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Commentary

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Oxygenation in Acute Ischemic Stroke & Mortality

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Abstract: *In the management of acute ischemic stroke (AIS), researchers have investigated how oxygenation affects patient survival. They've found that both low oxygen (hypoxia) and high oxygen (hyperoxia) levels are linked to worse outcomes. Interestingly, keeping oxygen saturation levels within the optimal range of 94-98% is associated with better outcomes. These findings emphasize the significance of prompt addressing of oxygenation levels in AIS treatment, stressing the importance of careful monitoring and personalized interventions to lower the risk of death. Developing guidelines based on this evidence could greatly improve patient outcomes and lessen the burden of stroke-related deaths.*

Keywords: *Acute ischemic stroke; Oxygen therapy; Hypoxia; Hyperoxia*

Introduction

Acute ischemic stroke (AIS) is a leading cause of morbidity and mortality globally. Timely management of AIS is crucial to improve patient outcomes, and optimizing oxygenation levels is a fundamental aspect of stroke care. The association between mortality of stroke patients and their oxygenation in the first few hours of admission was investigated by Akca O, et al. (2020) [1]. This retrospective study aimed to investigate the impact of varying oxygenation levels on mortality in both reperfused and non-reperfused AIS patients. Oxygenation levels were measured using pulse oximetry (SpO_2), with the intent to focus on oxygenation by creating a ratio between fraction of inspired oxygen (FiO_2) to oxygen saturation (SpO_2/FiO_2). The rationale for this shift in focus was based on the hypothesis that hyperoxia could also be detrimental to these patients. They argued that targeting a higher than physiological normal oxygen tension in the setting of an elevated FiO_2 may lead to tissue injury. Therefore, they aimed to clarify the potential mal effects of both hyper- and hypoxia. They found that in AIS patients, higher oxygenation levels (SpO_2/FiO_2 > 250) were associated with lower risk of mortality, with these patients experiencing a 5% mortality rate, during their hospital stay compared to their counterparts in the low oxygenation group (SpO_2/FiO_2 < 250), who experienced a mortality rate of 26%. They also demonstrated an inverse correlation between SpO_2/FiO_2 and mortality (R^2 = 0.973), with patients in the highest oxygenation group (SpO_2/FiO_2 > 400) experiencing the lowest mortality rate of 2.6%, compared to an overall mortality rate of 5.7%. A U-shaped relationship when they plotted mortality stratified by SpO_2. Interestingly, while there was an observed reduction in mortality with the avoidance of hypoxia (SpO_2 > 95%) there was also an increased odds of mortality when SpO_2 was > 99%. Although the increased risk of mortality with low and high levels of oxygenation was not unexpected, these differences were not statistically significant compared to the overall mortality of AIS patients.

This association between mortality and degree of oxygenation has been reaffirmed across multiple studies and different populations, including patients with covid pneumonia, in the emergency department, and in the ICU [2-5]. One such study examined the role of varying levels of oxygenation on mortality in 3464 critically ill patients. They found that hypoxic patients (SpO_2 < 92%) had statistically increased odds of in-hospital mortality across all FiO2 levels (21-100%) with OR ranging from 1.9 (1.5–2.6) to 17.8 (10.1–31.4). They also found that when patients were hyper-oxygenated (SpO_2 > 98%) by receiving high FiO_2 (> 50%), there was an associated increase in mortality risk ranging from 1.5 (1.1–2.2) to 7.7 (4.3–13.5). Caution should be taken in interpreting the results of these trials as the definition of normoxia was variable. Some of the referenced studies included patients with SpO_2 < 94% in the normoxic groups. While this management strategy may be appropriate for patients with non-neurological illness, current AHA/Stroke guidelines recommend SpO_2 > 94% in AIS patients [6]. While there is evidence that hyperoxia is potentially harmful to many patients, the optimal oxygenation range continues to be

unknown in AIS.

More recently, Farag E, et al. (2022), examined the effects of oxygenation in the first 48 hours post-thrombectomy on mortality in AIS patients. They found a similar U-shaped association between SpO_2 and mortality finding a statistically increased risk of mortality (OR 3.8 (2.1–6.9), p < .001) at the highest oxygenation (SpO_2 > 98%) [7]. The lower SpO_2 group (SpO_2 < 96%) showed a slightly increased risk for mortality (OR 1.8 (0.9–3.4) p=.08) compared to the comparison group (SpO_2=96-98%), but this was not a statistically significant difference. This finding of no increased risk of mortality in the lower oxygenation group differed from the results of the Akca O, et al. study, and this was likely due to the lower oxygenation group not including hypoxic range patients (i.e., SpO_2 < 92%) in Farag E, et al.'s work, and only being consisted of patients with a SpO_2 between 92-96%. Based on the findings of this study and the previously discussed findings, a target SpO_2 goal of 94-98% may be reasonable to avoid worsening mortality in AIS patients.

Discussion

The findings discussed underscore the critical role of early oxygenation management in AIS care. Hypoxemia at admission was identified as a significant predictor of mortality, emphasizing the need for prompt recognition and intervention to improve oxygenation status in stroke patients. Hypoxia induces multiple neurophysiological changes that can lead to cellular death if not quickly corrected [8]. In AIS, where disruption of blood flow also decreases glucose deliver, hypoxia further impairs the already diminished capacity for ATP production. The loss of ATP production quickly leads electrolyte dysregulation and eventual cell death. With regards to CBF, in normocapnic patient's hypoxia leads to a resultant vasodilation and increases CBF. In patients where ICP concerns are present this change could lead to worsening mass effect; accordingly, hypoxia should be corrected. Optimizing oxygenation levels, through supplemental O_2 therapy or other interventions, may mitigate mortality risk and enhance patient outcomes. However, overuse of high levels of FiO_2 may lead to worse outcomes due to the deleterious effects of hyperoxia, which has been shown to increase free radical levels that inactivate nitric oxide thereby resulting in vasoconstriction and a resultant decrease in CBF [9]. In patients who are normoxic, prophylactic use of supplemental O_2 has not been shown to improve outcomes, and therefore, it is not recommended [10].

Conclusion

Early oxygenation levels in the acute period after neurological injury are associated with mortality in AIS patients. Hypoxia and hyperoxia within the initial hours following AIS onset are linked to adverse outcomes. This association between oxygenation and mortality was observed in AIS regardless of the reperfusion status. Clinicians should prioritize the assessment and optimization of oxygenation status in stroke patients to improve survival and reduce morbidity. Future studies should explore the efficacy of targeted oxygenation interventions and establish evidence-based guidelines for oxygenation management in AIS. Addressing this critical aspect of stroke care can potentially enhance patient outcomes and reduce the burden of stroke-related mortality.

Author Contributions Statement

All authors listed are responsible for their contributions in drafting and editing this manuscript. The authors have approved the final version of the manuscript before submission.

Conflict of Statement

The authors declare that they have no competing interests that could influence the work reported in this paper.

References

1. Akca O, Nichols J, Stewart B, Elliott C, Remmel K, Lenhardt R. Association of Early Oxygenation Levels with Mortality in Acute Ischemic Stroke - A Retrospective Cohort Study. J Stroke Cerebrovasc Dis. 2020 Feb;29(2):104556. https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.104556

2. Douin DJ, Anderson EL, Dylla L, Rice JD, Jackson CL, Wright FL, et al. Association Between Hyperoxia, Supplemental Oxygen, and Mortality in Critically Injured Patients. Crit Care Explor. 2021 May;3(5):e0418. https://doi.org/10.1097/cce.0000000000000418

3. Martin-Rodriguez F, Lopez-Izquierdo R, Del Pozo Vegas C, Delgado-Benito JF, Ortega GJ, Villamor MAC, et al. Association of Prehospital Oxygen Saturation to Inspired Oxygen Ratio With 1-, 2-, and 7-Day Mortality. JAMA Netw Open. 2021 Apr 1;4(4):e215700. https://doi.org/10.1001/jamanetworkopen.2021.5700

4. Satici MO, Satici C, Aksel G. The Role of a Noninvasive Index 'Spo2/ Fio2' in Predicting Mortality among Patients with COVID-19 Pneumonia. Am J Emerg Med. Jan 2023;63:171. https://doi.org/10.1016/j.ajem.2022.10.033

5. Akca O. Hyperoxia: is it a Biomarker for Mortality? Intensive Care Med. 2015 Oct;41(10):1873-4. https://doi.org/10.1007/s00134-015-3975-y

6. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. Guidelines for the Early Management of Patients with Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2019 Dec;50(12):e344-e418. https://doi.org/10.1161/STR.0000000000000211

7. Farag E, Liang C, Mascha EJ, Toth G, Argalious M, Manlapaz M, et al. Oxygen Saturation and Postoperative Mortality in Patients with Acute Ischemic Stroke Treated by Endovascular Thrombectomy. Anesth Analg. 2022 Feb 1;134(2):369-379.

https://doi.org/10.1213/ane.0000000000005763

8. Ferdinand P, Roffe C. Hypoxia after Stroke: A Review of Experimental and Clinical Evidence. Exp Transl Stroke Med. 2016 Dec 7;8:9. https://doi.org/10.1186/s13231-016-0023-0

9. Watson NA, Beards SC, Altaf N, Kassner A, Jackson A. The Effect of Hyperoxia on Cerebral Blood Flow: A Study in Healthy Volunteers using Magnetic Resonance Phase-Contrast Angiography. Eur J Anaesthesiol. 2000 Mar;17(3):152-9. https://doi.org/10.1046/j.1365-2346.2000.00640.x

10. Roffe C, Nevatte T, Sim J, Bishop J, Ives N, Ferdinand P, Gray R, et al. Effect of Routine Low-Dose Oxygen Supplementation on Death and Disability in Adults with Acute Stroke: The Stroke Oxygen Study Randomized Clinical Trial. JAMA. 2017 Sep 26 ;318(12):1125-1135. https://doi.org/10.1001/jama.2017.11463