Evaluation and outcome of triage for patients with transient ischemic attack

A two-year analysis of the TIA Clinic of the University Hospitals Leuven

Nicolas Vandenbussche, MD

Promotor: Robin Lemmens, MD, PhD

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ABSTRACT

Background: Urgent evaluation of transient ischemic attack (TIA) has shown to lower the risk of recurrent cerebrovascular events in multiple TIA clinic models. We present the results of our TIA clinic model in the first two years of practice. In addition, we compared our results with TIA patients with matching clinical profiles who were admitted in our hospital during 2013 and 2014.

Methods: The TIA Clinic model was developed for triage and fast-track evaluation of TIA patients with neurological, imaging and vessel evaluation, with subsequent secondary cardiovascular preventive interventions. Only patients with ABCD2 score ≥ 4, carotid stenosis ≥ 50% or presence of diffusion weighted imaging (DWI) lesions were scored as high risk patients and admitted to hospital. We prospectively collected data on the rate of recurrence at 90 days, hospitalization rate, patient characteristics and patient assessment. Finally, we retrospectively collected corresponding data from TIA patients with similar profiles during 2013 and 2014 and compared the results with the TIA Clinic patients.

Findings: The total risk of recurrence at 90 days for TIA Clinic patients was 3,6%, similar to 6,8% in the period 2013-2014 (p=0,70). None of the low-risk TIA clinic patients had a recurrent cerebrovascular event at 90 days follow up, compared to two patients in the high-risk group. The rate of hospital admissions was similar during TIA Clinic period compared to the 2013-2014 period (67,9% vs 72%; p=0,61). The TIA Clinic protocol resulted in faster access to MRI scans (p = 0,001), more usage of MRI brain scans (p=0,0017) and CT angiography (p = 0,0058), less CT whole brain scans (p < 0,001), more prescriptions of statin therapies at discharge (p < 0,0001) and more follow-up visits (p=0,0085) in comparison to the patients assessed in 2013 and 2014.

Conclusions: The TIA Clinic model resulted in low rates of recurrent cerebrovascular event at 90 days after TIA and is a safe and efficacious model for management of low risk TIA patients in an outpatient setting. The TIA Clinic model improved patient assessment in comparison to the earlier approach towards TIA patients and resulted in equal percentage of recurrence at 90 days.

INTRODUCTION

The clinical approach towards transient ischemic attack (TIA) has been evolving over the last decade. Due to the high risk of stroke after TIA, with a 90-day risk of about 10,5% and a highest risk of recurrence in the first 48 hours, fast assessment of patients with TIA and starting secondary prevention are important to lower the burden of cerebrovascular disease [1] [2]. Several scoring systems have been developed to estimate the risk of recurrence of new vascular events [3]. These systems are being used to stratify patients in groups with high risk of recurrence or low risk of recurrence, according to their personal risk profile. Studies have shown that urgent evaluation and therapeutic intervention does lower the risk of recurrent cerebral vascular events, by as much as 80% [4]. Although in-hospital assessments can deliver good care for these patients, recent studies have shown that not all TIA patients need hospitalization because their work-up can be done in fast-track or in an out-patient setting. Results from different TIA clinics show that low-risk TIA patients can receive an equally beneficial therapeutic regimen in an early-management, non-hospitalization setting [4–9].

Starting from January 1st 2015, we initiated a fast-track TIA clinic for rapid evaluation of patients presenting in the emergency room with a potential TIA. By using a risk assessment based on clinical and imaging parameters patients would be classified as high versus low risk. In this paper, we present the results of the first two-years of practice, in terms of the characteristics of TIA clinic patients, diagnostic efficacy, treatments, outcome measurements and follow-up. In addition, we compared the recurrence rates, characteristics of patient assessment and therapeutic interventions of the patient assessment of the TIA clinic patients with the assessment of TIA patients with matching clinical profiles who were admitted in our hospital during 2013 and 2014.

METHODS

The TIA Clinic

The TIA Clinic protocol in the University Hospitals Leuven was initiated on January 1st 2015. The validated protocol with flowchart was published and accessible for all medical staff of the hospital (Figure 1). Opening hours for the TIA Clinic are between 8 A.M. and 4 P.M. The clinic operates only on working days from Monday until Friday, except on official holidays, as part of the Stroke Unit. Patients presenting to the hospital with symptoms suggestive of TIA, with or without referral by their general practitioner, are seen first by the neurology service in the emergency ward. Patients were eligible for

an evaluation by the TIA clinic based on the following criteria: transient symptoms suggestive of TIA, no neurological deficit on entering the hospital, no loss of consciousness and full ability to walk in the emergency room (ER). Patients with possible TIA in whom these criteria were not met, were first evaluated on the ER before admission at the stroke unit was considered

Patient assessment in the TIA Clinic:

Upon arrival in the TIA Clinic patients were neurologically evaluated which also included obtaining the ABCD2 score [10,11] (Figure 2). The diagnosis of definite, probable or possible TIA was then made by the neurologist supervising the stroke unit. The definition of transient ischemic attack according to the World Health Organization criteria was used: a sudden clinical phenomenon affecting motor, sensory, sensorial, speech, brainstem or cerebellar functions due to vascular insufficiency and lasting less than 24 hours.

After evaluation, one of the following trajectories was chosen: 1/ no clinical evidence of TIA: patient is discharged or referred to other department; 2/ clinical examination reveals a persistent neurological deficit, the patient is admitted to the Stroke Unit; 3/ TIA with ABCD2 score ≥ 4: the patient is admitted to the Stroke Unit for workup and cardiac telemetry; 4/ TIA with ABCD2 score < 4: urgent evaluation of intra- and extracranial arteries and brain magnetic resonance imaging (MRI) within the same day. If neuro-imaging would reveal a diffusion weighted imaging (DWI) positive lesion and/or a ≥50% stenosis of the extra- or intracranial vessels patients were admitted to the stroke unit. If these abnormalities were not documented patients in this group were discharged from the TIA Clinic the same day.

Patients admitted to the stroke unit received cardiovascular workup: MRI of the brain, imaging of the extracranial vessels and cardiac monitoring during admission. Echocardiography and additional 24hr or long-term cardiac monitoring was planned during or following admission on an individual based decision. Secondary cardiovascular prevention therapies (e.g. antithrombotics, anticoagulants, antihypertensives, statins) were initiated during admission. All patients in whom a final diagnosis of TIA or stroke was made, received appointments for follow-up 90 days after discharge from the hospital.

Data collection, data analysis and statistical analysis

We analyzed data of patients who entered the TIA Clinic from January 1st 2015 until December 31st 2016. This data was collected prospectively during hospitalization and follow-up appointment in our out-patient clinic. The main objective of this study was to determine the rate of recurrence at 90 days in each subgroup of TIA Clinic patients. This endpoint was determined by the neurologist

responsible for the stroke unit (RL). We compared the rate of recurrence at 90 days in the low-risk and high-risk groups. High-risk patients were defined as patients with an ABCD2 score ≥ 4, stenosis of a cervical artery ≥ 50% or DWI-positive lesions on MRI of the brain. In addition, we collected data on the TIA Clinic patient demographic characteristics, cardiovascular risk factors, rates of hospitalization, timing to several investigations and therapeutic interventions.

For the second part of the study, we retrospectively reviewed patient files and collected data from a cohort of TIA patients who entered the hospital (emergency room and stroke unit) from January 1st 2013 to December 31st 2014. We searched our databases for patients discharged during the specified period with the same profile as the TIA Clinic patients. These criteria were as follows: transient symptoms suggestive of TIA, Neurology department as the first contact in the hospital, admission in the hospital during working days between 8 A.M. and 4 P.M., no neurological deficit on entering the hospital, no loss of consciousness and full ability to walk in the ER.

Statistical analysis was performed using Microsoft Excel version 15.32 and Graphpad Prism version 7. Continuous variables were analyzed as means with standard deviations, or medians with interquartile ranges. We used Student T-tests for age comparison, and Mann-Whitney U non-parametric tests for variables with unknown distribution. For dichotomous variables, we used chi-squared tests or Fisher exact tests where applicable. All tests were two-tailed. We considered the significance level of $p < 0,05$ as statistically significant.

Ethics

All TIA clinic patients gave written informed consent. The study was approved by the Ethical Boards of the University Hospitals of Leuven and the KU Leuven.

RESULTS

Characteristics of TIA Clinic patients

Seventy-seven (n=77) patients were admitted to the TIA Clinic between January 1st 2015 and December 31st 2016. Fifty-six (n=56) patients were eventually diagnosed with the diagnosis of definite, probable or possible TIA and included for further analysis. Twenty-one (n=21) patients were diagnosed with a mimic of TIA or non-vascular causes (Table 1). 50% of patients (28/56) were admitted in 2015 and 50% of patients (28/56) were admitted in 2016. The baseline characteristics of TIA patients in the TIA Clinic are shown in table 2. The mean age was 67,71 years (SD 12,26). 51,8% of patients were female. The median ABCD2 score was 4 (IQR 3-5).

Distribution of Clinical Syndromes (n=77)	
Transient ischemic attack (TIA)	56
Migrainous aura	6
Transient visual disturbances of non-vascular origin, not otherwise specified	2
Confusion, non-vascular origin, not otherwise specified	2
Syncope	2
Dizziness caused by orthostatism	2
Aspecific dizziness	2
Aggravation of symptoms caused by previous stroke	1
Transient Global Amnesia	1
Stroke	1
Focal epilepsy	1
Unexplained	1

Table 1: Distribution of clinical syndromes in the TIA Clinic

	TIA Clinic 2015 2016 (n=56)			TIA 2013 2014 (n=75)			P-Value
Baseline Characteristics	**Mean**	**SD**		**Mean**	**SD**		
Age, years	67,71	12,26		69,92	13,50		p = 0,33
	Median	**IQR**		**Median**	**IQR**		
ABCD2 Median (IQR)	4,00	2 (2)		4,00	2 (2)		p = 1
	Number	**Percentage**	**Missing Data**	**Number**	**Percentage**	**Missing Data**	
Female	29	51,8%		34	45,3%		p = 0,46
Hypertension	29	51,8%		56	74,7%		**p = 0,007 ***
Diabetes mellitus	5	8,9%		20	26,7%		**p = 0,01 ***
Hypercholesterolemia	36	64,3%		41	54,7%		p = 0,26
Current Smoker	10	18,2%	n=1	8	10,7%		p = 0,24
History of stroke/TIA	15	26,8%		18	24,0%		p = 0,72
History of coronary artery disease	4	7,1%		16	21,3%		**p = 0,03 ***
Atrial Fibrillation	8	14,3%		13	17,3%		p = 0,64

Table 2: Baseline characteristics of TIA Clinic patients during 2015 and 2016, and the corresponding TIA patients from 2013 and 2014. IQR = interquartile range, SD = standard deviation, TIA = transient ischemic attack. * = statistically significant, in bold

High-Risk TIA clinic patients vs Low-Risk TIA Clinic patients

Patients in the TIA Clinic were divided by protocol into low-risk patients and high-risk patients according to their ABCD2 score (low-risk: < 4, high-risk: ≥ 4), presence or absence of significant stenosis of a cervical artery, or the presence or absence of DWI lesions on MRI of the brain. Sixteen patients (n=16) were classified as low-risk patients and forty patients (n= 40) as high-risk patients. Twenty-one patients in the high-risk group had one risk factor, 10 patients had two risk factors, none had all three risk factors. The baseline characteristics are shown in table 3.

	Low-Risk Group (n=16)			High-Risk Group (n=40)			
Baseline characteristics	**Mean**	**SD**		**Mean**	**SD**		**P-value**
Age, years	61,75	10,29		70,10	12,28		**p = 0,014 ***
	Median	**IQR**		**Median**	**IQR**		
ABCD2 median (IQR)	3,00	1 (2-3)		4,00	1 (4-5)		**p < 0,001 ***
	Number	**Percentage**	**Missing Data**	**Number**	**Percentage**	**Missing Data**	
Female	10	62,5%		19	47,5%		p = 0,31
Hypertension	5	31,3%		24	60,0%		p = 0,07
Diabetes mellitus	0	0,0%		5	12,5%		p = 0,14
Hypercholesterolemia	10	62,5%		26	65,0%		p = 0,86
Current Smoker	3	18,8%		7	17,9%	n=1	p = 1
History of stroke/TIA	3	18,8%		12	30,0%		p = 0,51
History of coronary artery disease	0	0,0%		4	10,0%		p = 0,31
Atrial fibrillation	1	6,3%		7	17,5%		p = 0,42
Use of antithrombotic medication	8	50,0%		22	55,0%		p = 0,73
Use of statin	3	18,8%		22	55,0%		p = 0,01

Table 3: Baseline characteristics of the Low-Risk Group and High-Risk Group. IQR = interquartile range, SD = standard deviation, TIA = transient ischemic attack. * = statistically significant, in bold

A total of thirty-eight (n=38) patients (67,9%) were admitted to the hospital from the TIA Clinic. In the low-risk group 4 patients were hospitalized for the following reasons: no availability of extracranial vessel imaging (n=1) or MRI of the brain (1) and overestimation of stenosis by duplex ultrasound (>50%) not confirmed by CT angiography the following day (n=2).

The total risk of recurrence at 90 days was 3,6% (95% CI 0,98% - 12,1%) (table 5). Zero patients (0%, 95% CI 0% - 19,4%) in the low-risk group had a recurrent cerebrovascular event after 90 days, whereas 2 patients (5%, 95% CI 1,38% - 16,5%) in the high-risk group experienced a new cerebrovascular event within the 90 days of follow-up. All patients in both low and high-risk groups had cervical artery imaging during their workup in the TIA Clinic or hospital admission. MRI brain scanning was performed in all patients of the low-risk group (16/16, 100%), but only in 36 of 40 (90%) patients in the high-risk group due to presence of an internal cardiac defibrillator (n=2) or MRI-incompatible pacemaker (n=1) (p=0,31). One patient did not have MRI brain imaging due to unknown

reasons. The MRI procedure had to be stopped during examination of one patient because of claustrophobia. In fifteen out of 52 patients (28,8%) who had a MRI scan, we found evidence of DWI lesions.

	Low-Risk Group (n=16)		High-Risk Group (n = 40)		
	Number	Percentage	Number	Percentage	P-value
Number of hospitalizations	4	25%	34	0,85	**p < 0,0001 ***
Recurrence at 90 days	0	0%	2	5%	p = 1
Imaging of Cervical Arteries	16/16	100%	40/40	40	p = 1
MRI brain scan	16/16	100%	36/40	90%	p = 0,31
Diagnosis clinically significant stenosis	0	0%	1	2,50%	p = 1
Diagnosis (symptomatic) dissection	0	0%	1	2,50%	p = 1
New diagnosis Atrial Fibrillation	0	0%	3	7,50%	p = 0,55
DWI lesions	0	0%	15/35	42,90%	**p < 0,0019 ***
Discharged on antitrombotic treatment	16/16	100%	40/40	100,00%	p = 1
Discharged on statin treatment	16/16	100%	37/40	92,50%	p = 0,55

Table 4: Diagnostic procedures, recurrence rates, hospitalization rates and secondary preventive therapies installed. DWI = Diffusion Weighted Imaging, MRI = Magnetic Resonance Imaging, TIA = transient ischemic attack. * = statistically significant, in bold

The TIA Clinic compared to historical in-hospital assessment

We retrospectively reviewed patient files and collected data from TIA patients admitted in 2013 and 2014, with corresponding criteria for entering the TIA Clinic if they would have presented themselves to our hospital in 2015 or 2016. After carefully reviewing the reports from the emergency ward and stroke unit and strictly applying all entrance criteria for the TIA Clinic, 75 patients were included for analysis and comparison. Table 2 presents the baseline characteristics of the group of TIA patients with similar profile who entered the hospital during 2013 and 2014. The cardiovascular profile of the 2013-2014 group showed some differences with the TIA Clinic patients from 2015-2016, with more patients suffering from hypertension (74,7% vs 51,8%; p = 0,007), diabetes mellitus (26,7% vs 8,9%; p = 0,01) and history of coronary artery disease (21,3% vs 7,1%; p = 0,03).

Table 5 shows the results of comparison between patients included in the TIA Clinic during 2015-2016 versus similar profile TIA patients during 2013-2014. A similar rate of recurrence at 90 days (3,6% vs 6,8%; p = 0,7) and similar amount of hospital admissions (67,9% vs 72%; p = 0,61) were found. The TIA Clinic resulted in a reduction in CT brain scans (25% versus 89,3% of patients; p < 0,001), an increase in MRI brain scans (92,9% versus 77,3%; p = 0,0017) and faster access to MRI of the brain (median delay 0 days (IQR 0) versus 1 days (1,75); p < 0,0001). More patients received CT angiography of the extracranial cervical and intracranial vessels (73,2% versus 49,3%; p = 0,0058) which corresponded to a reduction of the use of duplex echography of the extracranial vessels (33,9% versus

65,3%; p < 0,0001). In 2015-2016 more patients received a transesophageal echocardiography (73,2% versus 48%; p = 0037). A higher proportion of TIA Clinic patients were discharged on statin treatment in comparison to patients in 2013-2014 (92,9% versus 60%; p < 0,0001). Both groups received equal appropriate antithrombotic treatments on discharge from the hospital. There were no differences in delays between symptom onset and hospital admission, hospital admission rates or recurrence rates at 90 days. More patients were seen at 90 days in the outpatient clinic in the cohort from the TIA clinic compared to the TIA patients in 2013-2014 (85,7 % versus 64,5%; p = 0,0085).

	TIA CLINIC 2015 2016 (n=56)	TIA 2013 2014 (n=75)	P-Value
No Cholesterolevels measured, n (%)	3 (5,4%)	16 (21,3%)	**p = 0,01 ***
CT whole brain scans, n (%)	14 (25%)	67 (89,3%)	**p < 0,001 ***
MRI whole brain scans, n (%)	52 (92,9%)	58 (77,3%)	**p = 0,0017 ***
DWI lesions on MRI, n (%)	15/51 (29,4%)	11/58 (19%)	p = 0,20
Delay until MRI, days, median (IQR)	0 (0)	1 (1,75)	**p = 0,001 ***
Imaging of cervical arteries, n (%)	56 (100%)	73 (97,3%)	p = 0,51
Delay until cervical artery imaging, days, median (IQR)	0 (0)	0 (0)	p = 1
CT angiography cervical and intracranial arteries, n (%)	41 (73,2%)	37 (49,3%)	**p = 0,0058 ***
Duplex echography, n (%)	19 (33,9%)	49 (65,3%)	**p < 0,001 ***
Significant cervical artery stenosis, n (%)	1 (1,8%)	6/73 (8,2%)	p = 0,14
1-day cardiac monitoring (if AF unknown), n (%)	38/48 (79,2%)	48/62 (77,4%)	p = 0,83
7-days cardiac monitoring (if AF unknown), n (%)	3/48 (6,3%)	2/62 (3,2%)	p = 0,45
Transesophageal echocardiography, n (%)	41 (73,2%)	36 (48%)	**p = 0,0037 ***
Transthoracal echocardiography, n (%)	9 (16,1%)	19 (25,3%)	p = 0,20
Discharged on statin treatment, n (%)	52 (92,9%)	45 (60%)	**p < 0,0001 ***
Discharged on antithrombotic treatment, n (%)	56 (100%)	73 (97,3%)	p = 0,50
Delay until admission, days, median (IQR)	1 (2,75)	0 (1)	p = 0,07
Hospital admissions, n (%)	38 (67,9%)	54 (72%)	p = 0,61
Duration of hospitalization, days, mean (SD)	1 (1)	1 (2)	p = 0,08
Follow-up in outpatient clinic, n (%)	48 (85,7%)	49 (64,5%)	**p = 0,0085 ***
Recurrence at 90 days, n (%)	2 (3,6%)	5/73 (6,8%)	P = 0,70

Table 5: Analysis and comparison of patient assessment, therapeutic interventions, recurrence and follow-up, between patients included in the TIA Clinic during 2015-2016 vs. similar profile TIA patients during 2013-2014. CT = Computed Tomography, DWI = diffusion weighted imaging, MRI = Magnetic Resonance Imaging, TIA = transient ischemic attack. * = statistically significant, in bold,

DISCUSSION

Multiple studies with different TIA clinic models have been published recently [12–14]. These models were developed due to the urgent nature of TIA which, if not investigated or treated properly, can lead to devastating consequences due to stroke [3,14,15].

The ABCD2 score was used at baseline evaluation, because of its validation in TIA patients and rapid availability at entrance. However, its value in reliably discriminating true low and high-risk patients has been contested. The ABCD2 score on its own performs rather poor in the identification of high-risk patients with carotid stenosis or atrial fibrillation and discrimination of true TIA patients and TIA mimics in the high-risk groups [16–18]. For our TIA Clinic model, we didn't solely rely on the ABCD2 score to determine in-hospital or outpatient assessment. Urgent imaging of cervical arteries and DWI lesions were also used as determinants for admission. Stenosis of extra- and intracranial arteries are well known risk factors for early recurrence of stroke after TIA [19,20]. DWI lesions in TIA patients, a paradigm shift in our contemplation of TIA as being a reversible condition in terms of timing but not in tissue, has also been found to express a higher risk of subsequent stroke and scoring systems (e.g. the ABCD3-I scores) were created accordingly [21–23]. To our knowledge, this is the first time DWI lesions are implemented in a TIA clinic protocol in an effort to detect even more high-risk patients.

The recurrence rate at 90 days of 3,6% for all patients of the TIA Clinic (median ABCD2 score 4, IQR 3-5) is in line with previous reports and comes close to the equivalent result of a meta-analysis of TIA cohorts and clinics recently published [13]. This recurrence rate is also lower than the expected risk based on the data from the validation study of the ABCD2 scoring system (expected risk of recurrence at 90 days for ABCD2 score 4 = 9,8%, based on Johnston et al. 2007)[10]. Although our sample size is admittedly small, we are satisfied to report no recurrences of cerebrovascular events at 90-days follow up in the low-risk group. This result supports the hypothesis that our TIA Clinic model performs well in selecting patients suited for outpatient setting, hereby avoiding unnecessary hospital admissions and prioritizing beds for high-risk patients, used for monitoring and urgent treatment if necessary [12,24].

TIA mimics are a large portion of diagnoses in the TIA Clinic, with 21 of the 77 patients ultimately not diagnosed with TIA. This confirms earlier reports that TIA Clinics have high proportions of mimics, and that a correct diagnosis of TIA is often difficult to be made in the emergency room by doctors without neurovascular expertise [8,25].

By comparing our diagnostic and therapeutic approaches towards TIA in the TIA Clinic with our earlier practice, we found some improvements in the clinical pathways provided by the clinic. First, a

shift from CT scans towards MRI scans was detected. MRI imaging provides higher sensitivity for detecting recent ischemic lesions, has a more important role in risk stratification and is free of radiation [26]. However, a recent meta-analysis questions the cost-effectiveness for secondary stroke prevention in TIA patients [27]. Second, CT angiography of extra- and intracranial vessels provides higher spatial resolution of potential relevant stenosis (which can be overestimated or missed due to their location by duplex echography). Although inquiries can be made about the exposure to radiation and use of contrast-enhancing products, we believe CT angiography is the preferred modality and has more benefits over duplex echography due to higher diagnostic yield and greater spatial resolution [28,29]. Third, a significant rise by 32,9% in the prescriptions of statins was seen in the TIA Clinic group, in line with guidelines for secondary prevention after stroke [30]. Fourth, a steep rise of 21,2% in follow up visits was detected, also aiding secondary cardiovascular preventive management [30].

Our study has multiple limitations which need to be addressed. First of all we only managed to document the 90-day recurrence rate, but not the 7-days or 1-year recurrence rate as documented in multiple studies. We were only able to study a rather small number of patients in comparison to other reports of TIA Clinic models. Although we used reliable readily available parameters, the retrospective and/or non-randomized nature of our study groups is a major constraint to draw definitive conclusions. Finally, we did not perform economic analyses on the impact of the TIA Clinic on the usage of resources in comparison to an in-hospital assessment.

CONCLUSION

We presented the results of the TIA Clinic in terms of assessment and outcome of TIA patients during the first two years of use. Our TIA Clinic model resulted in low rates of subsequent, short-term cerebrovascular event after TIA. The model is most likely a safe and efficacious model for management of low-risk TIA patients in an outpatient setting. The TIA Clinic model improved the quality of care in comparison to our earlier approach towards TIA patients and resulted in equal percentage of recurrence at 90 days.

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Figure 1: Flowchart for admission to the TIA Clinic (in Dutch)

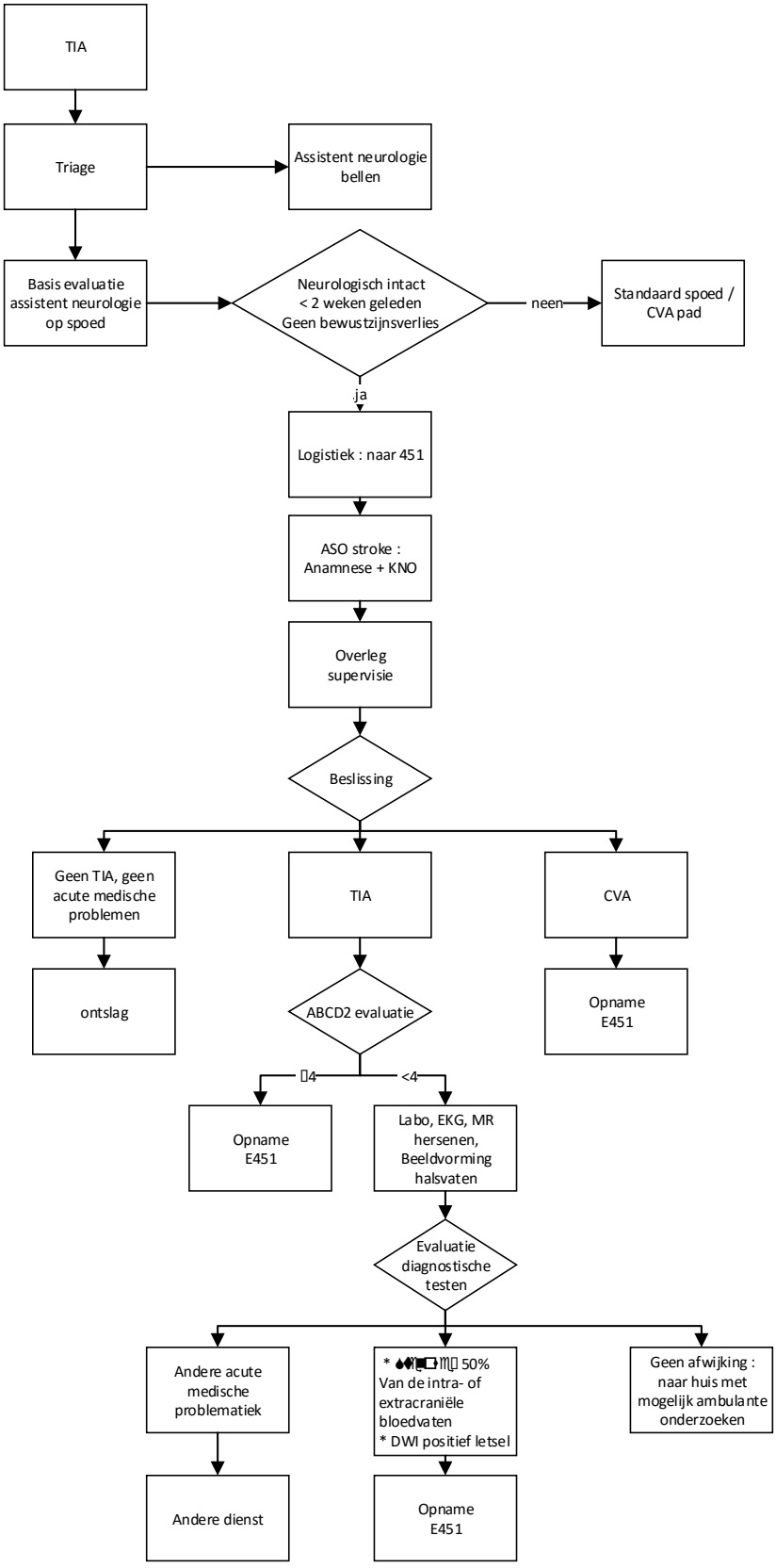

Figure 2: ABCD2 Score

ABCD2 score [10,11]	
Age ≥ 60	Yes = +1
Blood pressure ≥ 140/90 mmHg	Yes = +1
Clinical features of TIA	Unilateral weakness = +2 Speech disturbance without weakness = +1 Other symptoms = 0
Duration of symptoms	≥ 60 minutes = +2 10-59 minutes = +1 < 10 minutes = 0