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Impact of COVID-19 on the Volume of Acute Stroke Admissions: A Nationwide Survey in Japan

Takeshi YOSHIMOTO,[1] Hiroshi YAMAGAMI,[2] Nobuyuki SAKAI,[3] Kazunori TOYODA,[4] Yoichiro HASHIMOTO,[5] Teruyuki HIRANO,[6] Toru IWAMA,[7] Rei GOTO,[8] Kazumi KIMURA,[9] Satoshi KURODA,[10] Yuji MATSUMARU,[11] Susumu MIYAMOTO,[12] Kuniaki OGASAWARA,[13] Yasushi OKADA,[14] Yoshiaki SHIOKAWA,[15] Yasushi TAKAGI,[16] Teiji TOMINAGA,[17] Masaaki UNO,[18] Shinichi YOSHIMURA,[19] Nobuyuki OHARA,[20] Hirotoshi IMAMURA,[3] and Chiaki SAKAI[3]

[1]Department of Neurology, National Cerebral and Cardiovascular Center, Suita, Osaka, Japan
[2]Department of Stroke Neurology, National Hospital Organization Osaka National Hospital, Osaka, Osaka, Japan
[3]Department of Neurosurgery, Kobe City Medical Center General Hospital, Kobe, Hyogo, Japan
[4]Department of Cerebrovascular Medicine, National Cerebral and Cardiovascular Center, Suita, Osaka, Japan
[5]Department of Neurology, Kumamoto City Hospital, Kumamoto, Kumamoto, Japan
[6]Department of Stroke and Cerebrovascular Medicine, Kyorin University, Tokyo, Japan
[7]Department of Neurosurgery, Gifu University Graduate School of Medicine, Gifu, Gifu, Japan
[8]Graduate School of Business Administration, Keio University, Tokyo, Japan
[9]Department of Neurology, Nippon Medical School Hospital, Tokyo, Japan
[10]Department of Neurosurgery, Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama, Toyama, Toyama, Japan
[11]Department of Neurosurgery, Tsukuba University, Tsukuba, Ibaraki, Japan
[12]Department of Neurosurgery, Kyoto University, Kyoto, Kyoto, Japan
[13]Department of Neurosurgery, Iwate Medical University, Morioka, Iwate, Japan
[14]Departments of Cerebrovascular Medicine and Neurology, National Hospital Organization Kyushu Medical Center, Fukuoka, Fukuoka, Japan
[15]Department of Neurosurgery, Kyorin University, Tokyo, Japan
[16]Department of Neurosurgery, Tokushima University Graduate School of Medicine, Tokushima, Tokushima, Japan
[17]Department of Neurosurgery, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan
[18]Department of Neurosurgery, Kawasaki Medical School, Kurashiki, Okayama, Japan
[19]Department of Neurosurgery, Hyogo College of Medicine, Nishinomiya, Hyogo, Japan
[20]Department of Neurology, Kobe City Medical Center General Hospital, Kobe, Hyogo, Japan

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Abstract

This study aimed to measure the impact of the COVID-19 pandemic on the volumes of annual stroke admissions compared with those before the pandemic in Japan. We conducted an observational, retrospective nationwide survey across 542 primary stroke centers in Japan. The annual admission volumes for acute stroke within 7 days from onset between 2019 as the pre-pandemic period and 2020 as the pandemic period were compared as a whole and separately by months during which the epidemic was serious and prefectures of high numbers of infected persons. The number of stroke patients declined from 182,660 in 2019 to 178,083 in 2020, with a reduction rate of 2.51% (95% confidence interval [CI], 2.58%-2.44%). The reduction rates were 1.92% (95% CI, 1.85%-2.00%; 127,979-125,522) for ischemic stroke, 3.88% (95% CI, 3.70%-4.07%, 41,906-40,278) for intracerebral hemorrhage, and 4.58% (95% CI, 4.23%-4.95%; 13,020-12,424) for subarachnoid hemorrhage. The admission volume declined by 5.60% (95% CI, 5.46%-5.74%) during the 7 months of 2020 when the epidemic was serious, whereas it increased in the remaining 5 months (2.01%; 95% CI, 1.91%-2.11%). The annual decline in the admission volume was predominant in the five prefectures with the largest numbers of infected people per million population (4.72%; 95% CI, 4.53%-4.92%). In conclusion, the acute stroke admission volume declined by 2.51% in 2020 relative to 2019 in Japan, especially during the months of high infection, and in highly infected prefectures. Overwhelmed healthcare systems and infection control practices may have been associated with the decline in the stroke admission volume during the COVID-19 pandemic.

Keywords: coronavirus disease-2019, stroke, admission, nationwide survey, Japan

Introduction

On March 11, 2020, the World Health Organization declared coronavirus disease-2019 (COVID-19) a pandemic,[1,2] which triggered an increase in emergency medical system activation. COVID-19 variants are still rampant worldwide,[3] and the pandemic has induced profound changes in healthcare system organization.[4,5] In Japan, the first COVID-19 infected patient was found on January 16, 2020, and 1727013 people were infected with COVID-19 in the two years up to 2021.

Despite geographic variations, COVID-19 has been associated with a global decline[6] in the volume of overall stroke admissions-from comprehensive stroke centers in highly resourced countries[7,8] to primary stroke centers (PSCs) without endovascular capability in low- or middle-income countries.[9,10] The reasons for such a decline are unclear. There is little information about the worldwide changes in stroke admissions during the pandemic and pre-pandemic periods obtained using an annual survey involving a large population.

The present study aimed to measure the impact of COVID-19 on stroke care assessed by the changes in annual admission volumes to stroke centers for overall stroke and each stroke type across the pre-pandemic (2019) and pandemic periods (2020) in Japan.

Materials and Methods

Our data are available upon request to the corresponding author. The present study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[11] A completed STROBE checklist is included in the Data Supplement.

Study design

Between January 2019 and December 2020, we conducted a cross-sectional, observational, retrospective survey across Japan on the monthly volumes of consecutive patients admitted to PSCs certified by the Japan Stroke Society within 7 days of ischemic stroke (IS), intracerebral hemorrhage, or subarachnoid hemorrhage onset. The certified centers in Japan include both PSCs and comprehensive stroke centers. A physician or stroke coordinator verified the cases.

Setting, participants, variables, and outcome measures

The Japan Stroke Society conducted the present survey regarding the admission volume for acute stroke. The questionnaire was sent *via* e-mail to 974 PSCs in Japan (Figure S1). The responses were sent to the Japan Stroke Society, which provided a complete dataset for the 2-year period, including any associated analyses. The survey protocol conformed to the Declaration of Helsinki. The institutional review boards from the coordinating sites (Kobe City Medical Center General Hospital and National Hospital Organization Osaka National Hospital) considered that the investigators did not have access to identifiable protected health information, and thus, no informed consent or institutional review board oversight was required because the study did not meet the Japanese Ethical Guidelines for Medical and Biological Research Involving Human Subjects.

The monthly volumes of admissions for overall stroke

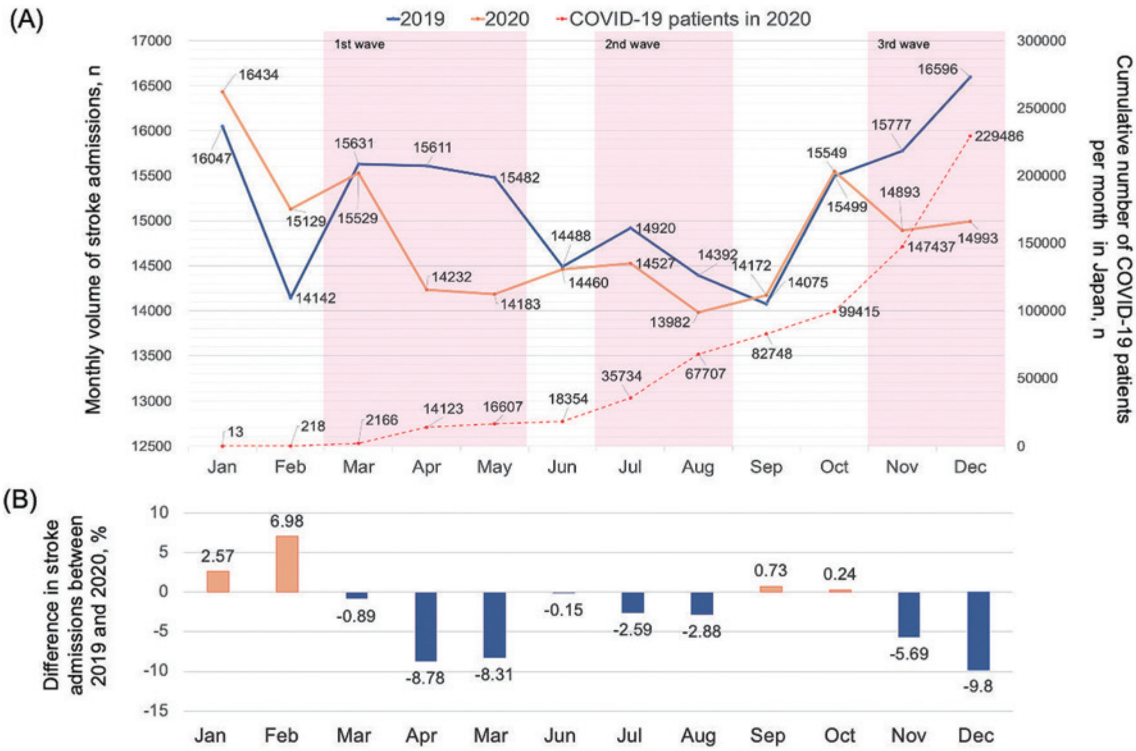

Fig. 1 Monthly volume of stroke admissions and cumulative number of COVID-19 patients in 542 Japanese PSCs during the study period.
(A) Monthly volume of stroke admissions and cumulative number of COVID-19 patients per month in Japan. (B) Difference in stroke admissions between 2019 and 2020.
A state of emergency was declared on April 7, 2020, and was lifted on May 25, 2020. Based on openly available data from the Ministry of Health, Labour and Welfare, Japan. <https://www.mhlw.go.jp/stf/covid-19/open-data.html, in Japanese>

and its subtypes were compared between the pre-pandemic (January-December 2019) and pandemic periods (January-December 2020).

Statistical analyses

As a primary analysis, we compared the annual numbers of hospitalized stroke patients (any stroke, IS, intracerebral hemorrhage, or subarachnoid hemorrhage) between 2019 and 2020. We calculated the percentage change in patient numbers between the two periods and their 95% confidence intervals (CIs) using the Wilson method without continuity correction.[12]

Subsequently, we repeated the analyses by dividing the 12 months of 2020 into two-time groups according to the pandemic severity as a secondary analysis. In Japan, there were three waves of COVID-19 in 2020: March-May, July-August, and November-December. We defined those 7 months as the spreading months (Fig. 1) and January-February, June, and September-October as the non-spreading months.

Furthermore, as a third analysis, according to the cumulative infection rate in 2020, we repeated the analyses by dividing Japan's 47 prefectures into highly infected prefectures and other prefectures. We defined highly infected prefectures as the top five with the highest cumulative number of infected people per million population as of December 31, 2020.[13] Furthermore, we expressed the relative changes in admissions for all types of stroke or its subtype (IS, intracerebral hemorrhage, and subarachnoid hemorrhage) as an incidence rate ratio (IRR) along with its two-sided 95% CI: IRR = incidence rate 2020/incidence rate 2019 (where the incidence rate 2020 = number of event admissions in the spreading months in 2020/number of event admissions in the non-spreading months of 2020, and where the incidence rate 2019 = number of event admissions in the spreading months of 2019/number of event admissions in the non-spreading months of 2019). Then, we calculated the IRR using mixed Poisson regression[14] to test whether the rate of events changed by year (2019 or 2020), spreading status (spreading or non-spreading months), and interaction of year and spreading status (reflecting the impact of COVID-19) (model 1).

Finally, we repeated our analyses separately by trisected groups of PSCs (low-, intermediate-, and high-volume PSCs) according to the annual number of stroke admissions in 2019, depending on the number of stroke admissions in the same year for each PSC.

We evaluated the descriptive statistics for differences in

Table 1 Annual and monthly volume of acute stroke during the pre-pandemic (2019) and pandemic (2020) periods

	N	Annual volume			Monthly volumes per stroke center		
		2019	2020	Percent change (95% CI), %	2019, mean ± SE	2020, mean ± SE	P value*
All stroke	542	182,660	178,083	−2.51 (−2.58 to −2.44)	28.08 ± 0.71	27.38 ± 0.69	<0.0001
Stroke type							
Ischemic stroke	542	127,979	125,522	−1.92 (−2.00 to −1.85)	19.68 ± 0.53	19.30 ± 0.53	0.0054
Intracerebral hemorrhage	542	41,906	40,278	−3.88 (−4.07 to −3.70)	6.44 ± 0.18	6.20 ± 0.17	0.0003
Subarachnoid hemorrhage	542	13,020	12,424	−4.58 (−4.95 to −4.23)	2.00 ± 0.07	1.91 ± 0.06	0.0086

Abbreviations: CI, confidence interval; N, number of hospitals; SE, standard error.
* *P*-value with reference to monthly volume per primary stroke center in 2019 using the Wilcoxon signed-rank test.

Table 2 Comparison of acute stroke admission volumes between the spreading and non-spreading months during the pre-pandemic (2019) and pandemic (2020) periods

	Annual volume*			Monthly volumes per stroke center*		
	2019	2020	Change (95% CI), %	2019, mean ± SE	2020, mean ± SE	Change (95% CI), %
All stroke						
Spreading months	108,409	102,339	−5.60 (−5.74 to −5.46)	16.67 ± 0.42	15.73 ± 0.40	−4.27 (−6.00 to −2.54)
Non-spreading months	74,251	75,744	2.01 (1.91 to 2.11)	11.42 ± 0.49	11.65 ± 0.30	4.69 (2.43 to 6.95)
Ischemic stroke						
Spreading months	76,015	72,103	−5.15 (−5.31 to −4.99)	11.71 ± 0.32	11.15 ± 0.30	−3.05 (−5.04 to −1.07)
Non-spreading months	51,774	53,374	3.09 (2.94 to 3.24)	7.98 ± 0.22	8.24 ± 0.23	6.69 (4.19 to 9.19)
Intracerebral hemorrhage						
Spreading months	24,580	23,226	−5.51 (−5.80 to −5.23)	3.79 ± 0.11	3.58 ± 0.10	−0.82 (−3.78 to 2.13)
Non-spreading months	17,235	17,118	−0.68 (−0.57 to −0.81)	2.65 ± 0.07	2.64 ± 0.07	9.24 (3.74 to 14.76)
Subarachnoid hemorrhage						
Spreading months	15,494	14,097	−9.02 (−9.48 to −8.58)	2.38 ± 1.19	2.18 ± 1.09	8.02 (0.54 to 15.49)
Non-spreading months	10,546	10,732	1.76 (1.53 to 2.03)	1.62 ± 0.81	1.65 ± 0.83	22.78 (14.80 to 30.76)

The spreading months were Mar.–May, July.–Aug., Nov.–Dec. 2020, and the non-spreading months were Jan.–Feb., June, Sept.–Oct. 2020. Each month was compared with the same month of the previous year (2019).
Abbreviations: CI, confidence interval; SE, standard error.
* $P < 0.0001$ between the spreading and non-spreading months for any events using the z-test or Wilcoxon signed-rank test.

the measures between the pandemic and pre-pandemic periods in all analyses other than the percentage changes using the Wilcoxon signed-rank test. The percentage changes in the overall stroke and its subtype admission volume were tested using the two-proportion Z-test. All studies were conducted using StataMP 17 (StataCorp LLC, College Station, TX), and significance was tested at $P < 0.05$ for the two-tailed tests.

Results

Of the 974 PSCs, 576 responded; of those, 34 were excluded due to incomplete data. Thus, we analyzed the data from the remaining 542 PSCs (55.6%).

Overall analysis

The annual volumes of stroke admissions were 182,660 in 2019 and 178,083 in 2020-indicating a decline of 2.51% (95% CI, 2.44%-2.58%, $P < 0.0001$, Fig. 1). Of the 542 PSCs, 235 (43.4%) had more stroke admissions in 2020 than in 2019. The monthly volumes for admissions according to stroke type are presented in Figure S2. The admission volume for IS decreased from 127,979 in 2019 to 125,522 in 2020; the adjusted mean (standard error) monthly number of IS patients per center declined from 19.68 ± 0.53 to 19.30 ± 0.53 ($P = 0.0054$), which correspond to a 1.92% (95% CI, 1.85%-2.00%, $P = 0.0025$) reduction (Table 1). The admission volume for intracerebral hemorrhage decreased from 41,906 to 40,278 (6.44 ± 0.18 to 6.20 ± 0.17 monthly per center, $P = 0.0003$), which correspond to a 3.88% (95%

Table 3 Comparison of stroke admission volumes between highly infected and other prefectures during the pre-pandemic (2019) and pandemic (2020) periods

	Annual volume *			Monthly volumes per stroke center **		
	2019	2020	Change (95% CI), %	2019, mean ± SE	2020, mean ± SE	Change (95% CI), %
Stroke						
Highly infected prefectures	46,348	44,161	−4.72 (−4.92 to −4.53)	30.17 ± 1.52	28.75 ± 1.44	−4.83 (−7.56 to −2.10)
Other prefectures	136,312	133,922	−1.75 (−1.82 to −1.68)	27.44 ± 0.80	26.96 ± 0.79	−0.09 (−2.00 to 1.83)
Ischemic stroke						
Highly infected prefectures	32,039	30,574	−4.57 (−4.81 to −4.35)	20.86 ± 1.14	19.90 ± 1.10	−4.28 (−7.22 to −1.35)
Other prefectures	95,940	94,948	−1.03 (−1.10 to −0.97)	19.31 ± 0.60	19.11 ± 0.60	1.03 (−1.18 to 3.23)
Intracerebral hemorrhage						
Highly infected prefectures	11,189	10,632	−4.98 (−5.40 to −4.58)	7.28 ± 0.38	6.92 ± 0.35	2.00 (−6.97 to 10.97)
Other prefectures	30,717	29,646	−3.49 (−3.70 to −3.29)	6.18 ± 0.20	5.98 ± 0.19	3.01 (−6.97 to 10.97)
Subarachnoid hemorrhage						
Highly infected prefectures	3,274	3,096	−5.44 (−6.27 to −4.71)	2.13 ± 0.14	2.02 ± 0.13	0.41 (−7.66 to 8.58)
Other prefectures	9,746	9,328	−4.29 (−4.71 to −3.90)	1.96 ± 0.08	1.88 ± 0.07	10.05 (1.83 to 18.28)

Abbreviations: CI, confidence interval; SE, standard error.
* $P < 0.0001$ between the highly infected and other prefectures for any events using the z-test.
** $P < 0.0001$ between the highly infected and other prefectures for any events using the Wilcoxon signed-rank test.

CI, 3.70%-4.07%, $P < 0.0001$) decline. The admission volume for subarachnoid hemorrhage decreased from 13,020 to 12,424 (2.00 ± 0.07 to 1.91 ± 0.06 monthly per center, $P = 0.0086$), which correspond to a 4.58% (95% CI, 4.23%-4.95%, $P < 0.0001$) decline.

Subgroup analyses

The number of stroke admissions decreased by 5.60% (95% CI, 5.46%-5.74%) during the spreading months in 2020 compared with that during the same months in 2019; however, it increased by 2.01% (95% CI, 1.91%-2.11%) in the non-spreading months ($P < 0.0001$, Table 2). These results were similar for IS and subarachnoid hemorrhage.

Among the 47 prefectures in Japan, Tokyo, Okinawa, Osaka, Hokkaido, and Kanagawa had the highest cumulative number of infected people per 1 million population (Figure S3). We considered these as the five highly infected prefectures, and the cumulative number of infected people per 1 million population exceeded 2,300. The number of stroke admissions decreased by 4.72% (95% CI, 4.53%-4.92%) between 2019 and 2020 in these prefectures and by 1.75% (95% CI, 1.68%-1.82%) in the other 42 prefectures ($P < 0.0001$, Table 3). These results were similar for each stroke type. The IRR (95% CI) of stroke admissions using mixed Poisson regression was 0.9899 (0.9977-0.9998), and similar analysis revealed a significant decrease in the number of stroke admission in the highly infected prefectures (IRR, 0.9987; 95% CI, 0.9974-0.9998). The IRR for stroke and each stroke subtype admissions between highly infected prefectures and other prefectures is presented in Table S1.

The tertiles of the stroke admission volumes in each PSC were 231 and 380 in 2019. High-volume PSCs with ≥380 stroke admissions in 2019 indicated a significant decline in stroke admissions in 2020 (3.21%; 95% CI, 3.10%-3.22%, $P = 0.0001$), whereas the intermediate-volume PSCs (1.51%; 95% CI, 1.41%-1.62%; $P = 0.1399$) and low-volume PSCs did not exhibit a significant decline in acute stroke admission volume in 2020 (1.87%; 95% CI, 1.72%-2.04%, $P = 0.0785$, Table 4). The annual and monthly volumes of stroke admissions by different scales of stroke centers during the pre-pandemic (2019) and pandemic (2020) periods are presented in Table 4.

Discussion

This was a temporal analysis of ≈180,000 annual stroke admissions in Japan. The major finding was that there was a global decrease in stroke admissions by 2.51% in 2020, the pandemic period, compared with 2019, the pre-pandemic period. A drop in stroke admission volume was also seen concerning the equivalent period in the prior year for all stroke subtypes. Notably, the number of stroke admissions declined during the spreading months in 2020 but increased in the remaining months. The number of stroke admissions in the five prefectures with relatively severe pandemic significantly declined over the same period. To reduce the bias in the change in the number of stroke admissions annually with or without the impact of COVID-19, the IRR verification also confirmed a decrease in stroke admission in the pandemic period-especially in those five prefectures. Furthermore, the declines in stroke admissions were predominant among high-volume stroke centers.

Table 4 Annual and monthly volume of stroke admissions by different scales of primary stroke centers during the pre-pandemic (2019) and pandemic (2020) periods

	Annual admission volumes				Monthly volumes per center		
	N	2019	2020	Percent change (95% CI), %	2019, mean ± SE	2020, mean ± SE	*P*-value *
All stroke **							
Low-volume PSCs	180	28,079	27,554	−1.87 (−2.04 to −1.72)	13.11 ± 0.34	12.85 ± 0.35	0.0771
Intermediate-volume PSCs	182	53,735	52,922	−1.51 (−1.62 to −1.41)	24.84 ± 0.27	24.44 ± 0.36	0.1360
High-volume PSCs	180	100,846	97,607	−3.21 (−3.10 to −3.22)	46.34 ± 1.10	44.89 ± 1.08	0.0001
Stroke subtype							
Ischemic stroke ***							
Low-volume PSCs	180	18,923	18,951	0.15 (0.10 to 0.21)	8.76 ± 0.25	8.78 ± 0.27	0.9696
Intermediate-volume PSCs	182	37,188	36,442	−2.01 (−2.15 to −1.88)	17.03 ± 0.19	16.68 ± 0.29	0.1526
High-volume PSCs	180	71,868	70,129	−2.42 (−2.53 to −2.31)	33.27 ± 0.85	32.47 ± 0.85	0.0025
Intracerebral hemorrhage****							
Low-volume PSCs	180	5,410	5,565	−2.87 (−3.35 to −2.45)	2.50 ± 0.08	2.58 ± 0.09	0.2091
Intermediate-volume PSCs	182	12,579	12,192	−3.08 (−3.39 to −2.79)	5.76 ± 0.08	5.59 ± 0.12	0.1097
High-volume PSCs	180	23,917	22,521	−5.84 (−6.14 to −5.55)	11.07 ± 0.26	10.48 ± 0.25	<0.0001
Subarachnoid hemorrhage *****							
Low-volume PSCs	180	1,340	1,636	22.09 (19.95 to 24.39)	0.62 ± 0.02	0.76 ± 0.04	0.0002
Intermediate-volume PSCs	182	3,499	3,361	−3.94 (−4.64 to −3.35)	1.60 ± 0.02	1.54 ± 0.05	0.0580
High-volume PSCs	180	8,181	7,427	−9.22 (−9.86 to −8.61)	3.79 ± 0.11	3.44 ± 0.11	<0.0001

Abbreviations: CI, confidence interval; N, number of hospitals; PSC, primary stroke center; SE, standard error.
High-, intermediate-, and low-volume PSCs were categorized according to the number of hospitalizations for each stroke center in 2019.
* *P*-value with reference to monthly volumes per PSC in 2019 using Wilcoxon's signed-rank test.
** Low vs. intermediate, $P = 0.7917$; low vs. high, $P = 0.2570$; intermediate vs. high, $P = 0.1456$.
*** Low vs. intermediate, $P = 0.1679$; low vs. high, $P = 0.0030$; intermediate vs. high, $P = 0.3799$.
**** Low vs. intermediate, $P = 0.0073$; low vs. high, $P < 0.0001$; intermediate vs. high, $P = 0.0954$.
***** Low vs. intermediate, $P < 0.0001$; low vs. high, $P < 0.0001$; intermediate vs. high, $P = 0.1473$.

Several infections have long been recognized to increase the risk of stroke, and stroke was also found to induce immune suppression, which increases the risk of infection.[15] Initial reports from Wuhan, China, revealed a high risk of stroke among COVID-19-infected patients, with a frequency of ≈5%, especially those with severe infection.[16,17] Contrarily, consistent declines in the absolute volumes of IS admissions due to COVID-19 have been reported; however, the magnitude of the reduction varied according to the severity of the pandemic in the studied countries and the observation period. Studies involving a few months of observation in early 2020 observed reductions in visits or consultations among patients with acute IS by 30%-40%.[18-20] One study with a longer observation period found recovery of stroke volumes in the second quarter of 2020 following an initial steep decline.[21] Thus, the decrease in the initial volume did not seem to have been caused by decreased stroke incidence.

In this study, we observed that in 2020, the number of stroke admissions decreased during the 7 months when the epidemic was relatively serious. Behavioral modifications against the spread of COVID-19 by the general population appeared to have both decreased and increased the risk of stroke. Stroke patients-especially those with mild neurological deficits-may have avoided visiting healthcare facilities because of concerns about infection risk.[22-26] Going outside less often may have offered protection against the cold in winter, which could have decreased the risk of hemorrhagic stroke; in summer, staying indoors more often could have provided protection from dehydration, thereby decreasing the risk of thrombotic IS. Conversely, staying inside more often could have reduced physical exercise opportunities and also led to noncompliance with medication owing to reduced regular medical checkups, thereby increasing the risk of stroke.[27,28]

Estimates of changes in the volume of IS and its subtypes were reported to have been affected by hospital characteristics and cohort case-mix.[29] In this regard, COVID-19 appears to have had a greater effect in larger cohorts that included a greater proportion of high-volume PSCs than in smaller cohorts with intermediate- and low-volume PSCs;[21,30-35] these findings are supported by the results of the present study. Most high-volume PSCs were core hospitals in a city and needed to devote considerable care for COVID-19 patients; thus, the capacity for stroke care may have decreased in such institutions. Conversely, intermediate- and low-volume PSCs may have contributed more to stroke care. As a result, the number of stroke admissions in 2020 might have increased in 47% of the PSCs compared with that in 2019.

About 47% of the PSCs were found to have increased stroke admissions in 2020. The influence was also clearly observed in the metropolitan areas, such as the Tokyo, Osaka, and Kanagawa prefectures and the prefectures with regiments of tourists, such as Okinawa and Hokkaido. In these prefectures, the medical staffs and sources originally for stroke care might be partly exploited for COVID-19 patients.

The strength of this study was the participation of geographically evenly distributed 542 PSCs, which are more than half the certified PSCs in Japan. Furthermore, 180,000 patients were investigated annually, which was about 75% of the annual number of acute stroke patients in Japan. To the best of our knowledge, this is currently the most extensive nationwide survey evaluating the impact of the COVID-19 pandemic on stroke care.

This study has several limitations. First, 44.4% of Japan's PSCs did not respond to the survey or submitted incomplete data. Second, data on stroke patients who visited hospitals and clinics other than the certified PSCs (probably mainly because of mild stroke severity) were unavailable. Third, we did not obtain detailed individual data, such as stroke severity, therapy, and functional outcome. Fourth, the spreading months of COVID-19 varied among the prefectures.

Conclusion

The volume of acute stroke admissions declined in 2020 relative to 2019 in certified primary stroke centers (PSCs) in Japan, especially in high-volume centers, during the COVID-19 spreading months, and in highly infected prefectures. Overwhelmed healthcare systems and infection control practices may have been associated with the reduced number of acute stroke patients during the COVID-19 pandemic.

Supplementary Material

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Conflicts of Interest Disclosure

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Corresponding author: Hiroshi Yamagami, MD, PhD
Department of Stroke Neurology, National Hospital Organization Osaka National Hospital, 2-1-14 Hoenzaka Chuo-ku, Osaka, 540-0006, Japan.
e-mail: yamagami.hiroshi@ncvc.go.jp