Is transient ischemic attack a minor stroke?

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In the current literature, the utility of transient ischemic attack (TIA) diagnosis is under revision by the scientific community and experts.¹ If initially this term was considered a valid diagnostic category, over the years the definition of TIA has been completely subverted, underlining the scientific lability of this nosological entity. In 1975, a committee from the US National Institutes of Health decided to provide a temporal framework definition of TIA, including in this diagnosis all those focal neurological syndromes lasting between 2 and 15 minutes and sometimes up to 24 hours, characterized by a complete spontaneous resolution in the absence of apparent brain injury (Table 1).² Due to its transience and to the full-re-

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[®]Copyright: the Author(s), 2022 Licensee PAGEPress, Italy Bleeding, Thrombosis and Vascular Biology 2022; 1:31 doi:10.4081/btvb.2022.31 covery of the neurological disorder, for a long time TIA was considered a relatively benign condition compared with minor or major stroke, reflected in a strong minimizing of associated medium- and long-term consequences. Further studies on patients affected by TIA showed an increased long-term risk of recurrent stroke and accumulation of disability similar to patients affected by minor ischemic stroke (or minor stroke).³

In particular, it has been demonstrated that prediction of recurrent major stroke in patients with high risk factors, identified in a clinical score assigned by using the ABCD2 and ABCD3 I scale (Age, Blood pressure, Clinical features, Duration, Diabetes / Dual TIA) is comparable in patients affected at onset by TIA or minor stroke.⁴⁻⁶

The marked improvement of neuroimaging and the broader awareness of patients to rapidly access to emergency care allowed the acquisition of new insights regarding clinical presentation and course of stroke, thus making TIA an outdated stand-alone entity of scarce use in clinical neurological practice.

In particular, the introduction of magnetic resonance imaging (MRI) in the clinical practice since 1990 showed that many TIA diagnoses were characterized by a central nervous system (CNS) damage radiologically detectable. In 2009, the American Heart Association renamed TIA as a transient entity represented by focal ischemia of the brain, retina or spinal cord in the absence of acute radiological infarction. If this statement, on one hand, has led to a more accurate definition of the diagnosis, on the other hand it has increasingly contributed to the development of technology for high-field MRI (3T and more recently 7T) that have allowed to detect even relatively small or transient lesions associated with a brain injury. The increasingly widespread use of MRI in the study of neurological syndromes in hyperacute phase, which partially replaced computerized tomography over the years, allowed to further circumscribe the TIA as an acute transient neurological deficitary entity associated with a restricted diffusivity in the sequences of diffusion weighted images in the absence of findings in T2 sequences (i.e. T2 FLAIR), or absence of findings both in DWI and in T2 sequences,⁷ identifying brain infarction as a risk factor for increased long-term disability.8,9

This clarification allows TIA to be classified as a purely radiological entity, as it is indistinguishable from



Year	Reference	Definition
1975	US, National Institutes of Health (NIHSS), Bethesda	Focal neurological syndromes between 2 minutes to 24 hours with complete spontaneous resolution in absence of apparent brain injury
2009	American Heart Association (AHA)	Transient entity represented bifocal ischemia of the brain, retina or spinal cord in absence of acute radiological infarction
2014	Brazzelli <i>et al.</i> ⁷	Acute transitory neurological deficit associated in MRI with a restricted diffusivity in absence of findings in T2 sequences, or absence of findings both in DWI and in T2 sequences

Table 1. Time evolution of the definition of transient ischemic attack.

a minor stroke without residual clinical neurological deficits.

Furthermore, in recent studies comparing antiplatelet and anticoagulant drugs used in acute vascular-based neurological syndromes, patients with TIA or minor stroke are equated and placed in the same observation arm, effectively defining them as a single group. In the CHANCE trial it has been shown that in the first 90 days after the onset of an acute cerebrovascular event characterized by a low degree of disability (ANCE), such as a TIA or minor stroke, the use of dual antiplatelet therapy limits the risk of subsequent stroke after one year from the first event.¹⁰ This analysis, conducted in the same category of patients in the POINT trial, was subsequently deepened, confining to the first 21 days after the event the actual benefit of a dual antiplatelet therapy.¹¹

From those reports, in agreement with their similar outcome, stratification of clinical risk of evolution and therapeutic management, we suggest that the clinical difference between TIA and minor stroke is anachronistic and should be confined to a mere radiological classification of the same disease.

REFERENCES

- Easton JD, Johnston SC. Time to retire the concept of transient ischemic attack. JAMA 2022;327:813.
- 2. A classification and outline of cerebrovascular diseases II. Stroke 1975;6:564-616.
- 3. Lioutas VA, Ivan CS, Himali JJ, et al. Incidence of transient ischemic attack and association with long-term risk of stroke. JAMA 2021;325:373.
- 4. Giles MF, Rothwell PM. Systematic review and pooled analysis of published and unpublished validations of the ABCD and ABCD2 transient ischemic attack risk scores. Stroke 2010;41:667-73.
- Weimar C, Benemann J, Michalski D, et al. Prediction of recurrent stroke and vascular death in patients with transient ischemic attack or nondisabling stroke. Stroke 2010;41:487-93.
- Song B, Fang H, Zhao L, et al. Validation of the ABCD 3 -I score to predict stroke risk after transient ischemic attack. Stroke 2013;44:1244-8.
- Brazzelli M, Chappell FM, Miranda H, et al. Diffusionweighted imaging and diagnosis of transient ischemic attack. Ann Neurol 2014;75:67-76.
- Yu AYX, Coutts SB. Role of brain and vessel imaging for the evaluation of transient ischemic attack and minor stroke. Stroke 2018;49:1791-5.
- Mendelson SJ, Prabhakaran S. Diagnosis and management of transient ischemic attack and acute ischemic stroke. JAMA 2021;325:1088.
- Wang Y, Pan Y, Zhao X, et al. Clopidogrel with aspirin in acute minor stroke or transient ischemic attack (CHANCE) trial. Circulation 2015;132:40-6.
- Pan Y, Elm JJ, Li H, et al. Outcomes associated with clopidogrel-aspirin use in minor stroke or transient ischemic attack. JAMA Neurol 2019;76:1466.