Comments on stroke subtypes classifications

Correct identification of stroke aetiology is critical to both research and clinical practice. Various classification criteria of brain infarct are used in clinical trials and stroke registries (1). Most of these classifications were developed for specific research projects in specialist institutions, a quite different situation from routine clinical practice. The phenotypic A–S–C–O classification of stroke subtypes was designed and its main application is the design and review of case reports, clinical trials and meta-analysis studies by researchers and peer reviewers of journals, respectively (2). This new classification system recognises that many patients belong to several categories; some categories may be causally related to the index stroke, whereas others are simply concurrent. By introducing the 'level of diagnostic evidence', this classification recognises the completeness and quality of the diagnostic investigations to grade the underlying diseases (2) and it could be very useful in daily clinical practice. Because it is not possible to be always absolutely sure of a single true mechanism, the clinician must keep in mind that multiple mechanisms might be simultaneously involved. Patients may have two or more competing causes of cerebral ischaemia. Despite efforts to arrive an aetiologic diagnosis, the cause of infarction may remain undetermined, possibly due to inappropriate workup or unwillingness of the patient or the physician to perform a complete workup. The limitation of Stroke Data Bank criteria (3, 4) is most prominent in patients with multiple coexisting potential causes of ischaemic stroke.

The TOAST (5, 6) and Lausanne stroke registry (7) defined a mixed aetiologic category; however, aetiologic grading of the A–S–C–O classification (2) and Asian Stroke Criteria (ASC) (8) is able to guide physicians in management policy. This grading of each aetiologic subtype for atherosclerosis, cardioembiolism and unusual causes in A–S–C–O classification (2) and ASC (8) is developed for therapeutic decision-making purpose. The very restrictive definition for atherothrombotic stroke in the Stroke Data Bank classification (3, 4), result in underestimation of the overall burden of atherosclerotic disease and some of the patients with atherothrombotic aetiology are classified as cryptogenic stroke based on this criterion. The same limitation is present in TOAST classification (5, 6) in which patients with documented atherosclerotic disease who did not reach the 50% stenosis limit are not categorised as atherothrombotic stroke. This limitation is not present in Lausanne stroke registry criteria (7), A–S–C–O classification (2) and ASC (8) by widening the atherothrombotic group. Despite TOAST (5, 6) and Lausanne stroke registry (7) classifications of stroke subtyping, the A–S–C–O classification (2) and ASC (8) rely on $\geq$70% stenosis of the corresponding extracranial artery. Because endarterectomy is usually indicated in symptomatic $\geq$70% carotid stenosis and we need a therapeutic classification. This therapeutic strategy of the A–S–C–O classification (2) and ASC (8) is also accepted in Stroke Data Bank classification (3, 4); however, the latter did not solve problem of restrictive definition of atherosclerosis and overestimation of cryptogenic stroke (1). On the other hand, categorisation of atherosclerotic aetiology in the latter as atherothrombosis and tandem arterial pathology is a pathophysiologic concept, which has no therapeutic usefulness (1, 3, 4). However, TOAST classification (5, 6) tried to help the therapeutic decision-making process by consideration of high- and medium-risk cardioembolic causes of stroke. However, there are some limitations in this system, e.g. mitral valve prolapse without mitral regurgitation and patent foramen ovale without deep venous thrombosis or right heart thrombus are accepted as medium cardioembolic mechanisms in TOAST (5, 6) and Stroke Data Bank classifications (3, 4), while they have a doubtful role in the aetiology of stroke and are not considered in Lausanne stroke registry (7) and ASC (8). The main disadvantage of stroke classification systems is the necessity of complete diagnostic investigations for the detection of stroke aetiology. Incomplete aetiologic investigation of brain infarction is very common in routine clinical practice. The A–S–C–O classification (2) tried to solve this problem by grading of the diagnostic workup (2). Mixed aetiologies, negative evaluation and incomplete evaluation are all categorised as stroke of undetermined cause in the TOAST system (5, 6) while these subtypes are precisely defined in A–S–C–O classification (2) and ASC (8). Despite the A–S–C–O classification (2) and ASC (8), mixed aetiologies and incomplete evaluation are not considered in Stroke Data Bank classification (3, 4), and Lausanne stroke registry (7) did not include incomplete evaluation. Left atrial turbulence (smoke) and mitral annulus calcification are considered to be cardiac sources of embolism in the TOAST (5, 6) and A–S–C–O classifications (2) and were ignored in Lausanne stroke registry (7) and ASC (8) due to their very low emboligenic risk. It is clear that brain infarcts of all sizes and locations can be caused by atheroembolism and cardioembolism (9). There are clear examples of thrombotic or embolic small deep infarcts presenting as lacunar syndrome, because small emboli can occlude single perforating arteries to cause lacunar infarcts (9). Evidently, there is no longer a specific vascular occlusive pathology of lacunar stroke and there are no specific clinical risk factors for small artery occlusion (9, 10). Because various aetiologies could lead to brain infarct in small-vessel as well as large-vessel territories (9, 10), aetiologic classification of the ASC (8) includes all vascular territories. Based on these impressions, we could refuse to define small artery disease as a subtype of ischaemic stroke that

characterises lacunar infarcts (9, 10). However, other stroke classifications assumed lacune to be equivalent of small-vessel disease (1, 2).

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