Risk factors of short-term stroke recurrence in patients with minor ischemic cerebrovascular events

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Original Article

Abstract

BACKGROUND: Assessing the risk of recurrent ischemic events in patients with transient ischemic attack (TIA) and minor ischemic stroke (MIS) is of a great importance in clinical practice.

METHODS: Consecutive patients with TIA or MIS who were visited in Ghaem Hospital, (Mashhad, Iran) were enrolled in a prospective cohort study during 2010 to 2011. Diagnosis of TIA or MIS was accomplished by a stroke neurologist. Only those who presented within 24 hours from the onset of symptoms were recruited. MIS was considered as an ischemic stroke with National Institutes of Health Stroke Scale (NIHSS) < 4. The endpoint of the study was a new ischemic cerebrovascular event or vascular death in 90 days and additionally in 3 days. The decision to admit and type of treatment in each case was left to the discretion of the stroke neurologist. The association between 20 potential factors with recurrent ischemic events in 3 and 90 days was investigated using univariate and multivariate analysis (MVA).

RESULTS: 393 TIA patients (238 males and 155 females) and 118 MIS patients (77 males and 41 females) were enrolled in the study. Stroke occurred in 117 (23.2%) patients, TIA in 99 (19.6%), and there was 11 (2.2%) vascular deaths within 3 months in the total 511 patients with minor ischemic events. Crescendo TIAs and multiple TIAs were associated with greater risk of stroke in 3 days in a univariate analysis (OR = 5.12, P < 0.001) and (OR = 3.98, P = 0.003), respectively. Patients with index stroke had 11.5% lower risk of recurrent stroke in 3 days than patients with index TIA in multivariate analysis (OR = 0.115, P = 0.039). Diabetes was independently associated with 3 months stroke recurrence in the patients with minor ischemic events (OR = 2.65, P = 0.039).

CONCLUSION: Multiple and crescendo TIAs are the main predictors of stroke recurrence, derived from the univariate analysis of the patients with minor ischemic events.

Keywords: Transient Ischemic Attacks, Infarction, Brain, Recurrence, Risk

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Introduction

The approach for management of patients with transient ischemic attack (TIA) or minor ischemic stroke (MIS) has been remained variable and controversial.[1] Reliable and easily obtainable information on each patient risk profile should be promptly available in the emergency setting to guide the management.[2] A large number of TIA and MIS patients do not go on to experience an early stroke. These patients do not need to be exposed to potentially risky therapies from which they will drive no benefit, nor do they need to use high-intensity resources. The clinical imperative is to sort out those patients who need immediate attention and those who do not. Because there is no single prognostic factor for TIA patients differentiating who are going to suffer an event or not, it is very difficult to achieve perfect discrimination.[3] TIA heralds a relatively high risk of stroke between 10% and 20% in the ensuing 90 days and half of the risk of early stroke occurs in the first 2 days after TIA.[4,5] In managing patients with TIA or MIS, it would be

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useful to know a given patient risk for having a stroke in the near future.[6] Identification of predictive factors in short-term recurrence of ischemic cerebrovascular events in TIA and MIS patients constitutes the objectives of the present study.

Materials and Methods

Patients with consecutive TIA or MIS were prospectively evaluated in Ghaem Hospital and Stroke Clinic (Mashhad, Iran) during 2010-2011. This prospective cohort study included patients with initial TIA or MIS with or without (as control) subsequent ischemic cerebrovascular events. Diagnosis of TIA or MIS was done by a stroke neurologist. Only those who presented within 24 hours from the onset of symptoms were enrolled.[2] Whether the initial ischemic symptoms lasted less than or more than 24 hours, categorized the patients as TIA or MIS, respectively. Patients had to access the hospital or stroke clinic within 24 hours of post event to enhance precise recall of the type and duration of symptoms and to guarantee inclusion of very short-term strokes.[2] Patients were enrolled in this study if they had a Pre-morbid Modified Rankin Scale ≤ 1.[5] Ischemic stroke and TIA was defined as a sudden focal neurologic deficit of presumed arterial origin lasting ≥ 24 hours and < 24 hours, respectively with or without corresponding ischemic lesion on brain imaging.[8] MIS was considered as an ischemic stroke with National Institutes of Health Stroke Scale (NIHSS) < 4.[5] Exclusive criteria were clinical evaluation over 24 hours from the end of the transient event and a final diagnosis of non-ischemic causes of symptoms such as migraine, seizure and anxiety.[7] A known cognitive impairment and a significant comorbidity limiting participation in the study also was considered as exclusive criteria.[1] The patients with disabling stroke, defined as NIHSS ≥ 4 in 1 day after event to allow for a more reliable assessment of recurrent events were excluded from the study.[8] The endpoint of the study was a new ischemic cerebrovascular event or vascular death in 90 days and additionally in 3 days. Recurrent TIA, stroke and vascular death as well as the hospital admission and ongoing medication were recorded.[7] Recurrent stroke was considered as the exacerbation by at least 4 points in the initial NIHSS punctuation or clearly defined new symptoms of > 24 hours duration that suggested a new ischemic event.[9,10] A recurrent TIA was defined as a new neurologic symptom of < 24 hours duration that was caused by focal ischemia in the brain or retina.[1,11] Follow up data were obtained from direct patient visit in 3 and 90 days or by centralized telephone interview if patients failed to attend the visit.[9] Follow up was continued until death or 3 months from the date of the index event.[1] All recurrent TIA and stroke were assessed and investigated by a stroke neurologist.[7] Vascular death was defined by acute coronary syndrome or cerebrovascular syndrome certified as the cause of death or contributing directly to death.[1] In patients who had multiple recurrent events, the endpoint was classified as the first recurrence after the index ischemic event.[10] All patients underwent blood test, ECG, head scan and duplex ultrasound of neck arterial trunks.[6,12] The decision to admit and treatment in each case was left to the discretion of the stroke neurologist. A strict control of vascular risk factors after discharge in all cases was recommended. Antiplatelet therapy was recommended in acute phase of all the patients with exception of those with cardioembolic strokes, patients already pretreated with antiplatelet, patients with crescendo TIA or progressive stroke after antiplatelet treatment in whom anticoagulation was initiated.[9]

A detailed history was taken from each TIA or MIS patient with a standardized questionnaire which included following variables. As far as possible, variables were defined and categorized in the same way as had been predictive in previous studies.[1-13] Age was dichotomized at 60 years.[13] Clinical features were categorized as motor weakness (focal and unilateral weakness of one or more of face, arm, hand or leg) versus speech disturbances (defined as either dysarthria or dysphasia stroke or both).[13] Limb weakness required a clear description of loss of power as opposed to more vague terms such as clumsiness or heaviness.[13] Isolated sensory or visual symptoms were also recorded in the patients.[14] Duration of symptoms was categorized as less than 10 minutes, 10-59 minutes, and 60 minutes or longer.[13] Hypertension was defined as using antihypertensive medication or patients with two blood pressure values (at least 1 week interval) of > 140/90 mm/Hg.[6,15] Administration of antidiabetic medication or a fasting blood glucose > 6.4 mmol/L or > 126 mg/dL were definitions of diabetes mellitus.[2,9,15] Hyperlipidemia was defined as use of lipid lowering medication, serum cholesterol concentration > 5.2 mmol/L or > 220 mg/dL, LDL cholesterol > 130 mg/dL, or serum triglyceride concentration > 150 mg/dL.[9,15] Current smoking habits was also recorded.[9] Patients who smoked more than 5 cigarettes per day in recent year were defined as smoker.[15,16] Stroke was analyzed for the non-TIA

index event (the distinction between MIS and TIA was determined by the presence of symptoms lasting > 24 hours). Duplex ultrasound served for detection of ≥ 70% carotid stenosis corresponding to manifestations.[17,18] Acute stroke signs in brain CT performed within 24 hours post event, previous history of stroke or TIA, and prior TIA in previous 7 days named as multiple TIA.[9,19] Cardiac risk factors included atrial fibrillation (prior documented history or evidence in the baseline ECG);[2,19] coronary artery disease (evidence in the baseline ECG or documented prior history of angina pectoris or myocardial infarction);[9,19] other high risk cardioembolic sources (defined if long-term anticoagulation was indicated based on findings in previous medical record, ECG or echocardiography).[19,20] Crescendo TIAs was defined as two or more TIAs within the past week with increasing in duration and in severity of deficit.[21,22] The 3 days and 90 days risk of TIA or stroke was determined in relation to each variable[13]. The successful follow up percentage was 92% and patients without complete follow-up were not analyzed and omitted from the results. Data on demographics and above variables were recorded in a standardized questionnaire and entered in SPSS for Windows 16.0 (SPSS Inc., Chicago, IL, USA). The primary analysis estimated the proportion of patients with endpoints for each category of variables. Differences of all the variables in the univariate analysis were evaluated by chi-square and Fisher's exact tests. Multivariable odds ratios (OR) with 95% CI were calculated in the secondary analysis of recurrence predictors using a multiple logistic backward regression model. The research was approved by the Ethics Committee of Ghaem Hospital, and an inform consent was obtained from the patients. There was no delay in any of the therapeutic interventions in order to continue the present study.[9]

Results

A total of 511 patients (315 and 196 males and females, receptively) meeting the eligibility criteria were recruited and completed the follow-up study during 2010 to 2011. Three hundred and ninety three TIA patients (238 and 155 males and females, receptively) and 118 MIS patients (77 and 41 males and females, receptively) were enrolled in the study. 72.4% of the patients (370 out of 511) were admitted in the hospital and the others were recruited from the stroke clinic. The mean age of all the patients was 68.5 ± 4.7 years and 63.2% of the patients were ≥ 60 years of age. The elapsed time from symptom onset to evaluate the index event was less than 24 hours in all the cases (14.6 ± 2.2 hours). The mean age of TIA and MIS patients was 68.4 years and 66.2 years, respectively. 117 strokes (23.2%), 99 TIA (19.6%), and 11 vascular deaths (2.2%) occurred within 3 months of post event in total of 511 patients with minor ischemic events. The estimated risk of recurrent stroke, TIA and vascular death in the present cohort is illustrated in table 1. Evidence of new brain infarction was identified on brain CT of 2.03% patients (8 out of 393) with TIA, 39.8% (47 out of 118) of the patients with MIS, and 46.6% (55 out of 118) of the entire cohort. Duplex ultrasound disclosed symptomatic ≥ 70% extracranial internal carotid artery stenosis in 3.4% (4.118) of the patients with TIA, 3.6% (14 out of 393) patients with MIS, and 3.5% (18 out of 511) patients with minor ischemic event. The effects of 20 evaluated features on recurrence rate of TIA or MIS during 3 days and 3 months follow-up in patients with minor ischemic cerebrovascular events is described in table 2. From the univariate analysis (Table 2), 3 out of the 20 factors were statistically significant for predicting stroke and TIA at 3 days. Crescendo TIAs and multiple TIAs were associated with 5-fold and 4-fold greater risk of stroke in 3 days in a univariate analysis (χ^2 = 48.0, OR = 5.12, 95%CI 3.13-8.35, P < 0.001) and (χ^2 = 3.98, OR = 3.98; 95%CI 1.53-10.3, P = 0.003), respectively. MIS patients had significantly lower rate of stroke in 3 days comparing to TIA cases; (χ^2 = 24.6, OR = 0.109, 95%CI 0.028-0.289, P < 0.001). There was a significant association of 4 evaluated factors with 3 months recurrence of stroke in the univariate analysis (Table 2). Crescendo TIAs and multiple TIAs were associated with 3.7-fold and 3-fold greater risk of stroke in 3 months in a univariate analysis (χ^2 = 31.4, OR = 3.72, 95%CI 2.30-6.0, P < 0.001) and (χ^2 = 11.97, OR = 3.08, 95%CI 1.58-5.98, P < 0.001), respectively. The ABCD^2 score is a prognostic system based on clinical data designed to predict stroke risk within 7 days after TIA to guide the triage.[17] The ABCD^2 score is the most externally validated prediction tool currently available.[17,18] This score has been independently validated in different clinical settings and is now recommended for use in triaging TIA patients by several major clinical guidelines.[17,18,20] Among the ABCD^2 items, only weakness had a significant effect on recurrence of stroke at 3 months; (χ^2 = 5.21, OR = 2.09, 95%CI 1.09-4.01, P = 0.025) in univariate analysis. MIS patients had significantly

lower rate of stroke in 3 months comparing to TIA cases; (χ^2 = 15.19, OR = 0.26, 95%CI 0.12-0.53, P < 0.001). The association of the 20 factors with stroke and TIA recurrence at 3 days and 3 months in a similar multivariate model of our cohort were separately analyzed in table 3. On multivariate backward logistic regression analysis of the total 511 patients, only index TIA/stroke was significantly associated with 3 days stroke recurrence; (OR = 0.115, 95%CI 0.015-0.898; df = 1, P = 0.039). In other words, patients with index stroke had 11.5% lower risk of recurrent stroke in 3 days compared patients with index TIA. Weakness was the only factor associated significantly with 3 days TIA recurrence in multivariate analysis of our cohort; (OR = 4.61, 95%CI 1.014-20.97, df = 1, P = 0.048). This item increased 4.6-fold risk of 3 days TIA in patients with minor ischemic event. Diabetic patients had 2.6-fold more chance of recurrent stroke in 90 days in multivariate analysis of our whole cohort; (OR = 2.65, 95%CI 1.49-6.72, df = 1, P = 0.039). None of the other evaluated factors had a significant independent influence on stroke recurrence in 3 months follow-up of the study groups. Eleven vascular deaths (4 males, 7 females) occurred during 3 months of follow-up in the whole cohort and 6 vascular deaths happened in 3 days too. Among 20 evaluated factors, only coronary artery disease and atrial fibrillation had a significant association with 3 months vascular death in univariate analysis; (χ^2 = 8.91, OR = 5.48, 95%CI 1.57-19.04, P = 0.007) and (χ^2 = 18.91, OR = 10.41, 95%CI 2.86-37.85, P = 0.002), respectively. Due to low number of cases with vascular death, logistic regression analysis was not possible for association of 20 factors with vascular death in the present cohort.

Discussion

The 3 days and 3 months rate of recurrent stroke in the whole cohort with TIA or MIS was 20.6% and 23.1%, respectively. A prospective study of 345 TIA patients in Spain was associated with 20% risk of stroke within the next 90 days and half of this recurrent events occurred in first 3 days.[23] The risk of stroke was 2.5% at 2 days in an Italian study of TIA patients[19] and 11.1% at 90 days in another study in Canada.[5] 711 patients with TIA or MIS were prospectively recruited from five centers in the UK.[1] Recurrent stroke and TIA occurred in 90 days in 4% and 14% of the cohort respectively.[1] Review of a Canadian stroke registry found that the stroke risk in 30 days after a first TIA was 8%, with half of these strokes occurred within the first 2 days.[24] Thirty four percent risk of stroke in 3 days and 36% risk of stroke at 90 days in our TIA patients was much higher than other reported studies.[25-27] The main reason of this high frequency of recurrent stroke in our patients was diagnosis of index TIA by stroke neurologist which diminished recruiting migraine, seizure and neurotic patients as probable TIA. The main indication for admission of TIA patients in our center was appearance of multiple or crescendo TIAs. This group of TIA patients was more risky than other cases.[28] Since 71.2% of our TIA patients had multiple TIAs and TIA cases constituted 76.9% of our whole patients, the high rate of 3 days and 3 months stroke recurrence in our cohort was reasonable. A similar study performed in Spain in patients with TIA or MIS revealed 16.1% rate of 3 months and 9% rate of 7 days recurrent stroke.[9] This Spanish study did not find any different risk of recurrent stroke between patients with minor stroke compared to patients with TIA.[9] In a cohort study of TIA or MIS patients in the UK, estimated risk of stroke in 7 days, 30 days and 90 days was higher for MIS than TIA patients.[29] In multivariate regression analysis of the present cohort, only index TIA/stroke was associated with a significant effect on recurrence of stroke within 3 days. Stroke as index event had a significantly protective effect on recurrence of stroke and whole ischemic cerebrovascular events in 3 days and 3 months in our patients in univariate analysis Paradoxically, the risk of a subsequent ischemic stroke may be less after a completed stroke than after a TIA.[11]

Table 1. Number and percentage of patients with recurrent stroke, transient ischemic attack and vascular death during 3 days and 3 months follow-up of the whole cohort

Index event/ follow up event	3 days stroke	3 days TIA	3 days vascular death	3 months stroke	3 months TIA	3 months vascular death
TIA n = 393	132 (34%)	40 (10.2%)	2 (0.5%)	141 (35.9%)	108 (27.5%)	5 (1.3%)
MIS = 118	7 (5.9%)	37 (31.5%)	4 (3.4%)	29 (24.6%)	71 (60.2%)	6 (5.1%)
Total = 511	104 (20.4%)	41 (8.1%)	6 (1.2%)	117 (22.9%)	99 (19.4%)	11 (2.2%)

TIA: Transient ischemic attack; MIS: Minor ischemic stroke

Table 2. The analyzed factors and their association in the univariate analysis with stroke and transient ischemic attack recurrence in 3 days and 3 months in 505 patients

Analysed Factor (number)	3 days stroke risk		3 days TIA risk		3 days stroke + TIA risk		3 months stroke risk		3 months TIA risk OR		3 months stroke+TIA risk	
	OR	P	OR	P	OR	P	OR	P	OR	P	OR	P
Age group ≥ 60 (323)	1.242	0.403	0.872	0.734	1.118	0.602	1.183	0.493	0.948	0.899	1.192	0.382
Duration*	-	0.320	-	0.862	-	0.313	-	0.744	-	0.517	-	0.305
Gender (male:315)	0.861	0.554	0.518	0.090	0.705	0.117	1.013	1	0.980	0.358	1.066	0.496
Hypertension (357)	1.436	0.207	1.794	0.156	1.630	0.046	1.506	0.117	1.398	0.282	1.552	0.040
Diabetes (131)	1.431	0.186	1.246	0.574	1.438	0.107	1.484	0.128	1.424	0.206	1.776	0.007
Hyperlipidemia (166)	0.872	0.062	1.298	0.481	0.999	1	0.810	0.408	1.150	0.599	1.025	0.920
Smoking (74)	1.309	0.413	0.820	0.819	1.156	0.667	1.196	0.535	0.823	0.729	0.921	0.792
Atrial fibrillation (30)	0.554	0.446	0.926	1	0.635	0.386	0.321	0.132	0.694	0.782	0.446	0.136
Coronary disease (128)	1.048	0.893	1.536	0.251	1.232	0.409	1.021	1	1.383	0.251	1.094	0.741
Other cardiac disease (13)	0.815	0.139	0.968	1	0.232	0.20	0.791	0.080	0.444	0.702	0.157	0.070
≥70% carotid stenosis (18)	0.543	0.548	0.650	1	0.540	0.423	0.749	1	0.650	0.751	0.621	0.713
History of stroke(85)	1.211	0.533	2.717	0.007	1.799	0.028	1.347	0.294	2.041	0.019	1.601	0.072
Index (TIA-Stroke)**	0.109	0.000	1.671	0.170	0.376,	0.001	0.260	0.000	0.747	0.385	0.393	0.000
Weakness (410)	1.963	0.057	5.008	0.020	2.710	0.001	2.098,	0.025	1.817	0.121	2.047	0.006
Speech*** disturbance (113)	0.957	1	2.167	0.703	1.295	0.795	1.234	1	1.126	1	1.289	0.206
Sensory disturbances (313)	1.290	0.353	1.115	0.850	1.271	0.297	1.258	0.375	1.442	0.204	1.324	0.196
Amarosis fugax (10)	1.307	1	1.465	1	1.438	0.702	1.117	1	4.508	0.037	3.988,	0.068
New infarct on CT (55)	0.646	1	0.920	0.641	0.403	0.468	1.307	0.668	0.841	0.617	0.643	0.722
Multiple TIAs**** (280)	3.988	0.003	0.753	0.556	1.760	0.058	3.081	0.000	0.889	0.666	1.723	0.020
Crescendo TIAs**** (108)	5.120	0.000	0.628	0.328	3.363	0.000	3.722	0.000	1.605	0.097	2.963	0.000

*: Duration of symptoms categorized as <10 minutes (111), 10-59 minutes (133) and ≥60 minutes (261) in whole of the cohort; TIA: Transient ischemic attack; MIS: Minor ischemic stroke
: TIA (388) and MIS (117); *: Speech disturbance without weakness; ****: Analysed in 388 TIA patients
†: Six cases with vascular death at 3 days and 11 cases with vascular death at 3 months were omitted in analysis

Table 3. Factors with influence on recurrence rate of stroke or transient ischemic attack in final step of multivariate backward conditional regression analysis in the whole cohort

Outcome event, analysis in final step	Influencing factor	B	SE	P	OR	95% CI
Recurrence of stroke in 3 days, step (15)	Index TIA-stroke	-2.162	1.048	0.039	0.115	0.015-0.898
	History of stroke	1.048	0.591	0.076	2.853	0.896-9.078
Recurrence of TIA in 3 days, step (16)	Weakness	1.528	0.773	0.048	4.611	1.014-20.979
Recurrence of stroke in 3 months, step (15)	Diabetes Mellitus	0.976	0.474	0.039	2.655	1.049-6.722
	Index TIA-Stroke	-0.955	0.586	0.103	0.385	0.122-1.213
Recurrence of TIA in 3 months, step (15)	Index TIA-Stroke	-7.90	0.482	0.101	0.454	0.177-1.167

TIA: Transient ischemic attack; MIS: Minor ischemic stroke

Thus, patients with index TIA are actually more unstable in terms of a new stroke than those presenting an index stroke[11]. Increasing number of TIAs in the 3 months before index event TIA was the most significant adverse prognostic factor for recurrent stroke in the UK study.[30] Crescendo TIAs was the most significant predictor of subsequent stroke within 90 days (OR = 7.6) independently of other predictors in a Japanese study of TIA patients.[31] Crescendo TIAs and multiple TIAs were associated with 5-fold and 4-fold increase in stroke risk in 3 days in univariate analysis of our study group. Crescendo TIAs and multiple TIAs were also associated with 3.7-fold and 3-fold greater risk of stroke in 3 months in a univariate analysis of the present cohort. These clinical characteristics of TIA should be considered as indication of urgent admission and therapeutic interventions in TIA patients.[28] This finding could reflect an unstable vascular condition with higher risk.[9] Addition of multiple TIAs to ABCD^2 score might augment the predictive accuracy.[25] Our research work supported adding multiple or crescendo TIA to ABCD^2 score and giving score of 4 to this clinical item as suggested by North Hertfordshire rapid access TIA service referral form (accessible on-line at: http://www.enherts-tr.nhs.uk/gps-professionals/files/2010/04/ Rapid-Access-TIA-service-referral-form.pdf). The univariate variables analysis of REACH registry cohort revealed previous history of TIA or stroke, and diabetes as significant risk factors of stroke in a 1-year-follow-up of TIA or MIS patients, $p < 0.01$ and $P = 0.02$, respectively.[20] Previous history of stroke had a non-significant effect on recurrence of stroke in 3 days in multivariate analysis of our patients. Previous history of stroke had also a significant effect on recurrence of TIA in 3 months in univariate analysis of our patients. Diabetes had a significant effect on stroke recurrence in 90 days in multivariate model of our cohort. While, none of the other evaluated factors had a significant independent influence on stroke recurrence in 3 months follow-up of our study group. A population-based study of Alberta TIA patients revealed hypertension, diabetes and older age as predictive of stroke by adjusted risk estimate in one year but not earlier, and the early risk of stroke was not predicted by clinical and demographic factors.[32] The Stroke Prognosis Instrument II (SPI-II) designed for TIA and MIS patients in the U.S. and validated by using multiple American and European cohorts.[2] Prior history of stroke or TIA, coronary artery disease, atrial fibrillation and diabetes were associated with risk of stroke or death during two years in the unadjusted analysis of SPI-II derived cohort.[2] In multivariate model of SPI-II derived cohort, age > 70 years, prior history of stroke and diabetes were significantly associated with stroke or death in 2 years follow up[2]. Unilateral weakness was the sole ABCD^2 item associated with 90 days stroke risk in multivariate analysis of patients in Dublin TIA study.[33] Weakness was independently associated with 3 days TIA risk in our TIA group. Diabetes was the only ABCD^2 item which was independently associated with stroke risk in 3 months in our study group. In the similar Spanish study of patients with TIA or MIS, 3 months stroke recurrence was independently associated with weakness, speech impairment, duration of symptoms, multiple TIAs, heart failure and severe symptomatic arterial stenosis and with 7 days recurrence; they obtained the same independent factors except speech impairment.[9] The 90-day recurrence of stroke was independently associated with weakness, previous history of TIA and severe symptomatic arterial stenosis in separated groups analysis of Spanish TIA and MIS patients[9]. Hypercholesterolemia and diabetes were independent predictors of stroke risk in 30 days in Greek TIA patients[12]. Among subjects with TIA in WASID trial, the presence of cerebral infarct on neuroimaging was the only statistically significant predictor of higher risk of stroke within 90 days (hazard ratio = 4.7).[34] Among 4574 TIA

patients, new or old infarction was present in 24% of brain CTs and 28% of DWI.[35] New or old infarction was independently predictive of stroke in 7 days; OR = 4.2 for CT and OR = 6.2 for DWI.[35] Leukoaraiosis, new and old ischemic changes in CT were associated with 4-fold greater risk of stroke in 30 days in univariate analysis of Italian TIA patients[7]. New ischemic changes on CT have been shown by Douglas et al. to be predictive of stroke risk (OR = 4; P = 0.028);[36] however, this finding was not associated with stroke recurrence in univariate and multivariate analysis of our patients with minor ischemic events. Carotid stenosis was strongly associated with stroke risk in 90 days after TIA; (hazard ratio = 3.3; P = 0.002) in Dublin TIA study.[33] In multivariate analysis of Spanish TIA patients, only large artery occlusive disease remained independent predictor for stroke recurrence in 3 days and 90 days.[24] Although symptomatic severe carotid stenosis has been reported as an important predictor of stroke recurrence within 3 months,[37] no association was observed between symptomatic severe carotid stenosis and stroke risk in 3 days and 3 months in our study group. The risk of stroke recurrence within a month after cardioembolic TIAs was estimated to be 4.6%.[37] This relatively low risk cardioembolic etiology could stem from the fact that all the mechanisms were lumped together while not all the cardiac sources of emboli carry the same risk.[37] No association was found between atrial fibrillation and recurrent stroke in 7, 28, or 90 days in Duplin TIA study.[33] No association was found between atrial fibrillation, coronary artery disease and other high risk cardiac source of embolism and stroke risk in 3 or 90 days follow up of our TIA or MIS patients in the present study. Coronary artery disease, atrial fibrillation and other high risk cardiac disease were not significantly associated with 1-year stroke risk in REACH registry.[20] Validation of ABCD^2 scoring systems in our patients was published elsewhere.[38,39]

Conclusion

Multiple and crescendo TIAs is the main predictive of stroke recurrence, derived in univariate analysis of our patients with minor ischemic events. Patients with index stroke had significantly lower risk of recurrent stroke in 3 days than patients with index TIA. Diabetes was independently associated with 3 months stroke recurrence of our patients with TIA or MIS.

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Conflict of Interests

Authors have no conflict of interests.

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