An Evidence-Based Causative Classification System for Acute Ischemic Stroke

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At the time of this trial, the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification system was the most widely used method for identifying acute ischemic stroke mechanisms, to appropriately devise secondary prevention plans. However, the classification scheme possessed some drawbacks, including only moderate inter-examiner reliability and a tendency to over-assign patients into the "stroke of undetermined etiology" category, including those with more than one potential stroke etiology. Related to the latter, it had become increasingly important to create an updated algorithm to classify patients more uniformly according to their most likely stroke mechanism, even if more than one potential etiology had been identified. For this reason, the goal of the current study was to create an updated algorithm to the previous TOAST scheme, to address the above two drawbacks.

Experimental design and statistics: The study authors created a modified classification scheme based on the original TOAST criteria, labeled Stop Stroke Study TOAST (SSS-TOAST). SSS-TOAST was composed of the same five, major stroke subtypes as TOAST (large artery atherosclerosis, cardioaortic embolism, small artery occlusion, other causes, or undetermined causes; see pp. 691 – 693 for details). In addition, SSS-TOAST used an extended algorithm for assigning a level of confidence, subclassified as evident, probable, or possible, for a particular stroke mechanism based on the available diagnostic data (**Table 1, Figure 1**).[1] The authors differentiated "evident" from "possible" mechanisms based on prior literature that assigned primary risk to each particular mechanism, and they determined "probable" mechanisms based on specific clinical and imaging characteristics of the infarct. In addition, probable mechanisms were based on positive likelihood ratios (PLRs), or the likelihood that certain clinical and imaging characteristics of a given stroke were associated with a particular stroke etiology (**Table 3**). For example, a high PLR for large artery athero as a stroke etiology would be given to a patient with 1) a prior h/o recurrent TIAs, 2) the presence of an acute watershed infarction in the distribution of the index artery, or 3) a h/o several, prior watershed infarctions in the distribution of the index artery. Probable mechanisms had to have a PLR of >2.[2] Of note, the authors state that the SSS-TOAST classification scheme is optimally applied in patients who undergo standardized testing following an ischemic stroke, including an MRI brain, intra and extracranial vessel imaging, EKG/TTE, and standard labwork. Finally, with the above, the interexaminer reliabilities of the SSS-TOAST vs. TOAST schemes was assessed via 2 neurologists who evaluated 50 patients admitted with acute strokes. Stroke mechanisms were determined with TOAST and SSS-TOAST criteria, and a k-statistic was used to determine the interexaminer reliability (k of 1 suggests perfect agreement between examiners).

Results: There were some additional modifications to the 5 original stroke etiologies from TOAST and these are discussed throughout pgs. 691 – 693 (see **Table 2** for updated considerations of cardioembolic sources). Otherwise, regarding inter-examiner reliability data, with the original TOAST scheme, the k statistic was 0.78 based on the 50 patients examined. For the SSS-TOAST criteria, the k statistic was 0.90 when using the additional evident/probable/possible algorithm. More importantly, use of the SSS-TOAST algorithm greatly reduced the number of stroke etiologies classified as "undetermined-unclassified", from ~40% with TOAST to ~4% with SSS-TOAST (**Table 4**).

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[1] Evident: there is only one potential mechanism available; probable: if there are >1 "evident" mechanisms, the algorithm uses the stroke characteristics to identify the most likely mechanism; possible: if there are no evident mechanisms, the algorithm searches for a possible mechanism, which carries an unclear risk for stroke

[2] PLRs were also established for cardioembolic and small vessel occlusion subtypes

Conclusions: The updated SSS-TOAST scheme provided a reliable and comprehensive algorithm for classifying ischemic stroke mechanisms and etiologies, based on the most up to date imaging and diagnostic testing available. In addition, SSS-TOAST used published data to help identify risk thresholds, to appropriately assign the most likely stroke mechanisms. In doing so, the use of this updated scheme greatly reduced the chance that a stroke etiology was classified as "undetermined". Notably, SSS-TOAST does not readily identify interactions between multiple, potential stroke risk factors, so this should be left to clinician discretion. Otherwise, SSS-TOAST should be used routinely when assigning stroke mechanisms and when deciding on appropriate plans for secondary stroke prevention.

Additional Reading, if interested:

Adams, H.P., et. al., Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke (1993); 24:35 - 41.

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