Helsinki model cut stroke thrombolysis delays to 25 minutes in Melbourne in only 4 months

Atte Meretoja, MD, PhD, MScStrokeMed
Louise Weir, RN, NP, GradCertStrokeMgt, MANP
Melissa Ugalde, RN, GradCertNeurosci
Nawaf Yassi, MBBS, BSc(Med), FRACP
Bernard Yan, MBBS, FRACP
Peter Hand, MD, FRACP
Melinda Truesdale, MBBS, GradDipHSM, FACEM
Stephen M. Davis, MD, FRACP
Bruce C.V. Campbell, MBBS, BMedSc, PhD, FRACP

Correspondence to Dr. Meretoja: atte.meretoja@fimnet.fi

ABSTRACT

Objective: To test the transferability of the Helsinki stroke thrombolysis model that achieved a median 20-minute door-to-needle time (DNT) to an Australian health care setting.

Methods: The existing "code stroke" model at the Royal Melbourne Hospital was evaluated and restructured to include key components of the Helsinki model: 1) ambulance prenotification with patient details alerting the stroke team to meet the patient on arrival; 2) patients transferred directly from triage onto the CT table on the ambulance stretcher; and 3) tissue plasminogen activator (tPA) delivered in CT immediately after imaging. We analyzed our prospective, consecutive tPA registry for effects of these protocol changes on our DNT after implementation during business hours (8 AM to 5 PM Monday–Friday) from May 2012.

Results: There were 48 patients treated with tPA in the 8 months after the protocol change. Compared with 85 patients treated in 2011, the median (interquartile range) DNT was reduced from 61 (43–75) minutes to 46 (24–79) minutes ($p = 0.040$). All of the effect came from the change in the in-hours DNT, down from 43 (33–59) to 25 (19–48) minutes ($p = 0.009$), whereas the out-of-hours delays remain unchanged, from 67 (55–82) to 62 (44–95) minutes ($p = 0.835$).

Conclusion: We demonstrated rapid transferability of an optimized tPA protocol to a different health care setting. With the cooperation of ambulance, emergency, and stroke teams, we succeeded in the absence of a dedicated neurologic emergency department or electronic patient records, which are features of the Finnish system. The next challenge is providing the same service out-of-hours.
Neurology® 2013;81:1071–1076

GLOSSARY

DNT = door-to-needle time; **ED** = emergency department; **INR** = international normalized ratio; **OTT** = onset to thrombolysis; **tPA** = tissue plasminogen activator.

Numerous interventions to reduce delays in ischemic stroke thrombolysis have been studied,[1] and each is motivated by the fact that the sooner the treatment is delivered, the more the patient benefits.[2] The fastest results published to date, with median door-to-needle time (DNT) of 20 minutes, were reported from the Helsinki University Central Hospital in this journal last year.[3] The Helsinki model had been developed over a period of more than a decade and is composed of 12 separate interventions, all aimed at minimizing delays from patient arrival to the initiation of thrombolytic therapy (tissue plasminogen activator [tPA]). There are certain components of the Finnish health care system and the Helsinki thrombolysis model, such as province-wide electronic patient records, a dedicated neurologic emergency department (ED), and a highly centralized service with only one tertiary hospital in the whole province, that raise questions about the applicability of this approach to other health care settings.

The aim of this report is to describe the transferability of key components of the Helsinki stroke thrombolysis model to an Australian center, and how this almost halved the DNTs in just a few months.

From the Departments of Neurology and Medicine (A.M., L.W., M.U., N.Y., B.Y., P.H., S.M.D., B.C.V.C), Nursing (L.W.), and Emergency Department (M.T.), The Royal Melbourne Hospital, University of Melbourne, Parkville, Australia; and Department of Neurology (A.M.), Helsinki University Central Hospital, Finland.

Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

METHODS

Health care setting. Australia has universal health care coverage, and acute stroke patients are treated almost exclusively in government-funded hospitals. In the state of Victoria, there is a single ambulance service and patients with symptoms suggestive of acute stroke are systematically taken to the nearest hospital with a tPA service for stroke patients. Seven public hospitals admit acute stroke patients and offer tPA within a 20-km radius in the Greater Melbourne metropolitan area, which has a population of 4.2 million. The Royal Melbourne Hospital is the most centrally located and admits approximately 450 ischemic stroke patients annually. IV tPA was approved in Australia for use in acute ischemic stroke in 2003.

Registry setup. This report is based on The Royal Melbourne Hospital Stroke Registry, a prospective registry of consecutive stroke patients and stroke mimic patients who have been admitted to the hospital since 2003. Treatment delays were registered prospectively with no missing data. Symptomatic intracerebral hemorrhage was defined according to the SITS (Safe Implementation of Thrombolysis in Stroke) criteria.[4] The present analysis includes patients from January 1, 2003 to December 31, 2012.

Standard protocol approvals, registrations, and patient consents. This registry has been approved by institutional authorities. As a routine observational quality registry, no patient consent for registration was required and all consecutive patients were registered.

Previous Royal Melbourne Hospital thrombolysis model. A "code stroke" protocol was implemented at the Royal Melbourne Hospital in 2007 with a system of rapid notification to the stroke team by the ED via a linked paging system.[5] The code stroke was usually activated after an emergency physician had first evaluated potential patients in an ED cubicle. Ambulance prenotification of the ED was sometimes available, but not routinely passed on to the stroke team. The utility of prenotification was also limited by minimal clinical and demographic detail.

New model. In late December 2011, in light of the Helsinki data and Dr. Meretoja's move to Melbourne a month earlier, the stroke team analyzed the current tPA process and feasibility of implementing components of the Helsinki model. Enhancing the ambulance prenotification to include patient's name, date of birth, and more clinical details was identified as a key target to allow registration and access to history before arrival. Going direct to CT on the ambulance stretcher after brief assessment of cardiorespiratory stability on arrival was another key element. An informal working group from neurology, emergency, and Ambulance Victoria reached consensus agreement on the restructured model during the first months of 2012. After securing buy-in from all personnel, the new model was initiated during office hours (8 AM to 5 PM Monday–Friday) from May 2012. The changes introduced in the new model and comparison with the Helsinki model are presented in table 1. The out-of-hours service was not changed.

Common features in the Helsinki model and the previous Royal Melbourne model remained unchanged: patients were physically examined and the patients' histories were taken by fellowship-trained stroke neurologists, and NIH Stroke Scale evaluations were done before the administration of tPA; while formal blood samples were drawn in all patients, only finger-prick glucose and, if the patient was on anticoagulation or their anticoagulation status was unknown, international normalized ratio (INR) results were waited for before treatment decision; blood pressure was managed to achieve <185/110 mm Hg before tPA; the decision to treat with tPA was based on noncontrast CT whenever possible, with CT perfusion used to help decision-making in cases with diagnostic uncertainty (suspected stroke mimic) or unclear treatment risk-benefit ratio (e.g., mild or rapidly improving symptoms); imaging was interpreted by the stroke team without waiting for formal CT reports; and formal consent for treatment was not sought, although the patient or patient's relatives were involved in the decision when this was possible without

Table 1 Comparison of Helsinki and Royal Melbourne Hospital models

Step	Helsinki model	Existing RMH model	May 2012 additions to existing RMH model (estimated saved time per step)
Prenotification	Ambulance calls stroke consultant on mobile phone, who accepts patients, takes history, and alerts the team.	Ambulance calls hospital ED over open-air radio. Once ED has assessed patient, a "code stroke" page is sent to stroke team.	ED pages stroke team on receiving ambulance call—stroke team present on patient arrival (5–10 min saved). Stroke team calls ambulance dispatch center for patient details during transport (no time saved, allows for steps below).
Medical history	Electronic province-wide PACS since 2002. Electronic lab and patient records with limited access to GP text. GP never called.	Electronic local lab and PACS since 2007. Paper records. GP sometimes called to obtain detailed history.	When available, history, lab, and imaging evaluated and GP called before patient arrival (5 min).
Registration and CT request	Unique personal identification number at birth, used in all public and private systems. Patient registration and CT request electronically before patient arrival.	Noncentralized records with unique identifiers different for each hospital. CT requests only after patient had arrived and was registered in local hospital system.	Registration done before arrival to retrieve existing record or generate new record based on name and date of birth. CT request form prefilled (3 min).
Labs	Preordered blood tests for all tPA candidates. Blood samples always drawn before tPA by lab nurse. POC-INR, glucose available at tPA decision.	Routine blood samples often drawn after tPA initiation. Capillary glucose before tPA. Only wait for INR in known and suspected anticoagulated patients.	POC-INR available since 11/2012 (60 min in anticoagulated patients).
IV line	Ambulance always inserts large-bore antecubital cannula during transport.	IV access often available on arrival, otherwise inserted in ED.	IV access often available on arrival, otherwise inserted on CT table.
Straight to CT	Patients go straight to CT on ambulance stretchers.		Patients go straight to CT on ambulance stretchers (10 min).
tPA on CT table	tPA can be initiated on CT table, but usually in adjacent room where the drug is kept.		tPA and infusion kit brought to CT room beforehand. Bolus and infusion initiated on CT table (3 min).

Abbreviations: ED = emergency department; GP = general practice; PACS = picture archiving and communication system; POC-INR = point-of-care international normalized ratio; RMH = Royal Melbourne Hospital; tPA = tissue plasminogen activator.

incurring delay. In Melbourne, we only mixed the tPA after a treatment decision and did not insert urinary catheters before treatment.

Statistical analysis. Because of the nonnormal distribution of age, NIH Stroke Scale scores, and all treatment delays, data are presented as median and interquartile range, grouped by year for demonstration of trends in time. Mean and SD are given for the most recent data, to allow comparisons with other series. Groups were compared with the independent samples Mann-Whitney *U* or Kruskal-Wallis tests, with statistical significance set at 0.05 (2-sided). Analyses were performed using IBM SPSS 20 software (IBM Corp., Armonk, NY).

RESULTS

Numbers of patients and treatment characteristics. Before the new model, from 2003 to 2011, a total of 400 acute ischemic stroke patients had been treated with tPA at our hospital. An additional 48 patients were treated from May to December 2012 after the new direct-to-CT thrombolysis model (table 2). Over the years, there was a trend toward treating older patients ($p = 0.003$), with no change in stroke severity ($p = 0.135$). Both the use of advanced imaging and post-tPA intra-arterial interventions increased over the years (table 2).

The thrombolysis rate among all ischemic stroke patients admitted to our hospital increased from approximately 5% in 2003–2005 to 10% in 2007–2008, then 18% (82/468) in 2011, and 15% (47/324) in 2012.

From 2003 to 2011, we treated 8 of 400 patients (2.0%) who turned out to have stroke mimics after full workup (6 functional, 1 migraine, 1 epileptic). In 2012, the rate was unchanged with 1 stroke mimic (pulmonary sepsis, treated out-of-hours) of 48 total thrombolysis treatments (2.1%).

The complication of symptomatic intracerebral hemorrhage occurred in 15 of 400 patients (3.8%) between 2003 and 2011 and 1 of 48 patients (2.1%) in 2012.

Door-to-needle times. Treatment delays gradually diminished from year to year, with a significant decrease after the implementation of the new protocol (figure 1). The median (interquartile range) DNT time was 61 (43–75) minutes in 2011, down to 46 (24–79) minutes ($p = 0.040$) in 2012. All of the effect came from the change in the in-hours DNT, down from 43 (33–59) to 25 (19–48) minutes ($p = 0.009$). Out-of-hours delays remained unchanged, from 67 (55–82) to 62 (44–95) minutes ($p = 0.835$). In 2012, the proportion of patients treated within 60 minutes of arrival was 80% in-hours, 48% out-of-hours, and 65% overall. CT angiography was available from 2007 and CT perfusion imaging was introduced in 2009. Multimodal CT was initially associated with DNT delays, but not beyond 2010, suggesting a "learning curve" (figure 2).

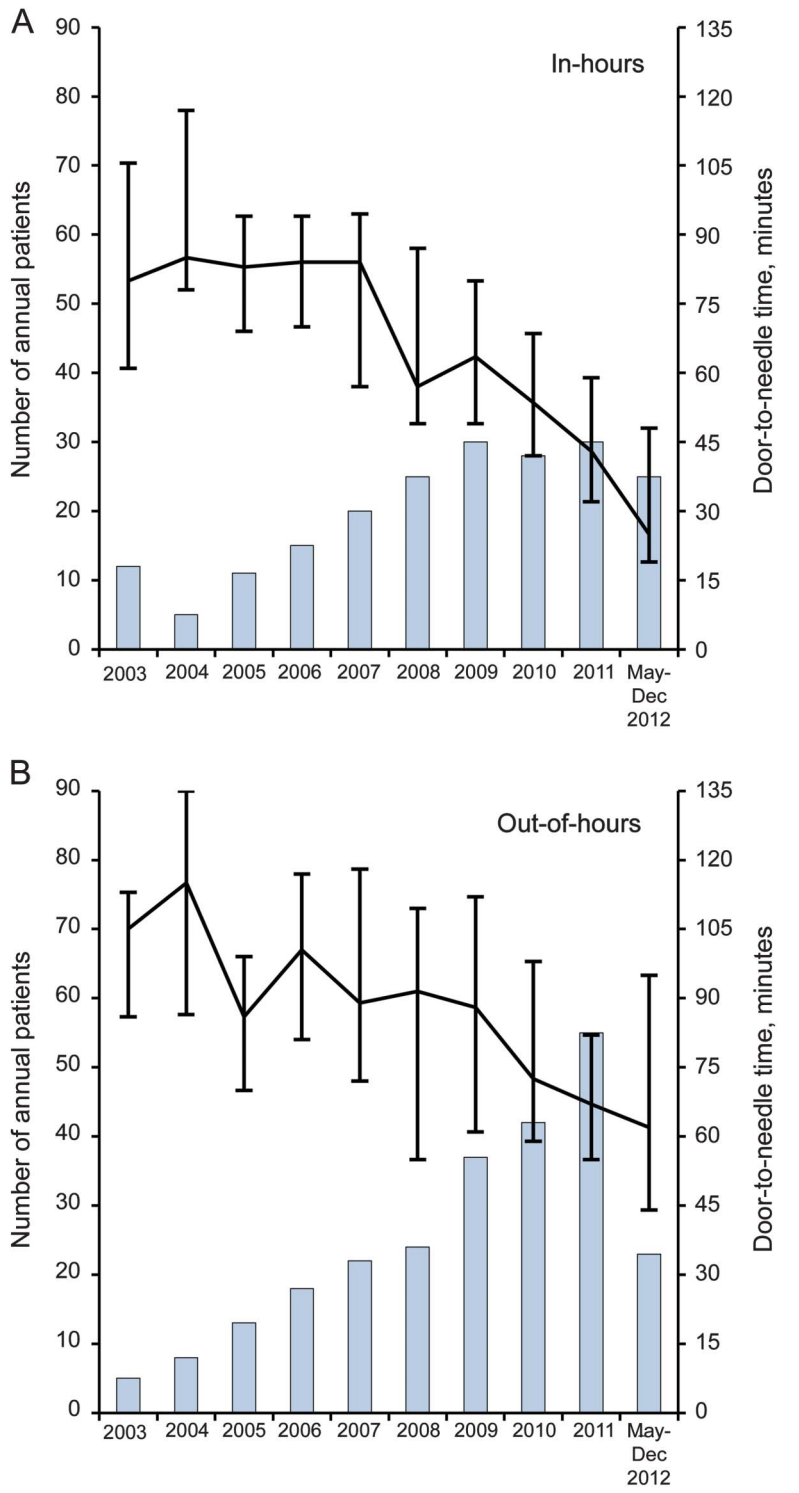
Onset-to-treatment times. The prehospital delay from stroke symptoms to hospital door remained unchanged, at median 77 (53–113) minutes in 2011 and 73 (50–108) minutes in 2012. The overall delay from onset to thrombolysis (OTT) decreased from 140 minutes in 2011 to 115 minutes in 2012 (figure 3). In 2012, there was a marked difference between in-hours (104 [88–155] minutes) and out-of-hours (165 [110–205] minutes) OTT times. In 2012, the mean ± SD in minutes DNT was 40 ± 31 in-hours, 72 ± 34 out-of-hours, and 55 ± 36 overall, and the OTT

Table 2 Baseline characteristics, imaging, and intra-arterial interventions of patients treated with IV thrombolytic therapy for acute ischemic stroke at the Royal Melbourne Hospital

Year	No.	Age, y	NIHSS at treatment decision	Patients with CT angiography or perfusion imaging[a] before therapy	Intra-arterial intervention after thrombolysis
2003	17	67 (56-75)	11 (7-18)	0	0
2004	13	72 (70-76)	13 (9-18)	0	0
2005	24	69 (58-80)	16 (11-19)	0	0
2006	33	68 (58-76)	14 (9-17)	0	0
2007	42	62 (49-74)	13 (11-18)	2 (5)	2 (5)
2008	49	70 (63-77)	15 (10-18)	10 (20)	4 (8)
2009	67	73 (59-80)	12 (7-17)	49 (73)	5 (7)
2010	70	72 (62-80)	13 (6-18)	53 (76)	10 (14)
2011	85	73 (65-80)	11 (7-19)	64 (75)	14 (16)
2012[b]	48	77 (66-85)	12 (5-18)	41 (85)	10 (21)
Total	448	72 (61-79)	12 (7-18)	219 (49)	45 (10)

Abbreviation: NIHSS = NIH Stroke Scale.
All values are median (interquartile range) or n (%).
[a] CT perfusion introduced in 2009 (total n = 183).
[b] Data for 8 months (May to December) after implementation of the new thrombolysis protocol.

Figure 1 Number of annually treated patients and median door-to-needle times



Annual patients (bars, left axis) and median door-to-needle times with interquartile range (line, right axis) in-hours (A) (8 AM to 5 PM Monday–Friday) and out-of-hours (B). Total n = 448. Data for year 2012 are for the last 8 months, after the protocol change.

was 121 ± 60 in-hours, 158 ± 58 out-of-hours, and 139 ± 61 overall.

DISCUSSION In only 4 months, we were able to plan and implement a new thrombolysis protocol that cut our median in-hours DNTs from 43 to 25 minutes. Importantly, this more-streamlined service was achieved without any additional costs or reduction in diagnostic quality. We demonstrated rapid transferability of this tPA model across different health care settings.

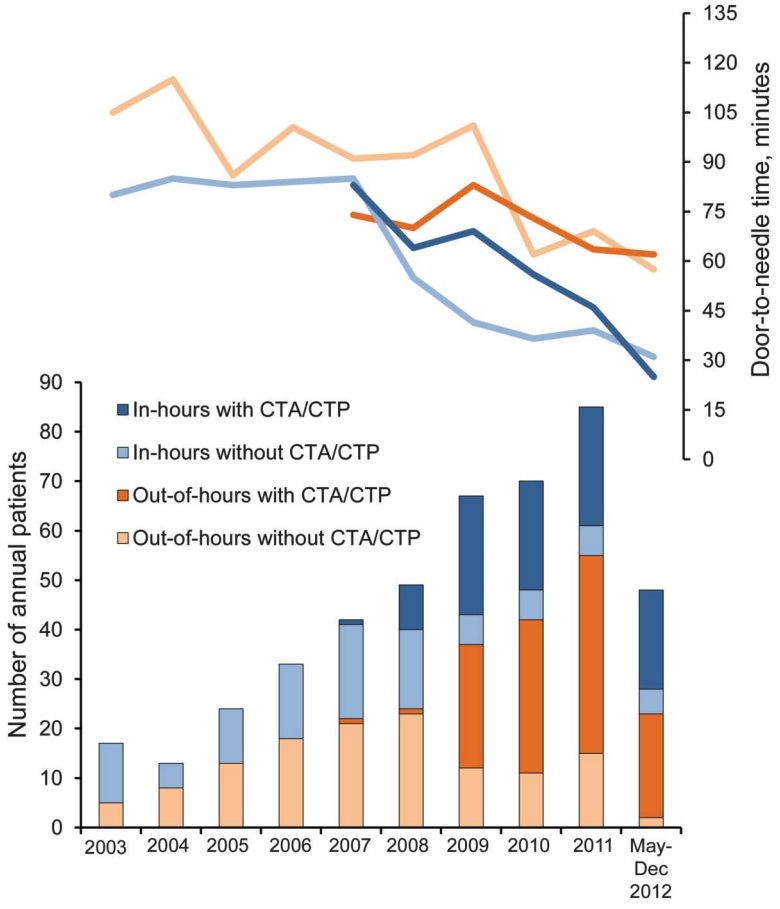
Several interventions are known to reduce thrombolysis delays.[1,6] A "code stroke" from the ED helps alert the stroke team,[7] but is often activated only after ED triage whereas notification before patient arrival would be more effective in reducing tPA delays.[6,8,9] However, prenotification alone does not allow for optimal preparation if patient details are not available. To make good use of the prenotification, the stroke team needs to know who is coming. Only then can they perform registration, prepare CT requests, access history and tests, and even call the patient's general practitioner. Getting the details of our patients has not been optimal, because ambulance communication is still via open-air radio and concerns regarding patient confidentiality have limited disclosure of personal details. The ambulance call center currently provides us with the details but a direct line with the personnel on-site would be more efficient.

While multimodal CT including perfusion and angiography was used in one-third of tPA cases in Helsinki and when used produced additional delays of 20 minutes, at the Royal Melbourne Hospital, >80% of patients had multimodal imaging and no extra delays were evident after a brief initial learning curve. The main factor that may be responsible for this difference is that image processing is performed immediately at the scanner terminal by the stroke team in Melbourne rather than waiting for radiology personnel to process and interpret the results as occurs in Helsinki. Also, in Melbourne, the treatment was often started before the multimodal imaging.

Optimal reduction in delays is not achievable by any single intervention, but rather results from the continuous analysis and improvement of the system as a whole,[6,10,11] as was shown already during the original National Institute of Neurological Disorders and Stroke trial.[12] A large American Heart Association/American Stroke Association initiative is systematically implementing a set of interventions to reduce DNT.[6] However, one component of the Helsinki model, going direct from ED triage to CT, is not part of that initiative. As in Helsinki, we found this "direct-to-CT" step to be the one in which the largest gains were made, and had no interference with regular CT operations from front-loading the imaging.

Not all of the components of our new model could be implemented simultaneously. We observed laboratory-related delays of approximately 60 minutes in many patients who were receiving anticoagulation therapy, and point-of-care INR tests were known to reduce these

Figure 2 Advanced imaging and in-hospital delays



Number of patients with and without either CT angiography (CTA) or CT perfusion (CTP) imaging and median door-to-needle times in patients treated with and without CTA/CTP.

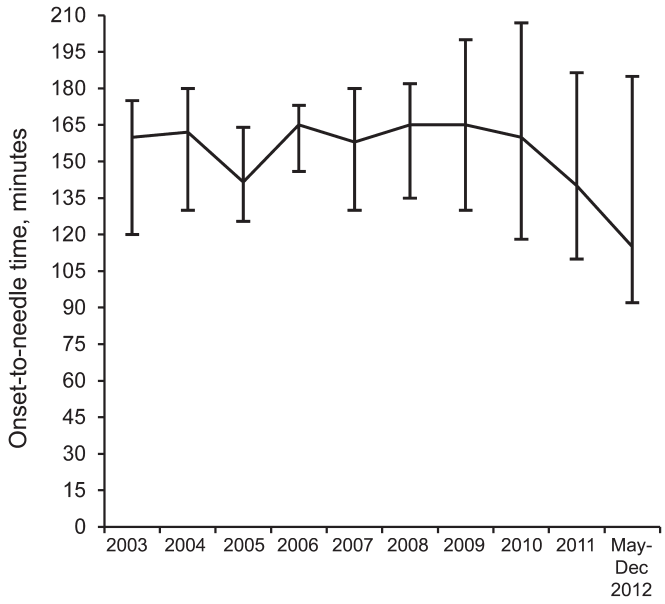
delays in Helsinki and elsewhere.[13] Still, procuring the device, followed by a thorough quality-assurance process in partnership with the Pathology Department took time; point-of-care INR testing was in use from November 2012 onward and was used pre-tPA in one patient (the resulting DNT of 14 minutes was the fastest in our series). The only remaining patients with extended delays after that were either those with in-hospital strokes (with no benefit of prenotification and increased CT transport time) or patients in whom ambulance and ED triage had failed to initially recognize stroke symptoms.

Being faster could potentially come at a cost on diagnostic quality. Importantly, our faster treatment protocol did not result in any misdiagnoses, as we had none during "office hours" with the new model. Overall, stroke mimic rates throughout the years have been low in Helsinki (1.4%)[14] and the Royal Melbourne Hospital (2.0%). This could be explained at both sites by a stroke consultant physically evaluating the patient and taking the history. At the Royal Melbourne Hospital, 6 of the 9 misdiagnoses over the years were "after hours," and 5 of these were functional stroke mimics where the diagnosis relies heavily on the expertise of the doctor performing the physical examination. Many other models around the world rely on phone consultations, which could partially explain higher mimic rates of up to 14%.[11,14]

On average, US centers treat 27% of their patients within 60 minutes of arrival, compared with 65% in our center.[15] To achieve the Helsinki rate of 94%, our out-of-hours service has to be improved; this is the next goal at the Royal Melbourne Hospital. Because we do not have any member of the stroke team in the hospital out-of-hours, significant delays currently stem from the need to call personnel in. Phone consultations have recently become more feasible with smart-phone PACS (picture archiving and communication system) access from late 2012. Telemedicine to allow seeing the patients is being assessed. Sufficiently skilled personnel on-site 24/7 would require a more centralized stroke service. The centralized system in Helsinki provides the same DNTs out-of-hours as in-hours.[16]

Our study has limitations. First, in a before-after setting, there is always a possibility that the observed changes had an external cause outside of the model being analyzed. In our series, this is unlikely because the stroke services remained otherwise unchanged. Our tPA protocol was identical from 2007 to 2011 with an average annual 14% decrease in median DNT because of a learning effect, compared with the 42% decrease in 2012 with the new protocol (figure 1). Second, because the individual steps of the model are dependent on each other, we cannot dissect the exact benefit of each protocol component. The experience of the team was that going direct to CT was the step in which most gains were made. Third, we do not have data on how many patients went direct to CT but were not given tPA. There was an initial concern that the CT would be prioritized unnecessarily for patients who would not eventually receive tPA. However, the treatment of all ischemic and hemorrhagic stroke patients benefited from faster diagnoses and most stroke mimics would have needed a CT in any case. Fourth, even though we demonstrated the rapid transferability of the Helsinki model to our system, some local elements such as the centralized ambulance service and an existing code stroke protocol did facilitate the process that could have otherwise been slower and more cumbersome. Lastly, although we demonstrated a marked decrease in our DNT in-hours when the whole stroke team was present, we have yet to expand this to out-of-hours. The options for achieving better coverage include a new roster with more on-site stroke personnel; calling the doctors in immediately on prenotification rather than awaiting assessment in emergency; or telemedicine consultations, with the latter being likely the most practical in our setting.

Figure 3 Onset-to-treatment times



Annual median onset-to-treatment times in minutes, with interquartile range.

To conclude, the Helsinki model of stroke thrombolysis, which includes prenotification with patient details to make good use of transportation time and going direct to CT on arrival, is applicable across different health care settings. In only 4 months, we were able to practically halve DNTs to a median of 25 minutes. Complicated theoretical frameworks are unnecessary with 2 common-sense rules of thumb: 1) do as much as possible before the patient arrives, and 2) do as little as possible after the patient has arrived. Similar results should be achievable elsewhere with the same principles.

AUTHOR CONTRIBUTIONS

Dr. Meretoja conceived the study, drafted the manuscript, and performed the statistical analyses. Ms. Weir, Dr. Truesdale, and Dr. Campbell coordinated the clinical practice change. Dr. Davis supervised and coordinated the study and obtained study funding. All authors acquired the data, analyzed and interpreted the data, and edited the manuscript for intellectual content.

STUDY FUNDING

Supported by the National Health and Medical Research Council of Australia (NHMRC) Centre for Research Excellence grant 1001216. The authors received additional support from Finnish Medical, Biomedicum Helsinki, and Sigrid Jusélius Foundations (A.M.), University of Melbourne, and Neurosciences Victoria (N.Y.), NHMRC Early Career Fellowship 1035688, Heart Foundation of Australia, National Stroke Foundation, and Cardiovascular Lipid Australia (B.C.V.C), and The Royal Melbourne Hospital Neurosciences Foundation (N.Y., B.C.V.C).

DISCLOSURE

M. Meretoja, L. Weir, M. Ugalde, and N. Yassi report no disclosures. B. Yan has received speaker's honoraria from Boehringer Ingelheim. P. Hand and M. Truesdale report no disclosures. S. Davis has received speaker's honoraria from Sanofi, Boehringer Ingelheim, Ever Neuro Pharma, and Allergan and has consulted for Boehringer Ingelheim, Ever Neuro Pharma, and Allergan. B. Campbell has received speaker's honoraria from Novartis and Boehringer Ingelheim and has consulted for Lundbeck. Go to Neurology.org for full disclosures.

Received February 18, 2013. Accepted in final form June 17, 2013.

REFERENCES

1. Meretoja A, Kaste M. Pre- and in-hospital intersection of stroke care. Ann NY Acad Sci 2012;1268:145–151.
2. Lees KR, Bluhmki E, von Kummer R, 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;375:1695–1703.
3. 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.
4. Strbian D, Sairanen T, Meretoja A, et al. Patient outcomes from symptomatic intracerebral hemorrhage after stroke thrombolysis. Neurology 2011;77:341–348.
5. Tai YJ, Weir L, Hand P, Davis S, Yan B. Does a 'code stroke' rapid access protocol decrease door-to-needle time for thrombolysis? Intern Med J 2012;42:1316–1324.
6. Fonarow GC, Smith EE, Saver JL, et al. Improving door-to-needle times in acute ischemic stroke: the design and rationale for the American Heart Association/American Stroke Association's target: stroke initiative. Stroke 2011;42:2983–2989.
7. Gomez CR, Malkoff MD, Sauer CM, Tulyapronchote R, Burch CM, Banet GA. Code stroke: an attempt to shorten inhospital therapeutic delays. Stroke 1994;25:1920–1923.
8. Belvis R, Cocho D, Marti-Fabregas J, et al. Benefits of a prehospital stroke code system: feasibility and efficacy in the first year of clinical practice in Barcelona, Spain. Cerebrovasc Dis 2005;19:96–101.
9. Lin CB, Peterson ED, Smith EE, et al. Emergency medical service hospital prenotification is associated with improved evaluation and treatment of acute ischemic stroke. Circ Cardiovasc Qual Outcomes 2012;5:514–522.
10. Kohrmann M, Schellinger PD, Breuer L, et al. Avoiding in hospital delays and eliminating the three-hour effect in thrombolysis for stroke. Int J Stroke 2011;6:493–497.
11. Ford AL, Williams JA, Spencer M, et al. Reducing door-to-needle times using Toyota's lean manufacturing principles and value stream analysis. Stroke 2012;43:3395–3398.
12. Tilley BC, Lyden PD, Brott TG, Lu M, Levine SR, Welch KM. Total quality improvement method for reduction of delays between emergency department admission and treatment of acute ischemic stroke. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Arch Neurol 1997;54:1466–1474.
13. Rizos T, Herweh C, Jenetzky E, et al. Point-of-care international normalized ratio testing accelerates thrombolysis in patients with acute ischemic stroke using oral anticoagulants. Stroke 2009;40:3547–3551.
14. Artto V, Putaala J, Strbian D, et al. Stroke mimics and intravenous thrombolysis. Ann Emerg Med 2012;59:27–32.
15. Fonarow GC, Smith EE, Saver JL, et al. Timeliness of tissue-type plasminogen activator therapy in acute ischemic stroke: patient characteristics, hospital factors, and outcomes associated with door-to-needle times within 60 minutes. Circulation 2011;123:750–758.
16. Curtze S, Meretoja A, Mustanoja S, et al. Does time of day or physician experience affect outcome of acute ischemic stroke patients treated with thrombolysis? A study from Finland. Int J Stroke 2012;7:511–516.