EDITORIAL

If Time is Neuron, What Are We Waiting for?

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Acute ischemic stroke (AIS) is a medical emergency with varied presentations and outcomes. The advent and availability of interventional therapies and devices have extended the timelines for attempted salvage of the ischemic brain. Thrombolytic therapy (TLT) with recombinant tissue plasminogen activator (rtPA) has remained the front-runner intervention among patients with AIS. The timelines for initiation of intravenous TLT, have also become well-established over the last decade. A well-defined timeline of 4.5 hours has been recommended by the American Heart Association.[1] Selection of patients who would benefit from such an intervention, necessitates quick clinical evaluation followed by focused imaging. The shorter the timetaken to initiate definitive TLT, the better the outcomes are expected to be. Any delay in triaging, imaging and treating patients with AIS results in loss of "healthy life – years". Almekhlafi et al. proposed 2.2 hours of healthy life lost for every second of delayed care among patients with AIS.[2] The authors identified several time lines which could influence the outcome among patients with AIS. These include last known well-to-door time, last well-known puncture time, last known well to reperfusion time, door-to-puncture time and door-to-reperfusion time. Programs targeted at improving the quality of stroke treatment could probably use these timelines are guidance for metrics. The authors found that 48% of patients received reperfusion therapy beyond 4 hours with consequent incomplete reperfusion. However, the authors also concede that all is not lost even if the timelines are exceeded and selected patients would still benefit from TLT.

It is therefore worthwhile looking at various touchpoints of stroke TLT where delays could be minimized for better outcomes. Four phases of delay are well documented[3] – (i) from symptom onset to decision to seek medical attention (ii) from decision to seek medical attention to first medical contact (iii) from first medical contact to evaluation (including transport time) and (iv) from admission to initiation of definitive therapy. As medical professionals, modifying the last two delay points is within our scope and improvement can be achieved. At an institutional level resources planning and coordination process engineering are key elements of streamlining stroke care.[3] Currently, an arbitrary benchmark for admission to TLT called door-to-needle time (DNT) has been set at 60 minutes. The AHA recommends that this target DNT should be achieved in 75% of all patients reaching the hospital.[4] The Helsinki model was the first to attempt reduction of DNT[5] and has been successfully implemented elsewhere. Majority of the centers which brought about a change in DNT did so by changing multiple areas of action for TLT.[6] In a systematic review of the factors delaying TLT, Sharobeam et al.[7] identified certain key in-hospital factors. Delay in Emergency Department registration and triage with consequent delays in computed tomography (CT) imaging were identified as major modifiable delays. Age related delays were also identified, with younger patients getting thrombolysed earlier, but having their stroke suspected later. Delays in imaging also play a big role, sometimes due to non-availability or due to airway and hemodynamic optimization taking precedence. The authors recommended a combined strategy of continued education, institution of stroke alert systems and the use of telemedicine to reduce the delays. Catangui et al.[8] emphasized the role of nursing education and empowerment as a viable and effective tool for reduction in DNT among patients with stroke. Mowlah et al.[9] identified that around 20% of eligible patients had a DNT greater than 60 minutes in a large stroke center in New York. Delays in imaging and control of hypertension were identified as major contributors to the delay. In addition, delays in obtaining consent and difficulty in ascertaining the time of symptom onset, seemed to have contributed to the delayed therapy. The metrics in a Chinese cohort were much different.[10] Huang et al. reported that the 75% percentile of DTN achievement was noted at 135 minutes rather than the recommended 60. Abraham et al.[11] reported the reasons for delay in TLT at a tertiary center in Southern India. The authors noted a mean in-hospital delay of 94 minutes and identified a gap between imaging and Stroke unit admission as a crucial contributor. Economic constraints leading to delays were encountered in 18% of eligible patients in this cohort. In an interesting observation, Nagendra et al.[12] noted that the distances that need to be covered to reach a health care facility with acute stroke care capabilities, become a major determinant of delayed TLT among Indian cohorts.

Several workers have attempted to provide solutions to these delays. Tran et al.,[13] reporting on a quality improvement

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initiative from a stroke center in California, suggested (i) ED management of hypertension (ii) TLT prior to laboratory results and (iii) administration of TLT in the radiology suite as viable and implementable steps to cut down DNT. They reported success in reducing the DNT by 23 minutes with this approach. Time taken for imaging has been noted in several reports as a key factor contributing to delayed TLT. Sadeghi-Hokmabadi et al.,[14] reporting on an initiative to reduce door to imaging time among an Iranian cohort, suggested prioritizing patients for imaging and lab analysis along with staff education as effective tools to reduce delays in TLT. With these simple interventions the mean door to CT time was reduced by 55 minutes in this cohort. A combination of initiatives is more likely to be successful in shortening the timelines for effective stroke TLT.[15]

In this edition of the journal, Shah et al.[16] report the results of their prospective observational study evaluating door-to-imaging and DNTs in an urban public academic hospital. During the study period, the proportion of patients with AIS who were thrombolysed was about 20%. This is lower than recommended, especially since more than 50% of eligible patients reached a care center within the window period. Majority of patients (73%) in this cohort were imaged within 60 minutes with 20% completing the investigation within 30 minutes. Eligible patients received TLT within 90 minutes of hospital arrival 60% of the time. There seems to be scope for improvement on this metric. The proportion of patients who were imaged on arrival was disproportionately higher than those who received the TLT. The authors have not discussed the reasons for drop out of a high proportion of eligible patients. However, consenting process or financial implications could have been contributory as was the case in earlier reports from India. Facilitating TLT while still in the imaging suite is an alternative strategy which should probably be considered for those with stable blood pressure presenting towards the limits of standard window periods. Education of medical, nursing and technical staff on the value of timelines and benefits of TLT are also probably essential tools.

Stroke TLT has improved the outcomes among patients with AIS. There is, however, scope for improvement in the timelines for DNT. A structured multi-tiered approach is likely to be the most effective way in achieving that goal.

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References

1. 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;50(12):e344–418.
2. Almekhlafi MA, Goyal M, Dippel DWJ, Majoie CBLM, Campbell CBV, Muir KW, et al. Healthy Life-Year Costs of Treatment Speed From Arrival to Endovascular Thrombectomy in Patients With Ischemic Stroke: A Meta-analysis of Individual Patient Data From 7 Randomized Clinical Trials. JAMA Neurol 2021;78(6):709–717. DOI: 10.1001/jamaneurol.2021.1055.
3. Lachkhem Y, Rican S, Minvielle É. Understanding delays in acute stroke care: a systematic review of reviews. Eur J Public Health 2018;28(3):426–433. DOI: 10.1093/eurpub/cky066.
4. American Heart Association/American Stroke Association. Target: Stroke Phase II, http://www.strokeassociation.org/STROKEORG/Professionals/TargetStroke/Target-Stroke-Phase-II_UCM_469859_Article.jsp#.WV59aTPMxn4 (2017, Accessed on: 6 July 2017).
5. Meretoja A, Strbian D, Mustanoja S, Tatlisumak T, Lindsberg PJ, Kaste M. Reducing in-hospital delay to 20 minutes in stroke thrombolysis. Neurology 2012;79:306–313. DOI: 10.1212/WNL.0b013e31825d6011.
6. Kamal N, Smith EE, Jeerakathil T, Hill MD. Thrombolysis: Improving door-to-needle times for ischemic stroke treatment – A narrative review. Int J Stroke 2018;13(3):268–276. DOI: 10.1177/1747493017743060.
7. Sharobeam A, Jones B, Walton-Sonda D, Lueck CJ. Factors delaying intravenous thrombolytic therapy in acute ischaemic stroke: A systematic review of the literature. J Neurol 2021;268(8):2723–2734. DOI: 10.1007/s00415-020-09803-6.
8. Catangui E, Baua E, Pizarro J, Almutairi AF. Timely Administration of Thrombolytic Therapy in Acute Ischemic Stroke: An Ethnographic Study. Int J Nurs Clin Pract 2020;7:331. DOI: https://doi.org/10.15344/2394-4978/2020/331.
9. Mowla A, Doyle J, Lail NS, Rajabzadeh-Oghaz H, Deline C, Shirani P, et al. Delays in door-to-needle time for acute ischemic stroke in the emergency department: A comprehensive stroke center experience. J Neurol Sci 2017;376:102–105. DOI: 10.1016/j.jns.2017.03.003.
10. Huang Q, Ma QF, Feng J, Cheng WY, Jia JP, Song HQ, et al. Factors Associated with In-Hospital Delay in Intravenous Thrombolysis for Acute Ischemic Stroke: Lessons from China. PLoS One 2015;10(11):e0143145. DOI: 10.1371/journal.pone.0143145.
11. Abraham SV, Krishnan SV, Thaha F, Balakrishnan JM, Thomas T, Palatty BU. Factors delaying management of acute stroke: An Indian scenario. Int J Crit Illn Inj Sci 2017;7(4):224–230. DOI: 10.4103/IJCIIS.IJCIIS_20_17.
12. Nagendra CV, Kumar TSS, Bohra V, Wilben V, Karan V, Huded V. Factors Affecting the Effective Management of Acute Stroke: A Prospective Observational Study. Indian J Crit Care Med 2018;22(3):138–143. DOI: 10.4103/ijccm.IJCCM_232_17.
13. Tran D, Zhu Z, Shafie M, Abcede H, Stradling D, Yu W. Three easily-implementable changes reduce median door-to-needle time for intravenous thrombolysis by 23 minutes. BMC Neurol 2019;19(1):300. DOI: 10.1186/s12883-019-1527-8.
14. Sadeghi-Hokmabadi E, Taheraghdam A, Hashemilar M, Rikhtegar R, Mehrvar K, Mehrara M, et al. "Simple In-Hospital Interventions to Reduce Door-to-CT Time in Acute Stroke", International Journal of Vascular Medicine 2016;2:pp. 6. Article ID: 1656212. https://doi.org/10.1155/2016/1656212.
15. Siarkowski M, Lin K, Li SS, Al Sultan A, Ganshorn H, Kamal N, et al. Meta-analysis of interventions to reduce door to needle times in acute ischaemic stroke patients. BMJ Open Qual 2020;9(3):e000915. DOI: 10.1136/bmjoq-2020-000915.
16. Shah A, Diwan A. Stroke thrombolysis: Beating the clock. Indian J Crit Care Med 2023;27(2):107–110.