



Management of Acute Retinal Ischemia

Follow the Guidelines!

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Acute retinal arterial ischemia, including vascular transient monocular vision loss (TMVL) and branch (BRAO) and central retinal arterial occlusions (CRAO), are ocular and systemic emergencies requiring immediate diagnosis and treatment. Guidelines recommend the combination of urgent brain magnetic resonance imaging with diffusion-weighted imaging, vascular imaging, and clinical assessment to identify TMVL, BRAO, and CRAO patients at highest risk for recurrent stroke, facilitating early preventive treatments to reduce the risk of subsequent stroke and cardiovascular events. Because the risk of stroke is maximum within the first few days after the onset of visual loss, prompt diagnosis and triage are mandatory. Eye care professionals must make a rapid and accurate diagnosis and recognize the need for timely expert intervention by immediately referring patients with acute retinal arterial ischemia to specialized stroke centers without attempting to perform any further testing themselves. The development of local networks prompting collaboration among optometrists, ophthalmologists, and stroke neurologists should facilitate such evaluations, whether in a rapid-access transient ischemic attack clinic, in an emergency department—observation unit, or with hospitalization, depending on local resources. *Ophthalmology* 2018;125:1597-1607 © 2018 by the American Academy of Ophthalmology



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Acute retinal arterial ischemic events are classic causes of acute painless monocular vision loss. Transient or permanent occlusion of the central retinal artery or a branch retinal artery reflects acutely impaired blood flow in the anterior cerebral and ocular circulation and is associated with high cerebrovascular and cardiovascular morbidity and mortality.^{1–3} Indeed, transient monocular vision loss (TMVL) of vascular origin is a retinal transient ischemic attack (TIA), whereas branch retinal artery occlusion (BRAO) and central retinal artery occlusion (CRAO) result in retinal infarctions, with mechanisms and causes identical to those of acute cerebral infarctions in the territory of the internal carotid artery.¹ Many health professionals and the public consider TIAs benign but regard strokes as serious. These views are incorrect. Strokes and TIAs are on a spectrum of serious conditions involving brain and eye ischemia, just as angina and acute myocardial infarction are part of the continuum of acute coronary syndromes.⁴ It is therefore logical to combine vascular TMVL, BRAO, and CRAO as “acute retinal arterial ischemia” and to propose the same systematic management for these 3 entities. Although their respective visual outcomes are different, their overall significance and their systemic and neurologic implications are similar. Vascular TMVL can be compared to a cerebral TIA, whereas BRAO and CRAO are best classified as minor strokes, and all must be managed accordingly. In 2011 and 2013, the National Stroke Association⁵ and the American Heart Association (AHA)^{6,7} published a consensus statement defining central nervous system infarction (stroke) as “brain, spinal cord, or

retinal cell death attributable to ischemia, based on neuro-pathological, neuroimaging, and/or clinical evidence of permanent injury.” This statement clearly emphasizes that acute retinal arterial ischemia is a stroke equivalent and represents an ophthalmologic and medical emergency. Numerous excellent publications originating in the ophthalmic literature have helped understand and clarify the spectrum of acute retinal ischemia over the past 40 years. However, although a few authors have emphasized the need to urgently care for these patients with isolated visual loss, there is ample evidence that appropriate care of patients with acute retinal ischemia is too often delayed.⁸ The aim of this article is to review the most recent data and recommendations regarding the acute management of patients with TIAs and minor strokes and to propose guideline-compliant strategies applicable to eye care providers who routinely see patients with acute visual loss from retinal arterial ischemic events. The outdated belief that acute retinal ischemia is of less concern than cerebral ischemia (and therefore may not need emergent care) must be revisited. It is time for a change in practice among eye care professionals.

Are Retinal Transient Ischemic Attacks Different From Cerebral Transient Ischemic Attacks?

Several studies^{9–18} have reported that the risk of stroke after a retinal TIA is lower than the risk of stroke after a cerebral

TIA. However, none of these studies concluded that retinal TIAs are benign, and most emphasized that although the risk of subsequent stroke may be lower than expected, the overall risk for cardiovascular events and death was the same as in the population of patients with cerebral TIAs, consistent with shared major vascular risk factors.^{10–12,19,20}

What can account for this apparently lower risk of stroke after TMVL? The most likely explanation is that retinal arterial ischemia as the cause of TMVL is overdiagnosed in most large studies, contributing to the seemingly better vascular prognosis after a retinal TIA. It is indeed often extremely difficult to determine the cause of an episode of transient visual loss, and despite a detailed history and ocular examination, a diagnosis of presumed vascular TMVL often remains uncertain.^{17,21,22} In our experience, nonvascular ocular causes and migrainous visual aura (often misinterpreted as being monocular by patients) explain many episodes of transient visual loss. Additionally, a number of recurrent isolated episodes of vascular TMVL may be related to central retinal artery vasospasm, which is a local (usually benign) disease not associated with higher cerebrovascular and cardiovascular risk²² (Fig S1, available at www.aajournal.org).

Even within the subgroup of patients with internal carotid artery stenosis and related ocular symptoms, there may be different individual responses to cerebral hypoperfusion. Collateral circulation plays a major role in protecting the ipsilateral hemisphere in patients with severe internal carotid artery stenosis. In these patients, flow is often diverted from the eye to the brain via the circle of Willis to maintain cerebral perfusion. Such patients classically have recurrent episodes of TMVL but no cerebral infarction because the brain is perfused at the expense of the eye.²³

It has also been suggested that very small platelet-fibrin emboli will more readily become manifest when reaching the eye than when reaching the brain. Indeed, it is probable that very small retinal emboli resulting in focal retinal hypoperfusion do result in transient visual symptoms, whereas it is very unlikely that similar small cerebral emboli would produce neurologic symptoms obvious enough to be noticed by patients.^{9,24} Additionally, because our eyes are constantly open when we are awake, we are more likely to perceive very brief episodes of visual loss than brief episodes of neurologic dysfunction, allowing us to notice “mini-ocular TIAs,” with relatively good prognosis. Such a theory would explain the not uncommon occurrence of small, multiple *asymptomatic* cerebral infarctions found acutely on magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI) sequences (DWI-MRI) in patients with TMVL.⁸

In the North American Symptomatic Carotid Endarterectomy Trial (NASCET),⁹ patients with TMVL were more likely to subsequently have retinal infarctions whereas patients with cerebral TIAs were more likely to have cerebral infarctions, with a resultant lower risk of cerebral infarctions after retinal ischemia. This could be explained by the intraluminal streaming phenomenon in which recurrent vascular emboli tend to go to the same arterial branch.²⁵ It has been theorized that because particles originating from the heart are usually of larger caliber

than those commonly originating from carotid atherosclerosis, cardiac emboli will more often reach the brain than the retinal circulation.²⁴ This is supported by laminar flow in large arteries in which various laminae are directed to different distal vascular beds. Large emboli tend to travel centrally in midstream and reach the most distal vascular bed, whereas small emboli originating from an atherosclerotic carotid wall will remain closer to the wall and be swept into the first arterial bifurcation they encounter (e.g., the ophthalmic artery), similar to the migration of rocks and debris in rivers (the streaming effect).^{24–26} Such phenomena may explain why retinal artery occlusions are more commonly caused by carotid disease than by cardiac sources of emboli, as previously suggested in another study comparing risk factors for cerebral versus ocular ischemic events.²⁶

Prognosis of Transient Ischemic Attacks

It is well established that TIAs offer an opportunity to initiate treatment that can forestall the onset of permanent disability.^{4,27} Major advances in the urgent evaluation of TIA patients and in secondary prevention strategies have resulted in a dramatic decrease in the risk for major stroke after a TIA or minor stroke.^{27–30} Previous studies conducted before the early 2000s estimated the risk of stroke and acute coronary syndromes between 12% and 20% during the first 3 months after a TIA or a minor stroke, with a large proportion of these strokes occurring very early after the first events.^{31,32} The recent TIAregistry.org project³³ included 4789 TIA patients (including 172 patients with TMVL) who were enrolled over 2.5 years in 61 specialized TIA clinics by experienced stroke specialists. Seventy-five percent of patients were evaluated and treated within 24 hours of symptom onset. The reported rate of stroke and acute coronary syndrome was only 1.5%, 2.1%, 2.8%, 3.7%, and 5.1% at days 2, 7, 30, 90, and 365, respectively. However, this very low risk for recurrent stroke is likely explained by the excellent immediate care received by these patients in specialized stroke centers. Indeed, previous studies relying on rapid assessment of TIA and immediate initiation of aggressive secondary prevention showed that proven management strategies for TIA can reduce the relative risk of subsequent stroke by 80%.^{34,35} A meta-analysis from 2007 evaluating the risk for stroke early after TIA³⁶ demonstrated a wide range of stroke risk among studies, with risks ranging from 0% to 12.8%, and a pooled stroke risk of 3.1% at 2 days (95% confidence interval [CI] 2.0–4.1) and 5.2% at 7 days (95% CI 3.9–6.5). Not surprisingly, the lowest risks (0.6% at 2 days [95% CI 0.0–1.6] and 0.9% at 7 days [95% CI 0–1.9]) were seen in studies of emergency treatment in specialized stroke services, and the highest risks (3.6% at 2 days [95% CI 2.4–4.7] and 11% at 7 days [95% CI 8.6–13.5]) were seen in population-based studies without urgent treatment. The publication of the EXPRESS study³⁴ and the SOS-TIA study³⁵ in 2007, both of which showed conclusively that immediate evaluation and treatment of TIA patients (cerebral and retinal TIAs) in specialized

stroke centers results in better outcomes, revolutionized the subsequent management of TIA patients. The impact of these studies was shown in another meta-analysis from 2017,³⁰ which reviewed studies published after 2007 and showed a pooled stroke risk of 1.36% at 2 days (95% CI 1.15–1.59), 2.06% at 7 days (95% CI 1.83–2.33), 2.78% at 30 days (95% CI 2.47–3.12), and 3.42% at 90 days (95% CI 3.14–3.74). There is no debate regarding the obvious benefit of urgent assessment of TIA patients to decrease the risk of stroke recurrence, including in patients presenting with acute vascular visual loss.^{4,28}

Stratification of Transient Ischemic Attack Patients

TIA is a warning sign of an impending stroke. Therefore, management of TIA on an emergent basis provides a great opportunity to avoid a subsequent stroke. However, many patients with TIAs never have a stroke and the diagnosis of TIA (including vascular TMVL) can be challenging, with numerous patients misdiagnosed as having TIAs.³⁷ Hence, a large number of studies have focused on identifying TIA patients with the highest risk of subsequent stroke. Clinical scores such as the ABCD2 score routinely used in emergency settings are helpful when triaging patients with transient neurologic symptoms.^{28,38} This score gives points to parameters such as **A**ge 60 or greater, **B**lood pressure 140/90 mmHg or more, **C**linical features of focal weakness or speech impairment, **D**uration of the neurologic symptom greater than 1 hour, and **D**iabetes. Higher scores are associated with a higher risk of stroke. The latest clinical scores have included results of cerebral and

vascular imaging, and it is now well established, for example, that evidence of cerebral infarctions on brain imaging in a patient with transient neurologic symptoms and large-artery atherosclerosis more than doubles the risk of stroke within the next few days.^{39,40} Brain imaging with computed tomography was always advocated in presumed TIA patients, mostly to rule out other causes of transient neurological dysfunction. However, the demonstration of at least 1 infarction somewhere in the brain in at least one third of TIA patients who receive an urgent DWI-MRI has revolutionized the urgent evaluation of TIA patients.^{33,39,40} Positive DWI is defined as areas of restricted diffusion, often small and multiple, that can be seen in any vascular territory (even unrelated to the TIA symptoms) (Fig 1). The presence of multiple cerebral infarctions on neuroimaging may be explained by plaque rupture with multiple distal emboli⁴¹ or a cardiac source of emboli,^{42,43} reinforcing why TIA patients who have abnormalities on DWI-MRI have a higher risk of recurrent ischemic events than those without such imaging abnormalities.^{33,39,40} These findings support the shift in emphasis of the characterization of TIA from a *time-based* (<24 hours, as defined by the World Health Organization TIA criteria proposed in 1988) to a *tissue-based* definition, requiring the absence of acute infarction on DWI-MRI.⁷ In 2009, the AHA⁷ revised the definition of TIA, describing it as “a transient episode of neurologic dysfunction caused by focal brain, spinal cord, or *retinal ischemia* without acute infarction.” The typical symptom duration is less than 1 or 2 hours; however, prolonged episodes do occasionally occur. Evidence of acute infarction detected by DWI-MRI (and ocular fundoscopic examination) among patients with transient events distinguishes between

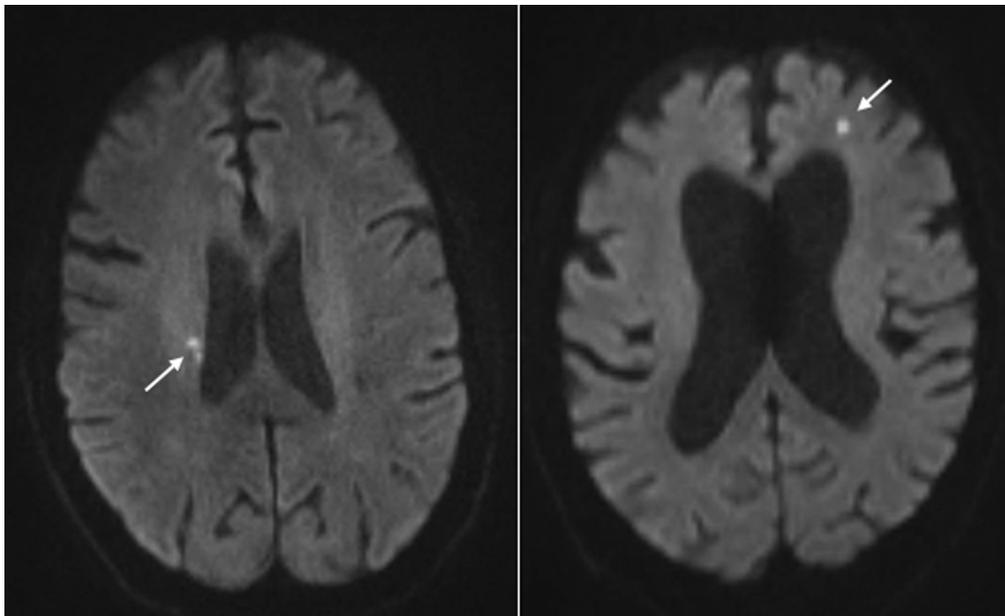


Figure 1. Brain magnetic resonance images (diffusion-weighted images) of 2 different patients obtained within 24 hours after a central retinal artery occlusion, showing a small area of restricted diffusion (hyperintense signal in *white arrows*), consistent with acute cerebral ischemia. The patients had no neurologic symptoms.

true TIA and ischemic stroke and portends a higher risk of recurrent stroke after the transient event.

DWI-MRI results combined with results of vascular imaging and cardiac monitoring are a very powerful way to triage TIA patients, allowing identification of a subgroup of patients with very high risk of stroke who need to be hospitalized and urgently treated. In the TIAregistry.org,³³ 22% of recurrent stroke occurred in patients with preventable underlying causes such as atrial fibrillation and ipsilateral internal carotid artery stenosis of 50% or more, conditions easily treated promptly at the time of initial evaluation.

Why Magnetic Resonance Imaging with Diffusion-Weighted Imaging Sequences Should Be Obtained Urgently in All Patients with Acute Retinal Arterial Ischemia

Since the publication of the AHA guidelines in 2011,²⁸ 7 studies have reported the presence of multiple small cerebral infarctions in up to 31% of patients with vascular TMVL, acute BRAO, and CRAOs^{44–50} (Table 1). These 7 studies report strikingly similar results, with DWI-MRI abnormalities being found more often in patients with acute CRAO, followed by those with BRAO and then those with vascular TMVL. Acute cerebral infarctions were found in 27% to 76.4% of CRAO patients, and in 11.8% to 30.8% of TMVL patients, emphasizing that although CRAO is more concerning than vascular TMVL, patients with transient visual symptoms must also be appropriately diagnosed and triaged so as to identify the subgroup of patients requiring urgent evaluation. In these studies, the presence of silent (asymptomatic) cerebral infarctions on DWI-MRI was associated with a higher chance of identifying an embolic cause for the acute retinal ischemia, allowing identification of the subgroup of patients with very high risk of stroke and creating an opportunity for immediate treatment and prevention of recurrent stroke. The authors all emphasized the need to evaluate patients with isolated acute retinal ischemia urgently with brain imaging, ideally brain MRI with DWI, in addition to a stroke workup, analogous to the management of patients with acute cerebral ischemia. This recommendation was endorsed by the American Academy of Ophthalmology Retina/Vitreous Preferred Practice Pattern Panel in 2016⁵¹ and an update was included in the latest edition (2017–2018) of the Basic and Clinical Science Course Section 5, *Neuro-Ophthalmology* for ophthalmology residents.⁵²

Cerebrovascular and Cardiovascular Morbidity Is High in Patients with Acute Retinal Arterial Ischemia

Much has changed since the original descriptions of retinal arterial occlusions and retinal TIAs and their relationship to subsequent neurologic outcomes. Although these events have always been recognized as “retinal strokes,” there was a prevalent belief among health care professionals that, except for the disability of permanent visual loss, acute

retinal ischemia was relatively benign, especially compared with cerebral ischemia, justifying delayed and often incomplete evaluations in the outpatient setting. However, even a prospective cohort study from 1991⁵³ of 99 patients with nonarteritic retinal infarctions showed that patients who present with embolic retinal infarctions had not only a high risk of stroke, but a major risk of acute coronary events, emphasizing the systemic implications of acute retinal ischemia. Similarly, a 2007 large retrospective study⁵⁴ of 416 nonarteritic BRAO and CRAO patients reported a very high prevalence of major vascular risk factors and emphasized the need to thoroughly evaluate all patients with acute retinal ischemia. In 2009, Hayreh et al² also emphasized the high prevalence of cardiovascular diseases in a series of 375 patients with nonarteritic retinal arterial occlusions, with one third of patients having an ipsilateral internal carotid artery stenosis of at least 50% and half the patients having an abnormal echocardiogram. A report from the NASCET study in 2001⁹ provided results on the subgroup of 198 patients with TMVL included in the NASCET study. All these patients had ipsilateral atheromatous internal carotid stenosis and had a high risk for recurrent TIAs or stroke after a first presumed retinal TIA, with up to 24.2% of retinal TIA patients developing a stroke at 3 years. However, because this risk was lower than that for patients who had a cerebral TIA, emphasis was placed on the relative “good prognosis” of retinal TIAs compared with cerebral TIAs, contributing to the misconception that retinal TIAs are relatively benign. The NASCET study additionally showed that the overall vascular risk (including myocardial ischemia and cardiovascular death) is as high for patients with a retinal TIA as it is for those with a cerebral TIA, emphasizing the need for immediate evaluation and treatment after a retinal TIA.⁹

All sources of emboli may cause acute retinal ischemia and it is now clear that TMVL, BRAO, and CRAO indicate a very high risk of cerebrovascular and cardiovascular complications. Large recent population studies^{55–60} (Table 2) have emphasized that patients with isolated retinal infarctions have numerous major vascular diseases that need to be treated urgently. These studies have also shown a high risk of subsequent cerebral infarction, confirming the need to initiate an urgent and detailed stroke workup in all BRAO and CRAO patients so as to identify and aggressively treat disorders exposing these patients to a high risk for cerebrovascular and cardiovascular events and death.

Current Referral Patterns

Despite the publication of the National Stroke Association/AHA guidelines in 2011^{5,28} and 2013,⁷ and the new American Academy of Ophthalmology Preferred Practice Pattern Guidelines in 2016,⁵¹ patients with acute retinal ischemia, whether transient or permanent, are only rarely evaluated emergently in a manner similar to patients with acute neurologic symptoms. A study from 1995¹⁴ emphasized that the average time of delay from the onset of TIA to

Table 1. Summary of Seven Recent Studies Evaluating Brain Magnetic Resonance Imaging in Patients with Acute Retinal Ischemia

Study	Study Period/ Type Patients*	Clinical Presentation, [†] N	Workup	DWI-MRI Results	Correlation with Abnormal DWI-MRI [†]
Hellenius et al ⁴⁴ (USA) 2012	2000–2008 Retrospective N = 129 64 ± 16 yo	Isolated TMVL: 66 Isolated BRAO/CRAO: 46 Neuro sx + TMVL: 8 Neuro sx + RAO: 9	≤7 days of VL Detailed stroke workup	DWI+ in 31/129 (24%) (CRAO/BRAO: 33% vs. TMVL: 18%) Same vascular territory as VL in 28/31 Small, multiple (65%) infarctions	Neuro sx + Permanent VL > TMVL Identified cause Embollic cause
Lee et al ⁴⁵ (Korea) 2014	2005–2012 Retrospective N = 33 58 ± 14 yo	Isolated BRAO: 12 Isolated CRAO: 13 Neuro sx + BRAO: 3 Neuro sx + CRAO: 5	≤7 days of VL Detailed stroke workup	DWI+ in 8/33 (24.2%) (CRAO: 27% vs. BRAO: 20%) Same vascular territory as VL in 8/8 Small, multiple (100%) infarctions	Neuro sx + Identified cause Embollic cause
Tanaka et al ⁴⁶ (Japan) 2014	2008–2009 Retrospective N = 13 71.2 ± 7.9 yo	Isolated TMVL: 12 Neuro sx + TMVL: 1	≤7 days of VL Detailed stroke workup	DWI+ in 4/13 (30.8%) No description	NA
Lauda et al ⁴⁷ (Germany) 2015	2008–2013 Retrospective N = 213 57–83 yo	TMVL: 68 BRAO: 44 CRAO: 101 Neuro sx + RAO: NA	≤7 days of VL Detailed stroke workup	DWI+ in 49/213 (23%) (CRAO: 53.1%; BRAO: 30.6% vs. TMVL: 16.3%) Same vascular territory as VL in 55.1% Small, multiple (34.7%) infarctions	Neuro sx + CRAO > BRAO > TMVL Identified cause Embollic cause
Cho et al ⁴⁸ (Korea) 2016	2009–2014 Retrospective N = 46 18–92 yo	Isolated BRAO: 46	≤14 days of VL Detailed stroke workup	DWI+ in 6/46 (13%) No description	Identified cause Embollic cause
Golsari et al ⁴⁹ (Germany) 2017	2008–2013 Prospective N = 112 59–75 yo	Isolated TMVL: 35 Isolated BRAO: 8 Isolated CRAO: 69	≤1 day of VL Detailed stroke workup	DWI+ in 17/112 (15%) (CRAO: 76.4%; BRAO: 11.8% vs. TMVL: 11.8%) Same vascular territory as VL in 70.6% Small, sometimes multiple infarctions	CRAO > BRAO > TMVL Identified cause Embollic cause
Tanaka et al ⁵⁰ (Japan) 2018	2011–2013 Prospective N = 40 63–75 yo	Isolated TMVL: 35 Neuro sx + TMVL: 5	≤7 days of VL Detailed stroke workup	DWI+ in 7/40 (18%)	NA

BRAO = branch retinal artery occlusion; CRAO = central retinal artery occlusion; DWI+ = patients with abnormal DWI-MRI; DWI-MRI = magnetic resonance imaging with diffusion-weighted imaging sequences; NA = information not available; Neuro sx = neurologic symptoms; RAO = retinal artery occlusion; TMVL = vascular transient monocular vision loss; VL = visual loss; yo = years old.
 *Patient ages are presented as either mean ± standard deviation or range, depending on the study.
[†]Neuro sx + indicates patients who had acute focal neurologic symptoms at the time of visual loss.

treatment was much longer for patients with retinal TIAs than for patients with hemispheric TIAs (48.5 vs. 15.2 days). A Canadian publication from 2012⁶¹ reported the same delay in a series of patients with carotid stenosis whose surgery was delayed when the symptom was a retinal TIA. Many optometrists and ophthalmologists choose to have patients with BRAO or CRAO evaluated as outpatients by their primary care physicians, which only delays appropriate evaluation and treatment. In a 2009 survey⁶² of ophthalmologists and neurologists practicing in the state of Georgia, only 35% of ophthalmologists, versus 73% of neurologists, reported sending acute CRAO patients to an emergency department (ED) for immediate evaluation. However, no progress was shown in a similar survey⁶³ of US retina specialists and US neurologists performed in 2013, with 18% and 73%, respectively, reporting sending acute CRAO patients to an ED.

The care providers are not the only ones to blame. Several studies have shown that stroke patients call 911 or present to an ED very inconsistently, and much less when neurologic symptoms spontaneously resolve (TIA) or when visual loss is isolated. A 2003 nationwide survey⁶⁴ in the

United States found that only 8% of laypersons were able to correctly define or identify 1 common manifestation of TIA. Studies from the United Kingdom published in 2009⁶⁵ and 2010⁶⁶ showed that more than one third of patients with a diagnosis of TIA do not seek medical attention within 24 hours of the event, resulting in delayed management. Similar recent studies performed in Europe^{67–69} and Australia⁷⁰ within the past few years have confirmed these findings and emphasize that delays are even longer when the symptom is visual. Additionally, these most recent studies^{67–70} highlight that given the high prevalence of internal carotid artery stenosis in patients with acute retinal ischemia,^{53,54,67,71} any delay in care results in longer time from symptom to carotid surgery, with resultant high early stroke rates. This is particularly important given the 2011 updated guidelines⁷² from the AHA and American Society for Vascular Surgery, which recommended that, when indicated, carotid endarterectomy should be performed within 14 days of the ischemic event. Indeed, the effectiveness of carotid endarterectomy is highly time-dependent, with the number needed to treat being 5 among those who undergo surgery within 2 weeks,

Table 2. Risk of Stroke and Cardiac Ischemia in Patients with Isolated Acute Retinal Ischemia in Recent Large Studies

Study	Study Period/ Type Patients*	Clinical Presentation and Follow-up	Vascular Risk Factors and Cardiovascular Diseases in RAO Patients	Risk of Stroke and of ACS
Chang et al ⁵⁵ (Taiwan) 2012	1999–2006 Retrospective N = 464 60 ± 14 yo	BRAO: 349 CRAO: 115 3-year f/u	Hypertension (38.1%) Diabetes (22.5%) Hyperlipidemia (10.3%)	91 of 464 (19.61%) had a stroke/TIA at 3 yrs compared with 280 of 2748 controls (10%) [CRAO: 27.8% vs. BRAO 16.9% (25.2% within 1 month after RAO; 59.3% within 6 months after RAO)] Risk of stroke higher if vascular risk factors, and higher with age (≥70 yo)
Chang et al ⁵⁶ (Korea) 2014	1999–2008 Retrospective N = 688 58 ± 14 yo	BRAO: 531 CRAO: 157 1-year f/u	Hypertension (42.7%) Diabetes (24.1%) Hyperlipidemia (12.5%) Atrial fibrillation (1.2%)	37 of 688 (5.4%) had ACS at 1 yr compared with 138 of 4128 controls (3.3%) CRAO: 9.6% vs. BRAO: 4.1% Risk of ACS higher if vascular risk factors and higher with age (≥70 yo)
Park et al ⁵⁷ (Korea) 2015	2007–2011 Retrospective N = 1585 Age NA	CRAO: 1585 1-year f/u	Stroke or ACS within previous 6 months (3.7%)	152 of 1585 (9.6%) had a stroke at 1 yr [33.8% within 1 month after CRAO (higher within 1st week after CRAO); 43.9% within 6 months after CRAO]
Callizo et al ⁵⁸ (Germany) 2015	2007–2011 Prospective N = 77 24–75 yo	CRAO: 77 4-week f/u	Hypertension (73%) Diabetes (14%) Hyperlipidemia (23%) Atrial fibrillation (20%) Ischemic heart disease (22%) Valvular heart disease (17%) ICA stenosis ≥70% (40%)	15/1585 (9.5%) had AMI at 6 months 3 of 77 (9.6%) had a stroke within 4 weeks after CRAO 1 of 77 (1.3%) had a TIA within 4 weeks after CRAO No patients had AMI within 4 weeks after CRAO
Rim et al ⁵⁹ (Korea) 2016	2004–2013 Retrospective N = 401 Age NA	BRAO: 32 CRAO: 119 10-year f/u	Hypertension (77.1%) Diabetes (61.1%) Hyperlipidemia (74.3%) Atrial fibrillation (9%) Ischemic heart disease (44.4%)	60 of 401 (15%) had a stroke at 1 yr compared with 160/2003 controls (8%) [59% within 2.5 yrs after RAO (higher immediately after RAO)] Risk of stroke higher if vascular risk factors, and higher with age (≥65 yo)
Hong et al ⁶⁰ (Korea) 2017	2003–2013 Retrospective N = 151 61 ± 15 yo	BRAO: 32 CRAO: 119 1-year f/u	Hypertension (57.6%) Diabetes (23.2%) Hyperlipidemia (23.2%) Atrial fibrillation (6%) LA atherosclerosis (41.1%) Previous stroke (10.6%)	13 of 151 (8.6%) had a stroke at 1 yr [57% within 1 month after RAO; 78.6% within 3 months after RAO] Risk of stroke higher if LA atherosclerosis 1 of 151 (0.7%) had AMI at 1 yr

ACS = acute coronary syndrome; AMI = acute myocardial infarction; BRAO = branch retinal artery occlusion; CRAO = central retinal artery occlusion; f/u = follow-up; ICA = internal carotid artery; LA = large artery; NA = information not available; RAO = retinal artery occlusion; TIA = transient ischemic attack; yo = years old.

*Patient ages are presented as either mean ± standard deviation or range, depending on the study.

compared with a number to treat of 125 among those receiving surgery after 12 weeks.⁷³ A 2016 study⁷¹ evaluating the risk for recurrent stroke of ≥50% in symptomatic carotid stenosis awaiting revascularization showed a high-risk for stroke of 2.7% at 1 day, 5.3% at 3 days, 11.5% at 14 days, and 18.8% at 90 days. Delayed access to appropriate care resulted in delayed surgery, and because these patients were not managed acutely by stroke specialists, it is very likely that they did not receive optimal medical therapy while awaiting surgery, hence the very high risk of recurrent stroke observed in this study. In order to comply with these recommendations, there need to be radical changes in the way patients are evaluated and treated. In addition to increasing public awareness of the need to seek urgent medical advice, there is also a need for health care providers to reassess management pathways so as to expedite delivery of medical and surgical treatment strategies.^{74–76} However, as shown in a UK study published in 2014,⁶⁸ such changes are difficult to implement. Despite

education of providers and institution of a streamlined, rapid referral system for patients with TMVL in 1 department, many ophthalmologists remained unaware of the 14-day target for performing carotid endarterectomy and many continued to hesitate to refer TMVL patients to a rapid-access TIA clinic.

What Should the Eye Care Provider Do?

An ocular examination is always necessary to rule out a nonvascular ocular problem or confirm a diagnosis of vascular TMVL, BRAO, or CRAO (Fig S1, available at www.aajournal.org). Telephone diagnosis of visual loss is impossible, and there should be a pathway for same-day appointments for patients with acute visual loss. Ideally, the ocular examination should be performed in the ED or close to an ED of an institution with a stroke center. Because many EDs do not have an ophthalmologist readily available,

Table 3. Typical Evaluation Performed Urgently in Certified Stroke Centers for Patients with Acute Retinal Ischemia (Vascular Transient Monocular Vision Loss, Branch Retinal Artery Occlusion, or Central Retinal Artery Occlusion) Based on the American Heart Association and National Stroke Association Recommendations^{5-7,19,28,29,77}

Step	Action
1	Evaluation as soon as possible after the onset of acute visual loss, with accelerated triage in an emergency center affiliated with a stroke center or rapid-access TIA clinic/stroke center, depending on availability and local resources.
2	Routine blood tests* (complete blood count with platelets, chemistry panel, hemoglobin A1C, prothrombin time and partial thromboplastin time, and fasting lipid panel) are reasonable. Erythrocyte sedimentation rate and C-reactive protein are necessary in patients older than 50 years to screen for inflammation, which may suggest giant cell arteritis.
3	Electrocardiography* should occur as soon as possible after the event. Prolonged cardiac monitoring* (inpatient telemetry or Holter monitor) is useful in patients with an unclear etiology after initial brain/vessel imaging and electrocardiography.
4	Patients should preferably undergo neuroimaging evaluation* within 24 hours of symptom onset. MRI without contrast, including DWI, is the preferred brain diagnostic imaging modality. If MRI is not available, head CT should be performed.
5	Noninvasive imaging of the cervicocephalic vessels* should be performed routinely as part of the evaluation of patients with suspected vascular TMVL and those with BRAO or CRAO. MRA or CTA, or carotid ultrasound/transcranial Doppler, should be obtained, depending on local availability and expertise (it is often easier to obtain an MRA if a brain MRI is obtained or a CTA [with contrast] if a head CT is obtained).
6	Echocardiography* (at least transthoracic echocardiography) is reasonable, especially when the patient has no cause identified by other elements of the workup. Transesophageal echocardiography is useful in identifying left atrial thrombus, patent foramen ovale, aortic arch atherosclerosis, and valvular disease and is reasonable when identification of these conditions will alter management. Depending on local resources, outpatient echocardiography may be obtained after discharge in patients with otherwise normal cardiac evaluation. ⁷⁸
7	It is reasonable to hospitalize patients with TIA, BRAO, or CRAO if they present within 72 hours of the event and any of the following criteria are present: Abnormal brain DWI-MRI showing evidence of acute cerebral infarction(s) Large artery atherosclerosis found on noninvasive vascular imaging (such as internal carotid artery stenosis) Abnormal cardiac evaluation Recurrent episodes (crescendo TIAs), or inability to provide expedited outpatient follow-up

BRAO = branch retinal artery occlusion; CRAO = central retinal artery occlusion; CT = computed tomography; CTA = computed tomography angiography; DWI = diffusion-weighted imaging; DWI-MRI = magnetic resonance imaging with diffusion-weighted imaging sequences; MRA = magnetic resonance angiography; MRI = magnetic resonance imaging; TIA = transient ischemic attack; TMVL = transient monocular vision loss.

*These tests are obtained immediately in the emergency facility over a 23-hour observation period, during which the patient receives cardiac monitoring. These tests are part of the standard “stroke protocol” recommended by the American Heart Association/National Stroke Association. If no cause is identified, the patient can be discharged home after 24 hours with optimal secondary prevention of stroke. If a test identifies an embolic cause requiring immediate treatment (such as internal carotid artery stenosis of at least 50% or cardiac source of emboli), the patient should be admitted to a stroke unit. In all cases, the patient is discharged with appropriate secondary stroke prevention measures, including an antithrombotic agent, statin for hyperlipidemia, and blood pressure control, and an outpatient follow-up with a neurologist with stroke expertise is arranged within 2 weeks after discharge to review the tests obtained and to promote optimal secondary prevention of stroke and other cardiovascular diseases. These recommendations apply to patients in whom the diagnosis of giant cell arteritis is *not* considered.

an emergent ophthalmic examination by an outside ophthalmologist or optometrist may be necessary before referral to an ED. The differential diagnosis of transient visual loss is wide and an eye care provider should serve as the “gate-keeper” to facilitate correct diagnosis of retinal vascular ischemia. Recognition of a BRAO or a CRAO is usually straightforward, although very acute presentations of CRAO can be challenging. Transient visual loss can occur in many ocular conditions (other than retinal arterial TIA) that an eye care provider should recognize. (Fig S1, available at www.aojournal.org).²⁰⁻²²

Once the diagnosis of vascular TMVL, BRAO, or CRAO is confirmed, the patient should be immediately referred to the closest ED affiliated with a stroke center or to a rapid-access TIA clinic, where available. Many hospitals have ED-affiliated observation units, which allow rapid (usually within 24 hours) outpatient workup with a predefined accelerated diagnostic protocol^{73,75-80} (Table 3). Giant cell arteritis needs to be ruled out in patients older than 50 with immediate blood tests including complete blood count, platelets, erythrocyte sedimentation rate, and C-reactive protein, before a stroke workup is initiated^{4,5,7,22,28,29}

(Table 3). Hospitalization is indicated only if a dedicated outpatient center is not available, or if the evaluation cannot be completed within 24 hours.⁷⁸⁻⁸¹ The best setting for TIA and BRAO/CRAO management can be individualized for each center, but it should include an assessment by a stroke specialist and immediate brain and vascular imaging and cardiac monitoring. Such centers are readily available in the United States, and it is worth instructing patients to go where such expertise is available (Table 4).

Conclusion

The combination of clinical features and urgent brain MRI and vascular imaging can distinguish TMVL, BRAO, and CRAO patients at highest risk for recurrent stroke, providing the opportunity to start early preventive treatments to reduce the risk of subsequent stroke and cardiovascular events. Because the risk of stroke is maximum within the first few days after the onset of visual loss, prompt diagnosis and triage are mandatory. Eye care

Table 4. “Nuts and Bolts” for Eye Care Providers

Step	Action
1	Establish a relationship with the nearest certified stroke center open 24/7 (https://hospitalmaps.heart.org/AHAMAP/map/qimap.jsp) to create a pathway for the rapid evaluation of patients with suspected vascular visual loss.* Collaborate with the stroke center to create a clear and simple referral form to be used for future easy urgent referrals.
2	Offer same-day appointments for patients with acute painless monocular vision loss, whether transient or permanent.
3	Once the correct diagnosis of presumed vascular TMVL, BRAO, or CRAO is confirmed, consider giant cell arteritis and inquire about systemic symptoms.
4	Send the patient immediately to the nearest emergency department affiliated with a certified stroke center or rapid-TIA clinic, depending on local resources.* with a note indicating “Ocular TIA” or “Ocular Stroke.” Inform the patient of the risk of stroke and acute coronary syndrome and explain that such immediate evaluation results in fast-track access to a specialist, to diagnostic investigation, and to a multidisciplinary network, and allows immediate secondary prevention of cardiovascular disease. Call the center to warn them that “a stroke patient is on the way.”
5	Patients seen a few days after the episode of visual loss still need to receive an urgent stroke workup, which can be obtained by the neurologist with stroke expertise as an outpatient. These patients should be started on an antiplatelet agent without delay. Contact your local neurologist with stroke expertise in order to have these patients seen urgently when necessary.

BRAO = branch retinal artery occlusion; CRAO = central retinal artery occlusion; TIA = transient ischemic attack; TMVL = transient monocular vision loss.

*The ideal patient disposition obviously varies based on local resources and may include a visit to an emergency department in a hospital affiliated with a certified stroke center (sometimes in an observation unit), or a specialized outpatient rapid-access TIA clinic, or sometimes a direct admission to a stroke unit.

professionals should make a rapid and accurate diagnosis and recognize the need for timely expert intervention by immediately referring patients with acute retinal arterial ischemia without attempting to perform any further testing themselves. Obviously, these recommendations only apply to patients seen within a few days of visual loss; management should be adjusted based on how late patients are seen by the eye care provider. Direct communication with the local stroke team will help determine appropriate management.^{74,82} Education of health care providers is essential to promote emergent evaluation and referral of all patients with acute retinal arterial ischemia (Table 4). An additional benefit will be efficient access to future protocols evaluating treatments designed to reverse acute retinal ischemia and improve visual outcomes.⁸³ The factors that will result in system change are multiple and include increased public awareness of stroke and 911 response,⁷⁶ but mostly involve educating all eye care providers. As previously suggested,^{76,84} revision of the “Act FAST” public education campaign to “Act VFAST” (Very FAST) or to “BE-FAST” to include vision loss as one of the main symptoms of stroke may be an important next step. The development of local networks prompting collaboration among optometrists, ophthalmologists, and neurologists with stroke expertise should facilitate such evaluations, whether in a rapid-access TIA clinic, in an ED observation unit, or with hospitalization, depending on local resources.^{51,85} Follow the guidelines!

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Abbreviations and Acronyms:

AHA = American Heart Association; **BRAO** = branch retinal artery occlusion; **CI** = confidence interval; **CRAO** = central retinal artery occlusion; **DWI** = diffusion-weighted imaging; **DWI-MRI** = magnetic resonance imaging with diffusion-weighted imaging sequences; **ED** = emergency department; **MRI** = magnetic resonance imaging; **NASCET** = North American Symptomatic Carotid Endarterectomy Trial; **TIA** = transient ischemic attack; **TMVL** = transient monocular vision loss.

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