VIEWPOINT

Time to Retire the Concept of *Transient Ischemic Attack*

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Transient ischemic attack (TIA) has been a useful clinical term even though agreement on the diagnosis for individual cases has been far from perfect even among experts.[1] The utility of the diagnosis has waned with improvements in brain imaging and a deeper understanding of the natural history of acute cerebral ischemia. The current concept of TIA characterizes an ischemic episode in which symptoms are transient and not associated with brain injury. But recent evidence suggests that such episodes do not occur or are vanishingly rare and that brain injury almost always occurs during these events. Accordingly, it is time to reevaluate the conceptual soundness and utility of the term *TIA*.

In 1975, a US National Institutes of Health committee considered the issues regarding classification and diagnosis of cerebrovascular diseases.[2] Their considerations included transient focal cerebral ischemic attacks about which the committee stated, "These are episodes of temporary and focal cerebral dysfunction of vascular origin, rapid in onset (no symptoms to maximal symptoms in less than 5 minutes and usually less than a minute), commonly lasting 2 to 15 minutes but occasionally lasting as long as a day (24 hours)." These episodes were called TIAs, and the maximum duration was arbitrarily set at 24 hours. This definition was constructed to provide a common basis for distinguishing patients who were likely harboring underlying cerebral infarction (ischemic stroke) and patients likely not harboring underlying cerebral infarction (TIA). This approach assumed that TIAs are associated with complete resolution of brain ischemia occurring rapidly enough to cause only transient symptoms and no permanent brain injury.

> Based on the 2009 TIA definition, this would mean TIAs (brief episodes of brain ischemia occurring rapidly enough to cause only transient symptoms and no permanent brain injury) do not exist.

As magnetic resonance imaging (MRI) was used more frequently in the 1990s, it became clear that many patients who experienced a TIA had evidence of infarction on brain imaging. Consequently, a TIA working group of stroke neurologists convened to consider and then proposed a new definition of TIA that was published in 2002.[3] Furthermore, many health professionals and the public tend to consider TIAs benign, whereas they regard strokes as serious. The working group considered that this perception regarding TIAs was incorrect and viewed TIA and stroke as both on a continuum of serious conditions involving brain ischemia. Both are markers of current or impending disability and a risk of death. The new imaging studies made clear that the traditional time-based definition of TIA was not differentiating a group of individuals without permanent brain injury, as originally intended. Furthermore, there is nothing specific about a symptom duration of 24 hours, or 6 hours, or 1 hour, or 5 minutes with respect to prognosis. The group proposed a new tissue-based, rather than time-based, definition: "a TIA is a brief episode of neurologic dysfunction caused by focal brain or retinal ischemia, with clinical symptoms typically lasting less than one hour, and without evidence of acute infarction."[3] Regrettably, the inclusion of the 1-hour duration persisted as a remnant of the traditional time-based definition.

In 2009, the American Heart Association/American Stroke Association's Stroke Council issued a scientific statement for health care professionals titled "Definition and Evaluation of Transient Ischemic Attack."[4] The statement settled on the final tissue-based definition of TIA: "a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction."[4] Because ischemic events involving the spinal cord are uncommon and not usually considered strokes, these episodes easily could have been omitted from the definition. However, in this statement, time was no longer mentioned. In 2013, Sacco and colleagues[5] addressed the issue of continuing to consider both the tissue-based and time-based definition of TIA given the varied use worldwide of different imaging modalities and techniques, especially when temporal trends in stroke incidence over a long period are being assessed.

Advances in imaging have rendered untenable the view that brain ischemia sufficient to cause transient symptoms often does not produce any brain injury. If the brain is imaged with computed tomography after an ischemic event, some infarcts may be visible. If the same brain is imaged with MRI at 0.15-Tesla (T), more infarcts may be apparent.[6] At 1.5 T, and then 3 T, even more infarcts are likely to be visualized, even among patients with clinical symptoms and signs that were transient. Currently, 7 T and even 11 T superconducting magnets are available, and new highly sensitive methods for identifying cerebral infarction from blood are in development. In addition, histopathologic studies have shown that even when frank tissue infarction does not occur, neuronal dropout does.[7] Given the extreme pace of loss of neurons, synapses, and myelinated fibers during each minute of ischemia,[8] it is likely that the preponderance of those events defined as TIA, even under the modern definition, are associated with enduring

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cerebral tissue injury, provided the clinician can be confident that the clinical event was due to transient ischemia or infarction rather than a TIA mimic (eg, focal seizure, migraine aura, metabolic disturbance, or syncope).

Based on the 2009 TIA definition, this would mean TIAs (brief episodes of brain ischemia occurring rapidly enough to cause only transient symptoms and no permanent brain injury) do not exist. Rather, all symptomatic focal cerebral ischemic events should be considered to be cerebral infarctions,[7] which may be minor, moderate, severe, or fatal and may or may not be detected or detectable using modern imaging techniques. Previous descriptions that "TIAs are mini-strokes" were correct after all.

Symptomatic cerebral infarctions range, based on the National Institutes of Health Stroke Scale scores, in presentation from minor (0), mild (1-5), moderate (6-14), severe (≥15), or fatal. In short, all are ischemic strokes on a continuum from minimum to maximum. TIAs are minor ischemic strokes. These events should be named such, and the term *TIA* should be retired.

Cardiologists have grappled with a similar conundrum of definitions and criteria for acute coronary syndrome (ACS). In ACS, with progression from measuring serum aspartate aminotransferase (AST) to lactic dehydrogenase (LDH), to creatine kinase (CK), to CK-MB, to troponins, the prevalence of infarction appears to increase and true angina without infarction decreases.[9] The term *unstable angina* has been folded into ACS and used less frequently on its own. The commonality between unstable angina and myocardial infarction is much more important than any difference. Cerebral and coronary arteries and their ischemic events are not substantially different.

Even if true, tissue-negative transient ischemic attacks exist as a rare entity when ideal evaluation for brain infarction is performed, the utility of distinguishing TIA from minor stroke remains unclear. Both are at high risk for future brain ischemia, both respond to similar treatments, and both may have similar effects on the patient. Again, this assumes the clinician can be confident the episode was not an ischemic mimic. The ABCD^2 (age, blood pressure, clinical features, duration of TIA, and presence of diabetes) score can offer a substantial measure of confidence. Given this, the time and effort spent in defining TIA seems misplaced. Rather, it is time to embrace the previously suggested term *acute ischemic cerebrovascular syndrome*[10] and retire the term *TIA*. Just as cardiologists have addressed the evolution of their redefinition of ACS, neurologists should address the evolution of their redefinition of acute ischemic cerebrovascular syndrome.

ARTICLE INFORMATION

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