ORIGINAL PAPER/*ARTYKUŁ ORYGINALNY*

Assessment of ABCD^2 scale in patients with transient ischaemic attack or stroke

Ocena skali ABCD^2 u pacjentów z napadem przemijającego niedokrwienia mózgu lub udarem mózgu

Kavian Ghandehari, Fahimeh Ahmadi, Saeed Ebrahimzadeh, Keyvan Shariatinezhad, Kosar Ghandehari

Department of Neurology, Ghaem Hospital, Ahmadabad Street, Mashhad, Iran

Neurologia i Neurochirurgia Polska 2012; 46, 5: 421-427
DOI: 10.5114/ninp.2012.31351

Abstract

Background and purpose: Stroke risk prediction scores have been designed to stratify risk of recurrent cerebrovascular events in patients with transient ischaemic attack (TIA) or minor ischaemic stroke (MIS).
Material and methods: Consecutive patients with TIA or MIS referring to Ghaem Hospital, Mashhad presenting within 24 hours from the onset of symptoms were recruited to the prospective cohort study between 2010 and 2011. MIS was defined as an ischaemic stroke with National Institutes of Health Stroke Scale (NIHSS) score < 4. The end-point of the study was a new ischaemic cerebrovascular event or vascular death at 90 days and, additionally, at 3 days after the index TIA or MIS. The decision to admit and of method of treatment in each case was left to the discretion of the stroke neurologist. The predictive accuracy of the ABCD^2 scoring system for recurrent stroke or TIA was quantified by the area under the curve (AUC), using the *c*-statistics.
Results: The study included 393 patients with TIA (238 males, 155 females) and 118 patients with MIS (77 males, 41 females). Among 511 patients with minor ischaemic events, 117 strokes (23.2%), 99 TIAs (19.6%), and 11 vascular deaths (2.2%) occurred within 3 months after the index event. The ABCD^2 score had a weak predictive value for 3-month and 3-day recurrent stroke in patients with TIA (AUC = 0.599 and 0.591, respectively), but a high predictive value for 3-month and 3-day recurrent stroke in patients with MIS (AUC = 0.727 and 0.728, respectively).

Streszczenie

Wstęp i cel pracy: Punktację oceny ryzyka wystąpienia udaru mózgu opracowano w celu stratyfikacji ryzyka nawrotowego incydentu naczyniowego mózgu u pacjentów z napadem przemijającego niedokrwienia mózgu (*transient ischaemic attack* – TIA) lub niewielkim udarem niedokrwiennym mózgu (*minor ischaemic stroke* – MIS).
Materiał i metody: Do badania włączono kolejnych chorych zgłaszających się w latach 2010–2011 do szpitala Ghaem w Mashad w ciągu 24 godzin od wystąpienia TIA lub MIS. Niewielki udar niedokrwienny mózgu definiowano jako udar niedokrwienny mózgu powodujący ubytkowe objawy neurologiczne ocenione w skali *National Institutes of Health Stroke Scale* (NIHSS) na < 4 pkt. Punktem końcowym badania było wystąpienie kolejnego incydentu naczyniowego mózgu lub zgon w ciągu 90 dni, a dodatkowo również w ciągu 3 dni od pierwszego zachorowania. Decyzję o przyjęciu do szpitala i o sposobie leczenia podejmował neurolog specjalizujący się w chorobach naczyniowych mózgu. Dokładność rokowniczą skali ABCD^2 w przewidywaniu wystąpienia nawrotowego udaru mózgu lub TIA oceniono liczbowo i określono ilościowo metodą pola pod krzywą (*area under the curve* – AUC) z użyciem statystyki *c*.
Wyniki: W badaniu wzięło udział 393 chorych na TIA (238 mężczyzn i 155 kobiet) oraz 118 chorych na MIS (77 mężczyzn i 41 kobiet). W grupie obejmującej łącznie 511 chorych z lekkimi incydentami naczyniowymi mózgu w okresie 3 miesięcy od wystąpienia pierwszego incydentu

Correspondence address: Dr Kavian Ghandehari, Department of Neurology, Ghaem Hospital, Ahmadabad Street, Mashhad, Iran, P.O. Box: 91766-99199, phone: 05118012398, fax: 05118429828, e-mail: Ghandeharik@mums.ac.ir
Received: 27.01.2012; accepted: 21.05.2012

Conclusion: The ABCD^2 score is highly predictive for short-term recurrent stroke in patients with MIS but not in patients with TIA, although it was originally designed for patients with TIA.

Key words: transient ischaemic attacks, infarction, brain, recurrence, risk.

naczyniowego mózgu wystąpiło 117 udarów mózgu (23,2%), 99 TIA (19,6%) i 11 zgonów z przyczyn naczyniowych (2,2%). Wartość predykcyjna punktacji ABCD^2 w odniesieniu do wystąpienia nawrotowego udaru mózgu w okresie 3 miesięcy lub 3 dni po pierwotnym incydencie naczyniowym była niewielka u pacjentów z TIA (wartość AUC odpowiednio 0,599 i 0,591), a duża u pacjentów z MIS (wartość AUC odpowiednio 0,727 i 0,728).

Wniosek: Punktacja ABCD^2 ma dużą wartość predykcyjną wczesnego wystąpienia nawrotowego udaru mózgu u pacjentów z MIS, ale nie z TIA, chociaż pierwotnie została zaprojektowana do użycia w drugiej z tych populacji.

Słowa kluczowe: napady przemijającego niedokrwienia mózgu, zawał, mózg, nawrót, ryzyko.

Introduction

Identification of those transient ischaemic attack (TIA) and minor ischaemic stroke (MIS) patients at high risk of recurrent stroke is an important aspect of management to ensure an optimal risk- and cost-benefit relation. A large number of TIA and MIS patients do not go on to experience an early stroke. Defining who is at risk for a subsequent event and what actions should be taken immediately remains an important clinical issue.

Predictive scores could help to raise awareness of recurrent stroke risk in patients, which in turn might improve adherence to prevention strategies [1]. Clinical prediction rules may be the most helpful in triaging these patients [2]. Stronger predictors of stroke recurrence are needed to enable practitioners to take clinical decisions [3]. Clinical prediction scores have been developed with the aim of improving identification of TIA subgroups at higher and lower early stroke risk, thus aiding triage decisions in primary and secondary care [4]. The usefulness of risk scores depends on predictive value, consistency of performance in different studies and ease of calculation.

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 [5]. The ABCD^2 score is the most externally validated prediction tool currently available [6]. 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 [6]. Multiple validations of the ABCD^2 system have reported inconsistent results, ranging from excellent predictive value to little better than chance [5,6]. Evaluation of the use of the ABCD^2 score in predicting incident vascular events in TIA and MIS patients constitutes the aim of our study.

Material and methods

Consecutive TIA or MIS patients were prospectively evaluated in our hospital and stroke clinic between 2010 and 2011. Diagnosis of TIA or MIS was made by a stroke neurologist. Only those presenting within 24 hours from the onset of symptoms were enrolled [7]. Patients had to access the hospital or stroke clinic within 24 hours after an event to enhance precise recall of the type and duration of symptoms and to guarantee inclusion of very short-term strokes [8]. Patients were enrolled in this study if they had a premorbid modified Rankin scale ≤ 1 [8]. Ischaemic stroke and TIA were defined as a sudden focal neurological deficit of presumed arterial origin lasting ≥ 24 hours and < 24 hours, respectively, with or without a corresponding ischaemic lesion on brain imaging [1]. Minor ischaemic stroke was considered as ischaemic stroke with a National Institutes of Health Stroke Scale (NIHSS) score < 4 [4]. Exclusion criteria were clinical evaluation beyond 24 hours from the end of the transient event and a final diagnosis of non-ischaemic causes of symptoms such as migraine, seizure and anxiety [7]. Known cognitive impairment and significant comorbidity limiting participation in the study were also considered as exclusion criteria. We excluded patients with disabling stroke, defined as NIHSS ≥ 4 at 1 day after the event, to allow for a more reliable assessment of recurrent events [1]. The end point of the study was a new ischaemic cere-

brovascular event or vascular death at 90 days and additionally at 3 days. Recurrent TIA, stroke and vascular death as well as hospital admission and ongoing medication were recorded [7]. Recurrent stroke was diagnosed in patients in whom the initial symptoms had already substantially or fully recovered (or reached stabilization). We considered recurrent stroke as worsening by at least 4 points in the initial NIHSS score or clearly defined new symptoms of > 24 hours duration that suggested a new ischaemic event [3,9]. Although there may be natural stroke progression in the first 3 days, this progression would be unusual in patients with initial NIHSS < 4. A recurrent TIA was defined as a new neurological symptom of < 24 hours duration that is caused by focal ischaemia in the brain or retina [10,11]. Follow-up data were obtained from direct patient visits at 3 and 90 days or by centralized telephone interview if patients failed to attend the visit [3]. Follow-up was continued until death or 3 months from the date of the index event [10]. All recurrent TIA and strokes 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 [10]. In patients who had multiple recurrent events, the end point was classified as the first recurrence after the index ischaemic event [9]. All patients had blood test, electrocardiogram (ECG), head scan and duplex ultrasound of neck arterial trunks [3,12]. The decision to admit and of method of treatment in each case was left to the discretion of the stroke neurologist. We recommended strict control of vascular risk factors after discharge in all cases. Antiplatelet therapy was recommended in the acute phase of all patients with the exception of those patients with cardioembolic strokes, patients already pretreated with antiplatelet therapy, and patients with crescendo TIA or progressive stroke after antiplatelet treatment in whom anticoagulation was initiated [3].

Using the ABCD^2 score criteria, we analysed the following variables: age ≥ 60 years (1 point), initial hypertension > 140 mm Hg (systolic) and/or > 90 mm Hg (diastolic) (1 point); weakness (2 points); speech impairment (without weakness 1 point); duration of symptoms ≥ 1 hour (2 points), 10 minutes to 1 hour (1 point); and diabetes (1 point) for calculation of ABCD^2 score in each TIA or MIS patient. The ABCD^2 score is calculated by summing up points for five independent factors [13]. The score assigns 0 to 7 points. The ABCD^2 score is a risk assessment tool designed to improve the prediction of short-term stroke risk after a TIA. The score is optimized to predict the risk of stroke within 2 days after a TIA, but also predicts stroke risk within 90 days [14].

Estimation of discriminative ability of ABCD^2 score in TIA and MIS patients

The predictive accuracy of the ABCD^2 scoring system for TIA or stroke at 3 days and 90 days was quantified by the area under the curve (AUC) from the receiver operating characteristic curves (ROC) analysis (*c*-statistic) [1,4]. Values of AUC range from 0.5 (chance prediction and no discrimination) to 1.0 (perfect prediction) [1,4]. The sensitivities and specificities of prediction were determined at each cut-off of the score [1,4].

The research was approved by the ethics committee of Ghaem Hospital and each patient gave informed consent to participate. There was no delay in any of the therapeutic interventions in order to carry out the present study [6].

Results

A total of 511 patients (315 males, 196 females) meeting the eligibility criteria were recruited and completed the follow-up study during 2010 and 2011. Three hundred and ninety-three TIA patients (238 males, 155 females) and 118 MIS patients (77 males, 41 females) enrolled in the study. 72.4% of the patients (370/511) were admitted in hospital and the remainder were recruited from our stroke clinic. The mean age of all patients was 68.5 years (standard deviation [SD], 4.7) and 63.2% of the patients were ≥ 60 years of age. The elapsed time from symptom onset to evaluation of the index event was < 24 hours in all cases (mean, 14.6 hours; SD, 2.2). The mean age of TIA and MIS patients was 68.4 years and 66.2 years, respectively. One hundred and seventeen strokes (23.2%), 99 TIAs (19.6%), and 11 vascular deaths (2.2%) occurred within 3 months after the index event in the whole group of 511 patients with minor ischaemic events. The estimated risk of recurrent stroke, TIA and vascular death in our cohort is illustrated in Table 1. Eleven vascular deaths (4 males, 7 females) occurred during 3-month follow-up of our whole cohort and 6 vascular deaths happened at 3 days.

The values for ROC analysis for best results of the ABCD^2 score in predicting 3-day and 3-month

Table 1. Number and percentage of patients with recurrent stroke, transient ischaemic attack and vascular death during 3-day and 3-month follow-up of whole cohort

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

TIA – transient ischaemic attack, MIS – minor ischaemic stroke

recurrent ischaemic cerebrovascular events are provided in Table 2. On ROC analysis, the AUC (c-statistic) for 3-month and 3-day recurrent stroke in our TIA patients is 0.599 and 0.591, respectively. The ABCD^2 score was weakly predictive of 3-month and 3-day risk of stroke recurrence in follow-up of our TIA patients. The ABCD^2 score was trichotomized into low scores (0-3), intermediate scores (4-5) and high (6-7) scores [15].

Among our 393 TIA patients, 21.6% (85/393) had low (0-3) ABCD^2 scores, 52.9% (208/393) had intermediate scores (4-5) and 24.2% (95/393) had high (6-7) scores. Low, intermediate and high ABCD^2 scores were observed in 24.2% (32/132), 36.4% (48/132) and 40.2% (53/132) of TIA patients with stroke recurrence at 3 days. Low, intermediate and high ABCD^2 scores constituted 22.7% (32/141), 36.9% (52/141) and 40.2% (57/141) of TIA patients who had stroke in 3-month follow-up. The relation between 3-day and 3-month recurrence of stroke, TIA or both and distribution of ABCD^2 score in our TIA patients was not significant ($p > 0.05$).

Among our 118 MIS patients, 3.4% (4/118) had a low (≤ 3) ABCD^2 score, 49.2% (58/118) had a moderate (4-5) score and 46.6% (55/118) had a high (6-7) score. None of our 7 MIS patients who had recurrent stroke in 3-day follow-up had a low or intermediate ABCD^2 score and all of them had a score of 6 or 7. Recurrence of stroke occurred in 29 MIS patients during 3-month follow-up. Low, intermediate and high ABCD^2 scores constituted 0% (0/29), 10.3% (3/29) and 89.6% (26/29) of our MIS patients who had stroke recurrence in 3-month follow-up. The relation between 3-day and 3-month recurrence of stroke, TIA or both in our MIS patients was not significant ($p > 0.05$).

Table 3 illustrates the relation of outcome events with distribution of ABCD^2 score in index groups. On ROC analysis, the AUC (c-statistics) for 3-month and 3-day recurrent stroke in our 118 MIS patients is 0.727 and 0.728, respectively. The ABCD^2 score was highly pre-

Table 2. Values for receiver-operating curve (ROC) analysis for ABCD^2 score in predicting 3-day and 3-month recurrent ischaemic cerebrovascular events

Index event/outcome event*	ROC analysis, area under the curve (95% confidence interval)	Assessment of best ABCD^2 score**		
		Sensitivity	Specificity	Best ABCD^2 score
TIA/3-month recurrent stroke	0.599 (0.536-0.663)	100%	97.2%	≥ 2.5
MIS/3-month recurrent stroke	0.727 (0.602-0.852)	100%	76.9%	≥ 4.5
TIA/3-month recurrent TIA	0.535 (0.457-0.613)	100%	97.5%	≥ 1.5
MIS/3-month recurrent TIA	0.547 (0.403-0.692)	100%	96.1%	≥ 3.5
TIA/3-day recurrent stroke	0.591 (0.526-0.657)	100%	97.3%	≥ 1.5
MIS/3-day recurrent stroke	0.728 (0.588-0.868)	100%	45.6%	≥ 5.5
TIA/3-day recurrent TIA	0.569 (0.457-0.666)	100%	89.8%	≥ 2.5
MIS/3-day recurrent TIA	0.495 (0.349-0.641)	100%	96.2%	≥ 3.5

TIA – transient ischaemic attack, MIS – minor ischaemic stroke

**Six cases with vascular death at 3 days and 11 cases with vascular death at 3 months were omitted in c-statistics analysis*

***The result variables of the best predictive ABCD^2 score*

dictive of 3-month and 3-day risk of stroke recurrence in follow-up of our MIS patients. Among our whole cohort of 511 patients with minor ischaemic events, 17.4% (89/511) had low, 52.1% (266/511) had intermediate and 29.4% (150/511) had high ABCD^2 scores. One hundred and four recurrent strokes (20.3%) occurred in 3 days of the whole cohort with minor ischaemic events. Low, intermediate and high ABCD^2 scores constituted 29.8% (31/104), 35.6% (37/104) and 34.6% (36/104) of our patients with recurrent stroke in 3 days after the index event. One hundred and seventeen strokes were observed during 3-month follow-up of our whole group of 511 patients with minor ischaemic events. Low, intermediate, and high ABCD^2 scores constituted 26.5% (31/117), 35% (41/117) and 38.5% (45/117) of patients who had recurrent stroke during 3-month follow-up. Distribution of ABCD^2 score in the whole cohort was not significantly related to recurrent stroke at 3 days and 3 months ($p > 0.05$).

Table 3. The relation of outcome events with distribution of ABCD^2 score in index groups

Index event/outcome event*	χ^2 statistics	df	*P*-value
TIA/3-day stroke or TIA	11.384	7	0.123
Stroke/3-day stroke or TIA	4.050	5	0.542
Whole cohort/3-day stroke or TIA	7.770	7	0.352
TIA/3-day stroke	9.664	1	0.208
Stroke/3-day stroke	4.926	5	0.425
Whole cohort/3-day stroke	4.408	7	0.734
TIA/3-day TIA	4.049	7	0.774
Stroke/3-day TIA	2.245	5	0.814
Whole cohort/3-day TIA	4.341	7	0.701
TIA/3-month stroke or TIA	5.604	7	0.587
Stroke/3-month stroke or TIA	6.838	5	0.233
Whole cohort/3-month stroke or TIA	15.109	14	0.258
TIA/3-month stroke	6.931	7	0.436
Stroke/3-month stroke	3.595	5	0.609
Whole cohort/3-month stroke	10.379	7	0.183
TIA/3-month TIA	4.883	7	0.674
Stroke/3-month TIA	5.240	5	0.387
Whole cohort/3-month TIA	14.204	14	0.309

**Six cases with vascular death at 3 days and 11 cases with vascular death at 3 months were omitted in analysis.*
TIA – transient ischaemic attack

Discussion

The 3-day and 3-month rate of recurrent stroke in our whole cohort with TIA or MIS was 20.4% and 22.9%, 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 these recurrent events occurred in the first 3 days [15]. The risk of stroke was 2.5% at 2 days in an Italian study of TIA patients [7] and 11.1% at 90 days in another study in Canada [4]. 711 patients with TIA or MIS were prospectively recruited from five centres in the UK [10]. Recurrent stroke and TIA occurred at 90 days in 4% and 14% of the cohort, respectively [10]. A review of a Canadian stroke registry found that the stroke risk at 30 days after a first TIA was 8%, with half of these strokes occurring within the first 2 days [16]. Thirty-four percent risk of stroke at 3 days and 36% risk of stroke at 90 days in our TIA patients is much higher than in other reported studies [14,17,18]. The main reason for this high frequency of recurrent stroke in our TIA patients is diagnosis of index TIA by a stroke neurologist, which diminishes recruitment of migraine, seizure and neurotic patients as probable TIA. The main indication for admission of TIA patients in our centre is appearance of multiple or crescendo TIAs. This group of TIA patients are at greater risk than other cases [19]. Because 71.2% of our TIA patients had multiple TIAs and TIA cases constituted 76.9% of our whole group, this high rate of 3-day and 3-month stroke recurrence in our TIA cohort is reasonable. An Italian cohort study of TIA patients revealed that an ABCD score < 4 carries a very low risk of subsequent stroke and could be advocated as a reason not to admit such patients [7]. Rothwell *et al.* as creators of the initial ABCD score found it highly predictive of 7-day risk of stroke in probable or definite TIA patients in an Oxfordshire population [20]. The initial ABCD system was highly predictive of 7-day, 30-day and 90-day stroke risk (AUC = 0.75) in TIA patients [7,21]. The initial ABCD score was also highly predictive of 30-day risk of stroke in Greek TIA patients [12]. Another validation study of 180 TIA patients confirmed high AUC of 0.78 for 90-day risk of stroke using the ABCD^2 score [4]. Although the ABCD^2 score validated well (AUC = 0.62-0.83) in its original validation cohorts in the UK and California [13,14], the predictive capability remains modest and this score cannot replace clinical judgment [22]. In a cohort of 559 probable TIA patients

residing in Oxfordshire, the relationship between the risk of stroke at 7 days and both ABCD and ABCD^2 scores was strong ($p < 0.0001$) [23]. However, since no score will presumably ever reach an absolute predictive value, clinicians should be aware that some, albeit few, patients deemed to be at very low risk will still go on to have a stroke [7]. In the Dublin TIA study, when each ABCD^2 item was analysed individually, there were no associations with stroke at 7, 28 or 90 days and the AUC for 7 days, 28 days and 90 days stroke was 0.49, 0.55 and 0.55, respectively [24]. The ABCD^2 score performed no better than chance for prediction of 90-day stroke in the Dublin TIA study, largely related to the fact that 24.2% of patients who experienced a recurrence had low scores [24]. When the ABCD^2 score was trichotomized into low (0-3 pts), intermediate (4-5 pts), and high (6-7 pts) categories in the Dublin TIA study, a trend toward higher 90-day stroke risk was observed in the intermediate (10.7%) group compared to high (5.3%) and low (4.8%) groups [24]. The ABCD^2 score was modestly predictive (AUC = 0.62, AUC = 0.62) of stroke recurrence after MIS at 7 days and 90 days, respectively, in the Oxfordshire area [25]. Another validation study of the ABCD system revealed that its discriminatory ability is not optimal and TIA patients with a score of 0 to 3 still had a significant probability of having stroke within 90 days [26]. Therefore, ABCD score had limited clinical utility in risk stratification of acute TIA patients [26]. Another prospective study of 500 TIA patients was performed by Rothwell *et al.* Recurrent TIA and stroke were detected in 11% and 10% of their cohort within 7 days [9]. The ABCD^2 score was highly predictive of major recurrent stroke (AUC = 0.80, $p < 0.0001$), weakly predictive of minor stroke (AUC = 0.57, $p = 0.26$), and inversely related to risk of recurrent TIA (AUC = 0.37, $p = 0.001$) [9]. Therefore, the ABCD^2 predicted severity of recurrent events after TIA [9]. In general, the score was predictive of the 7-day risk of any stroke after TIA (AUC = 0.71, $p < 0.001$) [9]. The ABCD^2 appeared to predict severity of recurrent events rather than risk of any recurrent event in TIA patients [9].

There are few published data on the risk of recurrent TIA after minor ischaemic cerebrovascular events [9]. It should be stressed, however, that the ABCD^2 score was developed for TIA patients alone. The duration factor, for instance, is useless for MIS patients [27], and all of them will take an ABCD^2 score of ≥ 2 based on the duration item.

The ASPIRE approach for TIA and MIS patients defined high-risk patients for stroke recurrence at 90 days as those with any of the following components: ABCD^2 score ≥ 4; motor or speech symptoms lasting longer than 5 minutes; patients with atrial fibrillation [28]. The ASPIRE approach had an AUC of 0.62 in discrimination of high-risk patients for stroke at 90 days [28]. However, none of the ASPIRE items were associated with risk of stroke in univariate and multivariate analysis of our patients.

The Essen stroke risk score was designed for prediction of stroke, myocardial infarction and vascular death in 1-year follow-up of the REACH registry which includes TIA or MIS patients [29]. The corresponding AUC of the Essen stroke risk score was low (0.56) [29]. The Essen stroke risk score and SPI-II were not better than chance for prediction of recurrent stroke at 7 days and 90 days in index TIA or MIS patients in another study (AUC = 0.50, AUC = 0.48) and they had a low positive predictive value [25]. Thus, physicians may question the usefulness of predictive scores in daily clinical practice [1].

Conclusions

1. In patients with minor ischaemic events, clinical scores will never replace clinical acumen, and a high-risk etiology should be managed urgently, whatever the risk is on a clinical score.
2. The ABCD^2 score is highly predictive of short-term recurrent stroke in MIS patients but not TIA cases, although it was originally designed for patients with TIA.

Acknowledgements

This research was funded by grant number 6500 by the research deputy, Mashhad University of Medical Sciences.

Disclosure

Authors report no conflict of interest.

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