



THE CEYLON MEDICAL JOURNAL

Established 1887

The Official Publication of the
Sri Lanka Medical Association

Volume 65, No. 1&2, June 2020

Quarterly ISSN 0009-0875

Editors Emeritus

Chris G Uragoda MD, FRCP
Colvin Goonaratna FRCP, PhD
Janaka de Silva DPhil, FRCP
Anuruddha Abeygunasekera MS, FRCS

Editors

Senaka Rajapakse MD, FRCP
A Pathmeswaran MBBS, MD

Section Editors

B J C Perera MD, FRCPCH
Shalini Sri Ranganathan MD, PhD

Assistant Editors

Carukshi Arambepola MBBS, MD
Ajith de Silva Nagahawatte MBBS, MD
Tiran Dias MD, MRCP
Ranil Fernando FRCS, PhD
Raveen Hanwella MBBS, MD
Renuka Jayatissa MD, MSc
Sarath Lekamwasam MD, PhD
Udaya K Ranawaka MD, FRCP
Sachith Mettananda MBBS, MD
Shamini Prathapan MBBS, MD

International Advisory Board

S Arulkumaran FRCP, PhD
London, UK

Zulfiqar Ahmed Bhutta FRCPCH, PhD
Karachi, Pakistan

Andrew Dawson FRACP
Sydney, Australia

Barbara Gastel MD, MPH
Texas, USA

Kalle Hoppu MD, PhD
Helsinki, Finland

David Lallo MD, FRCP
Liverpool, UK

Ian Pearce MBBS, FRCS
Manchester, UK

Peush Sahni MS, PhD
New Delhi, India

Anita KM Zaidi MBBS, SM

Transient ischaemic attacks: It's time for timely action!

DOI: <http://doi.org/10.4038/cmj.v65i1-2.9130>

Ceylon Medical Journal 2020; **65**: 5-8

Transient ischaemic attack (TIA) is now defined as a transient episode of neurological dysfunction caused by central nervous system ischemia without acute infarction [1]. This tissue-based definition with a focus on the absence of infarction has replaced the previous time-based definition. The new definition highlights the importance of TIA as an opportunity for stroke prevention, similar to the importance of urgent treatment of unstable angina in preventing the tissue death of myocardial infarction. TIA is a major warning of an impending stroke; 15-30% of ischaemic strokes are preceded by TIAs [2-6]. The risk of stroke is highest in the immediate period following an index TIA, with 42% of all strokes during the 30 days after a first TIA occurring within the first 24 hours [6-8]. Therefore, optimal management of the first 24 hours following a TIA is critical in preventing a stroke.

Early assessment and treatment of TIA have been shown to reduce recurrent stroke risk significantly. The EXPRESS study (Effect of urgent treatment of transient ischemic attack and minor stroke on the early recurrent stroke) showed a reduction of recurrent stroke risk by 80% at 90 days following an index TIA with urgent assessment and treatment using available medications. The study compared two different approaches to the management of patients with TIA and minor stroke over two time periods (phases 1 and 2). Both phases used the same treatment protocols, with the only difference being that patients in Phase 2 received more urgent assessment and treatment [9]. The median delay from symptom onset to assessment was 3 (IQR 2-5) days in phase 1 and 1 (0-3) day in phase 2. The median delay from assessment to initiation of medications, mainly aspirin, was 20 (8-53) days in phase 1 (started at primary care) and 1 (0-3) day in phase 2 (started at a TIA clinic). This intervention showed a reduction in the 90-day risk of recurrent stroke from 10.3% in phase 1 to 2.1% in phase 2. Similarly, the establishment of a hospital clinic with 24-hour access for TIAs (SOS-TIA Paris) reported a reduction of predicted 90-day stroke rate from 6.0% to 1.2% [10]. A systematic review which studied early stroke risk following TIA again highlighted the benefits of emergent management of TIAs [11]. Among 10126 TIA patients studied in 18 independent cohorts, the 7-day stroke risk following TIA was 0.9% in studies with emergency treatment, compared to 11.0% in population-based studies without urgent treatment. These studies emphasized the importance of treating TIA as an emergency way back in 2008 [12], and led to the implementation of emergency TIA clinics in many developed countries.



This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

The TIA registry.org project, which prospectively studied TIAs or minor strokes from 2009 through 2011 after the establishment of dedicated TIA clinics, reported lower stroke rates (3.7% at 90 days and 5.1% at 1 year) [13] and lower risk of all cardiovascular events (6.4% at 5 years) [14]. These data highlight the importance of urgent assessment and treatment of TIA as a medical emergency [15].

Several scoring systems were traditionally used for risk stratification of TIAs to guide patient selection for early treatment [16-20]. However, more recent evidence suggested that clinical risk scores alone without additional data on cerebral and carotid imaging were poor at discriminating low from high-risk TIAs. A systematic review and meta-analysis of all TIA studies published between 2005 and 2014 reported that the widely used ABCD2 score had high sensitivity (86.7%) but poor specificity (35.4%) in predicting recurrent stroke risk [21]. Further, it was noted that only 66% of true TIAs had an ABCD2 score ≥ 4 (indicating moderate to high risk). Patients with an ABCD2 score < 4 (low risk), 20% had a major risk factor for stroke ($> 50\%$ carotid stenosis or atrial fibrillation), and 35-41% were TIA mimics needing different pathways of management [21]. The current National Institute for Health and Care Excellence (NICE) guideline (2019) recommends not to risk stratify patients using scoring systems and to arrange all patients to be evaluated by a specialist within 24 hours [22].

Early assessment and treatment of TIA depend on the urgency of patients seeking medical assistance, and this in turn is dependent on public awareness [23-26]. However, studies from many countries have shown that awareness of TIAs is low among patients and the public. A population-based study in Oxford, UK found that 70% of patients did not recognize their TIA or minor stroke, 30% delayed seeking medical attention for > 24 hours, and 30% of recurrent strokes occurred before seeking medical attention [25]. Another survey of over 2,000 members of the public in the UK revealed that 68% had never heard of TIA, 68% did not recognize symptoms of a TIA, 74% would not seek emergency medical help even if TIA was recognized, and 40% were unaware that a TIA was a warning sign of a major stroke [27]. In a Dutch study, only 33% of patients interpreted their symptoms as a medical emergency, and less than half had correct general knowledge about TIA [25]. A study of a Swiss urban community reported only a third would seek immediate medical help following a TIA [27]. In a qualitative study in the UK, only four out of 20 patients were able to identify symptoms as that of a TIA [26], and in an internet-based survey among 11,121 Japanese individuals, only 22% would consider an immediate visit to a hospital in a TIA [28]. Timely management of TIA also depends on the urgency shown by treating physicians in evaluation and treatment, and this is influenced by their knowledge of symptom recognition and management. A study in Switzerland showed that knowledge of TIA was poor

among general practitioners and hospital physicians, and only 38% referred patients for emergency assessment [29]. More than 40% of French general practitioners and emergency department physicians were unaware of the current TIA definition, and more than one third were unaware of the relevant national guidelines [30]. Clearly, improving awareness at many levels is a key factor in ensuring the timely delivery of optimal care in TIA.

TIA in Sri Lanka: where are we, and what can we do?

Stroke is the fourth leading cause of hospital mortality and causes significant morbidity in Sri Lanka [31]. Its contribution to the health burden of Sri Lanka is increasing with the ongoing demographic and epidemiological transition leading to an increasingly ageing population. The proportion of Sri Lankans over 60 years is predicted to double by 2040 [32]. However, acute treatment options such as stroke units, thrombolysis, and endovascular treatment are not widely available in Sri Lanka (33). Therefore, prevention is the best way to minimize the burden of stroke.

There are many things we can do to improve the management of TIAs and to minimize stroke risk in the Sri Lankan setting. Educating the public on recognition of TIA symptoms and on the importance of seeking urgent medical treatment is of paramount importance. There is no data currently available on awareness of TIAs in Sri Lankan patients or the public. Previous studies have shown low levels of awareness of stroke among stroke victims, patients at high risk of stroke, and in the community [34, 35], and it is likely that awareness on TIA is similarly low. Awareness of diagnosis and emergency management of TIAs among first contact Sri Lankan doctors is inadequate [20], and efforts should be made to update their knowledge of TIAs and the need for timely referral of patients for specialist opinion. They should also be made aware that immediate initiation of aspirin is recommended to all suspected cases unless contraindicated even without brain imaging, as the benefits outweigh the risks of haemorrhage [15, 22].

The other key step is the establishment of fast track clinics for rapid assessment and management of TIAs, based on the experience of many developed countries. Resources needed for such clinics, especially for emergent evaluation (such as CT/ MRI scanning, carotid vascular imaging, ECG, 2D Echocardiography and risk factor assessment) are not readily available in most Sri Lankan hospitals. However, innovative mechanisms such as assessing all TIAs within 24 hours by an on-call medical team or referral to a routine medical clinic on the given day would be feasible and unlikely to pose a significant added burden. Arranging relevant brain imaging after proper assessment by a specialist will reduce the number of brain scans done, leading to significant cost savings in addition

to preventing patient exposure to unnecessary radiation. Negotiating with radiology departments for dedicated MRI and carotid doppler slots for TIAs will help in meeting timelines for optimal TIA management.

Implementation of current international guidelines is likely to be challenging with the limited resources at our disposal. However, a collaborative approach and restructuring of existing facilities would enable us to develop acute TIA care pathways in our hospitals to minimize the risk of stroke and the resultant death and disability.

References

1. Easton JD, Saver JL, Albers GW, Alberts MJ, Chaturvedi S, Feldmann E, *et al.* Definition and evaluation of transient ischemic attack. *Stroke* 2009; **40**(6): 2276-93.
2. Rothwell PM, Coull AJ, Giles MF, Howard SC, Silver LE, Bull LM, *et al.* Change in stroke incidence, mortality, case-fatality, severity, and risk factors in Oxfordshire, UK from 1981 to 2004 (Oxford Vascular Study). *Lancet* 2004; **363**(9425): 1925-33.
3. Bamford J, Sandercock P, Dennis M, Burn J, Warlow C. A prospective study of acute cerebrovascular disease in the community: the Oxfordshire Community Stroke Project-1981-86. 2. Incidence, case fatality rates and overall outcome at one year of cerebral infarction, primary intracerebral and subarachnoid haemorrhage. *J Neurol Neurosurg Psychiatry* 1990; **53**(1): 16-22.
4. Farrell B, Godwin J, Richards S, Warlow C. The United Kingdom transient ischaemic attack (UK-TIA) aspirin trial: final results. *J Neurol Neurosurg Psychiatry* 1991; **54**(12): 1044-54.
5. Group ECSTC. A randomized trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). *Lancet* 1998; **351**(9113): 1379-87.
6. Rothwell PMW. C. P. Timing of TIAs preceding stroke: time window for prevention is very short. *Neurology* 2005; **64**(5): 817-20.
7. Chandratheva A, Mehta Z, Geraghty OC, Marquardt L, Rothwell PM. Population-based study of risk and predictors of stroke in the first few hours after a TIA. *Neurology* 2009; **72**(22): 1941-7.
8. Johnston SC, Gress DR, Browner WS, Sidney S. Short-term prognosis after emergency department diagnosis of TIA. *JAMA* 2000; **284**(22): 2901-6.
9. Rothwell PM, Giles MF, Chandratheva A, Marquardt L, Geraghty O, Redgrave JNE, *et al.* Effect of urgent treatment of transient ischaemic attack and minor stroke on early recurrent stroke (EXPRESS study): a prospective population-based sequential comparison. *The Lancet* 2007; **370**(9596): 1432-42.
10. Lavallee PC, Meseguer E, Abboud H, Cabrejo L, Olivot JM, Simon O, *et al.* A transient ischaemic attack clinic with round-the-clock access (SOS-TIA): feasibility and effects. *The Lancet Neurology* 2007; **6**(11): 953-60.
11. Giles MF, Rothwell PM. Risk of stroke early after transient ischaemic attack: a systematic review and meta-analysis. *The Lancet Neurology* 2007; **6**(12): 1063-72.
12. Amarenco P, Benavente O. EXPRESS Transient Ischemic Attack Study. *Stroke* 2008; **39**(8): 2400-1.
13. Amarenco PL, Philippa C, Labreuche, Albers, Gregory W Bornstein, Natan M. Canhão, Patrícia Caplan, Louis R Donnan, Geoffrey A, Ferro JM, Hennerici MG, Molina C, Rothwell PM, Sissani L, *et al.* One-Year Risk of Stroke after Transient Ischemic Attack or Minor Stroke. *New England Journal of Medicine* 2016; **374**(16): 1533-42.
14. Amarenco P, Lavallée PC, Monteiro Tavares L, Labreuche J, Albers GW, Abboud H, *et al.* Five-Year Risk of Stroke after TIA or Minor Ischemic Stroke. *New England Journal of Medicine* 2018; **378**(23): 2182-90.
15. Rothwell PM, Algra A, Chen Z, Diener HC, Norrving B, Mehta Z. Effects of aspirin on risk and severity of early recurrent stroke after transient ischaemic attack and ischaemic stroke: time-course analysis of randomized trials. *Lancet* 2016; **388**(10042): 365-75.
16. Rothwell PMG, Flossmann MF, Lovelock E, Redgrave CE, Warlow JN, Mehta CP, Z. A simple score (ABCD) to identify individuals at high early risk of stroke after transient ischaemic attack. *Lancet* 2005; **366**(9479): 29-36.
17. Johnston SC, Rothwell PM, Nguyen-Huynh MN, Giles MF, Elkins JS, Bernstein AL, *et al.* Validation and refinement of scores to predict very early stroke risk after transient ischaemic attack. *Lancet* 2007; **369**(9558): 283-92.
18. Giles MF, Albers GW, Amarenco P, Arsava MM, Asimos A, Ay H, *et al.* Addition of brain infarction to the ABCD2 Score (ABCD2I): a collaborative analysis of unpublished data on 4574 patients. *Stroke* 2010; **41**(9): 1907-13.
19. Merwick A, Albers GW, Amarenco P, Arsava EM, Ay H, Calvet D, *et al.* Addition of brain and carotid imaging to the ABCD(2) score to identify patients at early risk of stroke after transient ischaemic attack: a multicentre observational study. *The Lancet Neurology* 2010; **9**(11): 1060-9.
20. Kelly PJ, Albers GW, Chatzikonstantinou A, De Marchis GM, Ferrari J, George P, *et al.* Validation and comparison of imaging-based scores for prediction of early stroke risk after transient ischaemic attack: a pooled analysis of individual patient data from cohort studies. *The Lancet Neurology* 2016; **15**(12): 1238-47.
21. Wardlaw JM, Brazzelli M, Chappell FM, Miranda H, Shuler K, Sandercock PAG, *et al.* ABCD2 score and secondary stroke prevention: meta-analysis and effect per 1,000 patients triaged. *Neurology* 2015; **85**(4): 373-80.
22. NICE. Stroke and transient ischaemic attack in over 16s: diagnosis and initial management 2019 May 2019.
23. Hachinski V. Awareness: the first step to action. *Stroke* 2002; **33**(5): 1173.
24. Mandelzweig L, Goldbourt U, Boyko V, Tanne D. Perceptual, social, and behavioral factors associated with

- delays in seeking medical care in patients with symptoms of acute stroke. *Stroke* 2006; 37(5): 1248-53.
25. Dolmans LS, Hoes AW, Bartelink MEL, Kappelle LJ, Rutten FH. Determinants of Patient Delay in Transient Ischemic Attack. *Eur Neurol*. 2019; **81**(3-4): 139-44.
 26. Mc Sharry J, Baxter A, Wallace LM, Kenton A, Turner A, French DP. Delay in seeking medical help following Transient Ischemic Attack (TIA) or “mini-stroke”: a qualitative study. *PLoS One* 2014; **9**(8): e104434.
 27. ICM Research survey on a random sample of 2,009 adults in GB October 2012.
 28. Akiyama H, Hasegawa Y. Knowledge of transient ischemic attack among the Japanese. *Journal of Stroke and Cerebrovascular Diseases* 2013; **22**(4): 457-64.
 29. Streit S, Baumann P, Barth J, Mattle HP, Arnold M, Bassetti CL, et al. Awareness of Stroke Risk after TIA in Swiss General Practitioners and Hospital Physicians. *PLoS One* 2015; **10**(8): e0135885-e.
 30. Massengo SA, Cisse M, Guiziou C, Leray E, Rajabally YA, Edan G. Knowledge of TIA among general practitioners and emergency department physicians. A questionnaire survey in a French semi-rural area. *Clin Neurol Neurosurg*. 2013; **115**(8): 1457-63.
 31. Medical Statistics Unit Ministry of Health, Nutrition, and Indigenous Medicine. Annual Health Bulletin – 2014, Sri Lanka. Colombo 2016.
 32. Michael Engelgau KO, Kumari Vinodhani Navaratne and Sundararajan Gopalan. Prevention and Control of Selected Chronic NCDs in Sri Lanka. Washington, DC 20433: World Bank; 2010.
 33. Ranawaka UK. Stroke Care in Sri Lanka: The Way We Were, the Way We Are, and the Way Forward. *Journal of Stroke Medicine* 2018; **1**(1): 45-50.
 34. Ranawaka UK, De Silva H, Balasuriya J, Puvanendiran S, Jayasekara B, Wijsekera JC. Stroke awareness in a Sri Lankan community. *Journal of the Ceylon College of Physicians* 2016; **47**(1): 31-35.
 35. Ranawaka U, Mettananda C, Thilakarathna C, Peiris A, Kasturiratna A, Tilakarathna Y. Stroke awareness in patients with incident stroke compared to patients without stroke or ischemic heart disease. *Journal of Stroke and Cerebrovascular Diseases* 2020; **29**: 104790

Chamila D Mettananda, Department of Pharmacology, Faculty of Medicine, University of Kelaniya, **Udaya K Ranawaka**, Department of Medicine, Faculty of Medicine, University of Kelaniya, Sri Lanka.

Correspondence: CDM, email: <chamila@kln.ac.lk>