PERSPECTIVES

Magnetic resonance imaging in patients with transient ischemic attack

Transient ischemic attack (TIA) is a temporary event, which portends a higher risk of a disabling stroke following the TIA. However, the evaluation and management of TIA vary worldwide and is debated and controversial. With the development of brain imaging, particularly diffusion weighted imaging-magnetic resonance imaging (DWI-MRI), the diagnosis of TIA changed from time-based definition to a tissue-based one. DWI-MRI became a mandatory tool in the TIA workup. The DWI-MRI provides not only the evidence to distinguish between TIA and acute ischemic stroke, furthermore it predicts TIA patients who are at higher risk of disabling stroke, which can be prevented by an immediate evaluation and treatment of TIA.

TIA was first clinically defined in 1964 as any transient neurological deficit lasting less than 24 hours due to focal cerebral or retinal ischemia (Marshall, 1964). This temporary event is generally an unstable condition and is associated with a higher risk of a stroke, especially in the early phase after TIA. It has been found that up to 20% of TIA patients suffer a stroke within 90 days after TIA (Hill et al., 2004; Kleindorfer et al., 2005). The most critical time to suffer a stroke is the 7 days following TIA. The stroke risk is 12.8% in the first 7 days after symptom onset, with half occurring in the first 48 hours (Lovett et al., 2003; Coull et al., 2004). Therefore, TIA has been considered a major warning signal of stroke. This is also apparent, if one considers patients admitted with a stroke. Up to 25% of these patients have experienced a TIA during the week before the stroke (Rothwell and Warlow, 2005).

Some investigations suggest that the risk of stroke after TIA can be predicted with the ABCD2 score, which includes age, blood pressure at admission (>140/90 mmHg), clinical features (weakness, speech dysfunction), duration of symptoms, and diabetes (Rothwell et al., 2005; Johnston et al., 2007).

The development of brain imaging tools including cranial computed tomography (CCT) as well as magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI) changed the assumption that TIA is a temporary event resolving within 24 hours without serious consequences. Several researches (Bogousslavsky and Regli, 1985; Awad et al., 1986; Dennis et al., 1990; Koudstaal et al., 1992) have shown that TIA patients had actually cerebral infarctions that can be detected by CCT, even though the CCT was performed days to weeks after the TIA. It has been found that 3-48% of patients with clinical TIA symptoms had acute cerebral infarctions that can be visualized by CCT. Furthermore, the DWI-MRI measurements have shown that up to 67% of patients with TIA demonstrate relevant cerebral infarction (Fazekas et al., 1996; Redgrave et al., 2007).

The development of brain imaging and its usage in daily diagnostic evaluation of patients with TIA has thus changed our view of TIAs. Particularly, the definition of TIA has shifted from a clinically time-based term to tissue-related one in the clinical day routine.

Albers et al. proposed 2002 a new definition, which includes a shorter duration of neurological symptoms (less than 1 hour) and the absence of a lesion detected by a DWI-MRI (Albers et al., 2002), thus suggesting that an investigation by MRI is a mandatory tool in the diagnostic accuracy of a TIA. Guidelines have recommended the use of MRI including DWI in diagnosing patients with transient neurological symptoms so as to distinguish a TIA from an acute infarction (Furie et al., 2011). Several CCT and MRI studies have shown that evidence of an acute infarction has a prognostic value and was associated with increased stroke risk following a TIA (Giles et al., 2011; Douglas et al., 2003). Therefore, it was suggested to enter the findings of the DWI-MRI in the ABCD2 score to predict the stroke risk after TIA (Giles et al., 2010).

On the contrary, epidemiological studies have shown that only a minority of TIA patients undergo a MRI investigation. Studies have shown that 3-5% of patients received an investigation by MRI as part of the diagnostic evaluation (Gladstone et al., 2004; Edlow et al., 2006). By contrast, the use of CCT as a diagnostic procedure in the TIA management was more frequent; it has found that 56% of patients with TIA who presented to hospitals underwent a CCT (Edlow et al., 2006). The sensitivity of CCT to detect infarcts is considerably lower than that of DWI-MRI, which is the gold standard tool of brain imaging in the evaluation of TIA patients (Forster et al., 2012; Totaro et al., 2010; Fazekas et al., 1996; Ay et al., 2002; Mullins et al., 2002). In daily clinical routine, CCT is performed more frequently than DWI in patients with TIA for several possible reasons, including the high availability, low cost, rapidness, and easy evaluation of CT.

The American Heart Association has revised the proposed definition of TIA to a tissue-based term without time limit, previously 1 hour. The recent definition of a TIA includes "any neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction" (Easton et al., 2009), of typical symptom duration of less than 1 to 2 hours. According to this definition, a prolonged TIA might occur. Diagnostic correctness depends on the extent of the evaluation.

As a consequence of advancements in cerebral imaging, patients with transient neurological symptoms who demonstrate high signal intensity lesions on DWI or low-density lesions on CCT are diagnosed as having an acute ischemic stroke (Easton et al., 2009).

In a large cohort study including 3,554 patients with TIA defined according to the WHO, we have found that 1,910 patients (54%) were evaluated by MRI (Al-Khaled et al., 2012). All patients were hospitalized and the TIA diagnosis was made during hospitalization after TIA work-up. Of 1,910 patients being investigated by MRI, 11.1% of patients showed a TIA-related acute infarct detected by MRI including DWI. The evidence of acute infarction was correlated with the severity of the neurological deficits and presence of motor weakness or aphasia.

The frequency of the acute infarction was comparable with that of other study (Schulz et al., 2004), but lower than most published data about the incidence of acute infarction detected by DWI-MRI (Giles et al., 2011; Giles et al., 2010; Redgrave et al., 2007).

We assumed that patients who demonstrated an acute infarction by MRI might have been diagnosed with an acute ischemic stroke according to the new tissue-based definition of a TIA, and, thus, were not included in this cohort. To avoid this bias selection, we performed MRI-study(Al-Khaled and Eggers, 2013) including 3,724 patients with transient neurological symptoms lasting less than 24 hours according to the definition put forth by the WHO, regardless whether patients were diagnosed with TIA or acute ischemic stroke after evaluation by MRI including DWI. In a previously reported study, 31% of TIA patients showed an acute infarction visualized by MRI including DWI. A strong association was found between neurological symptoms, speech dysfunction and weakness and an evidence of acute infarction by MRI including DWI (Al-Khaled and Eggers, 2013). However, a great variability exists in the literature as to the incidence of acute infarction detected by DWI-MRI among different cohorts of patients with TIA (Rovira et al., 2002; Crisostomo et al., 2003; Purroy et al., 2004; Schulz et al., 2004; Ay et al., 2005). Using DWI-MRI, one to two thirds of TIA patients showed an acute infarction, whereas the frequency of acute infarctions depended on study design and investigated cohort. However, most of the MRI studies are small or are pooled analyses of smaller investigations (Coutts and Cucchiara, 2013; Giles et al., 2011; Giles et al., 2010; Giles and Rothwell, 2010; Rovira et al., 2002; Redgrave et al., 2007).

On the other hand, studies showed that TIA patients who were not evaluated by DWI-MRI were older and had higher rates of unilateral weakness and speech dysfunction (Adeoye et al., 2010; Al-Khaled and Eggers, 2013). These results suggest that a TIA evaluation by MRI was mainly done in patients with unclear symptoms. It is well known that the diagnosis of TIA is unreliable (Castle et al., 2010; Koudstaal et al., 1989; Ferro et al., 1996; Sempere et al., 1996).

In summary, the brain imaging in patients with transient neurological symptoms can help to answer the question that whether patients with TIA who have an acute infarction should be classified as acute ischemic stroke. Furthermore, it has recognized that TIA patients who showed acute infarction by DWI-MRI or CCT are at a higher risk to suffer from disabling stroke (Al-Khaled et al., In press; Giles et al., 2011; Giles et al., 2010).

The risk of stroke after TIA in patients with evidence of acute infarction ranged between 3 to 18-fold higher than TIA patients without acute infarction detected by MRI (Al-Khaled and Eggers, 2013; Al-Khaled et al., In press; Giles et al., 2011; Giles et al., 2010; Giles and Rothwell, 2010; Douglas et al., 2003). Therefore, TIA should be dealt as an emergency event and patients suffering from TIA should be immediately treated to evaluate the etiology and to receive the secondary prophylaxis to prevent a stroke (The European Stroke Organization, 2008). The impact of the immediate evaluation of TIA patients on stroke prevention after TIA has been shown in ear-

lier studies (Al-Khaled and Eggers, 2014; Giles and Rothwell, 2007; Kennedy et al., 2007; Lavallee et al., 2007; Rothwell et al., 2007).

On the contrary, there are no uniform international guidelines and recommendations for TIA diagnosis and treatment, particularly in diagnostic and therapeutic procedures.

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