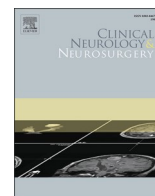




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Non-ischemic neurovascular emergencies at a supra-regional medical center during the SARS-CoV2-pandemia

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ABSTRACT

Objective: To assess the impact of the lockdown in Germany due to the SARS-CoV2-pandemic on the incidence and the outcome of neurovascular emergencies at a tertiary medical center.

Methods: From March 16th, 2020 (first lockdown in Germany) to January 31st, 2021, all neurosurgical emergencies were included and compared to a longitudinal case-cohort. Cases were descriptively recorded and retrospectively analyzed with respect to incidence and outcome.

Results: All emergencies referred to our tertiary medical center decreased by 10% during the pandemic, whereas, neurosurgical emergencies increased by 18.4% (764 vs. 905 cases). Number of specific non-ischemic neurovascular emergencies increased by 29% (95 vs. 123 cases). The difference was not statistically significant ($p = 0.53$). Mortality rate increased dramatically by 40% during the pandemic throughout all neurovascular cases. As all included patients were negative PCR-tested for SARS-CoV2 the observed increase is unrelated to the virus infection.

Conclusion: Unexpectedly, according to our data neurovascular emergencies raised in number and severity during the pandemic in Germany at our tertiary referral center. Furthermore, the case fatality increased. Even though our data lack proof of evidence for these findings, we might suggest two possible explanations for the absolute increase in numbers: firstly, patients might have refused to seek medical help while suffering only mild symptoms. Furthermore, as numerous lower-level medical centers restricted admissions, the referral times of patients in need of neurosurgical attention increased. We, therefore, suggest that even in a pandemic situation like the SARS-CoV2/COVID-19, it seems of utmost importance to retain dedicated neurovascular competence in designated centers to care for these emergencies.

1. Introduction

In December 2019, a new viral infectious disease, caused by the SARS-CoV2 (severe acute respiratory syndrome coronavirus type 2) causing the COVID19 (Corona Virus Disease 2019), was reported in Wuhan, China. The pathogen is a new beta-corona virus transmitting the

human respiratory system. Among others, COVID-19 might also affect the central nervous system as well as its vessels with an inflammatory response [1].

The pandemic took Germany approximately by February 2020. On March 16th, 2020, the first German lockdown was announced. In the wake of the lockdown, hospitals postponed all elective cases (if

Abbreviations: COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus type 2; GSNR, German Society of Neuroradiology; GSN, German Society of Neurosurgery; DSG, German Stroke Society; TIAs, transient ischemic attacks; PCI, percutaneous coronary interventions; ntSAH, non-traumatic subarachnoid hemorrhages; ntICH, non-traumatic intracerebral hemorrhages source; AVM, symptomatic arterio-venous malformations; ICH, intracerebral hemorrhage; AVF, arterio-venous fistula; SDH, subdural hemorrhage; cSDH, chronic subdural hemorrhage; IVH, intraventricular hematocephalus; mRS, Modified Ranking Scale; ICU, Intensive care unit.

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possible), outpatient departments were closed to non-emergency cases, and - as a consequence - patients-physicians contacts were stripped-down to a minimum [2].

From the registers of the German Stroke Society (DSG), as well as the German Cardiac Society, a significant decrease in heart attacks and strokes was already noted during this time.

Lately, the German Cardiac Society found a remarkable decline in catheter activity of 35%, and an increase of cardiac or cardiovascular mortality of 8%, and 12%, respectively. (NEF Clin Res Card 2021) In addition, the COVID-19 pandemic appears to have had a major impact on heart attack care in Europe, in numerous ways. As the results of the large multicenter ISACS-STEMI COVID-19 registry show, significantly fewer percutaneous coronary interventions (PCI) were carried out in European centers during the first corona wave than in the previous year (18.9%, $p < 0.0001$) [3,4].

Accordingly, the DSG reported a decline in hospitalization for acute ischemic stroke by 17.4% during the first couple of months of lockdown. Especially in patients suffering from mild symptoms (transient ischemic attack (TIA)), numbers fell to almost 23%, with severe strokes declining for about 17%. These figures are based on data from 1463 hospitals in Germany [5,6].

All third-level hospitals were instructed by the German government to provide sufficient intensive care unit (ICU) capacities for treating COVID-19 patients in need of invasive ventilator therapy. Routine operations were postponed (if possible) and admission to hospitals was restricted to emergencies. The medical professional societies released guidelines to define emergencies for each of their discipline [7]. Consequently, many patients kept away from seeking professional help as the lockdown continued and the incidence of SARS-CoV2 infections increased in Germany.

Because COVID-19 is a multi-system condition, we learned that SARS-Cov2 also affects the central nervous system, as well as its nurturing vessels with a mostly inflammatory response.

However, little information is found how this affected the clinical practice in neurovascular centers in Germany [1].

Similar trends could be seen in our hospital concerning neurovascular emergencies. Our hospital is one of the largest in North Rhine-Westphalia and the fourth largest municipal maximum care hospital in Germany offering all medical specialties. As advised by the German societies of stroke, neuroradiology and neurosurgery, tertiary medical centers treating neurovascular diseases are certified as "Neurovascular Network Center" by the German TÜV (Technischer Überwachungsverein Deutschland), if they meet the criteria as published before and serve as a regional referral center for adjacent (smaller) hospitals, that do not forfold all facilities to treat these conditions.

Our hospital has been certified as the coordinating center for such a neurovascular network, including 12 hospitals and rehabilitation facilities that all contribute to the standardized treatment of neurovascular emergencies as well as the elective cases. Therefore, the caseload of these has been considerably high at our center, even before the pandemic.

It is the aim of the current analysis to evaluate the impact of the SARS-CoV2 pandemic and the lockdown on non-ischemic neurovascular emergencies in a third-level medical referral center in a non-university setting.

2. Methods

Our study is a retrospective, non-randomized, non-blinded and non-placebo-controlled data analysis of neurovascular cases at a tertiary medical center in Germany.

The hospital is situated in an area with about seven million citizens maintaining a rural region of about one million inhabitants. For this reason, even though the study reflects data of a single center, the results represent a cohort of the German citizen as the congested urban area reflects nearly 10% of the 83 million German citizens (Destatis 2019)

[12]. Furthermore, the hospital is a dedicated specialized clinic for neurovascular diseases, board certified by the German Stroke Association (GSA), the German Society of Neuroradiology (GSNR) and the German Society of Neurosurgery (GSN).

The present study retrospectively analyses the medical records of all patients, who were treated for a neurovascular disorder identified by diagnostic ICD-10 codes during the first pandemic period from March 16th, 2020 to January 31st, 2021 at our center. A longitudinal control cohort was defined from the same time period 2019–2020.

Non-ischemic neurovascular diseases (N.I.N.E) were subsumed as follows: non-traumatic subarachnoid hemorrhages without identifiable bleeding source (ntSAH), non-traumatic intracerebral hemorrhages without identifiable bleeding source (ntICH), symptomatic aneurysms of the cerebral arteries (symptomatic by subarachnoidal hemorrhage (SAH) or a new neurological deficit), symptomatic arterio-venous malformations (AVM, symptomatic by intracerebral hemorrhage (ICH) or SAH, seizures or a new neurological deficit), symptomatic arterio-venous fistula (AVF, symptomatic by subdural hemorrhage (SDH), SAH or ICH), chronic subdural bleeding (cSDH), and intraventricular hemorrhage (IVH).

All other non-emergency neurovascular cases - scheduled admitted or treated - were neither included in the study nor analyzed (e.g. asymptomatic aneurysms, cavernomas and AVMs, vascular cross-compression of trigeminal neuralgia).

Statistical analysis was performed employing Excel 16.50 (Microsoft® Excel for Mac), using descriptive analysis and Chi-square-test for standard normal distribution. Statistical differences in categorical variables between patients were calculated using χ^2 test and for continuous variables using t test. $P < 0.05$ was defined as level of statistical significance.

All data of the present study are available upon request from the corresponding author upon reasonable intention.

The study protocol was approved by the ethic committee of the medical association of Westfalen-Lippe (2021–687-f-S). The study was carried out under the guidelines of Good Clinical Practice according to the WMA principles of the declaration of Helsinki.

3. Results

The total number of severe emergencies (defined as polytraumatized patients) referred to our tertiary medical center decreased by 10% during the pandemic ($n = 252$ in 2019–20; $n = 226$ in 2020–21).

The same applied for the non-polytrauma cases that were screened for study purposes. Amongst, 1669 cases were identified as neurosurgical emergencies in both time frames and further analyzed for study purposes.

Between March 16, 2019 and January 31, 2020 (period 1), 764 neurosurgical emergencies were identified. Of these, 95 were diagnosed with N.I.N.E. according to the criteria given above. During the second period, from March 16th, 2020 to January 31st, 2021, a total of 905 neurosurgical patients were identified. Among them, 123 patients were diagnosed with N.I.N.E. requiring urgent professional attendance (Table 1 and Table 2).

The patients' cohorts were comparable regarding gender and age, with a slight female preponderance, within both time periods.

All patients admitted to the hospital were tested for SARS-CoV2-infection by PCR testing. No SARS-CoV2 infection was observed in the cohort. As all included patients were negative PCR-tested for SARS-CoV2, we highlight that the following results unrelated to the virus infection itself.

A total of 218 patients suffering from N.I.N.E. were treated in both time periods. The absolute number of cases increased by 29.5% during the lockdown to a total of 123. Still, the increase was statistically not significant within the standard distribution ($\chi^2 p = 0.53$) as overall case-load raised to 905 patients during the latter time period, a plus of 113 patients or 18.4%.

Table 1
Patients with neurovascular emergencies.

	period 1 (cohort-control group, March 16th, 2019 – January 31st, 2020)	period 2 (Corona pandemic, March 16th, 2020 – January 31st, 2021)
female patients	63	83
male patients	32	40
duration total	1370	1365
hospital stay (days)		
duration in	441	480
peripheral wards (days)		
patients primary admitted at our hospital (n)	31	40
patients transferred from other hospitals (n)	64	83

Table 2
Comorbidities.

	period 1 (cohort-control group, March 16th, 2019 – January 31st, 2020)	period 2 (Corona pandemic, March 16th, 2020 – January 31st, 2021)
cardiovascular diseases	20	31
arterial hypertension	29	33
pulmonary diseases	4	2
cancer history	2	9
combination of more than one system diseases	35	25

While ntSAH and ntICH decreased by 25% and 15.79%, respectively, during the lockdown, admissions due to symptomatic aneurysms, AVMs or SDH substantially rose in numbers. Yet, the increase in symptomatic aneurysms was statistically not significant ($\chi^2 p = 0.77$).

Likewise, the incidences of cSDH and IVH were statistically not significant higher during the lockdown period ($\chi^2 p = 0.91$).

The number of patients suffering from AVMs and AVFs, respectively, grew in number during the lockdown, too. Yet, due to the small overall number, we only provide descriptive results rather than statistical analysis. The diagnoses are described in Table 3.

We observed an increase of patients pretreated with anticoagulation medication (of various kinds) during the pandemic (Table 4). Still, this increase was within the normal distribution not reaching statistical significance.

The patients of the cohort in time period 2, during the lockdown, were of higher age, and also had a worse outcome with respect to the modified Ranking Scale (mRS). The number of fatal outcomes increased by 40%, though not reaching statistical significance ($p = 0.77$) (Fig. 1).

Nevertheless, the total increase of case-load was not caused by a raised incidence of severely afflicted patients, solely. Contrarily, we observed an increase of patients leaving the hospital in excellent

Table 3
Diagnosis.

	period 1 (cohort-control group, March 16th, 2019 – January 31st, 2020)	period 2 (Corona pandemic, March 16th, 2020 – January 31st, 2021)
symptomatik aneurysms (n)	39	47
AVMs (n)	3	5
ntSAH (n)	12	9
ntICH and hematocephalus (n)	30	40
cSDH (n)	10	19
AVF (n)	1	3

Table 4
Anticoagulation.

	period 1 (cohort-control group, March 16th, 2019 – January 31st, 2020)	period 2 (Corona pandemic, March 16th, 2020 – January 31st, 2021)
acetylsalicylic acid (ASA)	16	20
antiplatelet medication	2	1
direct oral anticoagulants (DOAC)	7	21
combination	3	2
none	67	79

condition (mRS0), too.

The individual duration of total hospital stay decreased by 3 days during the second period (14 days/patient, vs. 11 days/patient). The total days of hospitalization treatment did not differ significantly (1370 days vs. 1365 days).

4. Discussion

This is the first detailed long-term analysis on incidence and severity of non-ischemic neurovascular emergencies (N.I.N.E.) at a tertiary medical referral center during the pandemic and the following lockdown.

Ischemic strokes were not included for two reasons: firstly, a nationwide registry analysis revealed a decrease of strokes during the beginning phase of the pandemic [5,6]. Secondly the true number of ischemic strokes will not be sufficiently reflected by the admissions in the surgical emergency department of our tertiary medical center.

It was expected that number of these cases decreased similar to non-hemorrhagic stroke or heart attacks. This assumption was supported by the recent publication of Nguyen et al., who found a decrease of the event of subarachnoid hemorrhage in a global cohort over a three-months-period [8]. In contrast to their findings, we instead observed an increase in the incidence of N.I.N.E. in our cohort over a nine-months-period.

Numerous publications have consistently reported that the total number of admissions of patients to hospitals across the disciplines have markedly declined during the pandemic. Different hypotheses are discussed. First, the social distancing presumably led to reduced interaction of patients with family and friends, whereas early and mild symptoms might not be recognized. The view of these non-physicians is known to have an impact on the decision-making process to seek professional medical help, even though it may even delay treatment [9].

Second, patients avoided consulting their physician, because they were afraid of getting infected of SARS-CoV2. Concurrently, many physicians reduced direct contact to patients, often just in case of evident emergencies. Thus, emerging warning signs, red-flags indicating an uprising severe condition were most likely to be ignored. It has been reported that patients generally tend to see their practitioner before going to an emergency or outpatient department at a hospital [10]. Reduction of numbers of emergencies was therefore suspected.

The need for standardized requirements in the treatment of non-hemorrhagic stroke to warrant the best possible outcome for the patients has led to a nationwide certification process of stroke units [11]. In the follow, it became evident that the same requirements defined by personal and medical standards should be warranted for the treatment of neurovascular diseases at “neurovascular centers”. As the term “neurovascular center” was neither protected nor assigned to any pre-conditions the hospitals had to fulfill, it became evident that in analogy to the certification of stroke units a similar certification for the treatment of neurovascular cases was needed. In a joint venture of the German stroke society, the German association of neuroradiology and

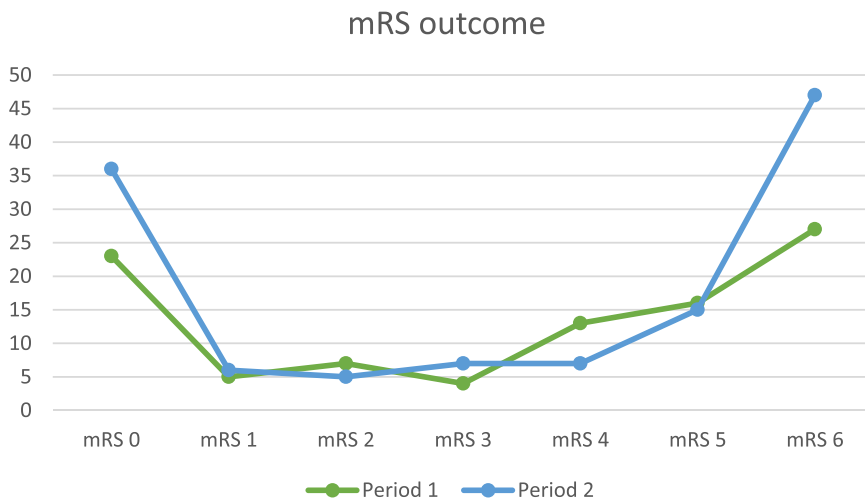


Fig. 1. Outcome at discharge of patients in both time periods using the modified Rankin Scale (mRS).

All patients were scored using the modified Rankin Scale (mRS). The scale runs from 0 to 6: 0 – no symptoms, 1 – no significant disability, able to carry out all usual activities, despite some symptoms, 2 – slight disability, able to look after own affairs without assistance, but unable to carry out all previous activities, 3 – moderate disability, requires some help, but able to walk unassisted, 4 – moderately severe disability, unable to attend to own bodily need without assistance, and unable to walk unassisted, 5 – severe disability, requires constant nursing care and attention, bedridden, incontinent, 6 – dead.

Patient during March 16th, 2019 – January 31th, 2020 were included for period 1 data (green line), period 2 was defined from March 16th, 2020 to January 31th, 2021 (blue line).

There was an increase of number of patients with fatal outcomes during the pandemic period (period 2) resulting in higher numbers of patients with mRS 6.

the German society of neurosurgery a consensus was filed, on whose base nowadays neurovascular networks with tertiary medical referral hospitals serving as coordinating centers are officially certified. This in turn has led to a successful certification process with 15 neurovascular networks being certified nationwide in Germany so far.

Interestingly, in our study non-ischemic neurovascular cases raised in number and severity during the pandemic-period in Germany. Furthermore, the case fatality increased. This may be explained by two circumstances during the lockdown. First, patients refused to seek medical help by their family physician while suffering only mild symptoms. Secondly, the referral times of patients in need of neurosurgical attention was much longer due to restricted admission at lower-level medical centers.

5. Conclusion

Even though, the incidence of N.I.N.E. did not raise statistically significant in our study database, the absolute numbers of occurring events rose at our third-level-center, requiring neurovascular competence even throughout unhandled exception situation like the first lockdown. However, the study showed that in both time-periods the intensive treatment of the patients with a neurovascular diagnosis maintains at the same high level. These results emphasize the importance for maximum care providers to generate sufficient and flexible capacities for non-COVID patients, as in the current study, for neurovascular diseases.

In addition, our data strengthens the need to maintain a dedicated neurovascular competence in designated centers to care for these N.I.N.E. during a pandemic situation like the current SARS-CoV2.

CRediT authorship contribution statement

K Lintas – data collection, analysis and evaluation, drafting the manuscript. S Rohde - Head Dept. Radiology/Interv. Radiology, providing data on interventionally treated NINE, revising the manuscript. G Ellrichmann – Head Dept. Neurology, providing data from the neurological emergency and outpatient department, revising the manuscript. T. Strohmann – Head Emergency Room/trauma center, providing data from the trauma registry, revising the manuscript. B El Hamalawi – senior consultant neurosurgeon, Section vascular neurosurgery, providing data on NINE surgically treated, revising the manuscript. R Sarge – senior consultant neurosurgeon, ICU neurosurgery, providing data on the intensive care of NINE patients, revising the manuscript. O Müller - Head Dept. Neurosurgery, drafting the study, ethic committee approval, data evaluation, final revision of the manuscript. The current study has been an interdisciplinary effort of the

management of patients suffering N.I.N.E.; even though the number of authors might appear rather high at a first glance, we would appreciate, if all concerned colleagues will be fully considered.

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None.

References

- [1] Epidemiologischer Steckbrief zu SARS-CoV-2 und COVID-19, Robert Koch Institut, (https://www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/Steckbrief.html), Accessed Januar 14, 2021.
- [2] C. Hoyer, A. Ebert, H.B. Huttner, V. Puetz, B. Kallmünzer, K. Barlinn, C. Haverkamp, A. Harloff, J. Brich, M. Platten, et al., Acute stroke in times of the COVID-19 pandemic: a multicenter study, *Stroke* 51 (2020) 2224–2227. (<https://www.ahajournals.org/doi/full/10.1161/STROKEAHA.120.030395>). Originally published 9 Jun 2020, Accessed May 23, 2021.
- [3] So hat sich die erste Corona-Welle auf die Herzinfarkte-Therapie in Europa ausgewirkt, *Kardiologie.org*, (<https://www.kardiologie.org/covid-19/aktuelles-koronarsyndrom/so-hat-sich-die-erste-corona-welle-auf-die-herzinfarkt-therapie-/18571748>). Originally published 10.11.2020. Accessed Januar 23, 2021.
- [4] G. Pessoa-Amorim, C.F. Camm, P. Gajendragadkar, et al., Admission of Patients with STEMI since the outbreak of the COVID-19 pandemic. A survey by the European Society of Cardiology, *Eur. Heart J. Qual. Care Clin.* 6 (3) (2020) 210–216. (<https://pubmed.ncbi.nlm.nih.gov/32467968/>). Accessed Februar 15, 2021.
- [5] Daniel Richter, Jens Eyding, Ralph Weber, Dirk Bartig, Armin Grau, Werner Hacke, Christos Krogias, Analysis of Nationwide Stroke Patient Care in Times of COVID-19 Pandemic in Germany, *Stroke*, (<https://www.ahajournals.org/doi/10.1161/STROKEAHA.120.033160>), 2021;52:716–721, Originally published 24 Dec 2020. Accessed May 19, 2021.
- [6] Zweite Corona-Welle: Ein Schlaganfall ist auch in Krisenzeiten ein medizinischer Notfall, *Deutsche Schlaganfall-Gesellschaft, German Stroke Society*, (<https://www.dsg-info.de/presse/pressemitteilungen/572-zweite-corona-welle-ein-schlaganfall-ist-auch-in-krisenzeiten-ein-medizinischer-notfall.html>), Accessed Februar 04, 2021.
- [7] Anna Slagman, Wilhelm Behringer, Felix Greiner, Matthias Klein, Dirk Weismann, Bernadett Erdmann, *Deutsches Ärzteblatt*, Jg 117, Heft 33 (2020) 17.
- [8] Thanh N. Nguyen # 1, Diogo C. Hauszen 2, Muhammad M. Qureshi 3, Hiroshi Yamagami 4, Toshiyuki Fujinaka 5 et al. Decline in subarachnoid haemorrhage volumes associated with the first wave of the COVID-19 pandemic, (<https://pubmed.ncbi.nlm.nih.gov/33771936/>), Accessed Juni 02, 2022.
- [9] American College of Emergency Physicians. American College of Emergency Physicians COVID-19. (<https://www.emergencyphysicians.org/globalassets/>)

- emphysicians/all-pdfs/acep-mc-Covid19-april-poll-analysis.pdf). Accessed August 19, 2020.
- [10] Gaertner Cornelia, Walz Linda, Bauernschmitt Eva, Ladwig Karl-Heinz, The causes of prehospital delay in myocardial infarction, *Dtsch. Arztebl Int.* 105 (15) (2008) 286–291.
- [11] O. Busse, J. Röther, J. Faiss, G.F. Hamann, T. Hupp, O. Jansen, J. Meixensberger, T. Neumann-Haefelin, G. Schackert, E.B. Ringelstein, Interdisziplinäres neurovaskuläres Netzwerk, *Nervenarzt* 84 (2013) 1228–1232.
- [12] (https://www.destatis.de/DE/Themen/GesellschaftUmwelt/Bevoelkerung/Bevoelkerungsstand/_inhalt.html#sprg352056). (Accessed 15 February 2021).