The Value of Neurological Assessment for Prediction of Subtle Cerebral Infarction

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ABSTRACT: We examined to what extent clinical assessment alone can predict subtle acute cerebral infarction on magnetic resonance imaging (MRI). Of the 72 patients presented to the emergency department (ED) with transient neurological deficits, 26 (36.1%) were predicted to be "positive" and 46 (63.9%) "negative" for transient ischemic attack/minor stroke by two independent neurologists. Twenty patients (27.8%) had acute restricted diffusion on MRI. Clinical assessment showed substantial agreement with MRI findings (Kappa = 0.75), sensitivity (95.0%), specificity (86.5%), positive-likelihood ratio 7.06, and negative-likelihood ratio 0.06. Neurological assessment has an excellent predicting value for MRI-confirmed acute cerebral infarction and a key role in the facilitation of effective patient care in the ED.

RÉSUMÉ : L'utilité des évaluations neurologiques dans la prédiction des infarctus cérébraux dont les signes sont subtils. Nous avons analysé dans quelle mesure une seule évaluation clinique peut permettre de prédire un infarctus cérébral aigu dont les signes subtils ont été révélés par IRM. Sur un total de 72 patients qui se sont présentés à un service d'urgence avec des déficits neurologiques transitoires, deux neurologues indépendants ont établi que 26 d'entre eux, soit 36,1 %, avaient été victimes d'un accident ischémique transitoire (AIT) ou d'un AVC mineur alors que les autres (63,9 %) ne l'avaient pas été. D'un autre côté, 20 patients (27,8 %) ont montré, en phase aiguë, des signes de diffusion restreinte observables par IRM. Les évaluations cliniques de ces patients ont donc rejoint, dans une très grande mesure, les résultats obtenus par IRM (coefficient de Kappa = 0,75 ; sensibilité = 95,0 % ; spécificité = 86,5 % ; rapport de vraisemblance positif = 7,06 ; et rapport de vraisemblance négatif = 0,06). Ces évaluations neurologiques possèdent donc une excellente capacité à prédire un infarctus cérébral aigu dont les signes ont été confirmés par IRM et à jouer un rôle clé en vue de faciliter la prise en charge de patients admis à un service d'urgence.

Keywords: Diffusion-weighted imaging, Stroke, Transient ischemic attack

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Transient ischemic attacks (TIAs) are brief episodes of neurological deficits suspected to result from cerebral ischemia without detectable permanent tissue injury. TIA is a diagnostic challenge. Studies have demonstrated that diffusion-weighted magnetic resonance imaging (DWI-MRI), the current diagnostic standard for a tissue-based definition (TIA versus minor stroke), may reveal ischemic changes in only up to 67% of patients with transient neurological deficits.[1] The 90-day risk of ischemic stroke following TIA or minor cerebral ischemia is estimated to range from 3% to 15%,[2] and it is well established that early initiation of stroke prevention strategies may reduce the total burden of stroke and its complications.[3] However, the high awareness and vigilance may also result in overdiagnosis. It was estimated that TIA mimics comprise 60% of referrals to rule out ischemic etiology.[4] These figures are in line with our local experience. Although new objective and sensitive diagnostic biomarkers are emerging,[5,6] at present, TIA diagnosis remains highly dependent on the clinical assessment in the emergency department (ED). We tested to what extent a neurological assessment by a trained neurologist can predict the presence of ischemic lesions on MRI. We hypothesize that a comprehensive neurological evaluation may reduce the rate of overdiagnosis and increase the pretest probability for positive DWI findings.

This prospective cohort study was held at a tertiary medical center in southern Israel between 2015 and 2017. We consecutively enrolled adult patients (≥18 years old) who presented to the ED with transient focal neurological deficits. All patients were evaluated by both ED and neurology attendings within less than 24 h, had an initial computed tomography (CT) scan showing no ischemic changes, and underwent brain MRI within <72 h from presentation. Patients with a new or known hemiplegic migraine, focal seizure, atrial fibrillation, structural cardiac anomaly, severe carotid stenosis, carotid dissection, or any acute intracranial lesion during ED workup (routine electrocardiogram and CT angiography of the brain and cervical arteries) were excluded. Patients with neurological deficits (objective or subjective) lasting more than 24 h were excluded. All participants signed an informed consent. The study protocol was approved by the Soroka Medical Center Institutional Review Board.

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Table 1 Baseline characteristics, radiological, and clinical findings at presentation

Characteristic		Likely ischemic[a] (n = 26)	Unlikely ischemic[a] (n = 46)	p-value
Mean age ± SD (years)		61.65 ± 13.72	56.91 ± 12.35	0.170
Male (%)		16 (61.5%)	25 (54.3%)	0.554
ABCD2	Age ≥ 60	15 (57.7%)	22 (47.8%)	0.421
	SBP ≥ 140 or DBP ≥ 90	15 (57.7%)	24 (52.2%)	0.652
	Unilateral weakness	7 (26.9%)	25 (54.3%)	0.024
	Duration >60 minutes	12 (46.2%)	29 (63%)	0.182
	Total	3.73(±1.373)	4.11(±1.370)	0.338
Risk factors	Hypertension	15 (57.7%)	24 (52.2%)	0.652
	Diabetes mellitus	8 (30.8%)	15 (32.6%)	0.872
	Smoking	8 (30.8%)	8 (17.8%)	0.207
	Heart disease or PVD	6 (23.1%)	7 (15.2%)	0.526
	Previous stroke	3 (11.5%)	8 (17.4%)	0.735
	Dyslipidemia	16 (61.5%)	21 (45.7%)	0.195
	Atrial fibrillation	2 (7.7%)	4 (8.7%)	1.000
	≥1 cardiovascular risk factor	21 (80.8%)	35 (76.1%)	0.646
DWI result	Nonischemic	7 (26.9%)	45 (97.8%)	<0.001
	Ischemic	19 (73.1%)	1 (2.2%)	
Clinical symptoms	Diplopia	0 (0%)	4 (8.7%)	0.289
	Loss of vision	1 (3.8%)	5 (10.9%)	0.408
	Limb weakness	8 (30.8%)	25 (54.3%)	0.054
	Facial drooping	6 (23.1%)	7 (15.2%)	0.526
	Paresthesia	8 (30.8%)	12 (26.1%)	0.670
	Confusion	1 (3.8%)	3 (6.5%)	1.000
	Speech impairment	10 (38.5%)	9 (19.6%)	0.081
	Dizziness	3 (11.5%)	6 (13%)	0.852
	Tremor	0 (0%)	3 (6.5%)	0.549
	Pain (any)	3 (17.6%)	14 (82.4%)	0.070
	Headache	3 (11.5%)	11 (23.9%)	0.203
Old infarct per CT on admission		8 (33.3%)	6 (14%)	0.067

DBP = diastolic blood pressure; DWI = diffusion-weighted imaging; PVD = peripheral vascular disease; SBP = systolic blood pressure.
[a]On clinical evaluation at presentation.

Two attending neurologists evaluated independently all patients. Assessment included history taking, complete neurological examination, and review of initial CT scans. Each neurologist categorized all patients based on the clinical evaluation as "positive" (the most likely diagnosis is cerebral ischemia, high likelihood of positive DWI findings) or "negative" (diagnosis of ischemic etiology is unlikely). All cases were reviewed immediately following the clinical evaluation and any disagreement was discussed to reach a consensus. All subjects were imaged on a 3T Philips Ingenia MRI. T1- and T2-weighted imaging, FLAIR, diffusion, and susceptibility weighted imaging data were acquired. An experienced neuroradiologist interpreted all MRI scans. Analyses were conducted using IBM SPSS Statistics version 24 (IBM, Armonk, NY, USA). Results are presented as mean ± SD for continuous variables and as percentages for categorical data. Mann–Whitney and chi-square tests were used for comparisons as appropriate. Sensitivity, specificity, predictive values, and positive- and negative-likelihood ratios were calculated to assess the performance of neurological assessment prior to MRI. Statistical significance was set at ≤0.05.

A total of 72 patients were included in the study. The clinical diagnosis prior to MRI was "positive" for cerebral ischemia in 26 patients (36.1%) and "negative" (i.e., likely nonischemic) in 46 (63.9%). No significant differences in demographic characteristics and baseline risk factors were found between groups (Table 1). The clinical assessment showed no association with the ABCD2 score, with specific signs, or symptoms at presentation. Unilateral limb weakness was more common among patients diagnosed as "negative" (Table 1). Acute ischemic lesions were found on MRI scans of 20 patients (27.8%). Restricted diffusion

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on MRI was more prevalent among patients diagnosed clinically as "positive" (19/26, 73.1%) compared with one patient (1/46, 2.2%) originally suspected to have a nonischemic etiology on clinical evaluation (Table 1). Substantial agreement was demonstrated between the predicted patient status according to the clinical evaluation and the actual DWI findings (Kappa = 0.75). The sensitivity, specificity, positive, and negative predictive values for accurate patient classification based on clinical evaluation alone were 95.0%, 86.5%, 73.0%, and 97.8%, respectively. The positive-likelihood ratio for a patient with restricted DWI lesion to be diagnosed as "positive" for cerebral ischemia prior to MRI was 7.06 (95% CI 3.52–14.16), and the negative-likelihood ratio was 0.06 (95% CI 0.01–0.39).

In the era of modern neuroimaging, the current diagnosis of TIA still relies on history taking and physical examination. However, a high rate of overdiagnosis and a low interobserver agreement in the ED setting have been reported.[7] In our cohort, clinical evaluation by a neurologist in the ED had a high diagnostic accuracy and patients with positive DWI were seven times more likely to be diagnosed as having an actual ischemic event on clinical evaluation alone. The currently accepted tissue-based definition of TIA/minor stroke on MRI is limited by high variability and availability.[8] Using the tissue-based definition, 20/72 (27.7%) patients with positive DWI findings were reclassified as cases of minor stroke. Among patients initially diagnosed as likely having cerebral ischemia, 7/26 (26.9%) could be labeled as TIA per se. This discrepancy emphasizes the need for a more objective and sensitive modality to diagnose subtle brain ischemia.[5] Future stroke prevention is an additional major consideration in the ED setting. A recent meta-analysis showed that the risk of stroke misdiagnosis is much greater when presenting neurologic complaints are transient, nonspecific, or mild (range 24%–60%).[9] MRI scans are not yet readily available in all clinical settings. Our findings suggest that clinical assessment by a neurologist has an excellent predicting value for ischemic brain lesion confirmed on MRI. This single-center study is limited by a relatively small sample size. Further replication studies should include larger cohorts and also compare the predictive capacity of clinical evaluation by neurology trainees, primary care practitioners, and ED physicians. Our findings reiterate the value of a neurologist in the ED,[10] for facilitation of effective patient triage and provision of quality care.

Disclosures

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Statement of Authorship

AH and YS contributed to literature search, study design, data analysis and interpretation, and wrote the manuscript. RE, RL, MS, AHonig, and GI contributed to recruitment of participants, data acquisition, analysis, and interpretation. All authors contributed to the critical revision of the manuscript and approved the final version before submission.

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