TOAST or A-S-C-O: Does the Method Matter?

Anne W. Alexandrov, AGACNP-BC, ANVP-BC, ASC-BC, CCRN, FAAN

The pathogenic mechanism categories that arose from the Trial of Org 10172 in Acute Stroke Treatment (TOAST)[1] are widely used to classify the cause of ischemic stroke. For those stroke teams that routinely and methodically work to determine etiology, TOAST has made a significant difference in application of secondary prevention strategies to reduce recurrent stroke risk due to increased awareness of causation. The 5 TOAST classification categories include large artery atherosclerosis, cardioembolism, small vessel disease, stroke of unusual etiology, and stroke of unknown etiology which is also referred to as cryptogenic stroke.

Some have argued that a major limitation of TOAST is its lack of precision which fails to take into consideration less well established etiologies and their probability of occurrence.[2] Given that TOAST first emerged in 1993, others have criticized the fact that it is not tied to specific criteria for the etiologic work-up that should be utilized today.[3]

The A-S-C-O pathogenic classification system reduces the number of categories to 4, namely, A = atherosclerosis; S = small vessel disease; C = cardiac source; and O = other causes of stroke.[2] A-S-C-O offers complete stroke phenotyping that takes into account the stroke etiology and the presence of all other underlying diseases. In comparison, TOAST subtypes stroke by taking into consideration only the most likely cause of stroke.[1] Grades are assigned to each of the 4 A-S-C-O phenotypes as follows: 1 = definitely a potential cause of the index stroke; 2 = causality uncertain; and 3 = unlikely a direct cause of the index stroke, but the disease is present. A grade of 0 is used when the disease is completely absent, and when grading is impossible because of an incomplete work-up, the grade is 9.[2]

To illustrate how A-S-C-O is used, the original article promoting its use[2] provides an example of a patient with a 70% ipsilateral symptomatic stenosis, leukoaraiosis, atrial fibrillation, and a platelet count of 700,000/mm^3 showing that this patient would be classified as A1-S3-C1-O3. Advocates for A-S-C-O classification assert that it makes clear the completeness and quality of the etiologic work-up since clinicians would have to classify each of the 4 elements in their patients.[3]

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In 2013, the A-S-C-O authors updated their classification to A-S-C-O-D with D standing for dissection since this is a common cause of stroke in the young.[4] In addition to this change, the level of diagnostic evidence ranks were reduced to just 9 (insufficient work-up) and 0 (diagnosis not present). Criteria for the "A" classification were revised to include 50% luminal stenosis and a neuroimaging cardioembolic stroke pattern was also added. Despite these changes, studies utilizing A-S-C-O almost always continue to use the original methods that incorporate the grading scale system, as this makes clear whether a thorough, exhaustive etiologic work-up was performed.

Two compelling original research studies utilizing A-S-C-O methods[5,6] have shed light on the significance of atherosclerosis as a stroke mechanism. Wolf and colleagues examined stroke mechanism in a cohort of 4,467 stroke patients 18-55 years of age assembled for the multinational European 'Stroke in Young Fabry Patients' (sifap1) study.[5] A-S-C-O scores were prospectively assigned based on a specified stroke etiologic work-up protocol. A grade 1 cause of stroke was evident in 29.3% of patients. The most common causes of stroke identified were cervical arterial dissection and persistent foramen ovale (PFO) in this young cohort. However, the study also found high prevalence of concomitant atherosclerosis and small vessel disease in the cohort.[5] A subsequent study examined a registry cohort assembled between 2004 to 2011 for patients with recurrent ischemic stroke to assign A-S-C-O classifications, finding that mechanism for recurrent stroke did not always reflect index stroke mechanism.[6] Recently, a retrospective follow-up study of etiologic subtypes was conducted in young stroke patients using both A-S-C-O and TOAST classification methods,[3] similarly finding diverse causative mechanisms.

Given the high prevalence of PFO in younger patients with stroke, in 2020, Elgendy and colleagues proposed updated nomenclature and classifications capable of capturing PFO-related ischemic stroke.[7] These authors propose use of the term, PFO-associated stroke as a separate category of stroke causation to guide directed care such as PFO closure to reduce subsequent recurrent stroke risk. The specific recommendation proposed by the writing group was a retitling of the cardioembolism classification within existing classification systems, to a name more reflective of PFO causation, namely, 'cardioembolic/transcardioembolic.'[7] These authors also suggest that progress in understanding the causative implications of PFO has consequences for the 'embolic stroke of uncertain source' (ESUS) construct which categorized numerous potential causative entities into a single category, including emboli arising from structural cardiac conditions, cardiac dysrhythmias, paradoxical embolism, artery-to-artery emboli due to atherosclerotic disease, and tumoral emboli. The authors posit that similar to PFO, the ESUS category fails to encourage detailed mechanistic work-ups beyond long-term cardiac monitoring for what may be multifaceted causes of embolic stroke.[7]

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What is abundantly clear is that the conduct of an exhaustive work-up resulting in a complete understanding of all actual and potential contributors to stroke causation must be fully understood and addressed by stroke clinicians. Sadly, more than 30 years since the publication of the TOAST criteria, this remains an elusive goal in many certified stroke centers. Stroke clinicians are encouraged to examine how well their program performs as providers of scrupulously thorough mechanistic stroke work-ups. When a program fails to perform adequately, there is a tremendous need to understand what drives lack of attention to stroke etiology. For example, programs should explore whether differences are driven by the education and training of physician leaders, or whether there are differences among private practice general neurologists when compared to specialty trained vascular neurologists. One area that has not been thoroughly explored is whether the use of internal medicine hospitalist-led teams supported by numerous specialist consultants improves or actually reduces the determination of stroke mechanism and timely application of appropriate secondary prevention. Whatever the reason, this article serves as a call to action for stroke clinicians to understand and ignite passion among their team members for attention to stroke mechanism determination.

American guidelines remain relatively silent on what constitutes an exhaustive work-up for different stroke pathologic mechanisms. Worse yet, certification agencies and core measures currently lack indicators for compliance with determination of stroke etiology. However, lack of indicators and pay-for-performance core measures should not keep each of us from ensuring that stroke mechanism is determined. Understanding stroke mechanism(s) is at the core of our work as stroke clinicians, and our stroke patients deserve nothing less to reduce the risk of recurrent stroke.

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