Risk Prediction of Subsequent Early Stroke in Patients with Transient Ischemic Attacks

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Key Words

Transient ischemic attack · Stroke recurrence ·
Symptom fluctuations · ABCD2 score · ABCD3-I score

Abstract

Background: Prognostic clinical scores (ABCD2 and ABCD3-I), as well as specific clinical signs and symptoms (e.g. fluctuations) have been used to predict early stroke risk in patients admitted to hospital after transient ischemic attacks (TIAs). We compared the utility of these scores and signs for prognosis and outcome. **Methods:** 235 patients with TIAs admitted to our Comprehensive Stroke Center entered the study. Patients were monitored over 3 days with detailed brain imaging [diffusion-weighted imaging (DWI) was performed either directly on admission or within 24 h from admission and was repeated in cases of stroke recurrence], vascular ultrasound imaging, repeated neurological scoring and continuous ECG monitoring. Duration, fluctuation of symptoms, clinical patterns of initial signs and/or symptoms as well as general patient characteristics and stroke risk factors, including atrial fibrillation (AF), were analyzed and recorded in our stroke databank. Fluctuation of symptoms was defined as the complete remitting and relapsing of TIA symptoms for ≥ 2 times in the acute phase within the first

24 h. This differs from the 'dual TIA' definition of the ABCD3-I score, which is defined as 'an earlier TIA within 7 days of the index event'. ABCD2 and ABCD3-I scores were calculated and the patients were placed into three categories: 'low', 'moderate' and 'high' risk for every score. Risk associations were assessed by the χ^2 test and the ϕ -coefficient. **Results:** Out of 235 patients, 17 patients (7.2%) experienced an early stroke during hospitalization (mean duration 7.4 ± 2.7 days). ABCD2 scores failed to predict early stroke ($p = 0.544$). ABCD3-I scores correlated better with early stroke recurrences ($p = 0.021$). Positive DWI findings (6/17; 35.3%), presence of carotid stenosis (3/17; 17.6%) or AF (1/17; 5.9%) alone failed to predict early stroke. Fluctuations of symptoms, however, showed a significant prediction for early stroke after TIA: 13/17 (76.5%) patients ($p < 0.001$). The combination of symptom fluctuation and MR-DWI-positive findings (4/17; 23.5%) also turned out to be statistically significant in this regard ($p = 0.003$), while the combination of symptom fluctuations with carotid stenosis $\geq 50\%$ did not ($p = 0.151$). Combining fluctuations with carotid stenosis and DWI-positive findings did not improve the result ($p = 0.029$). **Conclusions:** While the ABCD3-I score is indeed very useful, symptom fluctuations seem to be the best available and an easily accessible and applicable parameter for individual prediction of a high early stroke risk after TIAs. Copyright © 2013 S. Karger AG, Basel

Introduction

Patients with transient ischemic attack (TIA) are known to be at high risk with regard to subsequent early stroke [1–4]. Since this risk was realized, different scores and strategies have been suggested for stroke prediction after TIA. Early neuroimaging detection of cerebral ischemia has been suggested to be a strong prognostic factor, as infarction on diffusion-weighted images (DWI) has been shown to be associated with high early stroke risk [5–7]. The ABCD2 score was developed for acute risk stratification [8]. The ABCD3-I score additionally takes into consideration positive DWI findings, dual TIA episodes and relevant carotid stenosis [9, 10]. This combination has been claimed to be of particular value for individual stroke prediction. Previous studies have shown that ‘unstable’ TIAs, i.e. with symptom fluctuations, can identify patients at very high risk for subsequent stroke [11, 12]. We thus compared the different risk assessment scores with clinical fluctuations in a TIA patient cohort and with regard to early stroke risk prediction.

Methods

235 TIA patients consecutively admitted to our Stroke Competence Center were recruited for this study. The diagnosis of TIA was based on the traditional time-oriented definition with neurological symptoms of supposed cerebrovascular origin lasting less than 24 h. The standard operating procedure in our department requires all TIA patients to be admitted to the Stroke Unit. All patients underwent a thorough neurological examination and NIHSS scoring upon admission and every 6 h subsequently, according to the standards of Stroke Unit treatment. Prompt brain imaging was performed in all patients. Most patients (229; 97.5%) received MRI including DWI sequences, unless contraindications were present. In addition, cerebrovascular extra- and transcranial Doppler/duplex examinations were performed in all patients. DWI was performed either directly on admission or within 24 h from admission and was repeated in cases of stroke recurrence. Carotid stenosis was defined according to the ECST criteria. Every patient was ECG monitored for at least 24–72 h while in our Stroke Unit. Duration, fluctuation of symptoms, clinical patterns of initial signs and/or symptoms as well as general patient characteristics and stroke risk factors, including atrial fibrillation (AF), were analyzed and recorded in our stroke databank. Fluctuation of symptoms was defined as the complete remitting and relapsing of TIA symptoms (i.e. aphasia, dysarthria, ataxia, motor and/or sensory deficits) for ≥ 2 times in the acute phase within the first 24 h. Only symptoms that completely remitted in between were considered as fluctuations for the purpose of this study. This differs from the ‘dual TIA’ definition of the ABCD3-I score, which is defined as ‘an earlier TIA within 7 days of the index event’. All data were collected as a part of the investigation of the quality of care, in accordance with existing German law and regulations and with approval of the local

ethics committee. No patients were exposed to additional interventions, questioning or examinations because of this study. Accordingly, ABCD2 and ABCD3-I scores were calculated and the patients were divided into three categories: ‘low’, ‘moderate’ and ‘high’ risk for every score, according to recently published proposals [8–10].

Statistical Analysis

Risk associations were assessed by the χ^2 test and the ϕ -coefficient. Statistical analysis was performed using the SPSS, version 17.0 (IBM, USA).

Results

The mean age of patients was 66.1 years (SD = 13.9); 55.3% were male. Sixty-seven patients (28.5%) presented with symptom fluctuations at onset. Twenty-one (8.9%) patients exhibited AF and 36 (15.3%) a significant carotid stenosis $\geq 50\%$. In 50 (21.3%) patients, MR-DWI showed signs of acute cerebral ischemia corresponding to clinical signs/symptoms.

Using the ABCD2 score, classification was as follows: 99 (42.1%) patients with ‘low’, 114 (48.5%) with ‘moderate’ and 22 (9.4%) patients with ‘high’ risk. Using the ABCD3-I score, 74 (31.5%) patients were classified as ‘low’, 152 (64.7%) as ‘moderate’ and 9 (3.8%) as ‘high’ risk.

Seventeen (7.2%) patients suffered an early stroke during their hospitalization (mean duration: 7.4 ± 2.7 days). The ABCD2 score did not achieve a significant correlation with early stroke ($p = 0.544$, $\phi = 0.072$): 5 (29.4%) patients were in the ‘low’, 10 (58.8%) in the ‘moderate’ and 2 (11.8%) in the ‘high’ risk category (table 1). The ABCD3-I score reached statistical significance ($p = 0.021$, $\phi = 0.181$): 1 patient (5.9%) was in the ‘low’ category, 14 (82.4%) were in the ‘moderate’ and 2 (11.8%) in the ‘high’ risk group. The presence of AF (1 of 17 patients; 5.9%) was not significantly correlated with early stroke ($p = 0.647$, $\phi = -0.03$), nor was carotid stenosis $\geq 50\%$ (3 of 17 patients; 17.6%; $p = 0.782$, $\phi = 0.018$). MR-DWI-positive findings (6 patients; 35.3%) also failed to predict early stroke ($p = 0.143$, $\phi = 0.096$). Symptom fluctuations at onset showed the best correlation with early stroke: the majority of patients with an early stroke (13; 76.5%) presented with fluctuating TIA ($p < 0.001$, $\phi = 0.297$).

The combination of symptom fluctuation and MR-DWI-positive findings (4 patients; 23.5%) also turned out to show a good association with early stroke with high statistical significance ($p = 0.003$, $\phi = 0.196$), while the combination of symptom fluctuations with carotid steno-

Table 1. Patient characteristics

Parameter	Patients				p value
	all (n = 235)		with early stroke (n = 17)		
	n	%	n	%	
Age, mean ± SD, years	66.1±13.9		70.2±10.9		
Male gender	130	55.3	12	70.6	
ABCD2 score					
Low risk	99	42.1	5	29.4	0.544
Moderate risk	114	48.5	10	58.8	
High risk	22	9.4	2	11.8	
ABCD3-I score					
Low risk	74	31.5	1	5.9	0.021
Moderate risk	152	64.7	14	82.3	
High risk	9	3.8	2	11.8	
Atrial fibrillation	21	8.9	1	5.9	0.647
Carotid stenosis ≥50%	36	15.3	3	17.6	0.782
Positive MR-DWI	50	21.3	6	35.3	0.143
Symptom fluctuations	67	28.5	13	76.5	<0.001
Fluctuations plus acute infarction and/or carotid stenosis ≥50%	5	2.1	4	23.5	0.029
p values in italics are significant.					

sis $\geq$ 50% did not ($p = 0.151$; $\phi = 0.094$). Similarly, combining fluctuations with carotid stenosis and DWI-positive findings did not improve the result ($p = 0.029$, $\phi = 0.143$).

Discussion

Today, it is a well-known fact that TIAs are not as harmless as originally supposed. In our study, 7.2% patients suffered an early stroke during hospitalization. This figure is similar to those found in larger population-based studies, which showed an 8% stroke incidence in the first 7 days after TIA [1] or calculated the stroke risk at 8% at 30 days in a meta-analysis [4].

To assess the individual risk of early strokes, several parameters/scores have been proposed. The ABCD2 score was first introduced to assess acute stroke risk after TIA for outpatient emergency management [7, 8]. It has been validated in several studies and found to be of predictive value, as far as general risk associated with risk factors of atherosclerosis is concerned [8, 13–15]. Indeed, most of our patients who suffered an acute stroke after TIA were in the moderate- or high-risk group of the ABCD2 score. However, it did not reach statistical sig-

nificance as an individual predictor for an early subsequent stroke after TIAs in our population.

Early positive findings on MR-DWI have shown to be associated with subsequent early stroke [6, 7, 16]. However, although similar to numbers in these larger studies, only 6 of 17 patients with early stroke (35.3%) were MR-DWI positive in our series, which failed to reach statistical significance. This again mirrors results from previous studies, in which MR-DWI findings were usually combined with risk factors with different degrees of atherosclerosis or scores to reach statistical significance [6, 16].

Similarly, carotid stenosis was not correlated with early subsequent stroke in our study if used as a stand-alone parameter. However, we could demonstrate a favorable predictive value of the ABCD3-I score ($p = 0.021$), in which carotid stenosis is included. This means that each of the factors alone (ABCD2 score, brain imaging, carotid stenosis) have weak predictive power if not combined.

Although AF is a recognized risk factor for stroke and requires oral anticoagulation for stroke prevention, it has not been well examined independently as a risk factor for early stroke following TIA. A recent study showed no significant association between AF and risk of early stroke in 343 TIA patients; it was assumed that it was because of the relatively small sample size and the beneficial effect of

early oral anticoagulation [17]. This may also be the case in our study, where the presence of AF was not significantly correlated with early stroke.

Symptom fluctuations during or directly following TIAs proved to be of considerable value for predicting early stroke risk, provided prospectively repeated examinations are performed. Rates of up to 31% are described in the literature [12], and we have found similar percentages in a previous (27%) [11], as well as in our present study (28.5%). However, a direct comparison with other scores or associated diagnosis of AF, carotid stenosis, or early stroke signs in MRI has not been systematically addressed in any of these studies. Indeed, in our present study, symptom fluctuation turned out to be the best predictive parameter for early stroke ($p < 0.001$, $\phi = 0.297$). We defined 'symptom fluctuation' strictly as fluctuations of neurological clinical deficit of cerebrovascular origin during the acute phase of the first 24 h, in contrast to the definition of 'dual TIA' in the ABCD3-I score, which can

include TIAs within a time window of 7 days. Combining this parameter with positive DWI and/or carotid stenosis also led to an excellent, statistically significant correlation with early stroke.

Despite some limitations of this study, performed in a single-center design with limited sample size, confirming data now demonstrates the superiority of a single specific parameter versus general risk scores for early stroke risk prediction. Using this simple parameter is not costly, does not require additional, time-consuming technology and identifies individual patients at highest risk who will benefit from continuous stroke unit monitoring to be able to manage thrombolysis within the shortest time limits once subsequent ischemic events occur.

Disclosure Statement

The authors have nothing to disclose.

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