Ocular fundus photography of patients with focal neurologic deficits in an emergency department

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ABSTRACT

Objectives: We evaluated the frequency and predictive value of ocular fundus abnormalities among patients who presented to the emergency department (ED) with focal neurologic deficits to determine the utility of these findings in the evaluation of patients with suspected TIA and stroke.

Methods: In this cross-sectional pilot study, ocular fundus photographs were obtained using a nonmydriatic fundus camera. Demographic, neuroimaging, and ABCD² score components were collected. Photographs were reviewed for retinal microvascular abnormalities. The results were analyzed using univariate statistics and logistic regression modeling.

Results: Two hundred fifty-seven patients presented to the ED with focal neurologic deficits, of whom 81 patients (32%) had cerebrovascular disease (CVD) and 144 (56%; 95% confidence interval: 50%–62%) had retinal microvascular abnormalities. Focal and general arteriolar narrowing increased the odds of clinically diagnosed CVD by 5.5 and 2.6 times, respectively, after controlling for the ABCD² score and diffusion-weighted imaging. These fundus findings also significantly differentiated TIA from non-CVD, even after controlling for the ABCD² score.

Conclusions: Focal and general arteriolar narrowing were independent predictors of CVD overall, and TIA alone, even after controlling for the ABCD² score and diffusion-weighted imaging lesions. The inclusion of nonmydriatic ocular fundus photographs in the evaluation of patients presenting to the ED with focal neurologic deficits may assist in the differentiation of stroke and TIA from other causes of focal neurologic deficits. *Neurology*® 2015;85:256–262

GLOSSARY

ABCD² = age, blood pressure, clinical features, duration of TIA, presence of diabetes; **ARIC** = Atherosclerosis Risk in Communities; **CI** = confidence interval; **CVD** = cerebrovascular disease; **DWI** = diffusion-weighted imaging; **ED** = emergency department; **FOTO-ED** = Fundus Photography vs Ophthalmoscopy Trial Outcomes in the Emergency Department; **OR** = odds ratio.

Annually in the United States, 200,000 to 500,000 patients experience TIA,¹ with 7% to 14% subsequently having a stroke within 90 days.² A number of scores, particularly the widely used ABCD² score, were developed to determine which patients with TIA have the highest risk of stroke.² However, these scores have serious limitations.^{3–7} Diffusion-weighted imaging (DWI) has revolutionized the differentiation of stroke from TIA.¹ However, a negative DWI does not assist with the difficult, and arguably more important, task of differentiating TIA from non-cerebrovascular diseases, and TIA diagnosis remains very challenging. About 30% to 50% of patients diagnosed with suspected TIA by nonneurologists are ultimately determined not to have a TIA by a stroke neurologist.^{8,9} Even among nonstroke neurologists, agreement about TIA is only moderate to good.¹⁰

Epidemiologic investigations have shown an association between ocular fundus abnormalities and diabetes, cardiovascular disease, and stroke,^{11–17} suggesting that ocular funduscopic findings may be useful in the diagnosis of TIA and stroke in patients who present to the emergency department (ED) with focal neurologic deficits. Nonmydriatic fundus cameras can be used to assess for abnormalities of the ocular fundus, and the cameras are compact, easy to use, and do

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not require pupillary dilation, making them an ideal tool for nonophthalmologists. We undertook a pilot investigation to evaluate the role of ocular fundus abnormalities in TIA and stroke diagnosis using patients who presented to our ED with focal neurologic deficits during the Fundus Photography vs Ophthalmoscopy Trial Outcomes in the Emergency Department (FOTO-ED) Study.

METHODS **Standard protocol approvals, registrations, and patient consents.** The study was approved by our institutional review board. Informed consent was obtained from patients using a modified written consent procedure.

Study population. The FOTO-ED Study was a 2-phase sequential, cross-sectional study conducted between April 2009 and August 2011. The first phase evaluated the routine use of direct ophthalmoscopy by ED physicians.¹⁸ The second phase evaluated the routine use of nonmydriatic ocular fundus photography as interpreted by ED physicians.¹⁹ In both phases, all patients had ocular fundus photography with concurrent, masked interpretation of the photographs by 2 neuroophthalmologists, which served as the reference standard. In the FOTO-ED Study, adult patients who presented to our ED with the following chief complaints and triage findings were included: headache, acute focal neurologic deficits, acute visual changes, or triage diastolic blood pressure ≥ 120 mm Hg (16 kPa). Nonmydriatic ocular fundus photographs were obtained as previously described.^{18,19} This pilot investigation is a cross-sectional study of the subset of patients, from the FOTO-ED Study, who presented to the ED specifically with acute focal neurologic deficits. Patients included were required to have a focal neurologic deficit of acute onset, but we did not exclude patients based on duration of symptoms or based on time from symptom onset to presentation to the ED.

Patient characteristics. Patient demographics, including age and sex, along with presenting vital signs, were prospectively collected. Medical history, medications, imaging, consultations, and other interventions were ascertained by members of the study team masked to fundus photography results. Brain imaging interpretations were based on the final radiology reports. The ABCD² score was calculated at the time of initial presentation.² The diagnosis of TIA was based on a neurologist's review of the patient's history, physical examination, and initial stroke evaluation in patients with negative DWI, while being masked to fundus photography results. The diagnosis of acute stroke was performed in a similar fashion to that of TIA but required the presence of MRI DWI-positive lesions.¹

Nonmydriatic photography. Nonmydriatic photographs of the posterior pole of the ocular fundus (optic disc, macula, major retinal vessels, and portions of the peripheral retina) were obtained from both eyes of enrolled patients using a commercially available, Food and Drug Administration–approved, nonmydriatic ocular fundus camera (Kowa α -D; Kowa American Corporation, Torrance, CA) as previously described.^{18,19} In the original FOTO-ED studies, 2 neuroophthalmologists independently reviewed photographs for relevant findings defined as optic disc edema, optic disc pallor, acute retinal vascular occlusion (central or branch retinal artery or vein occlusions), retinal hemorrhages, and grade III/IV hypertensive retinopathy. Both neuroophthalmologists were masked to patient data at the time of photographic review. In

any case in which there remained diagnostic uncertainty, a third neuroophthalmologist made the determination of whether an abnormality was present or absent while being masked to the patient data, but aware of the finding disagreed upon by the 2 other reviewers. If there still remained uncertainty, an in-office examination was arranged.

For this study, the photographs were reviewed for additional funduscopic abnormalities, including cotton wool spots, microaneurysms, vascular tortuosity, generalized arteriolar narrowing, focal arteriolar narrowing, and arteriovenous nicking (figure, A). The Atherosclerosis Risk in Communities (ARIC) Study's circular grid (divided into 8 sectors and centered around the optic nerve) was used to evaluate the ocular fundus photographs for

Figure Example nonmydriatic fundus photograph, and the circular grid used in evaluating fundus photographs in the Atherosclerosis Risk in Communities Study

(A) Color nonmydriatic fundus photograph of the left eye of a patient diagnosed with cerebrovascular disease showing focal narrowing of one of the retinal arteries superior to the optic disc (arrow) and generalized arterial narrowing. (B) A standard grid is drawn around the disc. Zone A is a ring around the disc margin at a distance of 0.5 disc diameter. Zone B is a ring around 0.5 to 1 disc diameter away from the disc margin.

focal and general arteriolar narrowing and arteriovenous nicking (figure, B).²⁰ Focal arteriolar narrowing was defined as an arteriole estimated to be $\geq 50 \mu\text{m}$ in diameter that had a constricted area two-thirds or less than the width of the normal proximal and distal vessel segments.²⁰ Focal arteriolar narrowing was evaluated in all 8 sectors. General arteriolar narrowing was only evaluated in the outer 4 sectors of the grid and defined as an arteriolar-to-vein ratio of $\leq 50\%$ in any vessel segment.²⁰ The 8 sectors of the grid were also evaluated for arteriovenous nicking and arteriolar and venous tortuosity. The entire fundus photograph, not just limited to the ARIC grid, was evaluated for microaneurysms and cotton wool spots. When poor picture quality prevented evaluation of the photographs or the authors were not certain of a retinal finding, this was recorded.

For our study, “retinal microvascular” abnormalities included retinal hemorrhages, vascular occlusion, grade III/IV hypertensive retinopathy, cotton wool spots, microaneurysms, focal and generalized arterial narrowing, arteriovenous nicking, and arteriolar and venous tortuosity. “Nonmicrovascular” abnormalities included optic disc pallor and isolated optic disc edema.

Statistical analysis. Statistical analysis was performed using R: a language and environment for statistical computing (R Foundation for Statistical Computing, <http://www.R-project.org>). Two-tailed p values <0.05 were considered statistically significant. Descriptive statistics and logistic regression were performed, with cerebrovascular disease (CVD) as the outcome, ocular fundus abnormalities (coded as 2 indicator variables for microvascular and nonmicrovascular) as exposure of interest, and with age, blood pressure, diabetes status, DWI, clinical symptoms of focal weakness or speech impairment alone, and duration of symptoms as multiple predictors of interest. A p value–based backward elimination was used for variable reduction. Even though stroke requires a DWI-positive lesion, and was expected to be strongly associated with CVD, failure to include it in the model would prevent a determination of whether ocular fundus findings provide additional diagnostic information beyond that of DWI. In additional models, the ABCD² score was used rather than its individual components, and the model comparing patients with TIA and non-CVD did not include DWI. Bootstrap estimates were used to compare C statistics between nested logistic models.

RESULTS Among the 704 patients enrolled in the FOTO-ED Study, 257 patients (37%) presented with focal neurologic deficits. One hundred sixty-two patients (63%) were women, median age was 52 years (interquartile range: 37–65), and 136 (53%) had MRI performed. Forty-one patients (16%) had symptoms lasting less than 10 minutes, 29 (11%) for 10 to 59 minutes, and 187 (73%) for 60 or more minutes. Of the 257 patients with focal neurologic deficits, 81 (32%) were diagnosed with CVD (74 [91%] with MRI), among whom 22 (27%) had a stroke based on DWI. The remaining 59 (73%) were diagnosed with TIA.

Among the 257 patients who presented with focal neurologic deficits, 150 patients (58%; 95% confidence interval [CI]: 52%–64%) had one or more abnormalities of the ocular fundus, of whom 144 of 257 patients (56%; 95% CI: 50%–62%) had retinal microvascular abnormalities (table 1). Specifically,

patients with CVD were more likely to have retinal vascular occlusions, 2 or more sectors of focal arteriolar narrowing, or 4 or more sectors of generalized arteriolar narrowing. The presence of either 2 or more sectors of focal or 4 or more sectors of generalized narrowing had a sensitivity of 0.31, a specificity of 0.86, a positive predictive value of 0.51, and a negative predictive value of 0.73. Nonmicrovascular changes were more likely associated with a non-CVD diagnosis with a sensitivity of 0.07, a specificity of 0.98, a positive predictive value of 0.86, and a negative predictive value of 0.32. Overall, patients with CVD tended to be older, have higher systolic blood pressure, and have diabetes (table 1).

Among the 81 patients with CVD, patients with stroke were more likely to have higher systolic (median 160 vs 146 mm Hg, $p = 0.02$) and diastolic (median 82 vs 80 mm Hg, $p = 0.04$) blood pressures and were also more likely to have retinal vascular occlusions than patients with TIA (3 [14%] vs 1 [2%], $p = 0.03$). There were otherwise no significant differences between patients with stroke and TIA when comparing the remaining demographics and ocular funduscopic findings. Comparing patients with TIA and non-CVD diagnoses (i.e., excluding patients with stroke), patients with TIA tended to be older and to have higher systolic blood pressure, diabetes, and 2 or more sectors of focal and 4 or more sectors of generalized retinal arterial narrowing (table 1).

Backward elimination of a multivariable logistic regression model of fundus findings on CVD that initially controlled for age, sex, blood pressure, diabetes status, clinical presentation, symptom duration, and DWI showed that patients diagnosed with CVD were likely to be older, to be diagnosed with diabetes, and to have abnormal DWI (table 2). Among retinal microvascular findings, only 2 or more sectors of focal and 4 or more sectors of generalized arteriolar narrowing were associated with an increased odds of clinically diagnosed CVD (focal odds ratio [OR] 8.1; 95% CI: 1.8–36.1; $p = 0.006$; generalized OR 2.4; 95% CI: 1.01–5.7; $p = 0.049$) while nonmicrovascular retinal changes were associated with a significantly reduced odds of clinically diagnosed CVD (OR 0.10; 95% CI: 0.01–0.77; $p = 0.03$). When controlled for the ABCD² score instead of its individual components, the odds of CVD were 5.1 times higher when focal narrowing was present (95% CI: 1.4–19; $p = 0.02$) and 2.7 times higher when generalized narrowing was present (95% CI: 1.3–5.9; $p = 0.01$). The magnitudes were also similar when both the ABCD² score and DWI were controlled (focal OR = 5.5; 95% CI: 1.4–22; $p = 0.02$; generalized OR = 2.6; 95% CI: 1.2–5.7; $p = 0.02$).

The addition of focal and generalized narrowing and other fundus findings to the model led to a

Table 1 Univariate analysis comparing patients with CVD (stroke and TIA) vs those with other diagnoses

Variable	CVD							
	Stroke (n = 22)		TIA (n = 59)					
	Count or median	% or IQR	Count or median	% or IQR	Count or median	% or IQR	p Value, CVD vs other	p Value, TIA vs other
Demographics								
Women	12	55	37	63	113	64	0.57	0.84
Age, y	65	53-75	61	53-71	46	32-59	<0.001	<0.001
Systolic blood pressure, mm Hg (kPa)	160 (21.3)	147-170 (19.6-22.7)	146 (19.5)	136-156 (18.1-20.8)	135 (18.0)	123-151 (16.4-20.1)	<0.001	0.003
Diastolic blood pressure, mm Hg (kPa)	82 (10.9)	79-98 (10.5-13.1)	80 (10.7)	69-89 (9.2-11.9)	77 (10.3)	70-88 (9.3-11.7)	0.18	0.85
Diabetes	8	36	18	31	24	14	<0.001	0.003
Retinal hemorrhages	1	5	0	0	6	3	0.32	0.15
Hypertensive retinopathy	2	9	3	5	4	2	0.114	0.27
Retinal vascular occlusion	3	14	1	2	0	0	0.03	0.08
Cotton wool spots	1	5	2	3	2	1	0.17	0.24
Microaneurysms	2	9	1	2	4	2	0.51	0.79
AV nicking	8	36	13	22	40	23	0.58	0.91
Venous tortuosity	2	9	3	5	9	5	0.73	0.99
Arterial tortuosity	3	14	9	15	25	14	0.90	0.84
Focal narrowing (≥2 sectors)	4	18	6	10	5	3	0.003	0.02
General narrowing (≥4 sectors)	9	41	13	22	21	12	0.002	0.056
Optic disc pallor	1	5	1	2	4	2	0.92	0.79
Isolated optic disc edema	0	0	0	0	8	5	0.051	0.096
Summary of ocular abnormalities								
Nonmicrovascular	1	5	1	2	12	7	0.07	0.20
All retinal microvascular	16	73	33	56	97	55	0.42	1.00

Abbreviations: AV = arteriovenous; CVD = cerebrovascular disease; IQR = interquartile range.

Table 2 Multivariable logistic regression model with cerebrovascular disease as outcome among patients with focal neurologic deficits

Risk factor	OR (95% CI)	p Value
Age, per 10-y increase	1.46 (1.18-1.82)	<0.001
Blood pressure		
Systolic, per 10-mm Hg (1.3-kPa) increase	1.14 (0.92-1.42)	0.24
Diastolic, per 10-mm Hg (1.3-kPa) increase	0.76 (0.53-1.09)	0.14
Diabetes	2.74 (1.25-5.98)	0.01
Clinical presentation		
Speech	2.00 (0.71-5.64)	0.19
Unilateral weakness	1.75 (0.79-3.87)	0.17
Duration, ^a min		
10-59	1.93 (0.59-6.32)	0.28
≥60	0.71 (0.30-1.71)	0.45
Diffusion-weighted imaging, positive	19.72 (3.39-114.77)	<0.001
Funduscopy findings		
Focal narrowing (≥2 sectors)	8.11 (1.82-36.09)	0.006
General narrowing (≥4 sectors)	2.39 (1.01-5.68)	0.049
Nonmicrovascular	0.10 (0.01-0.77)	0.03

Abbreviations: CI = confidence interval; OR = odds ratio.

^aReference <10 minutes.

significant increase in the C statistic, even after accounting for ABCD² score and DWI (0.77 vs 0.71, $p = 0.02$). Excluding patients with stroke (i.e., retaining patients with TIA and non-CVD diagnoses), these fundus findings remained significantly associated with TIA (table 3) and improved the prediction of TIA vs non-CVD over and above ABCD² alone (0.71 vs 0.63, $p = 0.04$).

DISCUSSION Fifty-eight percent of patients who presented to our ED with focal neurologic deficits had one or more abnormalities of the ocular fundus; specifically, 56% of patients with focal neurologic deficits had retinal microvascular abnormalities. Among the retinal microvascular changes, 2 or more sectors of focal arteriolar narrowing increased the odds of clinically diagnosed CVD by 8 times, and 4

or more sectors of generalized arteriolar narrowing increased the odds of clinically diagnosed CVD by 2.5 times. When controlled for the ABCD² score, the odds of CVD were 5 times higher when focal narrowing was present and nearly 3 times higher when generalized narrowing was present. Nonmicrovascular changes, overall, reduced the odds of CVD by one-tenth.

Our findings are not surprising because the retina and optic nerve are an extension of the CNS tissue, and the retinal and cerebral microvasculature are similar embryologically, anatomically, and physiologically.¹¹ Extensive data from population-based studies have shown that retinal microvascular abnormalities are associated with diabetes, hypertension, and stroke. Population-based studies of subjects older than 40 years, including the Beaver Dam Eye Study and The Blue Mountain Eye Study, have found that about 10% to 16% have generalized arteriolar narrowing^{21,22} and about 8% to 13% have focal arteriolar narrowing.¹⁶ Even with our stricter cutoffs for narrowing, which require multiple quadrants of disease, and our younger population, we had similar prevalences (17% generalized; 6% focal), suggesting that our cohort has more severe disease, as would be expected.

The association of retinal microvascular abnormalities with stroke in population-based studies persists even after adjusting for diabetes and hypertension.²³⁻²⁶ Wang et al.²⁷ obtained dilated ocular fundus photographs of patients admitted to the hospital with TIA or acute stroke and found that their patients had 7.2 to 8.9 times the odds of having focal arteriolar narrowing compared with normal controls. Although our study occurred in the acute setting of the ED and was performed without pupillary dilation, we observed very similar ORs.

Perhaps even more interesting is the finding that both focal and general arteriolar narrowing remained significantly associated with TIA when patients with stroke were excluded from the analysis. In fact, these fundus findings improved the prediction of TIA vs non-CVD even after accounting for the ABCD² score. While we recognize that the ABCD² score is intended to be used as a risk stratification tool, some authors have suggested that the reason the ABCD² score is effective in predicting the risk of future events is its diagnostic capabilities in differentiating TIA from non-CVD.⁹ Thus, the results of this study suggest that ocular fundus abnormalities are an independent factor to be considered in the diagnosis of stroke and, especially, of TIA, which remains extremely difficult to differentiate objectively from noncerebrovascular causes of focal neurologic deficits in the ED. Indeed, numerous studies have emphasized the difficulty of making a definite diagnosis of TIA in the ED. TIA is a clinical diagnosis and up to 50% of patients

Table 3 Final multivariable logistic regression model with TIA as outcome

Risk factor	OR (95% CI)	p Value
ABCD ² score, per point	1.42 (1.15-1.76)	<0.001
Funduscopy findings		
Focal narrowing (≥2 sectors)	5.19 (1.27-21.22)	0.02
General narrowing (≥4 sectors)	2.37 (1.02-5.54)	0.046
Nonmicrovascular	0.11 (0.01-1.04)	0.053

Abbreviations: CI = confidence interval; OR = odds ratio.

Includes the 235 patients with focal neurologic deficits who were not diagnosed with stroke (i.e., comparing patients with TIA [$n = 59$] and patients without cerebrovascular disease [$n = 176$]).

presenting to the ED with suspected TIA have other conditions mimicking a TIA.^{28,29} The inclusion of systematic nonmydriatic fundus photographs in patients with acute transient focal neurologic deficits would potentially decrease overdiagnosis of TIA in the ED.

Given the portability of ophthalmoscopes, ocular funduscopic examinations can be done anywhere, including in the ED, but ophthalmoscopy is challenging, especially without pharmacologic pupillary dilation and constant practice.^{30–32} Ophthalmoscopy at bedside also has a low sensitivity for subtle findings, such as isolated retinal hemorrhages or retinal vascular changes, even in the hands of ophthalmologists.³³ In contrast, nonmydriatic fundus photography does not require the patient's pupils to be dilated, and provides high-resolution photographs with a wide field of view improving the sensitivity for abnormalities. The FOTO-ED Study previously showed the superiority of nonmydriatic fundus photography to direct ophthalmoscopy in the ED.³⁴ Indeed, in phase I of the FOTO-ED Study, when the ED physicians did not have access to the nonmydriatic fundus photographs, direct ophthalmoscopy was performed on only 5 of 33 patients who were found to have funduscopic abnormalities on photographs; the direct ophthalmoscopy results were erroneously recorded as normal for all 5 patients.³⁴ In phase II of the FOTO-ED Study, when the photographs were made available to ED physicians, they were able to identify 46% of the relevant abnormalities on the photographs without additional training.¹⁹ The cost of a nonmydriatic camera is currently more than the cost of outfitting several ED examination rooms with direct ophthalmoscopes (approximately \$25,000 vs \$5,000), but if photography became a useful adjunct in the evaluation of patients with possible TIA and stroke, it is worthwhile noting that it is substantially less than the cost of systematic brain MRI, which is standard care for these patients. The addition of nonmydriatic fundus photography to the diagnostic armamentarium available to an ED will likely prove cost-effective in the near future. Such cameras are already routinely used in clinical practice by nonophthalmologists in primary care (e.g., the national Veterans Affairs tele-screening program for diabetic retinopathy³⁵) and neurologist offices.

One limitation of the definition of generalized arteriolar narrowing based on venular diameter used in this and the ARIC Study is that arteriolar narrowing could instead represent venular widening, which has also been associated with stroke.³⁶ The FOTO-ED studies were not specifically designed to address the hypothesis of this study. However, the similarity of our effect sizes to those of other studies and the apparent value of adding focal and general arteriolar

narrowing to the ABCD² score in differentiating TIA from other non-CVD causes of focal neurologic deficits deserve confirmation in a dedicated study. In addition, it remains to be confirmed whether identification of these retinal microvascular abnormalities will assist in the risk prediction of short-term strokes following TIA. Finally, how photographs are evaluated for microvascular findings (e.g., by ED physicians vs ophthalmologists via telemedicine) will also require additional study.

Ocular fundus examination appears valuable in the differentiation of stroke and TIA from other causes of focal neurologic deficits in the ED setting. Our study shows that the presence of focal and general arteriolar narrowing increases the odds of clinically diagnosed CVD and helps in differentiating TIA from non-CVD events in the ED. Nonmicrovascular abnormalities, however, strongly suggested alternative diagnoses. We believe that the ease of use and commercial availability of nonmydriatic ocular fundus cameras will facilitate the incorporation of this examination technique into routine clinical practice.

AUTHOR CONTRIBUTIONS

L.N. Vuong: participated in the design of the study, in the collection, analysis, and interpretation of the data, and in the drafting and critical revision of the manuscript. P. Thulasi: participated in the design of the study, in the collection and interpretation of the data, and in the critical revision of the manuscript. V. Biousse: participated in the design of the study, in the analysis and interpretation of the data, and in the critical revision of the manuscript. P. Garza: participated in the collection and interpretation of the data, and in the critical revision of the manuscript. D.W. Wright: participated in the design of the study, in the analysis and interpretation of the data, and in the critical revision of the manuscript. N.J. Newman: participated in the design of the study, in the analysis and interpretation of the data, and in the critical revision of the manuscript. B.B. Bruce: participated in the design of the study, in the collection, analysis, and interpretation of the data, in the statistical analysis, and in the drafting and critical revision of the manuscript.

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DISCLOSURE

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REFERENCES

1. Easton JD, Saver JL, Albers GW, et al. Definition and evaluation of transient ischemic attack. *Stroke* 2009;40:2276–2293.
2. Johnston SC, Rothwell PM, Nguyen-Huynh MN, et al. Validation and refinement of scores to predict early stroke

- risk after transient ischemic attack. *Lancet* 2007;369:283–292.
3. Perry JJ, Sharma M, Sivilotti ML, et al. Prospective validation of the ABCD² score for patients in the emergency department with transient ischemic attack. *CMAJ* 2011;183:1137–1145.
4. Sanders LM, Srikanth VK, Blacker DJ, Jolley DJ, Cooper KA, Phan TG. Performance of the ABCD² score for stroke risk post TIA: meta-analysis and probability modeling. *Neurology* 2012;79:971–980.
5. Lee J, Shah K. In patients presenting with transient ischemic attack, does the ABCD² clinical prediction rule provide adequate risk stratification for clinical decision making in the emergency department? *Ann Emerg Med* 2013;62:14–15.
6. Chandratheva A, Geraghty OC, Rothwell PM. Poor performance of current prognostic scores for early risk of recurrence after minor stroke. *Stroke* 2011;42:632–637.
7. Amarenco P, Labreuche J, Lavallée PC. Patients with transient ischemic attack with ABCD² <4 can have similar 90-day stroke risk as patients with transient ischemic attack with ABCD² ≥4. *Stroke* 2012;43:863–865.
8. Nahab F, Leach G, Kingston C, et al. Impact of an emergency department observation unit transient ischemic attack protocol on length of stay and cost. *J Stroke Cerebrovasc Dis* 2012;21:673–678.
9. Quinn TJ, Cameron AC, Dawson J, Lees KR, Walters MR. ABCD² scores and prediction of noncerebrovascular diagnoses in an outpatient population: a case-control study. *Stroke* 2009;40:749–753.
10. Kraaijeveld CL, van Gijn J, Schouten HJ, Staal A. Interobserver agreement for the diagnosis of transient ischemic attacks. *Stroke* 1984;15:723–725.
11. Baker ML, Hand PJ, Wang JJ, Wong TY. Retinal signs and stroke: revisiting the link between the eye and brain. *Stroke* 2008;39:1371–1379.
12. Sharrett AR, Hubbard LD, Cooper LS, et al. Retinal arteriolar diameters and elevated blood pressure: the Atherosclerosis Risk in Communities Study. *Am J Epidemiol* 1999;150:263–270.
13. Ikram MK, Wittema JC, Vingerling JR, Breteler MM, Hofman A, de Jong PT. Retinal vessel diameters and risk of hypertension. The Rotterdam Study. *Hypertension* 2006;47:189–194.
14. Wong TY, Klein R, Nieto FJ, et al. Retinal microvascular abnormalities and 10-year cardiovascular mortality: a population-based case-control study. *Ophthalmology* 2003;110:933–940.
15. Wong TY. Is retinal photography useful in the measurement of stroke risk? *Lancet Neurol* 2004;3:179–183.
16. Wong TY, McIntosh R. Hypertensive retinopathy signs as risk indicators of cardiovascular morbidity and mortality. *Br Med Bull* 2005;73-74:57–70.
17. Wong TY, McIntosh R. Systemic associations of retinal microvascular signs: a review of recent population-based studies. *Ophthalmic Physiol Opt* 2005;25:195–204.
18. Bruce BB, Lamirel C, Wright DW, et al. Feasibility of non-mydriatic ocular fundus photography in the emergency department: phase I of the FOTO-ED Study. *Acad Emerg Med* 2011;18:928–933.
19. Bruce BB, Thulasi P, Fraser CL, et al. Diagnostic accuracy and use of non-mydriatic ocular fundus photography by emergency physicians: phase II of the FOTO-ED Study. *Ann Emerg Med* 2013;62:28–33.
20. Hubbard LD, Brothers RJ, King WN, et al. Methods for evaluation of retinal microvascular abnormalities associated with hypertension/sclerosis in the Atherosclerosis Risk in Communities Study. *Ophthalmology* 1999;106:2269–2280.
21. Klein R, Klein BE, Moss SE. The relation of systemic hypertension to changes in the retinal vasculature: the Beaver Dam Eye Study. *Trans Am Ophthalmol Soc* 1997;95:329–350.
22. Wang JJ, Mitchell P, Leung H, et al. Hypertensive retinal vessel wall signs in a general older population: the Blue Mountains Eye Study. *Hypertension* 2003;42:534–541.
23. Mitchell P, Wang JJ, Wong TY, Smith W, Klein R, Leeder SR. Retinal microvascular signs and risk of stroke and stroke mortality. *Neurology* 2005;65:1005–1009.
24. Witt N, Wong TY, Hughes AD, et al. Abnormalities of retinal microvascular structure and risk of mortality from ischemic heart disease and stroke. *Hypertension* 2006;47:975–981.
25. Wong TY, Klein R, Couper DJ, et al. Retinal microvascular abnormalities and incident stroke: the Atherosclerosis Risk in Communities Study. *Lancet* 2001;358:1134–1140.
26. Cooper LW, Wong TY, Klein R, et al. Retinal microvascular abnormalities and MRI-defined subclinical cerebral infarction. *Stroke* 2006;37:82–86.
27. Wang JJ, Baker ML, Hand PJ, et al. Transient ischemic attack and acute ischemic stroke associations with retinal microvascular signs. *Stroke* 2011;42:404–408.
28. Prabhakaran S, Silver AJ, Warrior L, McClenathan B, Lee VH. Misdiagnosis of transient ischemic attacks in the emergency room. *Cerebrovasc Dis* 2008;26:630–635.
29. Amort M, Fluri F, Schäfer J, et al. Transient ischemic attack versus transient ischemic attack mimics: frequency, clinical characteristics and outcome. *Cerebrovasc Dis* 2011;32:57–64.
30. Benbassat J, Polak BC, Javitt JC. Objectives of teaching direct ophthalmoscopy to medical students. *Acta Ophthalmol* 2012;90:503–507.
31. Mottow-Lippa L, Boker JR, Stephens F. A prospective study of longitudinal effects of an embedded specialty curriculum on physical examination skills using an ophthalmology model. *Acad Med* 2009;84:1622–1630.
32. Kelly LP, Garza PS, Bruce BB, Graubart EB, Newman NJ, Biousse V. Teaching ophthalmoscopy to medical students (the TOTeMS Study). *Am J Ophthalmol* 2013;156:1056–1061.
33. Mackay DD, Garza PS, Bruce BB, et al. Teaching ophthalmoscopy to medical students (TOTeMS) II: a one-year retention study. *Am J Ophthalmol* 2014;157:747–748.
34. Bruce BB, Lamirel C, Wright DW, et al. Nonmydriatic ocular fundus photography in the emergency department. *N Engl J Med* 2011;364:387–389.
35. Cavallerano AA, Conlin PR. Teleretinal imaging to screen for diabetic retinopathy in the Veterans Health Administration. *J Diabetes Sci Technol* 2008;2:33–39.
36. McGeechan K, Liew G, Macaskill P, et al. Prediction of incident stroke events based on retinal vessel caliber: a systematic review and individual-participant meta-analysis. *Am J Epidemiol* 2009;170:1323–1332.