





LEADING TOPIC

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International study: Global impact of COVID-19 on stroke care — the Polish contribution

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To the Editors

The most severe consequences of the COVID-19 pandemic were reported during its first wave in 2019. Although airway inflammation is part of the main clinical picture of COVID-19, the consequences of a SARS-Cov2 infection can also include coagulation disorders, cardiomyopathy and endotheliopathy, which lead to stroke in 1.5% of patients. With the global reach of the pandemic came collaboration between scientists and clinicians from around the world. This transfer of knowledge between various medical centres contributed to greatly improved understanding of the mechanisms of transmission and the different manifestations of infection.

To assess the global impact of the pandemic on stroke hospitalisations and outcomes, Prof. Nogueira inspired the international community of neurologists and neurointerventionalists from six continents, 70 countries and almost 500 hospital stroke centres to participate in large, cross-sectional, observational, retrospective studies. Thirteen Polish centres participated in this important project. This article presents a summary of the results from five analyses, focusing on ischaemic stroke, reperfusion therapy, subarachnoid haemorrhage, and cerebral venous thrombosis, before and during the pandemic, and includes the contribution of Polish centres.

To date, over 500 million cases of COVID-19 have been confirmed worldwide. Although respiratory infection is the main clinical feature of COVID-19, the consequences of

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a SARS-CoV-2 infection can also include coagulation disorders, cardiomyopathy and endotheliopathy, which are associated with stroke in up to 1.5% of patients. The sudden outbreak of the pandemic immediately favoured collaboration between Polish clinicians who have published several articles in this matter [1–7]. The transfer of knowledge between medical centres across the world was also important. This contributed to improved recognition and understanding of the mechanisms of transmission and the course of COVID-19 in patients with stroke and other neurological diseases.

As an example of international collaboration between stroke centres, Prof. Raul G. Nogueira, Director of the University of Pittsburgh Medical Centre (UPMC)'s Stroke Institute, initiated several studies on the course of cerebrovascular disease and the organisation of care provided to patients during the COVID-19 pandemic in relation to analogous parameters before the pandemic [8–12]. UPMC is an important stroke centre for patient care, teaching, clinical and basic research in several areas of neurology, including stroke, and Prof. Nogueira has played a global leadership role in many landmark stroke thrombectomy trials.

To assess the global impact of the pandemic on stroke hospitalisations and outcomes, Prof. Nogueira inspired the international community of neurologists and neurointerventionalists from six continents, 70 countries and almost 500 hospital stroke centres to participate in large cross-sectional, observational, retrospective studies [8–15]. As highlighted in an editorial by Prof. Bart M. Demaerschalk entitled: 'Where in the World Have All the Strokes Gone?' [16], Nogueira and his collaborators comprehensively described the global changes that took place in stroke care management at the height of the COVID-19 pandemic, and provided potential systemic explanations for these changes associated with COVID-19 or societal behaviour.

We had the opportunity to listen to a lecture by Prof. Nogueira during a conference organised by the Cerebrovascular Diseases Section of the Polish Neurological Society in 2021. An invitation to collaborate in the global COVID-19 stroke studies was received by Prof. Anna Członkowska, who was then Chair of the Cerebrovascular Diseases Section. This invitation was extended to the heads of neurology/stroke departments involved in the SITS and RESQ registers, and led to the participation of 13 Polish (not only academic) stroke centres (**listed below) in the global COVID-19 stroke studies.

Here, we present a summary of the results from five analyses, focusing on ischaemic stroke, reperfusion therapy, subarachnoid haemorrhage (SAH), and cerebral venous thrombosis (CVT) before and during the pandemic. The contribution of Polish centres is described — the names of the Polish clinicians involved can be found in the original papers.

The first paper entitled: 'Global impact of COVID-19 on stroke care and IV thrombolysis' compared the impact of the COVID-19 pandemic on intravenous thrombolysis (IVT), IVT transfers and stroke hospitalisations over four months during the height of the outbreak (from 1 March to 30 June 2020) with

two four-month pre-pandemic periods [8]. In total, 325 stroke centres from 70 countries, including 11 from Poland, participated in this study. Data was collected from 91,373 stroke patients hospitalised before and 80,894 stroke patients hospitalised during the pandemic. Data from 1,815 stroke patients hospitalised before and 1,749 hospitalised during the pandemic were submitted by Polish investigators.

Overall, stroke admissions declined by 11.5% [95% confidence interval (CI) –11.7 to –11.3, $p < 0.0001$] during the pandemic months compared to immediately before. Furthermore, in the four months preceding the pandemic, there were 13,334 IVT procedures compared to 11,570 therapies during the pandemic, which represents a 13.2% (95% CI –13.8 to –12.7, $p < 0.0001$) decline. In addition, the number of inter-facility IVT transfers decreased from 1,337 to 1,178, which represents an 11.9% decrease (95% CI –13.7 to –10.3, $p = 0.001$). The decline in patient volumes was greater in primary stroke centres and centres with higher COVID-19 volumes. Some recovery in stroke hospitalisation volumes was noted (9.5%, 95% CI 9.2 to 9.8, $p < 0.0001$) over the two later pandemic months (May, June) compared to the earlier two months (March, April). Overall, 1.48% of COVID-19 patients suffered from a stroke diagnosis and 3.3% of all stroke admissions were associated with SARS-CoV-2 infection.

After the first wave of the pandemic, a later study entitled: 'Global impact of the COVID-19 pandemic on stroke volumes and cerebrovascular events: One-year follow-up' compared the period from 1 March 2020 to 28 February 2021 to the year before (i.e. 1 March 2019 to 29 February 2020) [9]. Volume data was obtained for COVID-19 admissions and for four stroke metrics: ischaemic stroke and intracranial haemorrhage (ICH) admissions, IVT and mechanical thrombectomy procedures from 275 stroke centres in 56 countries. Nine Polish centres provided data for ischaemic stroke admissions (4,511 patients in the year before the pandemic, and 4,638 patients in the one-year pandemic period), ICH admissions (601 and 666 patients, respectively), IVT (1,142 and 1,066 patients, respectively) and mechanical thrombectomy procedures (527 and 601 patients, respectively).

Overall, there were 148,895 stroke admissions in the one-year period immediately before the pandemic and 138,453 admissions during the one-year pandemic period, which represents a 7% decline (95% CI 7.1 to 6.9; $p < 0.0001$). ICH volumes decreased by 4.8% (5.1 to 4.6; $p < 0.0001$) and IVT volumes by 6.1% (6.4 to 5.8; $p < 0.0001$). There were no significant changes in mechanical thrombectomy volumes (0.7%; 0.6 to 0.9; $p = 0.49$). These results suggest that during the first year of the pandemic, stroke care was maintained for more severe diseases.

Other interesting international findings on outcomes were described in the publication: 'Safety and outcome of revascularisation treatment in patients with acute ischaemic stroke and COVID-19: The Global COVID-19 Stroke Registry' [10] that was initiated by Dr. Patrik Michel and Dr. Joao Pedro Marto of the Lausanne University Hospital in collaboration with Professors Raoul Nogueira and Thanh Nguyen. This study examined

the association of acutely revascularised COVID-19 with ICH complications and clinical outcomes between March 2020 and June 2021. Of 15,128 included patients with acute ischaemic stroke from 105 centres, including nine Polish centres, 853 (5.6%) were diagnosed with COVID-19. In total, 38.7% of patients received IVT only and 61.3% had thrombectomy. Revascularised patients with COVID-19 had higher rates of symptomatic ICH (SICH); [adjusted odds ratio (OR) 1.53; 95% CI 1.16–2.01], symptomatic SAH (SSAH; OR 1.80; 95% CI 1.20–2.69), SICH and/or SSAH combined (OR 1.56; 95% CI 1.23–1.99), 24-hour (OR 2.47; 95% CI 1.58 to 3.86) and 3-month mortality (OR 1.88; 95% CI 1.52 to 2.33). COVID-19 patients also had an unfavourable shift in the distribution of the modified Rankin score at three months (OR 1.42; 95% CI 1.26–1.60).

The manuscript 'Global impact of the COVID-19 pandemic on subarachnoid haemorrhage (SAH) hospitalisations, aneurysm treatment and in-hospital mortality: 1-year follow-up' assessed differences in the incidence and severity of aneurysmal SAH (aSAH) presentation and ruptured aneurysm treatment modalities in the first year of the pandemic compared to the preceding year [11]. The analysis included 16,247 aSAH admissions, 8,300 ruptured aneurysm coilings and 4,240 ruptured aneurysm clipping procedures. Polish authors from nine centres included data from patients hospitalised before and during the pandemic for aSAH (163 and 169, respectively); endovascular coiling (101 and 115, respectively), surgical clipping (46 and 40, respectively), and non-traumatic SAH (221 and 217, respectively).

Overall, there was a decline in aSAH admissions (–6.4%; 95% CI –7.0% to –5.8%; $p = 0.0001$) in the first year of the pandemic compared to the year before. There was a trend towards a decline in mild and moderate SAH at presentation by Hunt Hess Grade, but there were no difference concerning higher SAH severity of presentation on admission. The rates of ruptured aneurysm clipping remained the same (30.7% vs. 31.2%; $p = 0.58$), whereas there was an increase in ruptured aneurysm coiling (53.97% vs. 56.5%; $p = 0.009$). No differences in in-hospital aSAH mortality rates were recorded (19.1% vs. 20.1%; $p = 0.12$) pre- and during the pandemic.

Finally, CVT and mortality were studied in the publication: 'Global impact of the COVID-19 pandemic on volume of cerebral venous thrombosis and mortality' [12]. Across the study period from January 2019 to May 2021, there were 3,210 CVT hospitalisations in 171 centres. Nine Polish centres contributed data on 82 patients.

No differences in CVT volumes or CVT mortality rates were noted between 2019 and 2020. During the pandemic, COVID-19 diagnoses were present in 7.6% of all CVT hospitalisations, while CVT was present in 0.04% of COVID-19 hospitalisations. In the first pandemic year of 2020, CVT mortality was higher in patients who were COVID-positive than in those who were COVID-negative [8/53 (15.0%) vs. 41/910 (4.5%); $p = 0.004$]. In the first five months of 2021, there

was a rise in CVT volumes in relation to 2019 (27.5%; 95% CI 24.2–32.0; $p < 0.0001$) and 2020 (41.4%; 95% CI, 37.0–46.0; $p < 0.0001$). There was also a rise in CVT mortality in the first five months of 2020 and 2021 in relation to the first five months of 2019 (2019 vs. 2020: 2.26% vs. 4.74%, $p = 0.05$; 2019 vs. 2021: 2.26% vs. 4.99%, $p = 0.03$). The increase in mortality during the first five months of 2021 may be partially attributable to 26 cases of vaccine-induced immune thrombotic thrombocytopenia, which resulted in six deaths [17].

The joint effort of this global coalition of stroke researchers and clinicians during very difficult times has contributed to advances in the knowledge and expertise related to the diagnosis and therapy applied to patients with cerebrovascular disease during the COVID-19 pandemic.

Acknowledgments: *On behalf of all Polish neurologists who participated, we would like to thank Prof. Nogueira and his team for the opportunity to collaborate on such an important project. We would also like to thank all our Polish colleagues who participated and we encourage active cooperation in further international scientific projects. More detailed subanalyses comparing Poland to other countries or regions are possible. If any researchers would like to submit a proposal to the coordinating centre — the data and statistical assistance will be provided.*

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****The list of Polish centres participating in the project:**

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4. Neurological Ward with Stroke Unit, District Hospital in Skarżysko-Kamienna
5. Department of Neurology, T. Marciniak's Hospital in Wrocław
6. Department of Radiology, Wrocław Medical University, Wrocław
7. Department of Neurology and Cerebrovascular Disorders Poznań
8. University of Medical Sciences; 107th Military Hospital with Polyclinic, Walcz
9. Department of Neurology, St. Queen Jadwiga, Clinical Regional Hospital No. 2, Rzeszów
10. Department of Neurology, Medical University of Lublin
11. Department of Neurology and Stroke Unit, Holy Spirit Specialist Hospital in Sandomierz, Collegium Medicum Jan Kochanowski University in Kielce
12. Neurology and Stroke Department, M. Kopernik's Hospital, Gdansk
13. Stroke Unit, Neurological Department, Stanislaw Staszic University of Applied Sciences, Pila

14. Department of Neurology, Institute of Medical Sciences, University of Opole, Opole
15. Department of Neurology, Central Clinical Hospital of the Ministry of Internal Affairs and Administration, Warsaw
16. Clinic of Neurology, Military Institute of Medicine, Warsaw
17. Department of Neurology, University Hospital, Jagiellonian University, Cracow
18. Department of Neurology and Stroke, St. John Paul II Western Hospital, Grodzisk Mazowiecki
19. Stroke Intervention Centre, Department of Neurosurgery and Neurology, Jan Biziel University Hospital, Bydgoszcz
20. Department of Neurosurgery and Neurology, Nicolaus Copernicus University in Torun, Ludwik Rydygier Collegium Medicum, Bydgoszcz
21. Department of Neurology, University of Warmia and Mazury, Olsztyn
22. Department of Radiology, Provincial Specialist Hospital, Olsztyn
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