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Academic Discussion

Comments on Asian Stroke Criteria☆●

Kavian Ghandehari

Department of Neurology, Ghaem Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad 91766-99199, Iran

Abstract: The Asian Stroke Criteria (ASC) was developed to detect etiology and topography of brain infarction. The ASC was designed by stroke neurologists and approved by the University of Alberta, Canada in 2003. In the first validation step, inter-rater reliability of ASC was evaluated. The inter-rater agreement, according to the ASC system, is much higher than other classifications with moderate inter-observer reliability. In the second validation step, ASC has been used successfully in Khorasan stroke registries.

Key Words: stroke; infarction; classification; etiology
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Kavian Ghandehari☆, M.D., FLSP. Professor of Cerebrovascular Disease, Department of Neurology, Ghaem Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad 91766-99199, Iran

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INTRODUCTION

Infarct subtypes have been used to determine reliance of clinical syndromes and co-existing risk factors. Advances in neurovascular imaging have improved clinical accuracy of ischemic stroke classification. Clinical impressions have been refined and supported by laboratory confirmation of infarct subtype. A complete diagnostic workup is required, because presenting clinical syndromes are typically not distinctive enough to infer the cause[1]. Because it is not always possible to determine a single mechanism, clinicians must keep in mind that multiple mechanisms might be simultaneously involved[2]. Patients might have two or more competing causes of cerebral ischemia[2]. Despite efforts to determine an etiological diagnosis, the cause of infarction may remain undetermined[1], possibly due to inappropriate workup or unwillingness of patient or physician to perform a complete workup[1]. Atheroembolisms and cardioembolisms can result in all sizes and locations of infarcts[1]. Clear examples of thrombotic or embolic small deep infarcts present as lacunar syndrome, because small emboli can occlude single perforating arteries, resulting in lacunar infarcts[3]. Based on these impressions, it is a mistake to define small artery disease as a subtype of ischemic stroke that characterizes lacunar infarcts[3]. The need for early differentiation of ischemic subtypes is important for thrombolysis therapy. Exclusion of patients with a high likelihood of spontaneous good functional recovery, such as lacunar infarct, or those less responsive to thrombolysis, such as patients with large artery thrombosis, as well as the selection of those with embolic occlusion of intracranial arteries, has become imperative in the classification of ischemic stroke[1]. All studies describing classification of brain infarction in Asia were sought. The following string of keywords was entered in Medline (OVID and PubMed), as well as Google, Proquest, Scopus, Cochrane Library, and ScienceDirect search engines: [Asia] and [Classification] and [Stroke] and [Criteria], with the final search performed on August 24, 2009. Surprisingly, no other Asian classification was determined for ischemic stroke. The Asian Stroke Criteria (ASC) has been developed as an academic tool to categorize brain infarction in Asia.

ASC DEVELOPMENT

Various classification criteria of brain infarct have been used in clinical trials and stroke registries. The ASC was designed for clinical practice. The correct identification of the cause of stroke is critical for research and clinical practice. Various mechanistic and syndromic systems have been developed to subtype ischemic stroke. In mechanistic classification systems, physicians classify

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Corresponding author: Kavian Ghandehari, M.D., FLSP. Professor of Cerebrovascular Disease, Department of Neurology, Ghaem Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad 91766-99199, Iran
E-mail: kavianghandehari@yahoo.com; Ghandeharik@mums.ac.ir

subtypes through a process of assigning guilt by association[4]. Syndromic subtyping systems rely on physicians recognizing patterns in the history and physical examination[5]. Many ischemic stroke subtyping systems have been developed for use in randomized clinical trials or epidemiological studies[4-5]. Each stroke subtyping system has some limitations and advantages. Presumed stroke subtype diagnosis guides both clinical evaluation and treatment decisions. Most classifications were developed for specific research projects in specialist institutions, which is much different from routine clinical practice. The ASC was designed for clinical practice in tertiary care hospitals, with and without stroke neurologists and magnetic resonance imaging (MRI) facilities. It was designed by stroke neurologists, and was approved by the University of Alberta, Canada in 2003. Topographic and etiologic classification of brain infarction, based on the ASC, is presented in Table 1.

VALIDATION OF ASC

Validation of ASC included two steps. In the first validation step, inter-rater reliability of ASC was evaluated[6]. In a total of 302 stroke patients, 20 patients (9 males, 11 females) were randomly selected. All patients underwent a standard battery of diagnostic investigation for stroke etiology and topography[6]. Two stroke neurologists and a general practitioner independently reviewed data from each randomly selected patient, and the patients were classified according to the ASC of stroke topography and etiology. Degrees of inter-rater reliability were measured using simple percentage of agreement and un-weighted *k* statistics. The three inter-rater agreement for topographic subtyping of patients was 0.95%; $k = 0.915$ (0.662–1), $P < 0.000\ 1$, and etiology diagnosis was 0.90 %; $k = 0.902\ 2$ (0.753–1), $P < 0.000\ 1$. Stroke neurologists were in agreement with topographic diagnosis for all 20 cases (100%; $k = 1$; 95% confidence interval, 1.0 to 1.0; $P < 0.000\ 1$)[6]. The general practitioner arrived at the same topographical diagnosis for 19 of the 20 cases (0.95%; $k = 0.875$; 95% confidence interval, 0.638 to 1.0; $P < 0.000\ 1$). Stroke neurologists were in agreement with etiological diagnosis in 18 of the 20 cases (0.90%; $k = 0.855$; 95% confidence interval, 0.66 to 1.0; $P < 0.000\ 1$)[6]. The general practitioner arrived at the same etiological diagnosis in 18 of the 18 cases (100%; $k = 0.875$; 95% confidence interval, 1.0 to 1.0; $P < 0.000\ 1$). The inter-rater agreement, according to the ASC system, is much higher than Trial ORG 10172 in Acute Stroke Treatment (TOAST) classification, which has moderate inter-observer reliability[7]. In a retrospective reliability study of 14 randomly selected patients, two neurologists and two internists agreed with subtype diagnosis of only 14%, according to TOAST criteria[7]. Development of a computerized diagnostic algorithm could increase the inter-rater agreement to 56%[7]. Limitations of mechanistic stroke subtyping are most prominent in patients with multiple coexisting potential causes of ischemic stroke[8]. TOAST[7] and ASC define a mixed etiological category. However, etiological grading of ASC provides physicians with a management policy. MRI is unavailable in many tertiary care centers, especially in developing countries.

Table 1 Asian Stroke Criteria for classification of brain infarction

Topographic Classification
I -Probable Large Vessel Territory (LVT): either A or B
A. New cortical signs (aphasia, agnosia, apraxia, sensory neglect, visual neglect, seizure, hemianopsia)
B. MRI/CT show a new cortical lesion compatible with stroke manifestations* and /or a new lesion ⩾ 2 cm* (if negative, repeated MRI/CT ⩾ 48 h post event is recommended)
I -Definite LVT: both A and B
II -Probable Small Vessel Territory (SVT): either A or B
A. Lacunar syndrome (pure motor hemiparesis, pure sensory stroke, mixed sensorimotor, ataxic hemiparesis, dysarthria clumsy hand) without new cortical signs
B. MRI/CT performed ⩾ 48 h post event show new subcortical lesion < 2 cm*, no new cortical lesion* and no new lesion ⩾ 2 cm*
II -Definite SVT: both A and B
Note: If there is new clinical or imaging evidence* of LVT, patient should be classified as LVT, regardless of new SVT evidence
Note: In brain stem imaging, new lesion* < 1.5 cm is considered SVT
Etiologic Classification
I -Atherosclerosis Grade 1: A and /or B
A: at least two of the following risk factors
aged ⩾ 60 years, hypertension, diabetes mellitus, smoking, hyperlipidemia
B: < 50% stenosis of the corresponding large intracranial artery, < 70% stenosis of the corresponding extracranial artery, aortic arch atheroma > 4 mm without mobile component
I -Atherosclerosis Grade 2: ⩾ 50% stenosis of the corresponding large intracranial artery, ⩾ 70% stenosis of the corresponding extracranial artery, aortic arch atheroma with mobile component
II -Cardioembolism Grade 1: right to left heart shunt with deep venous thrombosis or right heart thrombus, bioprosthetic mitral or aortic valve, mitral valve prolapsed with mitral regurgitation, severe mitral regurgitation, left ventricular aneurysm after acute myocardial infarction, left ventricular akinetic segment after acute myocardial infarction
II -Cardioembolism Grade 2: atrial fibrillation, mechanical mitral or aortic valve, acute myocardial infarction < 4 weeks, left heart thrombus, bacterial and nonbacterial endocarditis, congestive heart failure, dilative cardiomyopathy, rheumatic mitral stenosis, atrial myxoma
III -Miscellaneous Grade 1: hypercoagulability, migraine induced stroke, fibromuscular dysplasia *, aneurysmal sac*
III - Miscellaneous Grade 2: arterial dissection*, moyamoya syndrome*, arteriovenous malformation*, vasculitis*, cerebral venous thrombosis*
IV -Mixed: any combination of above etiologies
V -Undetermined: none of the above causes could be determined by complete diagnostic investigation
VI -incomplete diagnostic investigation

*compatible with stroke manifestations

ASC imaging criteria relies on brain CT scan ⩾ 48 hours after stroke onset. Based on ASC, diagnosis of large or small vessel territory infarct is based on either clinical or imaging results. Imaging of large vessel territory infarction rules out clinical evidence of small vessel territory stroke. This is not a disadvantage for ASC, because diagnostic accuracy of clinical signs of large or small vessel territory strokes is not very high. However, ASC enables clinicians with probable clinical

differentiation of large or small vessel territory infarction[9]. ASC includes cortical infarcts that are clinically diagnosed, but not detected by CT scan at the acute stage. By using cortical signs or lacunar stroke syndrome concepts, ASC enables the clinician to classify stroke topography, even in the absence of imaging studies[6]. Nevertheless, imaging studies, in particular MRI, offer further evidence for stroke localization. New symptoms suggesting cortical involvement are important criteria for definitive cardioembolic stroke in SPAF I–III trials[10]. Despite other mechanistic classifications of stroke subtyping[7-8], ASC relies on ≥ 70% stenosis of the corresponding extracranial artery. Because endarterectomy is usually indicated in ≥ 70% of symptomatic carotid stenosis, a therapeutic classification is needed. Because rheumatic valvular disease is still frequent in developing countries[11], severe mitral regurgitation is considered to be a cardiac source of embolus in ASC. Because various etiologies could lead to brain infarct in small vessel, as well as large vessel, territories[1, 12], etiological classification of ASC includes all vascular territories. The main disadvantage of stroke classification systems for etiological stroke identification is necessity of complete diagnostic investigations. The high rate of incomplete diagnostic investigations is common in stroke patients. This type of work up constitutes a separate entity in ASC, and is not assumed as a disadvantage for ASC. In the second validation step, ASC was used for the data bank of stroke registries. The Khorasan Stroke Registry (KSR)[10] was established for evaluation of incidence, clinical manifestations, risk factors, topography, and etiology of ischemic stroke in Khorasan, Iran, during 2001–2005. Consecutive stroke patients underwent a standard battery of diagnostic investigations by a stroke neurologist. Topography and etiology of brain infarction were determined according to ASC classification. A total of 1392 ischemic stroke patients (738 females, 654 males) were evaluated at the KSR[13]. The Khorasan Posterior Circulation Stroke Registry (KPCSR) is the first posterior circulation stroke registry in Iran that deals with clinical course and etiology of stroke based on different topographies of the vertebrobasilar territory[14]. Consecutive patients with vertebrobasilar territory brain infarction were admitted to Ghaem Hospital, Mashhad and were enrolled in a prospective study between 2006 and 2007. Vertebrobasilar territory infarcts were classified into five groups in the KPCSR according to the involved location: brainstem, thalamus, cerebellum, posterior cerebral artery, and mixed categories[14]. All stroke patients in the KPCSR underwent a standard battery of diagnostic investigations, and etiology of ischemic stroke was determined by the ASC. The ASC was also used for the Khorasan Pediatric Stroke Registry[15]. A population-based study was conducted to determine incidence, clinical manifestations, and etiology of pediatric ischemic stroke in Southern Khorasan, Iran, between 2002 and 2007. In this province, every child with a possible stroke diagnosis was referred to a stroke neurologist and routinely admitted to the Pediatric Division of Valie-Asr Tertiary Care Hospital[15]. The ASC has been reliably used for etiological evaluation of patients with transient ischemic attacks[16].

CONCLUSION

Various stroke classification systems have been designed in North America and Europe[7-8]. Despite guidelines for stroke medicine in Asia[17], an Asia-specific ASC does not exist. The ASC has therefore been dedicated to the diagnosis of ischemic stroke patients by physicians residing in Asia.

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