European Journal of Neurology 2013, 20: 1088–1093 doi:10.1111/ene.12141

Predictive value of brain and vascular imaging including intracranial vessels in transient ischaemic attack patients: external validation of the ABCD3-I score

F. Purroy[a], P. E. Jiménez-Caballero[b], G. Mauri-Capdevila[c], M. J. Torres[d], A. Gorospe[d], J. M. Ramírez Moreno[e], N. P. de la Ossa[f], D. Cánovas[g], J. Arenillas[h], J. Álvarez-Sabín[i], P. Martínez Sánchez[j], B. Fuentes[j], R. Delgado-Mederos[k], J. Martí-Fàbregas[k], A. Rodríguez Campello[l] and J. Masjuán[m] from the PROMAPA study: Stroke Project, Cerebrovascular Diseases Study Group, Spanish Neurological Society

[a]*Stroke Unit, Hospital Universitari Arnau de Vilanova, Lleida;* [b]*Department of Neurology, Hospital San Pedro de Alcántara de Cáceres, Cáceres;* [c]*Stroke Unit, Hospital Universitari Arnau de Vilanova, Lleida;* [d]*Hospital Universitari Son Dureta, Palma de Mallorca;* [e]*Hospital Universitario Infanta Cristina de Badajoz, Badajoz;* [f]*Hospital Universitari Germans Trias i Pujol, Badalona;* [g]*Hospital Parc Taulí, Sabadell;* [h]*Hospital Clínico Universitario de Valladolid, Valladolid;* [i]*Hospital Universitari Vall d'Hebron, Barcelona;* [j]*Hospital Universitario La Paz, Madrid;* [k]*Hospital Universitari de la Santa Creu i Sant Pau, Barcelona;* [l]*Hospital del Mar, Barcelona; and* [m]*Hospital Universitario Ramón y Cajal, Madrid, Spain*

Keywords:
cerebral ischaemia, diffusion-weighted, etiology, magnetic resonance imaging, outcome, prognosis, transient

Received 24 September 2012
Accepted 14 February 2013

Background and purpose: Recently, brain and vascular imaging have been added to clinical variables to identify patients with transient ischaemic attack (TIA) with a high risk of stroke recurrence. The aim of our study was to externally validate the ABCD3-I score and the same score taking into account intracranial circulation.

Methods: We analyzed data from 1137 patients with TIA from the PROMAPA study who underwent diffusion-weighted magnetic resonance imaging (DWI) within 7 days of symptom onset. Clinical variables and diagnostic work-up were recorded prospectively. The end-points were subsequent stroke at 7 and 90 days follow-up.

Results: A total of 463 (40.7%) subjects fulfilled all inclusion criteria. During follow-up, eight patients (1.7%) had a stroke within 7 days, and 14 (3.1%) had a stroke within 3 months. In the Cox proportional hazard multivariate analyses, the combination of large-artery atherosclerosis and positive DWI remained as independent predictors of stroke recurrence at 7- and 90-day follow-up [HR 8.23, 95% confidence interval (CI) 2.89–23.46, $P < 0.001$]. The ABCD3-I score was a powerful predictor of subsequent stroke. The area under the receiver operating characteristic curve was 0.83 (95% CI 0.72–0.93) at 7 days and 0.69 (95% CI 0.53–0.85) at 90 days. When we include intracranial vessel disease in the score, the area under the curve increases but the difference observed was non-significant.

Conclusion: The inclusion of vascular and neuroimaging information to clinical scales (ABCD3-I score) provides important prognostic information and also helps management decisions, although it cannot give a complete distinction between high-risk and low-risk groups.

Introduction

Stroke is the leading cause of acquired neurological discapacity. Transient ischaemic attacks (TIAs) preceded stroke in almost 20% of cases [1]. These warning events provide a great opportunity for \prevention. Recently, a new tissue-based definition of TIA has been proposed by the American Heart Association (AHA) scientific committee [2]. Nowadays, only imaging techniques such as diffusion-weighted magnetic resonance imaging (MRI; DWI) are able to detect acute brain infarction. Despite the transitivity of symptoms, DWI reveals an area of water restriction because of acute brain ischaemia in almost half of patients [3,4]. Patients with transient symptoms and a

Correspondence: F. Purroy, Stroke Unit, Department of Neurology, Professor Universitat de Lleida, Hospital Universitari Arnau de Vilanova de, Lleida, IRBLleida, Avda Rovira Roure, 80, Lleida 25198, Spain (tel.: 0034973248100; fax: 973248754; e-mail: fpurroygarcia@gmail.com).

EUROPEAN JOURNAL OF NEUROLOGY
THE OFFICIAL JOURNAL OF THE EUROPEAN FEDERATION OF NEUROLOGICAL SOCIETIES

restricted diffusion lesion on MRI are considered by the AHA scientific committee to have suffered a brain infarction. Moreover, classically defined patients with TIA (duration < 24 h) with abnormalities on DWI scans have a higher risk of recurrent stroke than those patients with transient episodes and normal DWI [4–9]. Therefore, neuroimaging is becoming an essential tool for the diagnosis, management and triage of patients with acute TIA. Recently, the ABCD3-I score that incorporates not only DWI findings but also carotid stenosis and the clinical variable 'dual TIA' defined as prior TIA within 1 week of the index event [10] has been proposed to enhance the predictive utility of ABCD2 score. Additionally vascular imaging of intracranial arteries is also recommended to identify patients with a high risk of subsequent stroke who will benefit from early treatments [11,12].

The aim of our study was to investigate the predictive accuracy of vascular and brain imaging, and to externally validate the original ABCD3-I score [10] and this score taking into account intracranial circulation.

Methods

The PROMAPA study [Proyecto Español del Manejo y evaluación de los pacientes con un ataque isquémico transitorio (in Spanish)] methodology has been described in detail previously [13]. In this subanalysis, we included patients from 30 Spanish stroke centers between January 2008 and December 2009. A TIA was defined as a reversible episode of neurological deficit of ischaemic origin that resolved completely within 24 h [14]. A neurologist treated all patients within the first 48 h after the onset of symptoms. We excluded patients with a modified Rankin Scale (mRS) score > 3 and/or patients with an alternative diagnosis other than TIA. The mRS was always measured at baseline after symptom resolution. In all patients of this sub-study, an MRI that included DWI was performed within 7 [4.10 (SD 3.58)] days after the onset of symptoms and previous to stroke recurrence.

The study was approved by the ethics committee of the Arnau de Vilanova University Hospital and all the institutions involved in the study. Written informed consent was obtained from all study participants. The duration and typology of clinical symptoms, vascular risk factors and etiological work-ups were prospectively recorded in a case report.

Transient ischaemic attacks were classified etiologically according to Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria [15] as due to large-artery atherosclerosis (LAA), small-vessel disease (SV), cardioembolism (CE), other cause or undetermined cause (UND). LAA was defined as > 50% narrowing of the ipsilateral internal carotid artery lumen or intracranial vessel lumen on imaging, including Doppler or duplex ultrasound, magnetic resonance angiogram or angiography computerized tomography.

The primary outcome measure was the occurrence of a subsequent stroke at 7- and 90-day follow-ups. Recurrence of a TIA was not considered an end-point. Clinical assessments were performed at 7 and 90 days by a neurovascular neurologist from each participating center.

Diffusion-weighted MRI hyperintensity (positive DWI) was defined as areas of high signal intensity on isotropic DWI reflecting an acute ischaemic lesion.

Determination of the ABCD2 [16], ABCD2-I [17] and ABCD3-I [10] risk scores was performed prospectively. The ABCD2-I score was calculated by assigning three points for the presence of acute ischaemic lesions on DWI. The ABCD3-I score was derived from the ABCD2 score by assigning two points for dual TIA (≥ 2 episodes of TIA within 7 days), two points for stenosis at least 50% on carotid imaging, and two points for abnormal DWI. Moreover, we calculated the ABCD3-I score taking into account symptomatic intracranial stenosis (IS; two points).

From an initial 1137 patients included in the PROMAPA study, a total of 463 fulfilled all inclusion criteria. The baseline characteristics of all patients with and without DWI performed are provided in Table 1. Patients with DWI performed were younger, with a higher frequency of valvulopathy, vertebrobasilar symptoms, longer episodes and LAA than patients without DWI performed.

Statistical analysis was performed with the SPSS (SPSS, Chicago, IL, USA) statistical package, version 15.0. Data are reported using standard descriptive statistics. Univariate analysis was performed to detect variables associated with a positive DWI. Finally, a forward stepwise multivariate logistic regression was conducted for variables that reached a value of $P < 0.05$ on the univariate analysis. Moreover, univariate analysis was performed to detect variables associated with the occurrence of a cerebral ischaemic event. Forward stepwise Cox proportional-hazards multivariate analyses were used to identify predictors of further cerebral ischaemic events in which age, sex, vascular risk factors and variables showing a value of $P < 0.05$ on univariate testing were included. A probability value < 0.05 was considered significant.

Predictive values for ABCD2, ABCD2-I and ABCD3-I scores were expressed as the area under the receiver operating characteristic curve (AUC) for a 95% confidence interval (CI) using standard methods. Ideal discrimination produces an AUC of 1.0, whereas discrimination that is no better than chance produces

Table 1 Baseline characteristics of patients with and without DWI performed

Variable	DWI performed (n = 463)	Not DWI performed (n = 792)	P
Risk factors			
Age, years (SD)	65.5 (13.5)	69.4 (12.8)	< 0.001
Male	274 (59.2)	467 (59.0)	0.993
Hypertension	274 (59.2)	503 (63.5)	0.124
Previous stroke	58 (12.6)	94 (11.9)	0.311
Diabetes mellitus	121 (26.1)	202 (25.5)	0.792
Coronary disease	69 (14.9)	124 (15.7)	0.710
Smoking	123 (26.6)	190 (24.0)	0.325
Valvulopathy	8 (1.7)	50 (6.3)	< 0.001
Hypercholesterolemia	180 (38.9)	299 (37.8)	0.710
Atrial fibrillation	40 (8.6)	97 (12.2)	0.053
Clinical features			
Dual TIA	110 (23.8)	194 (24.5)	0.959
Speech impairment	281 (60.7)	514 (64.9)	0.136
Motor weakness	218 (47.1)	375 (47.3)	0.915
Isolated sensory symptoms	38 (8.2)	68 (8.6)	0.792
Vertebrobasilar symptoms	82 (17.7)	75 (9.5)	< 0.001
Lacunar syndrome	148 (32.0)	264 (33.3)	0.617
Duration			
< 10 min	58 (12.6)	145 (18.3)	0.001
10–59 min	159 (34.5)	310 (39.1)	
1 h	244 (52.9)	337 (42.6)	
ABCD2, (SD)	4.58 (1.41)	4.55 (1.41)	0.765
Etiology			
LAA	100 (21.6)	119 (15.0)	0.035
CE	97 (21.0)	166 (21.0)	
UND	145 (31.3)	280 (35.4)	
SV	116 (25.0)	211 (26.7)	
OC	5 (1.1)	16 (2.0)	
IS	37 (8.0)	27 (3.4)	0.006
7-day stroke recurrence	8 (1.7)	24 (3.0)	0.153
90-day stroke recurrence	14 (3.1)	37 (4.7)	0.232

CE, cardioembolism; DWI, diffusion-weighted magnetic resonance imaging; IS, intracranial stenosis; LAA, large-artery atherosclerosis; OC, other cause; SV, small-vessel disease; TIA, transient ischaemic attack; UND, undetermined cause.

Table 2 Univariate analyses of variables associated with positive DWI

Variable	Normal DWI (n = 269)	Positive DWI (n = 194)	P
Risk factors			
Age, years (SD)	66.1 (13.5)	64.8 (13.5)	0.338
Male	144 (53.5)	130 (67.0)	0.004
Hypertension	156 (58.0)	118 (60.8)	0.541
Previous stroke	33 (12.3)	25 (13.0)	0.506
Diabetes mellitus	76 (28.3)	45 (23.2)	0.222
Coronary disease	35 (13.1)	34 (17.5)	0.184
Smoking	54 (20.1)	69 (35.6)	< 0.001
Valvulopathy			
Hypercholesterolemia	110 (40.9)	70 (36.1)	0.295
Atrial fibrillation	20 (7.4)	20 (10.3)	0.277
Clinical features			
Dual TIA	52 (19.5)	58 (30.2)	0.008
Speech impairment	162 (60.2)	119 (61.3)	0.808
Motor weakness	108 (40.1)	110 (56.7)	< 0.001
Isolated sensory symptoms	26 (9.7)	12 (6.2)	0.178
Vertebrobasilar symptoms	46 (17.1)	36 (18.6)	0.685
Lacunar syndrome	84 (31.2)	64 (33.0)	0.688
Duration			
< 10 min	40 (15.0)	18 (9.3)	0.101
10–59 min	95 (35.6)	64 (33.0)	
1 h	132 (49.4)	112 (57.7)	
ABCD2, (SD)	4.48 (1.47)	4.70 (1.31)	0.088
Etiology			
LAA	47 (17.5)	53 (27.3)	< 0.001
CE	40 (14.9)	57 (29.4)	
UND	114 (42.4)	31 (16.0)	
SV	64 (23.8)	52 (26.8)	
OC	4 (1.5)	1 (0.5)	
IS	19 (7.1)	18 (9.3)	0.206

CE, cardioembolism; DWI, diffusion-weighted magnetic resonance imaging; IS, intracranial stenosis; LAA, large-artery atherosclerosis; OC, other cause; SV, small-vessel disease; TIA, transient ischaemic attack; UND, undetermined cause.

an AUC of 0.5. We compared the respective AUC curves using the DeLong method [18].

Results

A total of 463 patients were included in the study. The mean age of patients was 65.5 (SD 13.5) years, and 59.0% were male (Table 1). Hypertension was the main vascular risk factor. Acute ischaemic lesions on DWI were identified in 194 (41.9%) patients. Regarding clinical risk scores, the mean ABCD2 score was 4.58 (SD 1.41) and the mean ABCD2-I score was 5.83 (SD 2.12). LAA was found in 100 (21.6%) patients; 37 (8.0%) patients had an IS. A 90-day follow-up was achieved in 454 (98.3%) patients.

The univariate analysis revealed (Table 2) that smoking, motor weakness and LAA or CE were associated with a positive DWI ($P < 0.001$). In the logistic regression model, motor weakness [odds ratio (OR) 1.85, 95% CI 1.26–2.72, $P = 0.002$] and LAA or CE (OR 2.65, 95% CI 1.80–3.90, $P < 0.001$) remained as independent predictors of a positive DWI.

Recurrent strokes occurred in eight (1.7%) patients at 7-day follow-up, and in 14 (3.1%) patients within the first 90 days after the index TIA. In univariate analyses (Table 3), only LAA and the composite variable of LAA and positive DWI were associated with stroke recurrence at 7 and 90 days after the onset of symptoms. Positive DWI was only associated with early risk of subsequent stroke at 7-day follow-up. In the Cox proportional hazard multivariate analyses, the composite variable LAA and positive DWI remained as an independent predictor of stroke recurrence after 7 and 90 days of follow-up [hazard ratio (HR) 7.89, 95% CI 1.77–35.26, $P = 0.007$; HR 5.16, 95% CI 1.73–15.34, $P = 0.003$, respectively] (Table 4).

The discriminatory power as measured by AUC of ABCD2, ABCD2-I, ABCD3-I and ABCD3-I including IS is shown in Table 4. The AUCs of both forms of ABCD3-I were higher than ABCD2, but the difference only reached statistical significance if we compared the predictive accuracy of ABCD3-I including IS and ABCD2 for stroke recurrence at 7 days ($P = 0.030$). The AUC of ABCD3-I including IS for both end-points was slightly higher than ABCD3-I and ABCD2-I, but without reaching statistical significance.

Discussion

In this multicenter cohort of patients with classical TIA and DWI performed within the first week after symptoms onset we observed, as in other previous studies [4,8], that those patients with positive DWI and LAA have the highest risk of early stroke recurrence. Patients with this composite variable have eight times more probability of having a subsequent stroke during the next 90 days than patients without it. As in the original population and in the first independent validation sample, the ABCD3-I score increases the AUC at each time interval compared with the ABCD2 score, reaching statistical significance when the risk of subsequent stroke at the 7-day follow-up was evaluated.

It is important to notice that none of the clinical variables from the ABCD2 score [16] was associated with the two end-points as in the entire cohort of patients of the PROMAPA study [13]. The ABCD2 score was published using population-based registries and was designed for initial primary care triage. A recent study has noted an adequate predictive utility of this score in non-specialist physicians but not in stroke specialists [19] by increasing the reliability of the diagnosis of true transient brain ischaemia [20]. The ABCD3-I was designed for secondary or tertiary care specialist setting. In our study, a vascular neurologist evaluated all patients.

Over the last decade, much attention has been placed on neuroimaging in TIA [21]. DWI is an objective marker of acute ischaemia. In our study, patients with positive DWI are three times more likely to have a subsequent stroke. We hypothesized that DWI not

Table 3 Univariate analysis of variables associated with stroke recurrence

	Stroke recurrence at 7-day follow-up			Stroke recurrence at 90-day follow-up		
Variable	No (n = 455)	Yes (n = 8)	P	No (n = 440)	Yes (n = 14)	P
Risk factors						
Age, years (SD)	65.5 (13.5)	69.9 (15.7)	0.359	65.5 (13.5)	66.7 (14.7)	0.738
Male	268 (59.0)	6 (75.0)	0.362	256 (58.2)	11 (78.6)	0.127
Hypertension	266 (58.6)	7 (87.5)	0.099	256 (58.2)	11 (78.6)	0.127
Previous stroke	56 (12.4)	2 (25.0)	0.556	56 (12.8)	2 (14.3)	0.981
Diabetes mellitus	118 (26.0)	2 (25.0)	0.949	117 (26.6)	3 (21.4)	0.666
Coronary disease	67 (14.8)	2 (25.0)	0.422	63 (14.4)	4 (28.6)	0.140
Smoking	121 (26.7)	2 (25.0)	0.914	116 (26.4)	4 (28.6)	0.858
Hypercholesterolemia	177 (39.0)	2 (25.0)	0.421	171 (38.9)	3 (21.4)	0.187
Atrial fibrillation	40 (8.8)	0 (0)	0.380	40 (9.1)	0 (0)	0.237
Clinical features						
Dual TIA	107 (23.8)	3 (37.5)	0.370	102 (23.4)	4 (28.6)	0.657
Speech impairment	274 (60.4)	6 (75.0)	0.401	264 (60.0)	11 (78.6)	0.162
Motor weakness	214 (47.1)	4 (50.0)	0.872	206 (46.8)	7 (50.0)	0.814
Isolated sensory symptoms	38 (8.4)	0 (0)	1	38 (8.6)	0 (0)	0.251
Vertebrobasilar symptoms	80 (17.6)	2 (25.0)	0.588	78 (17.7)	2 (14.3)	0.739
Lacunar syndrome	146 (32.2)	2 (25.0)	1	144 (32.7)	3 (21.4)	0.563
Duration $\geq$ 1 h	239 (52.9)	4 (50.0)	0.984	232 (53.0)	7 (50.0)	0.970
ABCD2, median (IQR)	4.0 (5.0–6.0)	4.5 (4.0–5.0)	0.891	5.0 (4.0–6.0)	5.0 (4.0–5.0)	0.968
Etiology						
LAA	95 (20.9)	5 (62.5)	0.05291 (20.7)	8 (57.1)	0.026	
CE	95 (20.9)	2 (25.0)	93 (21.1)	2 (14.3)		
UND	143 (31.5)	1 (0.7)	138 (31.4)	3 (21.4)		
SV	116 (25.6)	0 (0)	113 (25.7)	1 (7.1)		
OC	5 (1.1)	0 (0)		5 (1.1.)	0 (0)	
IS	34 (10.6)	3 (42.9)	0.007	33 (10.7)	4 (30.8)	0.027
Positive DWI	186	8 (1)	0.001	176 (42.3)	8 (66.7)	0.093
LAA and positive DWI	48 (10.6)	5 (62.5)	< 0.001	45 (10.3)	14 (3.1)	< 0.001

CE, cardioembolism; DWI, diffusion-weighted magnetic resonance imaging; IS, intracranial stenosis; LAA, large-artery atherosclerosis; OC, other cause; SV, small-vessel disease; TIA, transient ischaemic attack; UND, undetermined cause.

Table 4 Predictive accuracy of prognostic scores for stroke recurrent stroke at the 7- and 90-day follow-up

	Stroke recurrence at 7 days			Stroke recurrence at 90 days		
Clinical score	AUC	Comparison with ABCD3-I	Comparison with ABCD3-I including IS	AUC	Comparison with ABCD3-I	Comparison with ABCD3-I including IS
ABCD2	0.49 (0.32–0.66)	$P = 0.062$	$P = 0.030$	0.50 (0.37–0.62)	$P = 0.225$	$P = 0.191$
ABCD2-I	0.76 (0.66–0.85)	$P = 0.735$	$P = 0.587$	0.63 (0.49–0.78)	$P = 0.441$	$P = 0.365$
ABCD3-I	0.77 (0.65–0.89)	–	$P = 0.552$	0.66 (0.50–0.81)	–	$P = 0.545$
ABCD3-I including IS	0.79 (0.65–0.89)	$P = 0.552$	–	0.67 (0.51–0.83)	$P = 0.545$	–

AUC, area under the receiver operating characteristic curve; IS, intracranial stenosis.

only improves the diagnostic accuracy of brain ischaemia but also identifies unstable mechanisms of brain ischaemia. DWI also adds prognosis information to patients with an established high risk of subsequent stroke, for example subjects with high-grade IS or extracranial stenosis. Therefore, the combination of LAA and positive DWI remained as an independent predictor of stroke recurrence especially during the first 7 days after symptom onset. Patients with this combination may have more unstable vessel plaques. It is known that patients with high-grade stenosis who do not undergo early endarterectomy or carotid artery stenting have an extremely high risk of subsequent ischaemic cerebrovascular events [22], and they probably benefit from early high-dose statin therapy [23] or other aggressive therapies like double antiaggregation [24]. Previously, Calvet *et al.* [8] and Purroy *et al.* [4] pointed out similar results, and recommended the inclusion of vascular and imaging information in any prediction score of early risk of stroke after TIA. However, the AUC difference observed between ABCD2-I and both versions of ABCD3-I was non-significant. In addition, when we add intracranial information into the ABCD3-I score, its prognostic accuracy slightly increases without reaching statistical significance. It is previously reported that those patients with IS have very early risk of stroke recurrence [25]. We hypothesized that some of these patients were excluded because they have had a subsequent stroke before performing DWI. In the same direction, the variable dual TIA was not associated with stroke recurrence. It is known that patients with dual transient symptoms reflect an unstable situation and have a higher risk of subsequent cerebral infarction [26–28]. In the complete cohort of patients from the PROMAPA study, having multiple episodes of TIAs within 7 days was an independent predictor of stroke recurrence at 7 and 90 days [13]. Therefore, we thought that some patients with very early stroke recurrence were excluded.

Moreover, there are some other limitations that the small number of patients with stroke recurrence prevents us from making generalizations about the results. In addition, we included patients from 30 stroke centers in Spain, and there may have been variations in patient study and management methods. However, in all centers, patients were evaluated with a 1.5 TESLAS MRI and they used the same definition of positive DWI. Finally, in our study we used the TOAST system. But, if we want to help fast management decisions, a simple vessel imaging definition in the ABCD3-I score, like stenosis at least 50% on carotid or intracranial imaging, would be more useful than the TOAST system in a clinical setting. The TOAST system has limitations when it comes to classifying patients as UND because patients with multiple potentially contributory mechanisms and patients who have been investigated incompletely are classified in this category [29].

Transient ischaemic attack is recognized to require urgent medical attention, and the American Stroke Association [2] recommends hospitalization for patients who cannot complete an appropriate diagnostic evaluation within 48 h after TIA. According to our results, not only carotid imaging but also intracranial imaging and brain imaging including DWI are necessary to have enough prognostic information to establish the correct therapeutic or management strategy. Therefore, in an external validation study, ABCD3-I score provides prognostic information and also helps management decisions, although it cannot give a complete distinction between high-risk and low-risk groups.

Acknowledgements

The authors thank Marc Merin for language editing of the manuscript. This study was sponsored by Sanofi-Aventis.

Disclosure of conflict of interest

Dr F. Purroy received a grant from Instituto de Salud Carlos III FIS Number PIO81398. Dr B. Fuentes received a grant from Instituto de Salud Carlos III-programa de Intensificación and Agencia Laín Entralgo-Comunidad de Madrid (I3SNS). Dr J. Masjuán

serves on the scientific advisory board for Boehringer Ingelheim. The other authors report no disclosures.

References

1. Rothwell PM, Warlow CP. Timing of TIAs preceding stroke: time window for prevention is very short. *Neurology* 2005; **64:** 817–820.
2. Easton JD, Saver JL, Albers GW, *et al*. Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease. The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists. *Stroke* 2009; **40:** 2276–2293.
3. Redgrave JNE, Coutts SB, Schulz UG, *et al*. Systematic review of associations between the presence of acute ischemic lesions on diffusion-weighted imaging and clinical predictors of early stroke risk after transient ischemic attack. *Stroke* 2007; **38:** 1482–1488.
4. Purroy F, Begue R, Gil MI, , *et al*. Patterns of diffusion-weighted magnetic resonance imaging associated with etiology improve the accuracy of prognosis after transient ischaemic attack. *Eur J Neurol* 2011; **18:** 121–128.
5. Purroy F, Montaner J, Rovira A, *et al*. Higher risk of further vascular events among transient ischemic attack patients with diffusion-weighted imaging acute ischemic lesions. *Stroke* 2004; **35:** 2313–2319.
6. Ay H, Koroshetz WJ, Benner T, *et al*. Transient ischemic attack with infarction: a unique syndrome? *Ann Neurol* 2005; **57:** 679–686.
7. Boulanger J-M, Coutts SB, Eliasziw M, *et al*. Diffusion-weighted imaging-negative patients with transient ischemic attack are at risk of recurrent transient events. *Stroke* 2007; **38:** 2367–2369.
8. Calvet D, Touze E, Oppenheim C, *et al*. DWI lesions and TIA etiology improve the prediction of stroke after TIA. *Stroke* 2009; **40:** 187–192.
9. Prabhakaran S, Chong JY, Sacco RL. Impact of abnormal diffusion-weighted imaging results on short-term outcome following transient ischemic attack. *Arch Neurol* 2007; **64:** 1105–1109.
10. Merwick A, Albers GW, Amarenco P, *et al*. Addition of brain and carotid imaging to the ABCD(2) score to identify patients at early risk of stroke after transient ischaemic attack: a multicentre observational study. *Lancet Neurol* 2010; **9:** 1060–1069.
11. Purroy F, Montaner J, Delgado P, *et al*. Usefulness of urgent combined carotid/transcranial ultrasound testing in early prognosis of TIA patients. *Med Clin (Barc)* 2006; **126:** 647–650.
12. Meseguer E, Lavallee PC, Mazighi M, *et al*. Yield of systematic transcranial Doppler in patients with transient ischemic attack. *Ann Neurol* 2010; **68:** 9–17.
13. Purroy F, Jiménez-Caballero PE, Gorospe A, *et al*. Prediction of early stroke recurrence in TIA patients from the PROMAPA study. A comparison of prognostic risk scores. *Cerebrovasc Dis* 2012; **33:** 182–189.
14. Special report from the National Institute of Neurological Disorders and Stroke. Classification of Cerebrovascular Diseases III. *Stroke* 1990; **21:** 637–676.
15. Adams HP Jr, Bendixen BH, Kappelle LJ, *et al*. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. *Stroke* 1993; **24:** 35–41.
16. Johnston SC, Rothwell PM, Nguyen-Huynh MN, *et al*. Validation and refinement of scores to predict very early stroke risk after transient ischaemic attack. *Lancet* 2007; **369:** 283–292.
17. Giles MF, Albers GW, Amarenco P, *et al*. Addition of brain infarction to the ABCD2 Score (ABCD2I): a collaborative analysis of unpublished data on 4574 patients. *Stroke* 2010; **41:** 1907–1913.
18. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics* 1988; **44:** 837–845.
19. Sheehan OC, Merwick A, Kelly LA, *et al*. Diagnostic usefulness of the ABCD2 score to distinguish transient ischemic attack and minor ischemic stroke from noncerebrovascular events: the north Dublin TIA study. *Stroke* 2009; **40:** 3449–3454.
20. Quinn TJ, Cameron AC, Dawson J, *et al*. ABCD2 scores and prediction of noncerebrovascular diagnoses in an outpatient population: a case-control study. *Stroke* 2009; **40:** 749–753.
21. Giles MF, Albers GW, Amarenco P, *et al*. Early stroke risk and ABCD2 score performance in tissue- vs time-defined TIA: a multicenter study. *Neurology* 2011; **258:** 2107–2109.
22. Rothwell PM, Eliasziw M, Gutnikov SA, *et al*. Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery. *Lancet* 2004; **363:** 915–924.
23. Amarenco P, Goldstein LB, Szarek M, *et al*. Effects of intense low-density lipoprotein cholesterol reduction in patients with stroke or transient ischemic attack: the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial. *Stroke* 2007; **38:** 3198–3204.
24. Kennedy J, Hill MD, Ryckborst KJ, *et al*. Fast assessment of stroke and transient ischaemic attack to prevent early recurrence (FASTER): a randomised controlled pilot trial. *Lancet Neurol* 2007; **6:** 961–969.
25. Purroy F, Begue R, Quilez A, *et al*. Diagnostic lessons of recurrence pattern after transient ischemic attacks. *Med Clin (Barc)* 2009; **133:** 283–289.
26. Chatzikonstantinou A, Willmann O, Jager T, *et al*. Transient ischemic attack patients with fluctuations are at highest risk for early stroke. *Cerebrovasc Dis* 2009; **27:** 594–598.
27. Wilson SE, Mayberg MR, Yatsu F, Weiss DG. Crescendo transient ischemic attacks: a surgical imperative. Veterans Affairs trialists. *J Vasc Surg* 1993; **17:** 249–255.
28. Nakajima M, Hirano T, Naritomi H, Minematsu K. Symptom progression or fluctuation in transient ischemic attack patients predicts subsequent stroke. *Cerebrovasc Dis* 2010; **29:** 221–227.
29. Marnane M, Duggan CA, Sheehan OC, *et al*. Stroke subtype classification to mechanism-specific and undetermined categories by TOAST, A-S-C-O, and causative classification system: direct comparison in the North Dublin population stroke study. *Stroke* 2010; **41:** 1579–1586.