The Duration of Symptoms in Transient Ischemic Attacks

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ABSTRACT:

BACKGROUND:

The better understanding of the pathophysiology of brain ischemia ,the newer look provided by the increasingly available imaging techniques ,and the promising thrombolytic therapy have made the classical 24 hours time limit definition of Transient Ischemic Attack(TIA) outdated. A newer 1 hour time limit has recently been proposed and seems to be reasonable.

OBJECTIVE:

This study was designed to show the different aspects of TIA in relation to risk factors and imaging findings.

DESIGN AND SETTING:

A prospective study, patients were received at the neurology consulting clinic, examined clinically and by a set of investigations.

PATIENTS AND METHODS:

32 consecutive patients with TIA of variable duration and presentation were clinically examined within variable intervals from onset of symptoms by means of a specially designed questionnaire followed by a list of investigations including imaging of the brain within 4 weeks of the onset of symptoms.

RESULTS:

Most TIAs last less than ten minutes (18/32, 56.25% of all). Patients with longer duration TIAs found to have higher incidence of abnormalities in brain imaging than short duration ones .Most of patients with TIA have more than one attack of TIA on presentation and patients with multiple TIAs have less incidence of cardiac disease than those who have single prolonged TIA.

CONCLUSION:

Most TIAs last less than 10 minutes. The longer the duration of the symptoms, the higher the frequency of recent infarcts detected by brain imaging. MRI of the brain is much more sensitive than head CT-SCAN in the detection of changes in patients who present with TIA .Patients with brief duration TIAs may not seek for medical help until they are recurrent while those patients with longer duration TIAs ask for medical advice early.

KEY WORDS: TIA, CVA.

INTRODUCTION:

TIA has long been classically defined as a sudden, focal neurological deficit that lasts for less than 24 hours, is presumed to be of vascular origin, and is confined to an area of the brain or eye perfused by a specific artery.(1) TIA is not merely a transient episode but it is a marker of current or impending disability and a risk of death. [2] After a first TIA, 10 to 20 percent of patients have a stroke in the next 90 days, and in 50 percent of these patients, the stroke occurs in the first 24 to 48 hours after the TIA.(3,4,5). Rothwell and colleagues [6] developed the 6-point ABCD (age, blood pressure, clinical factors, and duration of symptoms) score (table 1) which was highly predictive of the 7-day risk of stroke in two independent validation cohorts. Table 1 compares the 7-day stroke risk derived from the population-based studies [6] with the similar model for 90-day risk of stroke by Johnston and colleagues.(3) The risk of stroke after retinal transient ischemic attack was about half the risk after nonretinal events.(7-9) The occurrence of carotid TIAs is a predictor not only of cerebral infarction but also of MI.(10) 15-20% of patients with stroke have a preceding TIA.(11) Time-based

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definitions of TIA were first advanced in the 1950s and 1960s. In 1958, an ad hoc committee on cerebrovascular diseases defined transient cerebral ischemia without infarcts as a cerebral ischemic event with a focal neurological deficit lasting less than 1 hour.[12] In 1964, Acheson and Hutchinson [13] supported a one-hour maximal duration of symptoms to distinguish TIA from stroke. That same year, Marshall [14] proposed 24 hours as the maximal duration of symptoms. In the 1975 revision of the National Institute of Health (NIH) classification document, episodes lasting less than 24 hours were classified as TIAs.[15] In 1990, the National Institute of Neurological Disorders and Stroke (NINDS) published the Classification of Cerebrovascular Diseases III, in which episodes lasting <24 hours are classified as TIAs, and indicating that the longer the episode, the greater the likelihood of finding a cerebral infarct by CT and MRI.[16] Although the 24 hours' time limit for TIA has been adopted but the majority of TIAs actually resolve within 60 minutes, and most of these resolve within 30 minutes.[17,18,19]. NINDS trial of tissue plasminogen activator for acute ischemic stroke showed that among placebo-treated patients who presented with a prominent ischemic focal neurological deficit that did not completely resolve within 1 hour or rapidly improve within 3 hours, only 2 percent had complete resolution within 24 hours.[20] Some have suggested that the 24 hours definition of TIA is outdated, confusing and potentially misleading and have proposed a new one hour time limit for definition of TIA.[1,21].Others have proposed sub classifying TIAs according to the presence or absence of infarction.[22] Multiple studies of patients with TIA who were evaluated with CT scanning have been reported.[23,24,25] Most of these studies reported a 15 to 20 percent incidence of cerebral infarction in a vascular territory relevant to the patient's symptoms. MRI identified infarction in up to 50% of patients without neurological deficits who meet the criteria for a TIA.[26,27,28] However CT is typically preferred if the patient is a potential candidate for thrombolytic therapy, because it can rapidly rule out brain hemorrhage and was the diagnostic imaging technique used in the successful studies of thrombolytic therapy.[29] Practitioners frequently disagree on whether a TIA has occurred.[30,31] The idea of tissue-based definition rather than the current time-based definition has been raised and proposed by some.[1] This study was designed to show the different aspects of TIA in relation to risk factors and imaging findings.

PATIENTS AND METHODS:

We reviewed the clinical records of 32 consecutive patients with TIAs who were admitted to Baghdad teaching hospital between January 2006 and September 2007 within 2 weeks of TIA onset. Patients consisted of 24 men and 8 women age 60 ± 9.5 years. Carotid TIA was diagnosed if the patient had a brief episode of unilateral motor dysfunction (i.e., weakness, paralysis, or clumsiness of extremities or face) or isolated aphasia that resolved within 24 hours based on the definition of the NINDS Classification III.[15] Patients with amaurosis fugax were excluded from the current study. Information about the approximate duration of a TIA was obtained from patients or their families in all cases. The symptom duration was reported as follows: <10 minutes in 18 patients, >=10 and <60 minutes in 8, >=60 and < 24 hours in 6.The patients were then classified into three groups for further analysis: 18 patients with TIAs <10 minutes (Group 1); 8 patients with TIAs >=10 minutes and <1 hours (Group 2); and 6 patients with TIAs >=1 hours (Group 3).

The following clinical characteristics were analyzed with respect to the duration of TIAs: 1) patient age and gender; 2) history of brain infarction, TIA, myocardial infarction, and definite angina pectoris; 3) risk factors for stroke, including hypertension, diabetes mellitus, hypercholesterolemia, cigarette smoking, and alcohol consumption; 4) use of antiplatelet agents or anticoagulants at onset of TIA; 5) potential cardiac sources of emboli; 6) significant arterial pathologies in the ipsilateral carotid system; 7) number of TIAs; and 8) evidence of recent brain infarction on CT or MRI. The following risk factors were identified: 1) use of antihypertensive agents, systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg on admission for hypertension; 2) use of oral hypoglycemic agents, insulin, or random blood sugar 180 mg/dL for diabetes mellitus; and 3) use of antihyperlipidemic agents or serum cholesterol level >220 mg/dL for hypercholesterolemia. To detect potential cardiac sources of emboli (emboligenic cardiac diseases), all patients were examined by 12-lead ECG, and transthoracic echocardiography. We carried out carotid ultrasonography (Doppler), and MR angiography (MRA) to evaluate significant arterial pathologies in the ipsilateral carotid system. Carotid Ultrasonography (Doppler) was performed in all patients. MRA in 3 patients (9.3%). CT was performed in all patients within 4 weeks of onset of the TIA to exclude nonischemic brain lesions

such as brain hemorrhage, chronic subdural hematoma, and brain tumors, and to detect relevant infarcts. A recent infarct was defined as a hypodense lesion in the vascular territory corresponding to the patient's symptoms. T1-weighted (repetition time [TR]/echo time [TE], 500/20) and T2-weighted (TR/TE, 1,800/110) MRI using a 1.5-T superconducting magnet was carried out within 28 days of TIA onset in 22 patients (68.7%).Ischemic lesions were considered to be recent if they were hyperintense on T2-weighted images and isointense to slightly hypointense on T1-weighted images(30-32) , which were located in the vascular region corresponding to the patient's symptoms. The lesions on CT or MRI were classified as cortical infarcts, lacunar infarcts (small, deep lesions less than 15 mm in diameter), and border zone infarcts (lesions located between two adjacent arterial territories). The risk factors, arterial or cardiac diseases, and CT and MRI findings were compared among the three groups using the [chi]$^{(2)}$ test. Based on this assessment, TIA patients were defined as having either long-duration or short-duration TIAs. Statistical analysis was performed using a commercially available software package (Stat-View, version 4.5; SAS Institute, Cary, NC)**.** Data are expressed as mean ± SD. The *p* values <0.05 were considered statistically significant.

RESULTS:

History of cerebral infarction was found to be significantly higher in groups 2 (>10 minutes and <1 hour in duration) and 3 (>1 hour) than in group 1 (<10 min.). Regarding risk factors history of atrial fibrillation was found in a total of 5 patients out of the 32 patients studied. Of them 3 was in group 3 out of 6 patients in this group a figure that is significantly higher than in the other groups. Regarding the number of TIAs, group 1 patients have significantly higher number of recurrent TIAs than in the other groups (table 2). There were otherwise no significant results regarding the other aspects of the history and risk factors or the medications taken by the patients in the different groups. The finding of atrial fibrillation whether by history or during examination of the patients was found to be significantly higher in the group with TIAs of more than 1 hour duration (in 3 out of 6 patients in this group and in 2 patients out of 26 patients in the group of patients with TIAs of less than or equal to 1 hour).There were no other significant differences regarding the finding of other cardiac diseases (table 3). MRI changes was found to be significantly higher in the group of patients with TIAs longer than 1 hour in duration than in the other group while CT-SCAN showed no significant difference in the 2 groups of the study . From another perspective , MRI of the brain done within 4 weeks of the onset of the presenting TIA showed significantly higher changes in both groups of patients in comparison to CT-SCAN of the head (table 4).

The frequency of finding a cardiac disease in patients with only 1 TIA on presentation was found to be significantly higher than in patients who presents with 2-4 TIAs or 5 or more TIAs represented in groups 2 and 3. From another perspective, patients with cardiac disease present with only 1 TIA frequently than with multiple TIAs (table 5). The 2 groups (group 1 of <= 1 hour , group 2 of > 1 hour duration) , showed no difference regarding the frequency of risk factors for TIA/stroke identified with the exception of atrial fibrillation and history of previous TIA/stroke that were significantly higher in group 2 than in group 1(table 6).

DISCUSSION:

In spite of the 24 hours time limit which has been adopted early and classically to define TIA [14-16] still most of them resolve completely within 60 minutes and the majority of these resolve within 30 minutes.[17,18] Furthermore, it has been shown that only 2% of patients presented with a prominent ischemic focal neurological deficit that did not resolve completely within 1 hour or rapidly improve within 3 hours had complete resolution within 24 hours.[20] Many studies utilized CT-SCAN for evaluation of patients with TIA reported that 15-20% of patients with TIA have cerebral infarction in a vascular territory relevant to the patients' symptoms and that the longer the duration of symptoms, the higher the rate of CT-SCAN evidence of brain lesions detected.[23-25] MRI is much more sensitive than CT-SCAN for detecting brain ischemia and infarction. MRI of the brain identified infarction in up to 50% of patients without neurological deficit who meet the criteria for TIA.[26-28] Therefore DW-MRI is recommended for patients suspected of having TIA.[1] The presence of recent infarcts on CT-SCAN or MRI have been reported to be associated with a higher incidence of significant cardiovascular disorders.[33].The current study shows that most of the patients with TIA have attacks that are less than 1 hour duration and that most of these patients have attacks that are less than 10 minutes in duration. The study demonstrated that the longer duration TIAs that are more than 1 hour in duration have a higher incidence of changes in CT-SCAN

or MRI of the brain in regions of the brain that are relevant to the presenting attack of TIA. These changes have been detected much more commonly in patients of the same duration of the attack who have been examined by MRI than those who have been examined by CT-SCAN in the same time period from the onset of the symptoms, a finding supported by what had other researchers ([26,27,28])already found in their studies on imaging in TIA .Our study shows that the longer duration TIAs (> 1 hour) have a higher incidence of a potentially emboligenic cardiovascular disease than the shorter duration TIAs (<= 1 hour) an observation found also by Kimura K, et al in 1999 in their study on TIA.[34] Accordingly the mechanism behind the longer duration TIAs seems to be different from the shorter duration attacks and extensive investigation for cardiovascular diseases is recommended for the longer duration TIAs including TEE (transesophageal echo study) in patients with normal transthoracic echo study to identify and treat these cardiovascular diseases that are relevant a point that was the most important difficulty in our study.

Table 1: The ABCD prognostic score for the 7-day risk of stroke in patients with transient ischemic attack.

	Risk factor	Points
ABCD SCORE		
Age	≥ 60 years	1
Blood pressure	Systolic ≥ 140 &/or Diastolic≥90mmHg	1
Clinical features	Unilateral motor weakness Speech disturbance without weakness Others	2 1 0
Duration	≥ 60 minutes 10-59 minutes < 10 minutes	2 1 0
CALIFORNIA SCORE		
Age	≥ 60 years	1
Motor weakness		1
Speech disturbance		1
Duration	> 10 minutes	1
Diabetes mellitus		1

Table 2: Demographic features of TIAs in Groups 1(<10 min.), 2(>10 min. &<1 hour) and 3(>1 hour) in duration.

	Group1(<10) No.18/32	Group2(>1& <60minute No.8/32	Group3(>1&<24hrs No.6/32	Pvalue
Age	60.0+/-9.2	59.1+/-10.2	63.5+/-8.1	0.3
History, n (%)				
TIA	2/18(11.1)	2/8(25)	2/6(33.3)	0.14
Cerebral infarction	2/18(11.1)	2/8(25)	4/6(66.6)	0.02*
Angina pectoris	2/18(11.1)	2/8(25)	2/6(33.3)	0.14
MI	2/18(11.1)	2/8(25)	2/6(33.3)	0.14
Risk factors, n (%)				
HT	10/18(55.5)	6/8(75)	4/6(66.6)	0.37
DM	6/18(33.3)	2/8(25)	2/6(33.3)	0.21
Hyperlipidemia	6/18(33.3)	4/8(50)	2/6(33.3)	0.4
Alcohol	2/18(11.1)	2/8(25)	0/6(0)	0.07
Smoking	10/18(55.5)	6/8(75)	2/6(33.3)	0.6
AF	2/18(11.1)	0/8(0)	3/6(50)	0.02*
Medication, n (%)				
Antico/antipla	6/18(33.3)	2/8(25)	2/6(33.3)	0.21
No. of TIAs				
1 only	2/18(11.1)	2/8(25)	2/6(33.3)	0.14
2-4	8/18(44.4)	6/8(75)	4/6(66.6)	0.6
5&more	8/18(44.4)	0/8(0)	0/6(0)	0.04*

Table 3: Cardiac Diseases identified in the 2 groups (<= 1 hour & > 1 hour in duration).

	GROUP 1 <= 1hr. No. 26/32(81.2%)	GROUP 2 > 1hr. No. 6/32(18.8%)	Pvalue
HT	16/26(61.5%)	4/6(66.6%)	0.0883
DM	8/26(30.76%)	2/6(33.3%)	0.29
AF	2/26(7.6%)	3/6(50%)	0.01*
Hyperlipidemia	10/26(38.4%)	0/6(0%)	0.4
Smoking	16/26(61.5%)	2/6(33.3%)	0.8
TIA/Stroke	8/26(30.76%)	5/6(83.3%)	0.018*
MI	4/26(15.4%)	2/6(33.3%)	0.3
*significant value			

Table 4: CT-SCAN & MRI changes in the 2 groups (<=1 hour & > 1 hour in duration of TIA)

	GROUP1<=1hr	GROUP2>1hr	Pvalue
AF	2/26(7.6%)	3/6(50%)	0.028
MI	4/26(15.2%)	2/6(33.3%)	0.3
ANGINA P.	4/26(15.2%)	2/6(33.3%)	0.3

Table 5: Cardiac changes in the 3 groups(only 1, 2-4 , & >=5 TIAs).

	GROUP1<=1hr	GROUP2>1hr	Pvalue
CT-SCAN	2/26(7.6%)	2/6(33.3%)	0.35
MRI	5/16(37.5%)	5/6(66.6%)	0.0288*

Table 6: Risk factors for TIA/Stroke in relation to the duration of TIA.

	GROUP1(1only)	GROUP2(2-4)	GROUP3(>=5)	Pvalue
With cardiac disease	4/6(66.6%)	2/20(10%)	2/6(33.3%)	0.016*
Without cardiac disease	2/6(33.3%)	18/20(90%)	4/6(66.6%)	0.016*

*significant value

CONCLUSION:

Most TIAs last less than 10 minutes. The longer the duration of the symptoms, the higher the frequency of recent infarcts detected by brain imaging. It has been shown that TIAs lasting longer than 1 hour associated with atrial fibrillation significantly more than in patients with TIAs that are shorter than or equal to 1 hour in duration. Apart from atrial fibrillation and history of previous TIA/stroke there is no significant difference between longer lasting TIAs and shorter lasting TIAs in the frequency of different risk factors for TIA.

Recommendations:

Patients with longer duration TIAs especially those who present TIA longer than 1 hour duration should be thoroughly investigated for underlying cardiac or arterial disease. Patients with TIA should be examined by MRI of the brain rather than by CT-SCAN of the head as soon as possible looking for any underlying changes in the brain whenever possible.

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