



**UNIVERSIDADE ESTADUAL DE CAMPINAS
SISTEMA DE BIBLIOTECAS DA UNICAMP
REPOSITÓRIO DA PRODUÇÃO CIENTÍFICA E INTELLECTUAL DA UNICAMP**

Versão do arquivo anexado / Version of attached file:

Versão do Editor / Published Version

Mais informações no site da editora / Further information on publisher's website:

https://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-282X2015000600526

DOI: 10.1590/0004-282X20150047

Direitos autorais / Publisher's copyright statement:

©2015 by Associação Arquivos de Neuro-Psiquiatria. All rights reserved.

DIRETORIA DE TRATAMENTO DA INFORMAÇÃO

Cidade Universitária Zeferino Vaz Barão Geraldo

CEP 13083-970 – Campinas SP

Fone: (19) 3521-6493

<http://www.repositorio.unicamp.br>

Lean thinking turns ‘time is brain’ into reality

Pensamento enxuto faz ‘tempo é cérebro’ virar realidade

Li Min Li^{1,2,3}, Sharon Johnson¹

ABSTRACT

Intravenous rt-PA is an effective recanalizing treatment for ischemic stroke within 4 and half hours from its onset (Onset-to-Treatment [OTT]), with the best result seen in those treated within 90 minutes OTT. Yet few patients currently are treated in this time frame. From the standpoint of process improvement or a lean thinking perspective, there is a potential opportunity to reduce the time by eliminating non-value-added steps in each element of the stroke survival chain. The reduction in one time element does not necessarily shift the OTT under 90 minutes. Most likely, the reduction in OTT requires a coordinated approach to track and improve all elements of OTT, from the patient’s ability to recognize the onset of stroke up to delivery of medication. Shortening this total time should be a considered an indicator of quality improvement in acute stroke care.

Keywords: stroke, thrombolysis, quality, safety.

RESUMO

Tratamento intravenoso com rt-PA é eficaz na recanalização do acidente vascular cerebral isquêmico (AVCI) no prazo de até 4 horas e meia de seu início (OTT), com o melhor resultado visto naqueles tratados dentro de 90 minutos OTT. Apesar disso, poucos são tratados neste período de tempo. Do ponto de vista da melhoria de processos ou uma perspectiva de pensamento enxuto, há uma oportunidade potencial para reduzir o tempo ao eliminar etapas que não agregam valor em cada elemento da cadeia de sobrevivência do paciente com acidente vascular cerebral. A diminuição da OTT requer uma abordagem coordenada em conjunto para controlar e melhorar todos os elementos de OTT, a capacidade do paciente para reconhecer o início do icto até à administração da medicação. Encurtar esse tempo total deve ser um considerado um indicador da melhoria da qualidade no atendimento AVCI agudo.

Palavras-chave: acidente vascular cerebral, trombólise, qualidade, segurança.

Thrombolysis with intravenous rt-PA is an effective recanalizing treatment for ischemic stroke within 4 and half hours from its onset¹. It is clear that by providing the treatment earlier the outcome is better with fewer complications^{2,3}. A pooled study⁴ demonstrated that short stroke-onset-to-treatment time (OTT) with rt-PA had better functional outcomes (modified Rankin Scale, mRS, score of 0 to 1) than patients treated beyond the 90 minute OTT, with odds of 2.8 (95%CI 1.8-4.5) for OTT between 0 to 90 min in comparison to odds of 1.6 (1.1-2.2) for OTT between 91 to 180 min. A more recent pooled reanalysis with additional data showed similar findings⁵; the number of patients needed to treat (NNT) to achieve an mRS score of 0 to 1 for OTT within 90 minutes is 4.5, whereas the NNT doubled to 9 for OTT between 91-180, and to 14 for OTT between 181-270 minutes.

Therefore, the goal for an optimal treatment should be to target an OTT under 90 minutes, as pictured in Figure 1. Based on the recommended American Heart Association (AHA) stroke guideline (the text and references^{6,7} in Figure 1 are derived from it⁸), the time limits for pre-hospital (30 minutes) plus hospital care (60 minutes) fill up the 90 minute window. Experience has demonstrated that process improvement can lower the time spent in the pre-hospital⁹ and hospital^{10,11,12,13} phases, and educational awareness campaigns can improve stroke recognition and time to seek help⁸. Therefore, combining best practices and available technologies, it is possible to respond within 90 minutes. The strategy and plan of action require commitment from the stakeholders, including society and in particular patients at risk. We need to move forward to interpret the 60 minute door to needle recommendation as more than a time to attain. The door-to-needle time needs to

¹Robert A. Foisie School of Business, Healthcare Delivery Institute, Worcester Polytechnic Institute, Worcester MA, USA;

²UMass Medicine School, Worcester MA, USA;

³Universidade Estadual de Campinas, Faculdade de Ciências Médicas, Departamento de Neurologia, Campinas SP, Brazil.

Correspondence: Li Li Min; Foisie School of Business, Washburn Shops 215, 100 Institute Road; 01609 Worcester MA, USA; E-mail: limin@fcm.unicamp.br

Conflict of interest: There is no conflict of interest to declare.

Support: Li Li Min is recipient of FAPESP Scholarship 2014/10911-3.

Received 09 December 2014; Received in final form 29 January 2015; Accepted 19 February 2015.



Figure 1. The best window time for rt-PA intravenous treatment is within 90 minutes from the stroke onset with adjusted odds of 2.55 (95%CI 1.44-4.52) for an outcome with minimal symptom at 3 months⁵. The guideline from the American Heart Association (AHA)⁸ suggests a hospital response in under 60 minutes (door-to-needle), and pre-hospital time under 30 minutes (alarm-to-door), which amounts to 90 minutes.

be considered as part of a broader process, with the goal to treat the patient within 90 minutes from the onset of stroke.

One could argue that the time for each step is already very tight. When the treatment window of 3 hours was first announced, many physicians viewed it with skepticism¹⁴, as a mission impossible that patients could arrive in this time window¹⁵. Time has shown otherwise, and paradoxically has created a “three hour effect”, with delays in providing treatment for those patients arriving earlier¹⁶. The increase to 4 and half hours for the window of treatment was warmly welcomed, increasing the number of people who can be treated; nevertheless we seem to be drifting from the goal of achieving a better result, which is the target of treating within 90 minutes of stroke onset.

From the standpoint of process improvement analysis or a lean thinking perspective, there is a potential opportunity to reduce time and eliminate non-value-added steps. For Formula 1 fans, as an example of the success of such techniques, Figure 2 shows the decrease in pit stop times over

time; in the 1970’s, pit stops were very slow as compared to today¹⁷. The latest record was set by Infiniti Red Bull Racing, with an impressive 1.923 seconds to change 4 tires during the 2013 US Grand Prix in Austin, breaking their former record of 2.05 in Malaysia in the same year. This record appears to be a pinnacle of what is possible; nevertheless, the same thing was said back in the early nineties, when pit stops were around 4.5 seconds (Figure 2).

The quest to reduce hospital door-to-needle times has yielded good results as demonstrated by Köhrnman et al. with an average time of 25 minutes¹³ in Erlagen, Germany; by Kim et al. with 29 minutes¹² in Busan, Korea; by Tveiten et al. with 38 minutes¹⁸ in Bergen, Norway; by Meretoja et al. with 20 minutes¹¹ in Helsinki, Finland; by Ford et al. with 39 minutes¹⁰ in Saint Louis, USA. In this regard, considering that 28.3% of stroke patients arrive within the ‘golden hour’¹⁶, only colleagues in Erlagen, Helsinki and Busan would be able to attain an OTT under 90 minutes. However, the

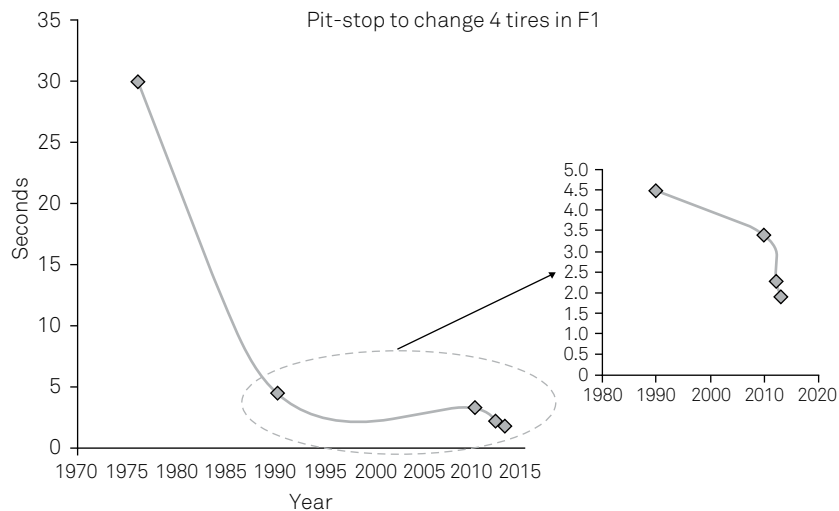


Figure 2. In the early nineties, a pit stop took around 4.5 seconds, and no one imagined that pit stops would be 2.34 times faster today¹⁷. However, the change took almost 20 years (1990-2010), when the Ferrari team recorded a pit stop time of 3.4 seconds during the Italian Grand Prix at Monza in 2010³⁰. The secrets to the improvement included training to perfection, modifications in the car, and new equipment designed for speed and efficiency in the pit stop. Over the next 3 years, there was a drastic drop in pit stop time to 2.31 seconds by the McLaren team during the 2012 German Grand Prix at Hockenheim, and 1.923 seconds by the Infiniti Red Bull Racing team during the 2013 US Grand Prix in Austin. These can be the decisive seconds for winning or losing a championship.

experience in Busan, Korea, demonstrates the importance of viewing the broad picture. In their process improvement effort, they were able to reduce door-to-needle time, but this led to an increase in pre-hospital care times, which overall did not impact the OTT. The same applies to the study carried out by Köhrmmman et al. and Meretoja et al., as their pre-hospital times were very long (> 70 minutes). In the USA, Ford et al.¹⁰ applied Value Stream Analysis (VSA) to the work flow of patients with stroke in an Emergency Department. Their experience showed that after changes, which involved completing a CT image first, there was a significant reduction in the door to needle time from a mean of 60 minutes (range from 46 to 73 minutes) to 39 minutes (range from 28 to 56 minutes). The average time from stroke onset to treatment was reduced from 131 minutes to 111 minutes. Despite this significant reduction in time, outcomes as measured by the mRS scale were not significantly different between the two groups. This was somewhat unexpected, but framed in OTT guidelines, the 111 minutes OTT after improvement as well as the 131 minutes OTT prior to improvement still fall into the same group of those treated between 91-180 minutes.

Therefore, if we expect to improve the odds of functional outcome we need to continue to pull the process towards the 90 minutes treatment limit from stroke onset. Process improvement is iterative, with the biggest improvements typically seen initially, followed by smaller improvements to continuously refine the process. Adopting a process perspective, the entire process could be viewed as elements in a stroke survival chain⁸. Rather than just encouraging speed – recognizing the stroke faster, getting to the hospital faster, and delivering the treatment faster – we need to first assess the entire value stream to avoid optimizing steps and

tasks that do not add value. Lean-Six-Sigma¹⁹ is a holistic approach to improvement that starts with a walk in the Gemba (the work area, where things are done) in order to examine the value of each process step. Processes and tasks that do not add value or that duplicate effort are removed, and bottlenecks and routing are scrutinized and redesigned to meet patient expectations. Once the non-value-added steps have been removed, the processes can be optimized iteratively through continuous improvement to reduce variation, and to ensure efficiency, resulting in faster execution.

As technology evolves, acute stroke care can also be delivered faster through mobile units²⁰. Ebinger et al. demonstrated a 15 minutes reduction in alarm-to-needle time using a stroke mobile unit equipped with a stroke neurologist, CT scan, point of care laboratory and technical personnel⁹. They were able to increase the number of patients with OTT under 90 minutes by 20% compared to hospital-based treatment (31% OTT < 90min)⁹, but the mean time remained around 107 minutes, within 91-180 OTT. Functional outcomes did not increase with this new approach, but only partial results were reported due to ethics protection so are not conclusive. Recently, Ebinger and colleagues²¹ demonstrated that this pack-and-load approach has increased 6-fold the number of patients treated within golden hour. Whether Berlin's experience can be generalized is open to debate²². In Brazil there are other challenges to overcome first, from the patients' ability to react²³ to tertiary hospital setup²⁴.

Other technologies include a wide range of information technologies that are available now, but which can be integrated to support more comprehensive care, ranging from detection sensors²⁵, smartphones²⁶, communication systems²⁷, big data, to logistics. Using such technologies does

not preclude a comprehensive process review to remove waste; otherwise the result could be a sophisticated, expensive process with little or no added value.

Quality assessment²⁸ and benchmarking²⁹ can be used to audit the quality of services, which is essential for hospitals in terms of preparedness, standard of care and continuous improvement. Quality assessment and benchmarking are typically centered on intra-hospital care, which can improve local issues such as stroke diagnosis, but do not take into account other elements of the healthcare system. From a patient perspective, if you had an ischemic stroke, how fast would you like to be treated? You likely answered 'as fast as possible', but the chance of receiving rt-PA under 90 minutes is not high today. For instance, less than one third of US hospitals have a door-to-needle time under 60 minutes⁸. If your answer was an 'OTT under 90 minutes',

this suggests a need to redesign acute stroke care delivery by considering a composite of independent processes, each contributing to the overall time; onset-to-alarm, alarm-to-door, door-to-needle. The reduction in one time element does not necessarily shift OTT under 90 minutes, as the experiences described above illustrate. Most likely, the reduction in OTT requires a coordinated approach to improve all elements of OTT, from the patient's ability to recognize the onset of stroke up to delivery of medication, and shortening this time should be considered an indicator of quality improvement in acute stroke care.

ACKNOWLEDGEMENT

Figure 1 was drawn by Mario Cau.

References

1. Hacke W, Kaste M, Bluhmki E, Brozman M, Dávalos A, Guidetti D et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. *N Engl J Med*. 2008;359(13):1317-29. <http://dx.doi.org/10.1056/NEJMoa0804656>
2. Ahmed N, Wahlgren N, Grond M, Hennerici M, Lees KR, Mikulik R et al. Implementation and outcome of thrombolysis with alteplase 3-4.5 h after an acute stroke: an updated analysis from SITS-ISTR. *Lancet Neurol*. 2010;9(9):866-74. [http://dx.doi.org/10.1016/S1474-4422\(10\)70165-4](http://dx.doi.org/10.1016/S1474-4422(10)70165-4)
3. Ahmed N, Kellert L, Lees KR, Mikulik R, Tatlisumak T, Toni D. Results of intravenous thrombolysis within 4.5 to 6 hours and updated results within 3 to 4.5 hours of onset of acute ischemic stroke recorded in the Safe Implementation of Treatment in Stroke International Stroke Thrombolysis Register (SITS-ISTR): an observational study. *JAMA Neurol*. 2013;70(7):837-44. <http://dx.doi.org/10.1001/jamaneurol.2013.406>
4. Hacke W, Donnan G, Fieschi C, Kaste M, Kummer R, Broderick JP et al. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. *Lancet*. 2004;363(9411):768-74. [http://dx.doi.org/10.1016/S0140-6736\(04\)15692-4](http://dx.doi.org/10.1016/S0140-6736(04)15692-4)
5. Lees KR, Bluhmki E, Kummer R, Brott TG, Toni D, Grotta JC et al. Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials. *Lancet*. 2010;375(9727):1695-703. [http://dx.doi.org/10.1016/S0140-6736\(10\)60491-6](http://dx.doi.org/10.1016/S0140-6736(10)60491-6)
6. Bock FB. Response system for patients presenting with acute stroke. *Proceeding of a National Symposium on Rapid Identification and Treatment of Acute Stroke*; 1996 Dec. Bethesda: National Institute of Neurological Disorders and Stroke; 2011 [cited 2014 Oct 7]. Available from: http://www.ninds.nih.gov/news_and_events/proceedings/stroke_proceedings/bock.htm
7. Acker JE 3rd, Pancioli AM, Crocco TJ, Eckstein MK, Jauch EC, Larrabee H et al. Implementation strategies for emergency medical services within stroke systems of care: a policy statement from the American Heart Association/American Stroke Association Expert Panel on Emergency Medical Services Systems and the Stroke Council. *Stroke*. 2007;38(11):3097-115. http://www.ninds.nih.gov/news_and_events/proceedings/stroke_proceedings/bock.htm
8. Jauch EC, Saver JL, Adams Jr HP, Bruno A, Connors JJ, Demaerchak BM et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2013;44(3):870-947. <http://dx.doi.org/10.1161/STR.0b013e318284056a>
9. Ebinger M, Winter B, Wendt M, Weber JE, Waldschmidt C, Rozanski M et al. Effect of the use of ambulance-based thrombolysis on time to thrombolysis in acute ischemic stroke: a randomized clinical trial. *JAMA*. 2014;311(16):1622-31. <http://dx.doi.org/10.1001/jama.2014.2850>
10. Ford AL, Williams JA, Spencer M, McCammon C, Khoury N, Sampson TR et al. Reducing door-to-needle times using Toyota's lean manufacturing principles and value stream analysis. *Stroke*. 2012;43(12):3395-8. <http://dx.doi.org/10.1161/STROKEAHA.112.670687>
11. Meretoja A, Strbian D, Mustanoja S, Tatlisumak T, Lindberg PJ, Kaste M. Reducing in-hospital delay to 20 minutes in stroke thrombolysis. *Neurology*. 2012;79(4):306-13. <http://dx.doi.org/10.1212/WNL.0b013e31825d6011>
12. Kim SK, Lee SY, Bae HJ, Lee YS, Kim SY, Kang MJ et al. Pre-hospital notification reduced the door-to-needle time for iv t-PA in acute ischaemic stroke. *Eur J Neurol*. 2009;16(12):1331-5. <http://dx.doi.org/10.1111/j.1468-1331.2009.02762.x>
13. Köhrmann M, Schellinger PD, Breuer L, Dohm M, Kuramatsu JB, Blinzler C et al. Avoiding in hospital delays and eliminating the three-hour effect in thrombolysis for stroke. *Int J Stroke*. 2011;6(6):493-7. <http://dx.doi.org/10.1111/j.1747-4949.2011.00585.x>
14. Bogousslavsky J. Thrombolysis in acute stroke. *BMJ*. 1996;313(7058):640-1. <http://dx.doi.org/10.1136/bmj.313.7058.640>
15. Caplan LR. Thrombolysis 2004: the good, the bad, and the ugly. *Rev Neurol Dis*. 2004;1(1):16-26.
16. Saver JL, Smith EE, Fonarow GC, Reeves MJ, Zhao X, Olson DM et al. The "golden hour" and acute brain ischemia: presenting features and lytic therapy in >30,000 patients arriving within 60 minutes of stroke onset. *Stroke*. 2010;41(7):1431-9. <http://dx.doi.org/10.1161/STROKEAHA.110.583815>
17. Graban M. Video: Formula 1 pit stops 1950 & today... a huge difference. 2014 Apr 18 [cited 2014 Oct 3]. In: Mark Graban's Lean blog [internet]. San Antonio; c2015. Available from <http://www.leanblog.org/2014/04/formula-1-pit-stops-1950-today/>
18. Tveiten A, Mygland A, Ljøstad U, Thomassen L. Intravenous thrombolysis for ischaemic stroke: short delays and high community-based treatment rates after organisational changes in a previously inexperienced centre. *Emerg Med J*. 2009;26(5):324-6. <http://dx.doi.org/10.1136/emj.2008.063610>

19. Li LM, Johnson S. Stroke care within the golden hour. *JAMA Neurol.* 2015;72(4):475. doi: <http://dx.doi.org/10.1001/jamaneurol.2014.4568>.
20. Ebinger M, Lindenlaub S, Kunz A, Rozanski M, Waldschmidt C, Weber JE et al. Prehospital thrombolysis: a manual from Berlin. *J Vis Exp.* 2013;(81):e50534. <http://dx.doi.org/10.3791/50534>
21. Ebinger M, Kunz A, Wendt M, Rozanski M, Winter B, Waldschmidt C et al. Effects of golden hour thrombolysis: a prehospital acute neurological treatment and optimization of medical care in stroke (PHANTOM-S) Substudy. *JAMA Neurol.* 2015;72(1):25-30. <http://dx.doi.org/10.1001/jamaneurol.2014.3188>
22. Warach S. Prehospital thrombolysis for stroke: an idea whose golden hour has arrived. *JAMA Neurol.* 2015;72(1):9-10. <http://dx.doi.org/10.1001/jamaneurol.2014.3389>
23. Panício MI, Mateus L, Ricarte IF, et al. The influence of patient's knowledge about stroke in Brazil: a cross sectional study. *Arq Neuropsiquiatr.* 2014;72(12):938-41. <http://dx.doi.org/10.1590/0004-282X20140167>
24. Tosta ED, Rebello LC, Almeida SS, Neiva MSS. Treatment of ischemic stroke with r-tPA: implementation challenges in a tertiary hospital in Brazil. *Arq Neuropsiquiatr.* 2014;72(5):368-72. <http://dx.doi.org/10.1590/0004-282X20140021>
25. Chandrasekaran V, Dantu R, Jonnada S, Thiyagaraja S, Subbu KP. Cuffless differential blood pressure estimation using smart phones. *IEEE Trans Biomed Eng.* 2013;60(4):1080-9. <http://dx.doi.org/10.1109/TBME.2012.2211078>
26. Dubey D, Amritphale A, Sawhney A, Amritphale N, Dubey P, Pandey A. Smart phone applications as a source of information on stroke. *J Stroke.* 2014;16(2):86-90. <http://dx.doi.org/10.5853/jos.2014.16.2.86>
27. Bladin CF, Cadilhac DA. Effect of telestroke on emergent stroke care and stroke outcomes. *Stroke.* 2014;45(6):1876-80. <http://dx.doi.org/10.1161/STROKEAHA.114.003825>
28. Fonarow GC, Zhao X, Smith EE, Saver JL, Reeves MJ, Bhatt DL et al. Door-to-needle times for tissue plasminogen activator administration and clinical outcomes in acute ischemic stroke before and after a quality improvement initiative. *JAMA* 2014;311(16):1632-40. <http://dx.doi.org/10.1001/jama.2014.3203>
29. Hall RE, Khan F, Bayley MT, Asllani E, Lindsay P, Hill MD et al. Benchmarks for acute stroke care delivery. *Int J Qual Health Care.* 2013;25(6):710-8. <http://dx.doi.org/10.1093/intqhc/mzt069>
30. Gray W. Tech talk: Can F1 pit stops get even quicker? In: Yahoo! Sport. 2013 Apr 9 [cited 2014 Oct 7]. Available from: <https://uk.eurosport.yahoo.com/blogs/will-gray/gray-matter-f1-stops-even-quicker-101951154.html>