Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Background: The COVID-19 pandemic caused public lockdowns around the world. We analyzed if the public lockdown altered the referral pattern of Code Stroke patients by Emergency Medical Services (EMS) to our Comprehensive Stroke Center.

Methods: Retrospective single-center study at a Bavarian Comprehensive Stroke Center. Patients who were directly referred to our stroke unit by EMS between the 1st of January 2020 and the 19th of April 2020 were identified and number of referrals, clinical characteristics and treatment strategies were analyzed during the public lockdown and before. The public lockdown started on 21st of March and ended on 19th April 2020.

Results: In total 241 patients were referred to our center during the study period, i.e. 171 before and 70 during the lockdown. The absolute daily number of Code Stroke referrals and the portion of patients with stroke mimics remained stable. The portion of female stroke patients decreased (55% to 33%; p = 0.03), and stroke severity as measured by the National Institutes of Health Stroke Scale (median 3 (IQR 0-7) versus 6 (IQR 1-15.5) points; p = 0.04) increased during the lockdown. There was no difference of daily numbers of patients receiving thrombolysis and thrombectomy.

Conclusions: Referral of Code Stroke patients by EMS could be maintained sufficiently despite the COVID-19 pandemic lockdown. However, patients’ health care utilization of the EMS may have changed within the public lockdown. EMS remains a useful tool for Code Stroke patient referral during lockdowns, but public education about stroke is required prior to further lockdowns.

Key Words: Hospital referral—COVID-19—Stroke mimic—Lockdown—Stroke

Introduction

During the coronavirus disease 2019 (COVID-19) pandemic the use of health care systems changed suddenly. Hospitals were overwhelmed as a result of the staggering COVID-19 patient numbers and/or modified their daily routine due to prophylactic allocation of resources. Public lockdowns with strict containment recommendations for the community have been announced around the world. Emergency Medical Services (EMS) and dispatch centers were confronted with increasing numbers of patients/calls and reorganization of the dispatch system including Code Stroke patient referral. Though COVID-19 disease is associated with vascular thrombotic events, several studies suggest a decline of patients with vascular diseases and strokes presenting to hospitals since the beginning of the pandemic. Probably, less severely affected stroke patients avoided emergent medical evaluation. It was speculated that patients changed their health care utilization patterns during the pandemic and...
its lockdowns. So far, it is unclear how EMS and their Code Stroke patient referral system were affected during the pandemic. Mostly, stroke patients are admitted to hospitals by EMS as Code Stroke patients. A sufficient maintenance of the interplay between EMS and stroke units during a pandemic and public lockdown is crucial to provide appropriate stroke care. In the present study, we analyzed numbers and patterns of Code Stroke patients dispatched by EMS during the COVID-19 pandemic at a German Comprehensive Stroke Center, which is located at one of the pandemic hotspots in Germany.

Methods

Study design

We retrospectively analyzed all consecutive patients with an activated Code Stroke by the EMS following pre-hospital triage and who were directly referred to our stroke unit between 1st January 2020 and 19th April 2020 using the electronic database IVENA eHealth of the Munich EMS dispatch. The time period 1st January 2020 to 20th March 2020 was defined as pre-lockdown and the time period during the Bavarian public lockdown between 21st March 2020 and 19th April 2020 as lockdown (Fig. 1). We extracted EMS admission patterns and analyzed patient data regarding age, sex, stroke severity as measured by the National Institute of Health Stroke Scale (NIHSS), diagnosis of discharge and mode of treatment in case of ischemic strokes. Based on the diagnosis of discharge, patients were categorized as stroke (ischemic stroke, hemorrhagic stroke, transient ischemic attack) or stroke mimic, respectively. Given the retrospective and anonymous design, approval by the local ethics committee and a need for written consent was waived based on the Bayerisches Krankenhaushaußgesetz (Section 27, paragraph 4). The study conforms with World Medical Association Declaration of Helsinki. Data that support the findings of this study are available from the corresponding author upon reasonable request.

Local COVID-19 measures and patient referral

In Bavaria the first COVID-19 patient was recorded the 27th of January 2020. To prevent further infections, among others, a public lockdown came into force between the 21st of March (Fig. 1) and all hospitals were obliged to allocate resources for expected COVID-19 patients. For all patients admitted to our hospital strict hygienic measures were applied. The standard procedure to refer patients to stroke units directly via EMS was continued during the pandemic. The referral is organized and monitored by the Integrierte Rettungsleitstelle München, which is the EMS dispatch center for Munich metropolitan area in Upper Bavaria.

Statistical analysis

Analysis were performed using GraphPad Prism version 7.04 (GraphPad). Quantitative differences between groups were analyzed using Student’s t-test or the non-parametric Mann-Whitney U test (two-tailed tests) depending on whether or not values followed a Gaussian distribution. Categorical differences were evaluated using bivariate analysis with Fisher’s exact test. Association between Stroke Unit availability and referral patterns were evaluated using Pearson correlation. The statistical significance threshold was p < 0.05. Values are provided as mean ± standard deviation (SD) if normally distributed, otherwise as median (25%–75% interquartile range (IQR)).

Results

During the lockdown, daily availability of our stroke unit to admit Code Stroke patients by EMS increased from 51% (12 ± 7 h) to 86% (20 ± 4 h; p < 0.001). During the study period, 246 direct Code Stroke referrals to our stroke unit were identified. Five patients were excluded from analysis, as they were transferred from other hospitals for thrombectomy with activated Code Stroke. This resulted in a study population of 241 patients. Mean age was 73.0 ± 16 years. 117 patients (48.5%) were female.
A total of 171 patients was referred to us during pre-lockdown and 70 patients during lockdown (Fig. 2A). There were no differences in EMS-based daily referral of Code Stroke patients between pre-lockdown and lockdown (Fig. 2B). Comparable portions of daily referred patients were categorized as stroke mimic during pre-lockdown (50% (IQR 13-100)) and lockdown (50% (IQR 31-67)). There were no differences in daily referral numbers of ischemic strokes, hemorrhagic stroke, and transient ischemic attacks between both periods (data not shown). By trend, we found a weak association between daily availability of our Stroke Unit and daily admission numbers (Pearson $r = 0.16$, $p = 0.10$).

Age between patients before and during the lockdown did not differ (73.8 ± 16 versus 71.0 ± 16 years; $p = n.s.$). The rate of female patients decreased significantly during lockdown (Fig. 3A). NIHSS scales of stroke at admission patients increased from 3 (IQR 0–7) to 6 (IQR 1–15.5) points during the lockdown (Fig. 3B). The portion of patients receiving invasive stroke treatment between both time periods did not change (Fig. 3C). No associations between daily Stroke Unit availability and stroke severity or sex were detected (data not shown).

---

**Fig. 2.** Code Stroke patient referral. A, Absolute daily number of all referred patients. B, median daily number of all referred patients.

**Fig. 3.** Patients’ characteristics. A; fraction of female patients. B, Median NIHSS (National Institutes of Health Stroke Scale) values. C, fraction of thrombolysis/thrombectomy in patients with ischemic stroke. * indicates $p$ values $<$0.05.
Discussion

In the present study, we present data about the interaction of EMS and a Comprehensive Stroke Center during the public COVID-19 pandemic lockdown. Our data suggest that EMS services operate stable and reliable during a lockdown, but patients’ health care utilization of the EMS may alter within a public lockdown.

We did not observe a clear change of daily referrals to our stroke unit during the lockdown. This suggests a sufficient maintenance of out- and inpatient care providers and EMS organization during the COVID-19 pandemic lockdown, which is in line to a recent Canadian study. As we did not study all hospitalized patients, but analyzed Code Stroke patients referred by EMS only, our finding is not contradicting previous observations of an overall decline of hospitalized stroke patients. Importantly, among admitted Code Stroke patients the proportion of patients with stroke and stroke mimics remained stable, indicating, that the prehospital management including triage of EMS is resilient during this current stress test. This is line to studies from Spain and France, displaying stable rates of stroke mimics during the COVID-19 pandemic. As none of the prior studies discussed this important point furtherly, we feel the need to highlight this particularly.

The increased availability of our stroke unit within the public lockdown is most likely explained by the legal measures to stop routine out- and inpatient visits, resulting in vast capacities in German hospitals. As we found a weak and non-significant association of daily referral numbers and availability of our stroke unit, we cannot rule out that this issue may affect our observations. In addition to first examples showing that in hospital stroke care can be upheld sufficiently during this crisis, our data suggest that strict containment measures do not necessarily disrupt the interplay of stroke units and EMS.

Since we detected a shift to male and more severely affected stroke patients during the lockdown, our data suggest a change in patients’ behavior and subsequent health care utilization. This fits well to prior studies. Possibly, patients avoid calling EMS and inpatient hospital care in fear of being infected with SARS-CoV-2. As such patients may benefit from therapy similarly, this aspect should be analyzed in detail during future studies. Providing stroke care to those patient subgroups during future pandemics will be crucial. Intense public education might be required prior to further lockdowns.

Our study has several limitations. Besides the retrospective data collection, our study is monocentric and does not address referral patterns in bigger areas. Multicenter studies covering whole districts are necessary to minimize the risk of skewed datasets. It should be noted that most actions to fight the pandemic were taken in a prophylactic manner and not as consequence of a health care system collapse in Germany. Thus, our findings might not be easily transferred to other regions in the world. However, since our hospital is located within a COVID-19 hotspot in Germany and treated more than 200 patients with COVID-19 till June 2020, our monocentric data provide important notes for coordination units and EMS to prepare for future lockdowns.

Declaration of Competing Interest

BH reports personal fees from Desitin, personal fees from Novartis, personal fees from AllergyCare, personal fees from TG Therapeutics, grants from Regeneron, outside the submitted work. BK reports grants from Novartis, during the conduct of the study; other from Novartis, grants from German Federal Ministry of Education and Research, grants from Technical University of Munich, School of medicine, outside the submitted work. BI, MD, KKG and SW have nothing to disclose.

Grant support

None.

Acknowledgments

None.

Sources of funding

No sources of funding were utilized for this project.

References

1. Armocida B, Formenti B, Ussai S, et al. The Italian health system and the COVID-19 challenge. Lancet Public Health 2020;5:e253.
2. Emanuel EJ, Persad G, Upshur R, et al. Fair allocation of scarce medical resources in the time of Covid-19. N Engl J Med 2020;382:2049-2055.
3. Koh D. COVID-19 lockdowns throughout the world. Occupation Med 2020.
4. Dami F, Berthoz V. Lausanne medical dispatch centre’s response to COVID-19. Scand J Trauma Resusc Emerg Med 2020;28:37.
5. Khosravani H, Rajendram P, Notario L, et al. Protected code stroke: hyperacute stroke management during the coronavirus disease 2019 (COVID-19) pandemic. Stroke 2020;51:1891-1895.
6. Dafer RM, Osteraa NS, Biller J. Acute stroke care in the coronavirus disease 2019 pandemic. J Stroke Cerebrovasc Dis 2020;29:104881.
7. Lodigiani C, Lapichino G, Carenzo L, et al. Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. Thromb Res 2020;191:9-14.
8. De Filippo O, D’Ascenzo F, Angelini F, et al. Reduced rate of hospital admissions for ACS during Covid-19 outbreak in Northern Italy. N Engl J Med 2020. Epub ahead of print.
9. Zhao J, Li H, Kung D, et al. Impact of the COVID-19 epidemic on stroke care and potential solutions. Stroke 2020;51:1996-2001.
10. Kerleroux B, Fabacher T, Bricout N, et al. Mechanical thrombectomy for acute ischemic stroke amid the COVID-19 outbreak: decreased activity, and increased care delays. Stroke 2020;51:2012-2017.
11. Onteddu SR, Nalleballe K, Sharma R, et al. Underutilization of health care for strokes during the COVID-19 outbreak. Int J Stroke 2020. 1747493020934362.
12. Tejada Meza H, Lambea Gil A, Sancho Saldana A, et al. Ischaemic stroke in the time of coronavirus disease 2019. Eur J Neurol 2020. Epub ahead of print.
13. Bersano A, Kraemer M, Touze E, et al. Stroke care during the Covid-19 pandemic: experience from three large European countries. Eur J Neurol 2020. Epub ahead of print.
14. Montaner J, Barragan-Prieto A, Perez-Sanchez S, et al. Break in the stroke chain of survival due to COVID-19. Stroke 2020. Epub ahead of print.
15. Siegler JE, Heslin ME, Thau L, et al. Falling stroke rates during COVID-19 pandemic at a comprehensive stroke center: cover title: falling stroke rates during COVID-19. J Stroke Cerebrovasc Dis 2020;29:104953.
16. Diegoli H, Magalhaes PSC, Martins SCO, et al. Decrease in hospital admissions for transient ischemic attack, mild, and moderate stroke during the COVID-19 era. Stroke 2020. Epub ahead of print.
17. Mantica G, Riccardi N, Terrone C, et al. Non-COVID-19 visits to emergency departments during the pandemic: the impact of fear. Public Health 2020;183:40-41.
18. Adeoye O, Lindsell C, Broderick J, et al. Emergency medical services use by stroke patients: a population-based study. Am J Emerg Med 2009;27:141-145.
19. Brechmann W. Vollzug des Infektionsschutzgesetzes (IfSG): Vorläufige Ausgangsbeschränkung anlässlich der Corona-Pandemie & Corona-Pandemie: Verschiebung elektiver Eingriffe und geplanter Behandlungen in Krankenhäusern. BayMBL. Nr.151/152 März/2020;Az. Zts-G8000-2020/122-98 & Az. G24-K9000-2020/125.
20. Zhang J, Zhou L, Yang Y, et al. Therapeutic and triage strategies for 2019 novel coronavirus disease in fever clinics. Lancet Respir Med 2020;8:e11-e12.
21. Bres Bullrich M, Fridman S, Mandzia JL, et al. COVID-19: stroke admissions, emergency department visits, and prevention clinic referrals. Can J Neurol Sci 2020;1-10.
22. Rudilosso S, Laredo C, Vera V, et al. Acute stroke care is at risk in the era of COVID-19: experience at a comprehensive stroke center in Barcelona. Stroke 2020;51:1991-1995.
23. Pop R, Quenardelle V, Hasiu A, et al. Impact of the Covid-19 outbreak on acute stroke pathways - Insights from the Alsace region in France. Eur J Neurol 2020. Epub ahead of print.
24. Agarwal S, Scher E, Rossan-Raghunath N, et al. Acute stroke care in a New York city comprehensive stroke center during the COVID-19 pandemic. J Stroke Cerebrovasc Dis 2020. Epub ahead of print.