD, Quy Viet Nguyen, MD, Thong Nhu Pham, MD, Trung Thanh Nguyen, MD, Hoang Thi Phan, MD, Mai Duy Ton, MD, Urs Fischer, MD, Patrik Michel, MD, PhD, Davide Strambo, MD, Sheila O. Martins, MD, PhD, Osama O. Zaidat, MD, MS, Raul G. Nogueira, MD

## Affiliation

From the Department of Neurology (T.N.N., P.K., Anvitha Sathya, H.C.L., Andreas Charidimou, Judith Clark, S.K.F., J.R.R.), Boston Medical Center, Boston University Chobanian & Avedisian School of Medicine; Department of Radiology (T.N.N., M.M.Q., P.K., Mohamad Abdalkader, Anvitha Sathya, H.C.L., N.L.K.), Boston Medical Center, Boston University Chobanian & Avedisian School of Medicine; Department of Radiation Oncology (M.M.Q.), Boston Medical Center, Boston University Chobanian & Avedisian School of Medicine; Department of Stroke Neurology (H.Y.), National Hospital Organization, Osaka National Hospital, Japan; Department of Neurology (R.M., Petra Sedova), International Clinical Research Centre, St Anne's University Hospital and Faculty of Medicine, Masaryk University, Brno, Czech Republic; 2nd Department of Neurology (Anna Czlonkowska, M.A.K.), Institute of Psychiatry and Neurology, Warsaw, Poland; Department of Internal Medicine and Cardiology (Petra Sedova), University Hospital Brno and Faculty of Medicine, Masaryk University, Brno, Czech Republic; Department of Neurology (O.Y.M.), Alexandria University Stroke and Neurointervention Unit, Egypt; Department of Neurology (H.R.V., K.U.), Cleveland Clinic; Centre Hospitalier de l'Université de Bordeaux (E.L.), INSERM, Bordeaux Population Health Research Center, France; Second Department of Neurology (Georgios Tsivgoulis, Lina Palaodimou), "Attikon" University Hospital, National and Kapodistrian University of Athens, Greece; Ohio Health Riverside Methodist Hospital (A.I.L.); Neurology Department (J.D., Robin Lemmens), Leuven University Hospital, Belgium; University of Tennessee Health Science Center (V.I., N.G.);

Cooper Neurological Institute (J.E.S., J.W.), Cooper University Hospital, Camden, NJ; Department of Neurology (Shadi Yaghi), Rhode Island Hospital, Brown University, Providence; Stroke Center (D.A.S.), Centro Hospitalar Universitário Lisboa Central—CHULC, Portugal, CEEM; Institute of Anatomy (D.A.S.), Faculdade de Medicina, Universidade de Lisboa, Portugal; Department of Neurology (Mahmoud Mohammadden, D.C.H.), Grady Memorial Hospital, Emory University School of Medicine, Atlanta, GA; Department of Neurology (E.S.K.), Akershus University Hospital, University of Oslo, Norway and Department of General Practice, University of Oslo, Norway; Division of Neurologia Vasculare (V.P.L.), Departamento de Neurologia, Institute for Neurological Research—FLENI, Buenos Aires, Argentina; Stroke Unit (S.D.S.), Ramos Mejia Hospital, Buenos Aires, Argentina; Department of Medicine and Neurology (B.C.V.C.), Melbourne Brain Centre at the Royal Melbourne Hospital, University of Melbourne, Parkville, Victoria, Australia; Royal North Shore Hospital (Alice Ma), Sydney, Australia; Department of Neurophysiology (J.O.T.), Liverpool Hospital, New South Wales, Australia; Department of Neurology (M.W.P.), Liverpool Hospital, New South Wales, Australia; Departments of Neurology (Shaloo Singal) and Radiology (L.-A.S.), Monash Medical Centre, Australia; Stroke and Aging Research Group (Shaloo Singhal), School of Clinical Sciences at Monash Health, Monash University, Australia; Department of Neurology (Rodrigo Tomazini Martins), Mater Hospital, Brisbane, Australia; Department of Neurology (Chris Enzinger), Medical University of Graz, Austria; Department of Neurology and Division of Neuroradiology (T.G.), Vascular and Interventional Radiology, Medical University of Graz, Austria; Department of Neurology (Aminur Rahman), Sir Salimullah Medical College, Mitford, Dhaka, Bangladesh; Hopital Erasme (T.B., N.L.), Brussels, Belgium; Department of Neurology (S.D.R., F.V.), Universitair Ziekenhuis Brussel, Center for Neurosciences, Vrije Universiteit Brussel, Belgium; Department of Neurology (P.V.), University Hospitals Antwerp; Department of Translational Neuroscience (P.V.), University of Antwerp, Belgium; Hospital das Clínicas (A.B.C., I.L.S.), São Paulo University, Brazil; Department of Neurology and Interventional Neuroradiology (R.C.T.H.), Hospital de Base de São José do Rio Preto, São Paulo, Brazil; Department of Neurology (L.O.N., I.B.S.), Hospital São Carlos, Fortaleza, Ceará, Brazil Stroke Unit (Rodrigo Targa Martins), Neurology, Nossa Senhora da Conceição Hospital, Porto Alegre, Brazil; Moinhos de Vento Hospital (D.L.M.C.), Brazil; Hospital de Base do Distrito Federal (L.C.R.), Brasília, Brazil; St. Anna University Hospital (T.S., Rosen Kalpachki, F.A.), Sofia, Bulgaria; Department of Neurology (Luciana Catanese), McMaster University, Hamilton, Canada; Department of Diagnostic Radiology (E.A.C.), Halifax Infirmary, Dalhousie University, Halifax, Canada; Departments of Clinical Neurosciences and Radiology (M.G., M.D.H.), Hotchkiss Brain Institute, Cummings School of Medicine, University of Calgary, Canada; Royal University Hospital (M.E.K., Lissa Peeling), Saskatoon, Saskatchewan, Canada; Department of Neurology (H.K.), Hurvitz Brain Sciences Program, Sunnybrook Health Sciences Centre, Division of Neurology, Department of Medicine, University of Toronto, Canada; Hopital Enfant Jesus (Pascale Lavoie), Centre Hospitalier de l'Université Laval, Quebec City, Canada; Toronto Western Hospital (A.P.), University of Toronto, Canada; Neuroradiology Department (R.R.), Instituto de Neurocirugía Dr. Asenjo, Santiago, Chile; Department of Neurology (H.-S.C.), General Hospital of Northern Theater Command, Shen Yang, China; Department of Neurology (Y.C., Shuiquan Yang), Foshan Sanshui District People's Hospital, China; Interventional Neuroradiology (X.H., Z.M.), Beijing Tiantian Hospital, China; Department of Neurology (M.R.B.), Sestre Milosrdnice University Hospital Center, Croatia; Department of Neurology (Marina Bralic), Clinical Hospital Center Rijeka, Croatia; Sveti Duh University Hospital - Zagreb (H.B.), Department of Neurology, Croatia; J.J. Strossmayer University of Osijek (H.B.), Faculty of Medicine, Department of Neurology and Neurosurgery, Osijek, Croatia; Department of Neurology (A.B.C.-Q.), Hospital Departamental Universitario del Quindío San Juan de Dios, Colombia; Department of Neurology (O.E.L.-S.), Clínica de la Costa, Barranquilla, Colombia; Department of Neurology (Martin Cabal), Faculty Hospital Ostrava, Czech Republic; Department of Neurology (D.T.), Blansko Hospital, Czech Republic; Oblastní Nemocnice Trutnov a.s. (Petr Fibrich), Czech Republic; Department of Neurology (R.H.), Comprehensive Stroke Center, Charles University Faculty of Medicine and University Hospital, Hradec Králové, Czech Republic; Neurology (H.H.), Hospital Příbram, Czech Republic; Uherskohradišská Hospital (E.H.), Czech Republic; Department of Neurology (D.H.), Thomayer University Hospital Prague, Czech Republic; Neurocenter (L.J.), Regional Hospital Liberec, Czech Republic; Neurology (Jana Kadcikova), Hospital Vyskov, Czech Republic; Regional Hospital Karlovy Vary (Igor Karpowicz), Czech Republic; Ostrava (L.K.), Czech Republic; Na Homolce Hospital (Martin Kovar), Czech Republic; Department of Neurology (D.L.), Third Faculty of Medicine, Charles University and University Hospital Kralovske Vinohrady, Czech Republic; Department of Neurology (J.N.E.S.O.), Krajská zdravotní, a.s.—Hospital Chomutov, Chomutov, Czech Republic; Karvina Mining Hospital (H.P.), Czech Republic; Neurology (Martin Reiser), České Budejovice Hospital, Czech Republic; Department of Neurology and Centre of Clinical Neuroscience (Petra Reková), First Faculty of Medicine, Charles University and General University Hospital in Prague, Czech Republic; Department of Neurology (V.R.), University Hospital Plzen, Czech Republic; Department of Neurology (O.S.), Hospital Jihlava, Czech Republic; Department of Neurology (M.S.), Masaryk University Faculty of Medicine, University Hospital Brno, Czech Republic; Oblastní Nemocnice Kladno (L.S.), Czech Republic; Central Military Hospital in Prague (Martin Sramek), Czech Republic; Nemocnice Trinec (Lenka Zakova), Czech Republic; Copenhagen University Hospital (H.C., N.D.), Denmark; Stroke Center (H.K.L., T.C.T.), Rigshospitalet, University of Copenhagen, Denmark; Neurovascular Center (T.W.), Zealand University Hospital, University of Copenhagen, Roskilde, Denmark; El hussein Alzahar University Hospital (Khalid Sobh), Egypt; Neurocenter (P.Y.), Turku University Hospital, Turku University, Finland; Department of Radiology (K.A.), Turku University Hospital, Finland; Department of Neurology (Daniel Strbian), Helsinki University Hospital and University of Helsinki, Finland; Bayonne Hospital Neurology (P.B.), Stroke Unit, France; Libourne Hospital Neurology (Philippe Casenave), Stroke Unit, France; Centre Hospitalier d'Arcachon—Neurologie (Maria Dan), France; Agen Hospital Neurology (J.-M.F.), Stroke Unit, France; Neuroradiologie Interventionnelle (J.-C.G.), Brest University Hospital, France; Neurochirurgie (E.M.), Brest University Hospital, France; Department of Neurology (C.S.), Rothschild Foundation Hospital, Paris, France; Lariboisiere Hospital (Peggy Reiner), Paris, France; Bordeaux University Hospital Neurology (F.R.), Stroke Unit, France; Department of Neurology (F.O.B.), University Hospital, Goethe University, Frankfurt,

Germany; Department of Neurology (Stefan Boskamp, Michael Rosenkranz), Albertinen Krankenhaus, Hamburg, Germany; Department of Neurology and Stroke (Joshua Mbroh, S.P.), Eberhard-Karls University, Tuebingen, Germany; Hertie Institute for Clinical Brain Research (Joshua Mbroh, S.P.), Eberhard-Karls University, Tuebingen, Germany; Department of Neurology (Simon Nagel), Klinikum Ludwigshafen, Ludwigshafen/Rhein, Germany; Department of Neurology (Simon Nagel, P.A.R.), Heidelberg University Hospital, Germany; Department of Neurology and Experimental Neurology (C.H.N.), Center for Stroke Research Berlin, Berlin Institute of Health, Charité-Universitätsmedizin Berlin, Germany; Universitätsklinikum Hamburg-Eppendorf (Götz Thomalla), Klinik und Poliklinik für Neurologie, Hamburg, Germany; Second Department of Neurology (Theodoros Karapanayiotides, Ioanna Koutroulou), AHEPA University Hospital, Aristotle University of Thessaloniki, School of Medicine, Faculty of Health Sciences, Greece; Stroke Unit (O.K.), Metropolitan Hospital, Piraeus, Greece; Hospital General San Juan de Dios (J.D.B.G.), Guatemala; Mazumdar Shaw Medical Center (V.H.), Bangalore, Karnataka, India; Department of Neurology (Bindu Menon), Apollo Specialty Hospitals Nellore, Andhra Pradesh, India; Department of Neurology (Shashank Nagendra), Grant Medical College and Sir JJ Hospital, Mumbai, India; Mazumdar Shaw Medical Center (C.P.), Bangalore, Karnataka, India; Sree Chitra Tirunal Institute for Medical Sciences and Technology (P.N.S.), Trivandrum, Kerala, India; Department of Neurology (N.A.K.P.), Faculty of Medicine Udayana University, Sanglah General Hospital Denpasar, Bali, Indonesia; Dr. Soetomo General Hospital Surabaya (A.F.S.), Universitas Airlangga, Indonesia; Stroke Research Group (A.G.), Head of Stroke Care Unit, Department of Neurology, Vali-e-Asr Hospital, School of Medicine, Zanjan University of Medical Sciences, Iran; Neurosciences Research Center (Mehdi Farhoudi, E.S.H.), Imam Reza Hospital, Tabriz University of Medical Sciences, Iran; Neurology Department (T.A.R., S.I.S.), Hillel Yaffe Medical Center, Hadera, Israel; Neurointerventional Unit (S.A.K., Levite Ronen), Shamir Medical Center, Israel; Stroke Unit (Maurizio Acampa), University of Siena, Italy; Stroke Center IRCCS Sacro Cuore Don Calabria (A.A.), Verona, Italy; Dipartimento di Neuroradiologia Diagnostica e Interventistica Policlinico Universitario IRCCS San Martino (Lucio Castellani, C.R.B.), Genova, Italy; Neurology and Stroke Unit (M.L., Michele Romoli), Ospedale Bufalini, Cesena, Italy; Neuroscience Section (R.O., Simona Sacco), Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, Italy; Interventional Neurovascular Unit (Leonardo Renieri), Careggi University Hospital, Florence, Italy; Neurological Department (Andrea Salmaggi, Davide Sangalli), "Alessandro Manzoni" Hospital, ASST Lecco, Via dell'Eremo, Italy; IRCCS Istituto delle Scienze Neurologiche di Bologna (A.Z.), Neurologia e Rete Stroke Metropolitana, Italy; Department of Neurosurgery (R.D., N.K.), Iwate Prefectural Central Hospital, Japan; Department of Neurology (H.F.), Japanese Red Cross Matsue Hospital, Japan; Department of Neurosurgery (T.F.), National Hospital Organization Osaka National Hospital, Japan; Department of Endovascular Surgery (K.F.), Tokyo Medical and Dental University, Japan; Department of Neurosurgery (H.I., N.S.), Kobe City Medical Center General Hospital, Japan; NTT Medical Center Tokyo (Takuya Kanamaru), Japan; Department of Neurology (Ryuhei Kono), Kin-kyo Chuo Hospital, Japan; Shiroyama Hospital (K.M.), Japan; Department of Neurology (Manabu Sakaguchi), Osaka General Medical Center, Japan; Department of Neurology (Kenichiro Sakai), The Jikei University School of Medicine, Japan; Department of Neurology (Kazutaka Sonoda), Saiseikai Fukuoka General Hospital, SFGH, Japan; Stroke Center (Kenichi Todo), Osaka University Hospital, Japan; Department of Neurology (Fumio Miyashita), Kagoshima City Hospital, Japan; Department of Neurology (N.T.), Japanese Red Cross Kyoto Daini Hospital, Japan; Department of Stroke and Cerebrovascular Diseases (Y.M.), University of Tsukuba Hospital, Japan; Comprehensive Strokeology (S.M.), Fujita Health University School of Medicine, Toyoake, Japan; Department of Neurology (N.O.), Kobe City Medical Center General Hospital, Japan; Department of Neurology (Seigo Shindo), Japanese Red Cross Kumamoto Hospital, Japan; Osaka Red Cross Hospital (Y.T.), Japan; Department of Neurology (Takeshi Yoshimoto), National Cerebral and Cardiovascular Center, Japan; Department of Cerebrovascular Medicine (Kazunori Toyoda), National Cerebral and Cardiovascular Center, Japan; Cerebrovascular Medicine (T.U.), Stroke Center, Saga Medical Centre Koseikan, Japan; Stroke Medicine (Yoshiki Yagita), Kawasaki Medical School, Japan; Department of Neurology and Stroke Treatment (Takehiro Yamada), Japanese Red Cross Kyoto Daichi Hospital, Japan; Advanced Brain Research (N.Y.), Tokushima University, Japan; Yokohama Brain and Spine Center (R.Y.), Japan; Department of Stroke Neurology (Yukako Yazawa), Kohnan Hospital, Sendai, Japan; Toyonaka Municipal Hospital (Y.S.), Japan; Kenyatta University Teaching (P.K.W.), Referral and Research Hospital, Kenya; Department of Neurology (J.-H.B.), Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, South Korea; Department of Neurology (S.B.L.), Uijeongbu St. Mary's Hospital, College of Medicine, The Catholic University of Korea, South Korea; Department of Neurology (K.-D.S.), National Health Insurance Service Ilsan Hospital, Goyang, Korea; Department of Neurology (S.-I.S.), Keimyung University Dongsan Hospital, Keimyung University School of Medicine, Daegu, Korea; Department of Urgent Neurology (A.A.A.), University Clinic of Neurology, University Ss. Cyril and Methodius-Faculty of Medicine, Skopje, North Macedonia; Hospital Sultan Abdul Halim (Y.C.C.), Malaysia; Department of Medicine (W.A.W.Z.), National University of Malaysia; Department of Surgery (A.S.J.), National University of Malaysia; Neurovascular Unit and Neurology Department (F.G.-R., A.I.-V.), University Hospital Jose Eleuterio Gonzalez, Universidad Autonoma de Nuevo Leon, Mexico; Department of Neurology (M.M.-M.), Hospital de especialidades del Centro Médico Nacional Siglo XXI IMSS, Mexico; "Nicolae Testemitanu" State University of Medicine and Pharmacy (S.G., Pavel Leahu); Emergency Medicine Institute (L.P., S.G.), Chisinau, Republic of Moldova; Amsterdam University Medical Centers Amsterdam (J.M.C., L.A.R.), the Netherlands; Departments of Neurology (D.W.J.D.) and Neurology and Radiology (D.H.K.D.-N.), Erasmus University Medical Center Rotterdam, the Netherlands; Department of Medicine (Annemarei Ranta), University of Otago—Wellington, and Department of Neurology, Wellington Hospital, New Zealand; Department of Neurology (T.Y.W.), Christchurch Hospital, New Zealand; Department of Medical Records (T.T.A.), Federal Medical Centre, Owo, Ondo State, Nigeria; Neurology Unit (A.H.B., K.W.W.), University of Ilorin, Nigeria; Neurology Unit (E.O.N.), Department of Medicine, Federal Medical Centre Owerri, Neurology Unit, Federal Medical Centre, Owerri, Nigeria; Neurology Unit, Department of Medicine, (T.A.S.) Federal Medical Center, Owo, Ondo State, Nigeria; Department of Neurology (O.M.R.), Akershus

University Hospital, Norway, and Institute of Clinical Medicine, University of Oslo, Norway; Department of Neurology (E.C.S.), Oslo, Oslo, Norway and The Norwegian Air Ambulance Foundation, Norway; Central Stroke Unit (A.M.A.H.), Neuroscience Directorate, Khoula Hospital, Ministry of Health, Oman; Lahore General Hospital (S.A., U.R.), Pakistan; Departamento de Neurología (L.R.-K., M.A.V.), Hospital Nacional Edgardo Rebagliati Martins, Essalud, Lima, Perú; St. Luke's Medical Center (P.M.Y.), Global City, Philippines; St. Luke's Medical Center (J.S.H.D., M.C.P.-F., C.O.C.), Quezon City, Philippines; Department of Neurology (W.B.), Specialist Hospital Konskie, Collegium Medicum, Jan Kochanowski University, Kielce, Poland; Clinic of Neurology (Aleksander Debiec, J.S.), Military Institute of Medicine, Warsaw, Poland; Department of Neurology (Malgorzata Dorobek), Central Clinical Hospital of the Ministry of Interior and Administration (M.D.), Warsaw, Poland; Department of Neurology (B.M.L.-R.), St. Jadwiga Provincial Specialist Hospital in Opole, Institute of Medical Sciences, University of Opole, Poland; Department of Neurology (A.L.-B.), Leszek Giec Upper Silesian Medical Centre of the Silesian Medical University in Katowice, School of Health Sciences, Medical University of Silesia in Katowice, Poland; 1st Department of Neurology (H.S.-J.), Institute of Psychiatry and Neurology, Warsaw, Poland; Department of Neurology in Sandomierz (Piotr Sobolewski), Collegium Medicum, Jan Kochanowski University in Kielce, Sandomierz, Poland; Department of Neurology (M.W.), Institute of Medical Sciences, Medical College of Rzeszow University, Rzeszow, Poland; Department of Neurology (J.Z.-T.), Central Clinical Hospital of the Ministry of Interior, Warsaw, Poland; Department of Neurology (J.Z.-T.), Central Clinical Hospital of the Ministry of Internal Affairs and Administration, Warsaw, Poland; Neuroradiology Department—Centro Hospitalar de Vila Nova de Gaia/Espinho (A.P.A.), Portugal; Neurology Department (Mariana Rocha), Centro Hospitalar Vila Nova de Gaia/Espinho; Department of Neurology (Pedro Castro), Centro Hospitalar Universitário de São João, Portugal; Stroke Unit—Hospital Pedro Hispano (V.T.C., P.V.F.), Matosinhos, Portugal; Stroke Unit (Patrícia Ferreira, A.P.N.), Centro Hospitalar Universitário de Lisboa Central, Portugal; Stroke Unit (Luísa Fonseca), Medicine Department, Centro Hospitalar Universitário de São João, Portugal; Department of Neurology (J.P.M.), Hospital de Egas Moniz, Centro Hospitalar Lisboa Ocidental, Lisbon, Portugal; Hospital de Santa Maria—Centro Hospitalar Lisboa Norte (T.P.M.), Portugal; Department of Neurology (Miguel Rodrigues), Hospital Garcia de Orta, Almada, Portugal; Centro Hospitalar Universitário de São João (M.L.S.), Portugal; Bucarest University Emergency Hospital (Adela Dimitriadu), Romania; Department of Neurology (C.F.-P.), County Clinic Hospital, Faculty of Medicine, Transilvania University, Brasov, Romania; Department of Neurology King Fahad Hospital of the University Imam Abdulrahman bin Faisal University Dammam (M.A.H.), Saudi Arabia; Raffles Hospital (N.V.), Singapore; Department of Neurology (G.K., Miroslav Mako), Faculty Hospital Trnava, Slovakia; Jessenius Medical Faculty (G.K., M.M.), Martin, Comenius University, Bratislava, Slovakia; Department of Neurology (G.K.), Slovak Medical University, Bratislava; Complejo Hospitalario Universitario de Albacete (O.A.-M., F.H.-F.), Albacete, Spain; Interventional Neuroradiology (J.B.), Hospital Clínic de Barcelona, Spain; Comprehensive Stroke Center (A.R.-V.), Hospital Clínic de Barcelona, Spain; Department of Neurology (Unidad de Ictus) (A.C.-C.), Hospital Universitario Ramón y Cajal, Madrid, Spain; Stroke Unit (Francisco Moniche), Neurology Department, Hospital Universitario Virgen del Rocío, Spain; Department of Neurology (Joan Montaner, S.P.-S.), Hospital Universitario Virgen Macarena & Neurovascular Research Laboratory, Instituto de Biomedicina de Sevilla-IbIS, Spain; Department of Neuroradiology (M.J.G.S.), Hospital Universitario Rey Juan Carlos, Spain; Department of Neurology (M.G.R.), Hospital Universitario Rey Juan Carlos, Spain; Institute of Neuroscience and Physiology (K.J., A.N.), Department of Clinical Neuroscience, Sahlgrenska Academy, University of Gothenburg; Department of Neurology (K.J., A.N.), Sahlgrenska University Hospital, Region Västra Götaland, Gothenburg, Sweden; Department of Neurology (M.V.M., T.T.P.M.), Karolinska University Hospital & Department of Clinical Neuroscience, Karolinska Institute, Stockholm, Sweden; Interventional Neuroradiology (G.B.), University Hospitals of Geneva, Switzerland; Department of Neurology (Morin Beyeler, U.F.), Inselspital, Bern University Hospital; Neurocenter (Manuel Bolognese), Cantonal Hospital of Lucerne, Switzerland; Department of Neurology (E.C.), University Hospitals of Geneva, Switzerland; Diagnostic and Interventional Neuroradiology (T.D.), Bern University Hospital, University of Bern, Switzerland; Radiology and Nuclear Medicine (G.M.K.), Cantonal Hospital of Lucerne, Switzerland; University Hospital (E.K.), University of Zurich, Switzerland; Department of Neurology (C.Y.H.), Tainan Sin Lau Hospital, Taiwan; Department of Radiology (Surawan Boonyakarnkul), Ramathibodi Hospital, Mahidol University, Thailand; Department of Radiology (Anchalee Churojana), Siriraj Hospital, Mahidol University, Thailand; Eskisehir Osmangazi University (O.A., M.D.O.), Turkey; Istanbul Aydin University (A.B., Songul Senadim), Florya Medicalpark Stroke Center, Turkey; Cleveland Clinic Abu Dhabi (S.I.H., S.J.), UAE; Department of Stroke Medicine (Soma Banerjee, Joseph Kwan), Imperial College Healthcare NHS Trust, Charing Cross Hospital, London, United Kingdom; Stroke (K.K.), Department of Medicine (K.K.), Nottingham University Hospitals NHS Trust, United Kingdom; Neuroradiology (Robert Lenthal), Nottingham University Hospitals NHS Trust, United Kingdom; Barking Havering and Redbridge University Hospitals (Ashok Matthews), Romford, United Kingdom; Royal London Hospital (K.W.), Barts Health NHS Trust, United Kingdom; St George's University Hospital (Liquan Zhang), London, United Kingdom; Valley Hospital Health System (D.A.), Neurosurgeons of NJ, New Jersey; Amita Health and University of Illinois-Chicago (K.S.A.); Inova Fairfax Hospital (Z.B.), Virginia; Neuroscience and Stroke Program (K.B., O.O.Z.), Bon Secours Mercy Health St Vincent Hospital, Toledo, OH; Loyola University Chicago Stritch School of Medicine (J.B.A.N.A., S.R.), Illinois; Inova Fairfax Hospital (S.A.C.), University of Virginia School of Medicine, Virginia; Rush University Medical Center (Michael Chen, Y.R.), Chicago, IL; Department of Neurology (Alex Chebl), Henry Ford Health System, Detroit, MI; Clinical Data Specialist (Jackie Cibulka), EBC Data Abstraction, University of Tennessee Health Science Center; Solution Architect II (Leon Cistrunk), Clinical Decision Support, University of Tennessee Health Science Center; Department of Radiology (Marco Colasurdo), University of Texas Medical Branch, Galveston, TX; Neurology (Alexandra Czap, S.A.S.), UTHealth McGovern Medical School, Houston, TX; Department of Neurology (A.H.), Yale University School of Medicine, New Haven; Brigham and Women's Hospital (S.D.A., A.A.D.), Boston; Baptist Health Medical Center—Little Rock (S.D., K.B.G.), Little Rock, AR; Neurointerventional Program (A.A.D.), Departments of Medical Imaging and Clinical Neurological Sciences, London Health

Sciences Centre, Western University, London, ON; Neuroendovascular Program (A.A.D.), Massachusetts General Hospital & Brigham and Women's Hospital, Harvard Medical School, Boston; Department of Neurology (M.R.E., N.S.R.), Massachusetts General Hospital, Boston; Department of Interventional and Vascular Neurology (Chizoba Ezeque), Neuroscience Center, SSM Health DePaul Hospital, St. Louis, Missouri; University of Iowa (Mudassir Farooqui, S.O.G.); Santa Barbara Cottage Hospital (Lauren Fink, R.A.T.), California; Department of Neurology (U.G.), Saint Louis University School of Medicine, Missouri; Department of Neurology (A.K.G., S.L.), Wake Forest Baptist Medical Center, NC; Wayne State University (M.H.G.N.P., A.M.K.), Detroit, MI; Department of Neurosciences and Comprehensive Stroke Center (M.H., Muhib Khan), Spectrum Health and Michigan State University College of Human Medicine; Department of Neurology (D.J.), Grady Memorial Hospital, Emory University School of Medicine; Department of Neurosurgery (P.T.K.), University of Texas Medical Branch; Department of Neurology (Rakesh Khatri), Texas Tech University Health Science Center, El Paso; HSHS St. John's Hospital (N.N.K.), Southern Illinois University School of Medicine, Springfield; Virginia Hospital Center (B.S.K.); Baptist Health Medical Group (M.K.K.), Baptist Health Lexington, KY; Division of Neurointerventional Radiology (A.L.K., A.S.P.), Department of Radiology, University of Massachusetts Medical Center, Worcester, MA; Community Memorial Hospital (S.L.-H.C.A., S.C.R.N., N.E.T.), Ventura, CA; Vascular and Neurointerventional Services (G.L.), Saint Louis University, Missouri; Miami Cardiac & Vascular Institute (I.L.), Miami Neuroscience Institute, FL; Dartmouth Hitchcock Medical Center (T.G.L., D.M.R.-S.), Lebanon, NH; Department of Neurology & Neurosurgery (S.S.M.), ECU Health Medical Center, Greenville, NC; Department of Neurology (L.M.), University of Kansas Medical Center; West Virginia University (John Mancin, Ansaar Rai); Department of Neurology (H.M., A.B.R.), SUNY Upstate, Syracuse, NY; Department of Neurology (G.A.M.), Medical University of South Carolina; Department of Neurosurgery (Andre Monteiro, A.H.S.), University at Buffalo; Department of Neurology (F.N.), Pediatrics, Emory University, Georgia; Department of Neurology (K.N.), University of Arkansas for Medical Sciences, Arkansas; Ascension St Johns Medical Center (R.H.R.), Tulsa, OK; Riverside Regional Medical Center (Pankajavalli Ramakrishnan), Newport News, VA; Department of Neurology (Aaron Rothstein), Hospital of the University of Pennsylvania, Philadelphia; University of Colorado School of Medicine (S.O.S.), Aurora, CO; Miami Neuroscience Institute (A.K.S.), Miami; UNC School of Medicine (M.J.W.), North Carolina; University of Utah (K.-H.W.); Hue Central (H.V.L., Q.V.N.), Vietnam; Da Nang Hospital (T.N.P., T.T.N.), Da Nang, Vietnam; Bach Mai Hospital (H.T.P., M.D.T.), Hanoi, Vietnam; Department of Neurology (U.F.), Basel University Hospital, University of Basel, Switzerland; Neurology Service (P.M., Davide Strambo), Department of Clinical Neurosciences, Lausanne University Hospital and University of Lausanne, Switzerland; Department of Neurology (S.O.M.), Federal University of Rio Grande do Sul, Porto Alegre; Hospital de Clinicas de Porto Alegre (S.O.M.), Brazil; and Department of Neurology (R.G.N.), University of Pittsburgh Medical Center, Pittsburgh. Ondrej Skoda is currently at the Department of Neurology, Third Faculty of Medicine, Charles University and University Hospital Kralovske Vinohrady, Prague, Czech Republic.

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## Appendix Authors

Authors, their locations, and their contributions are listed at [links.lww.com/WNL/C443](https://links.lww.com/WNL/C443)

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