Impact of the Coronavirus Disease Pandemic on the Number of Strokes and Mechanical Thrombectomies: A Systematic Review and Meta-Analysis

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Background: This systematic review and meta-analysis aimed to evaluate the impact of the coronavirus disease (COVID-19) pandemic on stroke care, including the number of stroke alerts/codes, number of reperfusions, and number of thrombectomies during the pandemic compared to those during the pre-pandemic period. *Methods:* A systematic literature search was performed using the PubMed, EuropePMC, and Cochrane Central databases. The data of interest were the number of strokes, reperfusions, and mechanical thrombectomies during the COVID-19 pandemic versus that during the pre-pandemic period (in a historical comparator group over a specified period of same period length). *Results:* The study included 59,233 subjects from 9 studies. Meta-analysis showed that the number of stroke alerts during the pandemic was 64% (56−71%) of that during the pre-pandemic period. The number of reperfusion therapies during the pandemic was 69% (61−77%) of that during the pre-pandemic period. Pooled analysis showed that the number of mechanical thrombectomies performed during the pandemic was 78% (75−80%) of that during the pre-pandemic period. The number of mechanical thrombectomies per stroke patient was higher during the pandemic (OR 1.23 [1.12−1.36], $p < 0.001$; I^2: 0%, $p = 0.845$). *Conclusion:* This meta-analysis showed that the number of stroke alerts, reperfusions, and mechanical thrombectomies was reduced by 36%, 31%, and 22%, respectively, during the pandemic. However, the number of patients receiving mechanical thrombectomy per stroke increased.

Keywords: Cerebrovascular Diseases—COVID-19—SARS-CoV-2—Stroke—Mechanical Thrombectomy

Introduction

As of 13th July 2020, there have been 12,768,307 cases of coronavirus disease (COVID-19), which has resulted in 566,654 deaths.[1] Although most COVID-19 patients are asymptomatic, a significant proportion develops severe manifestations that may lead to death. Patients with advanced age and preexisting comorbidities are more likely to develop severe disease.[2−8] The incidence of acute conditions such as myocardial infarction was shown to be "reduced" during the pandemic.[9] Because of the looming possibility of in-hospital COVID-19 transmission, people are more reluctant to visit the hospital. This was reflected in a study on patients with myocardial infarction, which showed that 27% of patients avoided hospitals because of the fear of COVID-19 transmission.[10] Similarly, a study showed that the COVID-19 pandemic disrupted prehospital and in-hospital care, resulting in a significant drop in admissions, thrombolysis, and thrombectomy.[11] However, other factors such as decreased pollution during pandemic may decrease myocardial infarction or stroke.[12,13]

Delays in the prehospital and in-hospital chain may lead to a prolonged time to presentation, beyond the golden hour for reperfusion, which may reduce the number of reperfusion and thrombectomy. Less result may result in increased morbidity and mortality. This systematic review and meta-analysis aimed to evaluate the impact of this pandemic on stroke care, including the

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number of stroke alerts/codes, number of reperfusions, and number of thrombectomies during the COVID-19 pandemic compared to the pre-pandemic period.

Material and Methods

Search Strategy

A systematic literature search was performed using the keywords "stroke," "cerebrovascular diseases," "cerebral infarction," "brain ischemia," "stroke alert," or "thrombectomy" and "COVID-19" or "Coronavirus Disease 2019" or "2019 n-CoV," or "SARS-CoV-2" or "pandemic" on PubMed, EuropePMC, and Cochrane Central Database. Hand-sampling from potential articles cited by other studies was also used to identify published studies from 1 January 2020 to 8 June 2020. This initial search was performed by two independent researchers, and the resulting discrepancies were solved by discussion. Inclusion and exclusion criteria were then applied to the retrieved records.

Inclusion and Exclusion Criteria

The inclusion criteria for this systematic review and meta-analysis were original articles, research letters, short reports, and case series containing primary data. The data of interest were the number of strokes, reperfusions, and mechanical thrombectomies during the COVID-19 pandemic versus the comparator period. The comparator group was a historical control over a specified period of time (same period length) before the pandemic. The exclusion criteria were preprints, case reports, review articles, and articles in a non-English language.

Data Extraction

Data extraction and quality assessment were performed by two independent researchers using extraction forms for the first author, year of publication, sample size, study design, number of stroke alerts/codes, number of reperfusions, and number of mechanical thrombectomies. Quality assessment was performed using Oxford CEBM Critical Appraisal tool.

The number of reperfusions was defined as the number of patients with acute ischemic stroke receiving thrombolysis and mechanical thrombectomy alone or with intra-arterial thrombolysis. Mechanical thrombectomy was defined as revascularization for acute ischemic stroke with either mechanical thrombectomy alone or with the addition of intra-arterial thrombolysis.

Statistical analysis

Meta-analysis of proportion was used to determine the number of stroke alerts/codes, reperfusions, and mechanical thrombectomies during the pandemic compared to that during the historical pre-pandemic control period. STATA 16.0 (StataCorp 2019 LLC) was used to perform the meta-analysis with a random-effects model, regardless of heterogeneity. Heterogeneity was calculated using I^2 statistics and Cochran's Q test, in which $I^2 > 50\%$ or $p < 0.10$ indicated significant heterogeneity. Assessment for publication bias and meta-regression analysis was not performed because of the limited number of studies (<10 studies).

Results

Study Selection and Characteristics

There were a total of 1,760 records, of which 1,305 remained after removal of duplicates. A total of 1,290 records were excluded after screening the titles and abstracts, leaving 15 eligible studies. After the full texts were screened for eligibility, we excluded 6 more articles for the following reasons: 1) no data on outcome of interest (n = 4), 2) preprint (n = 1), or 3) report was per 100,000 inhabitants (n = 1). We included 9 studies for our qualitative and quantitative analyses [Fig. 1]. There were a total of 59,233 subjects from 9 studies.[11,14–21] Characteristics of the included studies are presented in Table 1.

Stroke Alerts/Codes

The meta-analysis showed that the number of stroke alerts during the pandemic was 64% (56−71%) of that during the pre-pandemic period [Fig. 2].

Reperfusion Therapy

The number of reperfusion therapies undertaken during the pandemic was 69% (61-77%) of that during the pre-pandemic period [Fig. 3].

Mechanical Thrombectomy

Pooled analysis showed that the number of mechanical thrombectomies performed during the pandemic was 78% (75−80%) of that during the pre-pandemic period [Fig. 4]. However, the number of mechanical thrombectomies per stroke patient was higher during the pandemic (OR 1.23 [1.12−1.36], $p < 0.001$; I^2: 0%, $p = 0.845$).

Discussion

A meta-analysis of 9 studies showed that the number of stroke alerts/codes, reperfusions, and mechanical thrombectomies was less during the pandemic period than during the pre-pandemic period. However, the number of patients receiving mechanical thrombectomy per stroke increased.

The number of strokes was lower during the pandemic; this might be explained by hospital avoidance due to fear of contracting the COVID-19 virus. Nevertheless, further research is needed to better understand the reasons for not seeking care. It should be noted that COVID-19 is associated with coagulopathy[22,23] and may increase the risk of stroke.[2] Although the number of COVID-19-related

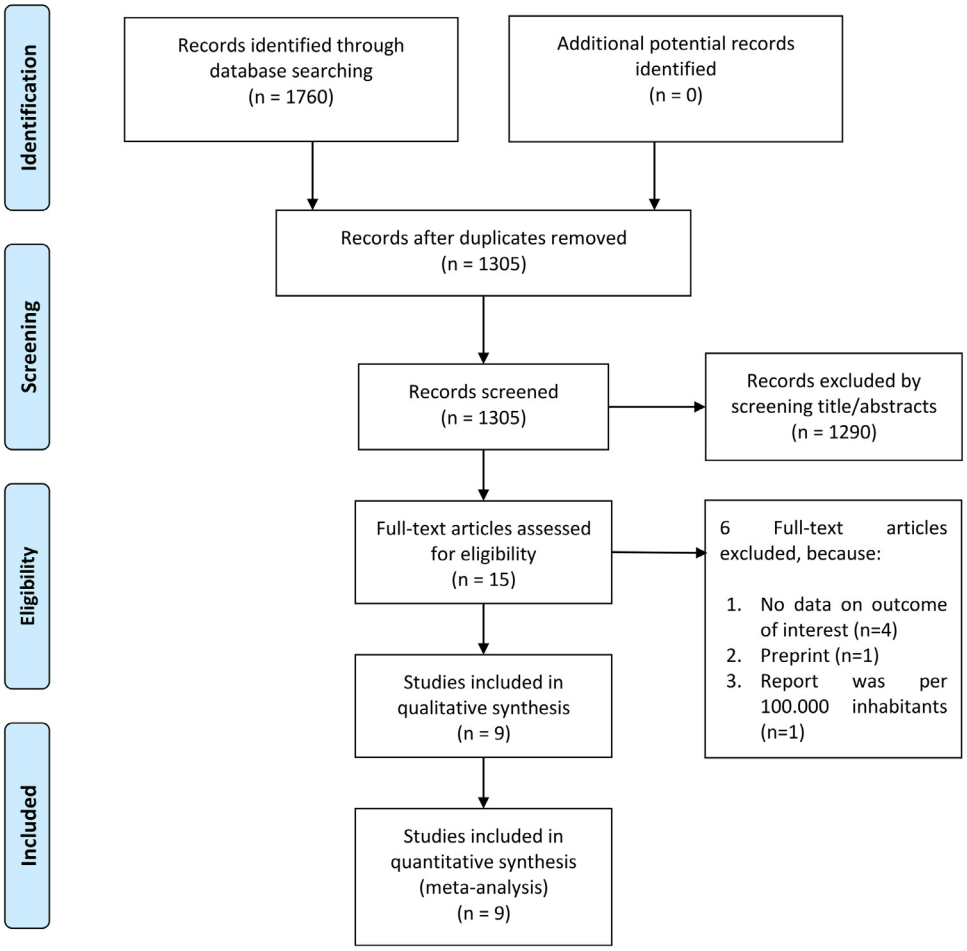

Fig. 1. *Study flow diagram.*

stroke cases is unclear—along with the non-compliance/non-adherence to chronic medications (due to accessibility or drug rumours unproven to be true)[24] and sedentary lifestyle[25]—the incidence of stroke might actually be higher than is usual. Reduction in the number of strokes in this pooled analysis reflects the unmet need for medical attention. However, reduced pollution due to lockdown and other restriction, shift in dietary patterns such as decreased consumption of high-sodium, fast-food intake, may lead to a decreased acute cardio-cerebrovascular events related to pollution.[12,13] Disruption in pre-hospital and in-hospital care may lead to delayed onset-to-door time. Teo et al. showed that only 54.8% of the patients were attended to within 4.5 h during the pandemic compared to 71.9% during the pre-pandemic period.[19]

Delayed presentation may lead to a reduced number of salvageable areas and also reduce the number of patients eligible for thrombolysis.[14,26] Our meta-analysis showed that the number of reperfusion episodes during the pandemic was only two-third of that during the pre-pandemic period. Our result strengthens the conclusion of prior observation that showed marked fall in stroke presentations and services due to COVID-19 in April 2020.[27,28] Mechanical thrombectomy—which carries the risk of transmission to health care workers—has become the procedure of choice in the late presenters.[29] The absolute number of mechanical thrombectomies performed was reduced; however, the number of patients receiving thrombectomy per patient with a stroke actually increased. This is possibly because of an increase in late presenters. Another possibility could be due to differences in proportions of patients with large vessel occlusion that are eligible for thrombectomy, or a greater tendency of more severe strokes, also those who would be candidates for thrombectomy, to present to emergency department during the pandemic compared to those with less severe stroke.[30] Regardless of severity of stroke, people experiencing symptoms of cardio-cerebrovascular diseases should be encouraged to seek emergency medical care.

The limitation of this systematic review and meta-analysis is that the limited data on clinical outcomes prohibit us from calculating the impact of the pandemic in terms of morbidity and mortality. The out-of-hospital deaths in

Table 1. *Characteristics of the included studies*

First Author	Study Design	Location	Sample Size (2020 vs Control)	Pandemic Period	Control Period	Age (years)	Male (%)	Mortality (%)
Pop R 2020	Multicenter; Retrospective Observational	Alsace, France	174 vs 288	1st March 2020 to 31st March 2020	1st March 2019 to 31st March 2019	N/A*	N/A*	N/A*
Schirmer 2020	Multicenter; Prospective and Retrospective Observational	United States	163 vs 320	February 2020 to March 2020	February 2019 to March 2019	N/A*	N/A*	N/A*
Hecht 2020	Single Center; Retrospective Observational	Berlin, Germany	18 vs 39	1st February 2020 to 15th April 2020	1st February 2019 to 15th April 2019	N/A*	N/A*	N/A*
Yang B 2020	Single Center; Retrospective Observational	Beijing, China	21 vs 34	23rd January 2020 to 7th March 2020	1st December 2019 to 14th January 2020	62.3±12.8 vs 65.2±13.1	71.4 vs 64.7	N/A*
Naccarato 2020	Single Center; Retrospective Observational	Trieste, Italy	16 vs 29	9th March 2020 to 9th April 2020	9th March 2019 to 9th April 2019	77 (67−81) vs 78 (70−85)	37.5 vs 41.4	12 vs 10
Teo 2020	Single Center; Retrospective Observational	Hong Kong, China	73 vs 89	23rd January 2020 to 24th March 2020	23rd January 2019 to 24th March 2019	70.1±16.2 vs 73.6±13.1	43.8 vs 50.6	N/A*
Zhao 2020	Multicenter; Retrospective Observational	China (National)	21581 vs 34725	February 2020	February 2019	N/A*	N/A*	N/A*
Rudilosso 2020	Multicenter; Retrospective Observational	Catalonia, Spain	68 vs 83	March 2020	March 2019	69 (64−73) vs 75 (73−80)	56 vs 55	11.8 vs 9.2
Kerleroux 2020	Multicenter; Prospective and Retrospective Observational	France (National)	668 vs 844	15th February 2020 to 30th March 2020	15th February 2019 to 30th March 2019	N/A*	N/A*	N/A*

Data in the table are presented by grouping during the pandemic period vs. the pre-pandemic period.
*Data was not presented by grouping of the pandemic period vs. the pre-pandemic period.

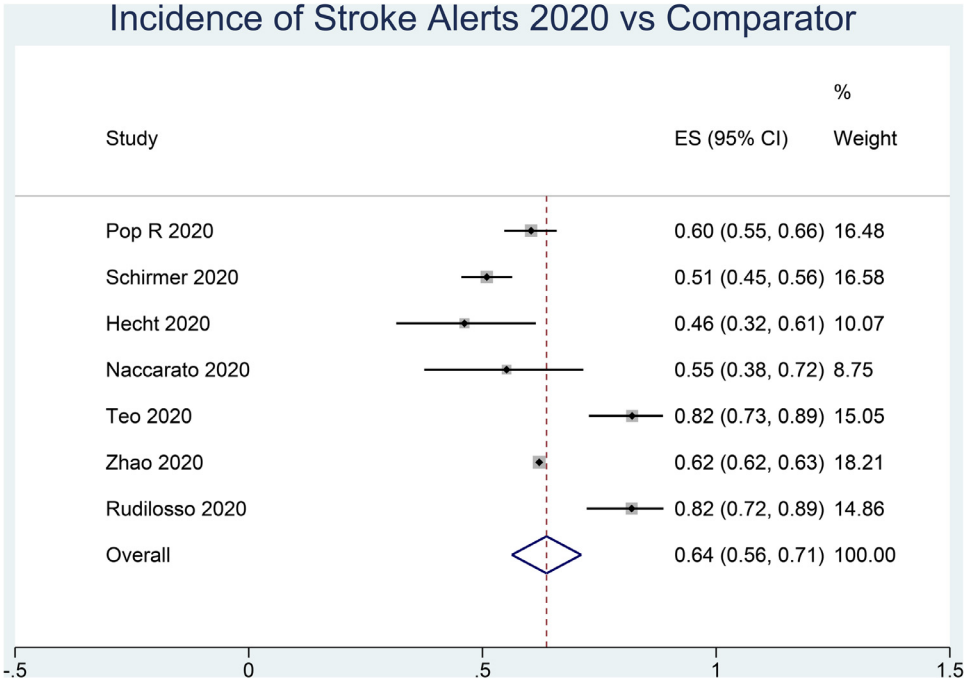

Fig. 2. *Forest plot showing the number of stroke alerts/codes during the pandemic compared with the pre-pandemic period.*

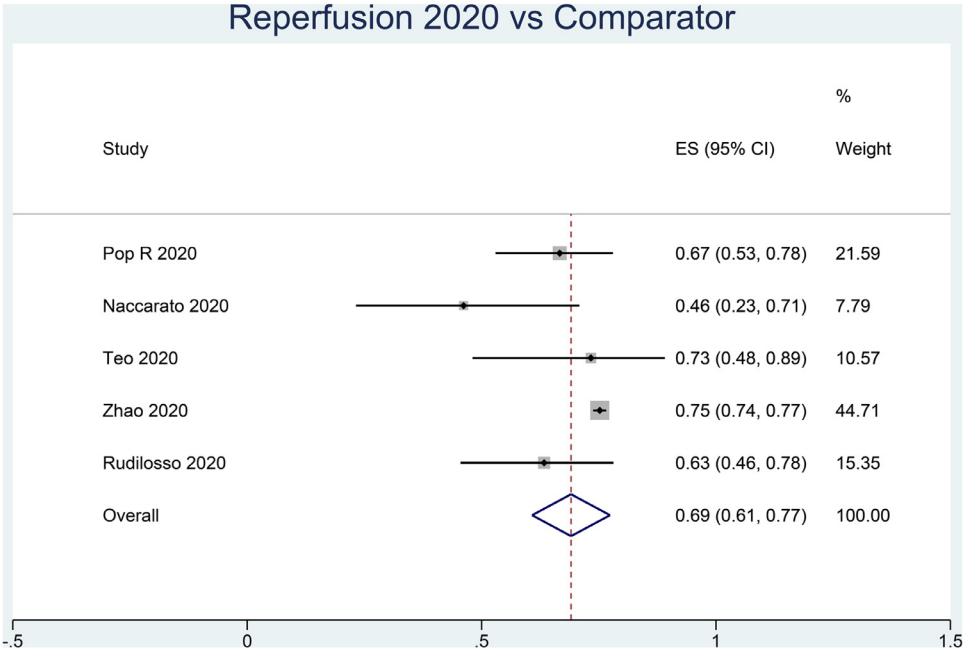

Fig. 3. *Forest plot showing the number of reperfusion therapies during the pandemic compared with the pre-pandemic period.*

specific regions, which may provide insight on patients with unmet medical needs, cannot be addressed in this meta-analysis. There might be an increasing trend of mechanical thrombectomy due to advances in technology and an increase/decrease in the real stroke incidence. There is no data on other possible factors such as pollution and dietary patterns that may affect the incidence of stroke. The data on proportion of patients with large vessel occlusion eligible for thrombectomy during pandemic compared to pre-pandemic is not thoroughly available.

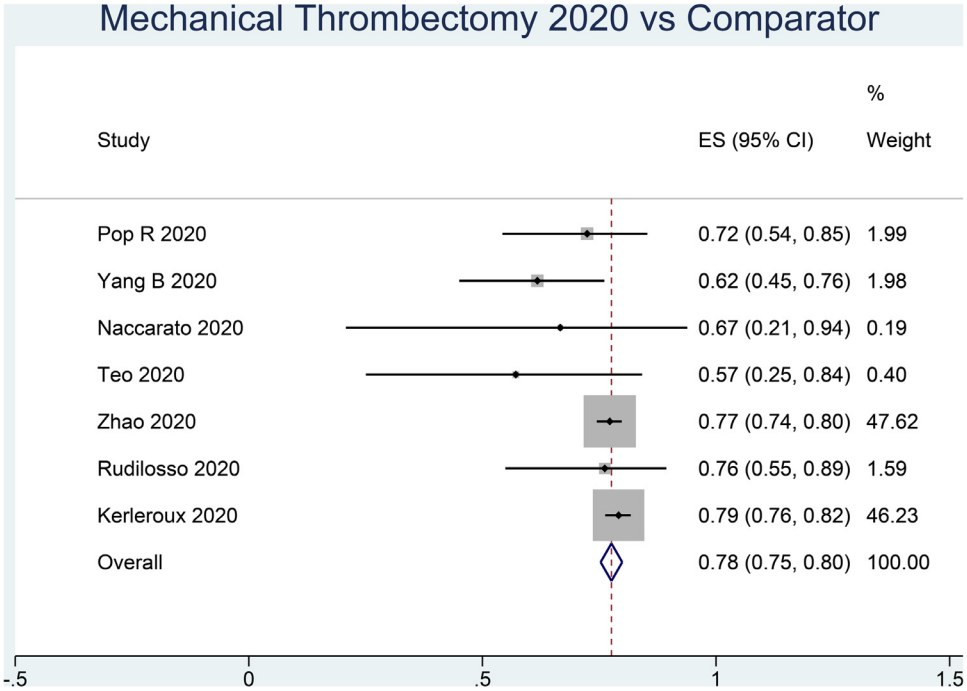

Fig. 4. *Forest plot showing the number of mechanical thrombectomies during the pandemic compared with the pre-pandemic period*

Conclusion

This meta-analysis showed that the number of stroke alerts/codes, reperfusions, and mechanical thrombectomies was reduced by 36%, 31%, and 22%, respectively, during the pandemic. However, the number of patients receiving mechanical thrombectomy per stroke increased.

Ethics approval and consent to participate

Not Applicable

Consent for publication

Not Applicable

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Conflict of interest

The authors declare that they have no competing interests.

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Author's Contribution

J.J. and R.P. conceived and designed the study and drafted the manuscript. J.J. and R.P. acquired the data and drafted the manuscript. J.J. and R.P. performed data extraction, interpreted the data, and performed extensive research on the topic. J.J and R.P. performed the statistical analysis. All authors contributed to the writing of the manuscript.

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None

References

1. World Health Organization. In: Coronavirus disease (COVID-19) situation report - 164; 2020. Geneva https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200713-covid-19-sitrep-175.pdf.
2. Pranata R, Huang I, Lim MA, Wahjoepramono EJ, July J. Impact of cerebrovascular and cardiovascular diseases on mortality and severity of COVID-19 – systematic review, meta-analysis, and meta-regression. J Stroke Cerebrovasc Dis 2020:104949. https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.104949.
3. Pranata R, Soeroto AY, Ian H, et al. Effect of chronic obstructive pulmonary disease and smoking on the outcome of COVID-19. Int J Tuberc Lung Dis 2020. https://doi.org/10.5588/ijtld.20.0278.
4. Pranata R, Lim MA, Huang I, Raharjo SB, Lukito AA. Hypertension is associated with increased mortality and severity of disease in COVID-19 pneumonia: A systematic review, meta-analysis and meta-regression. J Renin-Angiotensin-Aldosterone Syst 2020;21(2):147032032092689. https://doi.org/10.1177/1470320320926899.
5. Huang I, Lim MA, Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia – A systematic review, meta-analysis, and meta-regression. Diabetes Metab Syndr Clin Res Rev 2020;14(4):395-403. https://doi.org/10.1016/j.dsx.2020.04.018.

6. Huang I, Pranata R. Lymphopenia in severe coronavirus disease-2019 (COVID-19): systematic review and meta-analysis. J Intensiv Care 2020;8(1):36. https://doi.org/10.1186/s40560-020-00453-4.
7. Pranata R, Huang I, Lukito AA, Raharjo SB. Elevated N-terminal pro-brain natriuretic peptide is associated with increased mortality in patients with COVID-19: systematic review and meta-analysis. Postgrad Med J 2020. https://doi.org/10.1136/postgradmedj-2020-137884.
8. Pranata R, Lim MA, Yonas E, et al. Body Mass Index and Outcome in Patients with COVID-19: A Dose-Response Meta-Analysis. Diabetes Metab 2020. https://doi.org/10.1016/j.diabet.2020.07.005. S1262-3636(20)30097-5.
9. Solomon MD, McNulty EJ, Rana JS, et al. The Covid-19 Pandemic and the incidence of acute myocardial infarction. N Engl J Med 2020:NEJMc2015630. https://doi.org/10.1056/NEJMc2015630.
10. Hammad TA, Parikh M, Tashtish N, et al. Impact of COVID-19 pandemic on ST-elevation myocardial infarction in a non-COVID-19 epicenter. Catheter Cardiovasc Interv 2020:ccd.28997 https://doi.org/10.1002/ccd.28997.
11. Zhao J, Li H, Kung D, Fisher M, Shen Y, Liu R. Impact of the COVID-19 epidemic on stroke care and potential solutions. Stroke 2020. https://doi.org/10.1161/STROKEAHA.120.030225. STROKEAHA120030225.
12. Bhatt AS, Moscone A, McElrath EE, et al. Fewer hospitalizations for acute cardiovascular conditions during the COVID-19 pandemic. J Am Coll Cardiol 2020;76(3):280-288. https://doi.org/10.1016/j.jacc.2020.05.038.
13. Pranata R, Vania R, Tondas AE, Setianto B, Santoso A. A time−to−event analysis on air pollutants with the risk of cardiovascular disease and mortality: A systematic review and meta−analysis of 84 cohort studies. J Evid Based Med 2020;13(2):102-115. https://doi.org/10.1111/jebm.12380.
14. Kerleroux B, Fabacher T, Bricout N, et al. Mechanical thrombectomy for acute ischemic stroke amid the COVID-19 outbreak. Stroke 2020. https://doi.org/10.1161/STROKEAHA.120.030373. STROKEAHA120030373.
15. Naccarato M, Scali I, Olivo S, et al. Has COVID-19 played an unexpected "stroke" on the chain of survival. J Neurol Sci 2020;414(May):116889. https://doi.org/10.1016/j.jns.2020.116889.
16. 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;19:1-5. https://doi.org/10.1111/ene.14316.
17. 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. https://doi.org/10.1161/STROKEAHA.120.030329. STROKEAHA120030329.
18. Schirmer CM, Ringer AJ, Arthur AS, et al. Delayed presentation of acute ischemic strokes during the COVID-19 crisis. J Neurointerv Surg. 2020:639-642. https://doi.org/10.1136/neurintsurg-2020-016299.
19. Teo K-C, Leung WCY, Wong Y-K, et al. Delays in stroke onset to hospital arrival time during COVID-19. Stroke 2020(July). https://doi.org/10.1161/STROKEAHA.120.030105.
20. Yang B, Wang T, Chen J, et al. Impact of the COVID-19 pandemic on the process and outcome of thrombectomy for acute ischemic stroke. J Neurointerv Surg. 2020:664-668. doi:https://doi.org/10.1136/neurintsurg-2020-016177.
21. Hecht N, Wessels L, Werft F-O, Schneider UC, Czabanka M, Vajkoczy P. Need for ensuring care for neuro-emergencies-lessons learned from the COVID-19 pandemic. Acta Neurochir (Wien) 2020. https://doi.org/10.1007/s00701-020-04437-z.
22. Huang I, Pranata R, Lim MA, Oehadian A, Alisjahbana B. C-reactive protein, procalcitonin, D-dimer, and ferritin in severe coronavirus disease-2019: a meta-analysis. Ther Adv Respir Dis 2020;14:175346662093717. https://doi.org/10.1177/1753466620937175.
23. Lim MA, Pranata R, Huang I, Yonas E, Soeroto AY, Supriyadi R. Multiorgan failure with emphasis on acute kidney injury and severity of COVID-19: systematic review and meta-analysis. Can J Kidney Heal Dis 2020:7. https://doi.org/10.1177/2054358120938573.
24. Pranata R, Permana H, Huang I, et al. The use of renin angiotensin system inhibitor on mortality in patients with coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis. Diabetes Metab Syndr Clin Res Rev 2020. https://doi.org/10.1016/j.dsx.2020.06.047.
25. Lim MA, Huang I, Yonas E, Vania R, Pranata R. A wave of non-communicable diseases following the COVID-19 pandemic. Diabetes Metab Syndr Clin Res Rev 2020;14(5):979-980. https://doi.org/10.1016/j.dsx.2020.06.050.
26. Prabhakaran S, Ruff I, Bernstein RA. Acute stroke intervention. JAMA 2015;313(14):1451. https://doi.org/10.1001/jama.2015.3058.
27. Liu L, Wang D, Brainin M, Elkind MS V, Leira E, Wang Y. Approaches to global stroke care during the COVID-19 pandemic. Stroke Vasc Neurol 2020;5(2):107-109. https://doi.org/10.1136/svn-2020-000429.
28. Markus HS, Brainin M. COVID-19 and stroke—a global world stroke organization perspective. Int J Stroke 2020;15(4):361-364. https://doi.org/10.1177/1747493020923472.
29. Nguyen TN, Abdalkader M, Jovin TG, et al. Mechanical thrombectomy in the era of the COVID-19 pandemic: emergency preparedness for neuroscience teams. Stroke 2020;51(6):1896-1901. https://doi.org/10.1161/STROKEAHA.120.030100.
30. Perry R, Banaras A, Werring DJ, Simister R. What has caused the fall in stroke admissions during the COVID-19 pandemic. J Neurol 2020. https://doi.org/10.1007/s00415-020-10030-2. June.