Learning Objectives:

1. To understand the basis for the new definition of TIA and its consequences for TIA diagnosis and management.
2. To recognize the need for developing strategies for immediate evaluation and treatment of patients with transient visual loss presumably related to transient ischemia or the eye or brain.
3. To be able to predict the risk of stroke in patients with transient visual loss and adequately triage patients with transient visual loss based on risk stratification.

CME Questions:

1. Regarding patients presenting with transient visual loss, choose the correct answer:
A-Retinal TIA patients should be managed as outpatients because the risk of stroke is small and the prognosis usually good.
B-Retinal TIA patients do not need to have brain imaging.
C-Recent AHA guidelines recommend that patients with transient visual loss be evaluated emergently similar to patients with cerebral TIA.
D-The risk of cardiovascular death is lower in retinal TIA patients than in cerebral TIA patients.

2. Diagnostic recommendations after a TIA include the following (choose one correct answer):
A-Neuroimaging evaluation within 24 hours of symptom onset, preferably with magnetic resonance imaging, including diffusion sequences (DWI-MRI).
B-Noninvasive imaging of the cervical vessels.
C-Electrocardiography as soon as possible after TIA; prolonged cardiac monitoring and echocardiography in patients in whom the vascular etiology is not yet identified.
D-Hospitalization of patients with TIA if they present within 72 hours and have an ABCD2 score ≥ 4, indicating high risk of early recurrence, or if the DWI-MRI is abnormal, or if the evaluation cannot be rapidly completed on an outpatient basis.
E-All of the above.

3. Regarding the risk of stroke after a TIA (choose one correct answer):
A-Approximately 10 to 15% of patients have a disabling stroke within 3 months after a TIA, with half occurring within 48 hours after resolution of the TIA symptoms.
B-Hemispheric TIA from severe internal carotid artery stenosis is associated with the highest risk of stroke (20% at 3 months) compared with other causes.
C-The risk of stroke after a TIA is much higher when the DWI-MRI is abnormal, reinforcing the need to admit all TIA patients who have an abnormal DWI-MRI.
D-One of every 4 patients with acute retinal ischemia has acute brain infarction on brain DWI-MRI. 18% of patients with retinal TIA have positive brain DWI-MRI.
E-All of the above.

Keywords (Max 5):

1. Transient visual loss
2. Retinal transient ischemic attack
3. Transient ischemic attack
Introduction/Abstract (Please see instructions for formatting details):

Transient ischemic attacks (TIAs) are common and portend a high-short term risk of stroke. Recent guidelines from the American Heart Association and National Stroke Association suggest that all TIA patients should be evaluated emergently in a specialized unit, either as an inpatient or outpatient, based on local availability. The risk of stroke and vascular death is high after a retinal TIA, and patients with presumed vascular transient visual loss should be evaluated and treated similarly to those with transient cerebral ischemia or minor stroke. Neuro-ophthalmologists need to establish standardized protocols to assure rapid and complete evaluation and treatment for patients with TIA, with particular attention to urgency and close observation in patients at high risk of stroke.

Body (Please see instructions for formatting details):

Part I: Transient ischemic attacks (TIA): The Facts

Incidence and prevalence of TIA / Burden of stroke

- The estimated incidence of TIA in United States is around 200,000 to 500,000 per year with a population prevalence of 2.3% (translates into about five million individuals) [1,2,3].
- TIAs account for approximately 0.3% of ER visits [4].
- Precise estimates of the incidence and prevalence of TIAs are difficult to determine due to the varying criteria used in epidemiological studies to identify TIA.
- Lack of recognition of the transitory symptoms likely leads to gross underestimates.
- Approximately 15% of strokes are heralded by a TIA [3].
- The short-term risk of stroke after TIA is ~3% to 10% at 2 days and 9% to 17% at 90 days [3].
- Individuals who have had a TIA and survive the initial high-risk period have a 10-year stroke risk of approximately 19% and a combined 10-year stroke, myocardial infarction, or vascular death risk of 43% (4% per year) [3].
- Within 1 year of TIA, ~12% of patients will die [3].
- Stroke mortality has declined in recent years, but stroke remains the primary cause of disability in the US, and its resulting economic and social burden is enormous [3].

Lack of public awareness of TIA

- Most health professionals and the public consider TIAs benign but regard strokes as serious. These views are incorrect. Stroke and TIA 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 [5,6].
- Both TIA and stroke are markers of reduced cerebral and ocular blood flow and an increased risk of disability and death. However, TIAs offer an opportunity to initiate treatment that can forestall the onset of permanent disability.
- A nationwide survey in the US found that only 8% of laypersons were able to correctly define or identify one common manifestation of TIA [2].
- 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 [5,6].
- Physician compliance with current guidelines is poor, and more educational efforts to increase healthcare providers’ awareness of the danger of TIA are needed.

There is a new definition of TIA

The American Heart Association revised the most recent definition of TIA, describing it as “a transient episode of neurologic dysfunction caused by focal brain, spinal cord, or retinal ischemia without acute infarction” [8].

- The new definition of TIA includes the absence of acute brain infarction on diffusion-weighted imaging (DWI).
- This newly proposed definition of TIA by the American Heart Association implies that a brain MRI with DWI be performed immediately on all patients with suspected TIA (including those with retinal TIAs).

Urgency in the management of patients with TIA

- Large cohort and population-based studies reported in the last 10 years have demonstrated a higher risk of early stroke after TIA than generally suspected.
10 to 15% of patients have a stroke within 3 months, with half occurring within 48 hours after resolution of the TIA symptoms [7,8,9].

Acute treatments for TIA have also evolved, with new data supporting early (within 2 weeks, and ideally within 2 days of the TIA) rather than delayed carotid endarterectomy for TIA patients with carotid stenosis [10].

The risk of cardiac events is also elevated after TIA [7,8,9,10].

Any patient with suspected TIA should be evaluated urgently in order to identify those at high risk of immediate stroke and cardiac ischemia. This includes all patients with transient visual loss whether due to occipital TIA or retinal TIA.

New class I and class II evidence have led to recommendations for the risk stratification and management of all patients with suspected TIA.

Patients with TIAs are at high risk of early stroke, and their risk may be stratified by clinical scale, vessel imaging, and magnetic resonance imaging, including diffusion sequences (DWI-MRI) [7-17].

Diagnostic recommendations include [7-11]:
- TIA patients should undergo neuroimaging evaluation within 24 hours of symptom onset, preferably with DWI-MRI.
- Noninvasive imaging of the cervical vessels should be performed and noninvasive imaging of intracranial vessels is reasonable.
- Electrocardiography should occur as soon as possible after TIA and prolonged cardiac monitoring and echocardiography are reasonable in patients in whom the vascular etiology is not yet identified.
- Routine blood tests are reasonable (see below).
- It is reasonable to hospitalize patients with TIA if they present within 72 hours and have an ABCD2 score ≥ 4, indicating high risk of early recurrence, or if the DWI-MRI is abnormal (when DWI-MRI shows acute cerebral ischemia in any part of the brain), or if the evaluation cannot be rapidly completed on an outpatient basis.

Retinal TIAs are as bad as cerebral TIAs

Most health professionals and the public consider retinal TIAs benign with a low risk of subsequent stroke. This is incorrect.

The risk of stroke, cardiac events and death after a true retinal TIA is likely as high as for patients with a cerebral TIA [18].

One of every 4 patients with acute retinal ischemia has acute brain infarction (anywhere) on brain DWI-MRI [19]. 18% of patients with retinal TIA have positive brain DWI-MRI [19].

Part II: Journal Club - Major recent articles on TIA

Reviews on most current management of TIA:


Heart disease and stroke statistics:


National Guidelines (can be downloaded from respective websites):

National Stroke Association:

NICE (UK):

American Heart Association:

Stroke risk stratification after TIA:

TIA management and cost:

Retinal ischemia:

Part III: Cerebral transient ischemic attack (TIA)

Clinical vignette 1:
A 65-year-old man calls his physician immediately after recovering from a 10 minute episode of difficulty speaking and weakness of the right side of his face and right arm. His medical history is unremarkable. How should he be treated?

Recent scientific studies have revised our understanding of 3 key aspects of TIA:
1- How it is best defined.
2- What the early risk of stroke and other vascular outcomes is.
3- How it is best evaluated.

Definition of TIA

According to the World Health Organization criteria proposed in 1988, TIA is defined as rapidly developed clinical signs of focal or global disturbance of cerebral function, lasting less than 24 hours, with no apparent nonvascular cause [12].

The past decade has seen a shift in emphasis from the time-based (<24 hours) to the tissue-based definition of TIA, which includes symptom duration < 1 hour and the absence of acute infarction on diffusion-weighted imaging MRI (DWI-MRI) [13,14,15]. This has resulted in DWI-MRI being used to fulfill a key role in the diagnostic evaluation of patients with TIA. Indeed, numerous studies have shown that between 30 and 50% of patients with traditionally defined TIAs have evidence of infarction somewhere in the brain on MRI [14,15,16]. It is important to emphasize that these acute infarctions seen on DWI-MRI are often small and multiple and can be found anywhere in the brain, not necessarily corresponding to the clinical symptoms (for example, a patient with a retinal TIA may have an abnormal brain DWI-MRI, with acute infarcts obviously not corresponding to the clinical symptoms).

The American Heart Association recently revised the newly proposed definition of TIA, describing it as “a transient episode of neurologic dysfunction caused by focal brain, spinal cord, or retinal ischemia without acute infarction” [8,16]. 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 funduscopic examination) among patients with TIA distinguishes between TIA and ischemic stroke and portends higher risk of stroke after TIA.

Difficulties in diagnosing TIA:

Because neurologic and visual symptoms are by definition transient, the clinical examination is classically normal, and therefore the diagnosis relies exclusively on the clinical history alone, and specifically on the recollections of the patient who was neurologically or visually impaired during the event. This makes the diagnosis of TIA difficult for the non-specialist and the rate of falsely positive diagnosis of TIA is relatively high, particularly in the ED. Episodes misdiagnosed as TIAs are heterogeneous and include those due to migraine, seizure, vasovagal syncope, arrhythmia, hypoglycemia, anxiety, and conversion disorder [8,17,18,19]. However, specific symptoms are more reliable than others to make a presumed diagnosis of TIA.

-Hemispheric TIA (carotid artery TIA): relatively easy
   -Any acute hemiparesis, hemisensory loss, aphasia, dysarthria, hemianopia (often described as non-specific acute visual loss)

- Retinal TIA (carotid artery and ophthalmic artery TIA): more difficult
   -Acute, monocular visual loss; partial (altitudinal) or complete, but most often blackout of vision (not “blurry”, or “difficulty focusing”)

-Posterior circulation TIA (brainstem and occipital lobes): difficult – false positive diagnosis of TIA common
   -Acute vertigo, dizziness, gait instability, confusion, dysarthria, visual disturbances (including diplopia and binocular visual loss), particularly if more than one symptom at the same time
Two case scenarios with the same clinical history, but different outcomes:

<table>
<thead>
<tr>
<th>Acute binocular visual loss lasting 15 minutes and resolving completely.</th>
<th>Acute binocular visual loss lasting 15 minutes and resolving completely.</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Normal examination and normal visual fields</td>
<td>- Normal examination and normal visual fields</td>
</tr>
<tr>
<td>- Normal DWI-MRI of the brain</td>
<td>- Abnormal DWI-MRI of the brain (acute infarction in the left hemisphere)</td>
</tr>
</tbody>
</table>

**“TIA”**

**TIA evaluation and management per local stroke neurology protocol**

**“Stroke”**

**Admission to stroke unit for immediate evaluation and treatment**

**Risk of stroke after a TIA**

Overall, stroke is preceded by a TIA in approximately 15% of patients, and a quarter of these will occur shortly after the TIA [3,20,21].

For decades, it was clear that the long-term (3-5 years) outcome of ischemic stroke following TIA was as high as 30 to 40%. However, in 2000, new data suggested that much of this risk is front-loaded in the first hours to days after the TIA [22]. Numerous studies confirmed this subsequently. The risk of stroke is highest within the first 24 hours and decreases thereafter [23,24,25,26].

**Approximately 10 to 15% of patients have a disabling stroke within 3 months after a TIA, with half occurring within 48 hours after resolution of the TIA symptoms.**

Hemispheric TIA from severe internal carotid artery stenosis is associated with the highest risk of stroke (20% at 3 months) compared with other causes (5.7%), such as intracranial small vessel disease and cardioembolism [24].

Studies in northern California and Oxfordshire found the risk of stroke in the first 24 hours after TIA to be around 4%, which is about twice the risk of myocardial infarction or death in patients presenting with acute coronary syndrome (about 2% at 24 hours) [22,23].

Individuals who have had a TIA and survive the initial high-risk period have a 10-year stroke risk of approximately 19% and a combined 10-year stroke, myocardial infarction, or vascular death risk of 43% (4% per year) [3].

**Risk of cardiac events after a TIA**

The risk of cardiac events is also high after a TIA. In one large study of 1327 patients [27], 2.6% of TIA patients were hospitalized for major cardiovascular events (myocardial infarction, unstable angina, or ventricular arrhythmia) within 3 months.

Individuals who have had a TIA and survive the initial high-risk period have a 10-year stroke risk of approximately 19% and a combined 10-year stroke, myocardial infarction, or vascular death risk of 43% (4% per year) [3].

**Risk stratification after TIA**

There have been numerous attempts over the past decade to create a validated risk-stratification tool that is easy to apply and provides clinicians with realistic estimates of stroke risk after TIA. The California score (in 2000) [22], and the ABCD score (in 2005) [28] have both been shown to predict short-term risk of stroke well in independent populations of patients presenting acutely after a TIA.

The ABCD² score published in 2007 [29] represents the combined efforts of the authors of the California and ABCD scores and has demonstrated the best predictive ability. This score was designed to be used in primary and emergency care settings by identifying high-risk individuals to facilitate triage to specialist care and target secondary prevention [4]. The ABCD² score is based on clinical features identifiable at the time of initial assessment, before specialist evaluation, and deliberately does not include the results of brain imaging. However, although the ABCD² score was developed for use in cohorts of patients before investigation, the possibility has been raised that prognostication might be improved after evaluation in secondary care by the incorporation of information from investigations, particularly the presence of brain infarction on imaging [25,30]. Therefore, to enhance the discriminative ability of the ABCD² score,
several imaging enhanced scores have recently been developed (Tables 1,2,3) [31-38]. Many authors consider the presence of a new infarct on brain imaging (which was consistent with the classic definition of TIA but would now lead to a diagnosis of stroke) more valuable than clinical scores [31-38]. Indeed positivity of DWI is associated with an approximately 2- to 15-fold increase in subsequent short-term risk of stroke. Although, several studies have shown that the presence of brain infarction on DWI is associated with individual elements of the ABCD system [35], others have also demonstrated that brain infarction provides additional prognostic information and that incorporation of an infarction component into the scoring system (ABCD$^3$I) was justified [14]. Only the ABCD$^2$I score included CT data and found that it was equal to DWI-MRI in improving the predictive power of the ABCD$^2$ score [14]. Evidence of vessel occlusion on acute brain magnetic resonance angiography also has been associated with a 4-fold increased short-term risk of stroke [34].

The ABCD$^3$ scoring system, including brain and carotid imaging was subsequently suggested [36].

Table 1: Summary of ABCD prediction scores using imaging modalities and results of investigations

<table>
<thead>
<tr>
<th>Score</th>
<th>Date of publication</th>
<th>Imaging modality</th>
<th>Summary of changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABCD$^2$I</td>
<td>July 2009</td>
<td>DWI-MRI or CT</td>
<td>-Scores 3 points for the addition of abnormal imaging, defined as acute or old infarction on CT or DWI-MRI</td>
</tr>
</tbody>
</table>
| ABCD$^2$I | November 2010      | DWI-MRI + carotids      | -Scores 2 points for DWI-MRI lesions
-Scores 2 points for history of previous TIA within the preceding 7 days
-Scores 2 points for ≥50% ipsilateral carotid stenosis using ultrasound, CTA or MRA |
| ABCDE+ | January 2012        | DWI-MRI                 | -Scores 3 points for DWI-MRI lesions and large artery atherosclerosis
-Scores 1 point for cardioembolism, small arterial occlusion, or undetermined cause |

Table 2: Scoring system for the ABCD$^2$

<table>
<thead>
<tr>
<th>Score ABCD$^2$</th>
<th>Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Age ≥ 60 years</td>
</tr>
<tr>
<td>1</td>
<td>Blood pressure ≥140/90 mmHg on first evaluation</td>
</tr>
<tr>
<td>2</td>
<td>Clinical symptoms of focal weakness with the spell</td>
</tr>
<tr>
<td>1</td>
<td>(or) speech impairment without weakness</td>
</tr>
<tr>
<td>2</td>
<td>Duration ≥ 60 minutes</td>
</tr>
<tr>
<td>1</td>
<td>(or) 10 to 59 minutes</td>
</tr>
<tr>
<td>1</td>
<td>Diabetes</td>
</tr>
</tbody>
</table>

Table 3: 2-day risk of stroke using ABCD$^2$ score:

<table>
<thead>
<tr>
<th>Score ABCD$^2$</th>
<th>2 day-risk of stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>0%</td>
</tr>
<tr>
<td>2-3</td>
<td>1.3%</td>
</tr>
<tr>
<td>4-5</td>
<td>4.1%</td>
</tr>
<tr>
<td>6-7</td>
<td>8.1%</td>
</tr>
</tbody>
</table>

Although the addition of early DWI-MRI has aided the overall short-term stroke risk prediction in patients with TIA, it adds little insight into the underlying vascular mechanism responsible for the event, and therefore is limited in prognosticating future events [15,37].

It is important to emphasize that there are different uses of the ABCD$^2$ score:
- One is a pre-hospital triage tool that can be viewed as a “surrogate” for investigations to predict the risk in places where emergent evaluation (within hours after the TIA onset) is not possible. However, when TIA units are available, triage based on actual findings of immediate investigations should be preferred.
- Some use the ABCD$^2$ score after complete initial evaluation as a triage tool to determine who should be observed in the hospital for more than 24 hours. It has been suggested that all patients with TIA be evaluated as early as possible within 24 hours of call to medical attention regardless of ABCD$^2$ score to detect all patients needing immediate treatment to prevent a stroke [37].
Hospitalization after TIA

Because stroke risk after TIA is reduced by immediate medical or surgical intervention, emergent evaluation and treatment is warranted. Current guidelines recommend immediate evaluation and treatment of TIA patients by a specialized physician [8,9,10]. Therefore, structures able to provide services for acute stroke care should be available 24/7. Models vary among hospitals and both hospitalization and dedicated TIA evaluation units (often associated with an ED) have proven effective.

In many places, the best way to access this service is through the ED where immediate access to a specialist, laboratory testing, cardiac monitoring and brain imaging is readily available.

Hospitalization of all TIA patients is a definite way to accelerate evaluation and treatment. Additionally, close observation during hospitalization has the potential to allow more rapid and frequent administration of tPA should a stroke occur [39,40]. Other benefits of hospitalization include continuous telemetry monitoring, rapid diagnostic evaluation, and greater rates of adherence to secondary prevention interventions. However, hospitalization rates after TIA vary widely among practitioners, hospitals, regions, and countries [8-10,40-43]. A cost-utility analysis showed that hospitalization was cost-effective for patients with a 24-hour risk of stroke >4% (patients with ABCD² score ≥ 4) solely on this basis [39].

Theoretically, most TIA patients could be evaluated as outpatients and hospitalization may be avoided [42-44]. However, in many medical care systems, having the work-up accomplished as an outpatient within 48 hours is not logistically feasible. Alternatives to traditional hospitalization have been developed over the past 10 years and may offer as many advantages as inpatient evaluation, with a much lower cost.

Rapid-access TIA clinics, such as the ones described in the French SOS-TIA study [25] and the British EXPRESS study (Early use of Existing Preventive Strategies for Stroke) [26], provide outpatient alternatives (24-hour access to TIA clinics) to hospital admission and have been shown to reduce the 90-day risk of stroke by 80%. In the EXPRESS study model, there was a significant reduction of overall hospital bed days and associated health-care costs [45]. These rapid-access TIA clinics offer the advantage of ensuring rapid specialist evaluation, comprehensive testing, and an opportunity for direct referral from the patient’s primary care physician thereby bypassing the ED [25,26,45-47]. However, such models remain rare and it is difficult to provide 24/7 physician specialist coverage.

A more common model in the US is the use of ED-based observation units (EDOU) that use an accelerated diagnostic protocol (ADP) to evaluate patients with TIA [48,49]; similar units have been used for many years to evaluate patients with chest pain, and a national study of EDOU performed in 2010 showed that such units were found in more than one-third of EDs [50]. This number had increased compared with an estimated number of 19% in 2003 [50], confirming the popularity and success of such units. Similar to rapid-access TIA clinics, TIA evaluation in EDOUs have resulted in lower costs compared with inpatient admission, with comparable clinical outcomes [49].

Evaluation of TIA (Table 4)

Brain Imaging

Numerous studies have suggested that all patients with TIA (including those with isolated visual loss) should have immediate brain imaging looking for neuroimaging evidence of cerebral infarction; the presence of large vessel occlusion is also a predictor of new events [8,9,19,29,32,34-36]. Although MRI is more expensive and not as widely available as CT, DWI-MRI of the brain is the imaging of choice and should be obtained when possible [8,9].

Among patients who present to the ED with a TIA, studies show that approximately 50 to 70% have a CT performed. In the northern California study, a new infarct was identified in 4% of patients [51]. A nonvascular pathology (tumors, subdural hematomas for example) was identified on CT in 1 to 5% of patients in various series.

MRI is obviously much more sensitive than CT in demonstrating both old and new infarcts in TIA patients. Across various studies, MRI has shown at least one infarct somewhere in the brain in 46 to 81% of TIA patients [52,53]. It is important to emphasize that these acute infarctions seen on DWI-MRI are often small and multiple and can be found anywhere in the brain, not necessarily corresponding to the clinical symptoms (for example, a patient with a retinal TIA may have an abnormal brain DWI-MRI, with acute infarcts obviously not corresponding to the clinical symptoms).

The inclusion of DWI sequences facilitates the detection of acute cerebral ischemia, and provides a more precise evaluation of ischemic insult in TIA patients compared with standard CT and MRI studies [54].

Several studies have shown that DWI positivity has important prognostic implications [55]. Indeed, TIA patients who have abnormalities on DWI-MRI have a higher risk of recurrent ischemic events than those without such abnormalities. DWI positivity correlates with the ABCD and California scores for predicting the risk of stroke after a TIA [35,56]. Patients with retinal ischemia and abnormal DWI-TIA have a higher risk of having an underlying vascular or cardiac abnormality responsible for the ischemic events [19].

These studies suggest that MRI can help triage patients with TIA. All TIA patients with positive DWI-MRI should be admitted to a stroke unit for immediate treatment and observation. DWI can also assist with stroke localization and
understanding the mechanism of the stroke, and is therefore extremely useful acutely [8,56].

**Vascular imaging**

Ideally, patients with TIA should be evaluated expediously with tests assessing the extracranial and intracranial circulation. The choice of tests varies depending on local strengths and expertise. It is usually easy to perform a MRA of the intracranial and cervical vessels in conjunction with the initial brain MRI. In other cases, ultrasound and CT-angiogram are also very helpful in detecting cervical artery stenosis and occlusion. These tests are essential because lesions amenable to endarterectomy or stenting are common in patients with TIA [8].

**Cardiac evaluation**

All TIA patients should undergo an ECG looking for myocardial ischemia and arrhythmia. Cardiac monitoring is easily performed in the ED, TIA clinic or when the patient is hospitalized, and often replaces Holter monitoring [8].

Cardiac evaluation with echocardiography and Holter monitoring in patients with no cardiac history or absent signs of cardiac abnormalities on examination or ECG yields important abnormalities in a minority of patients. However, the yield of cardiac evaluation increases if other potential sources of cerebral symptoms have been ruled-out.

The echocardiographic method used is important. Transthoracic echocardiogram (TTE) is less sensitive than transesophageal echocardiogram (TEE) for atheroma of the aortic arch and abnormalities of the interatrial septum, atrial thrombi, and valvular disease. The use of contrast increases the detection of right to left shunts [8,57].

**Routine blood tests**

No systematic studies have been performed to assess the value of blood tests in patients with TIA. It is reasonable to perform the same routine blood tests in patients presenting with TIs as in patients presenting with ischemic stroke. These include a complete blood count with platelets, chemistry panel, and basic coagulation studies (prothrombin time, partial thromboplastin time). These tests are useful to exclude TIA mimics (such as hypoglycemia) and can help identify less common causes of thrombotic events (such as polycythemia or thrombocytosis). A fasting lipid profile is also appropriate [8,9].

Specialized coagulation tests can be considered in younger patients with TIAs, particularly when no vascular risk factor exists and no underlying cause is identified [8,9].

**Treatment of TIA**

The Effect of urgent treatment of TIA and minor stroke on early recurrent stroke (EXPRESS) [26] and effectiveness of round-the-clock access (SOS-TIA) [25] studies showed that urgent evaluation and initiation of preventive treatments such as antiplatelets, statins, anticoagulation, and carotid revascularization markedly reduce the risk of early stroke after a TIA or minor stroke.

Patients who have had a suspected TIA should have:
- Anti platelet agents started immediately.
- Specialist assessment and investigation within 24 hours of onset of symptoms.
- Measures for secondary prevention introduced as soon as the diagnosis is confirmed, including discussion of individual risk factors.
  - Patients who had a TIA but who present late (more than 1 week after their last symptom has resolved) should be treated as though they are at lower risk of stroke.
  - Specific guidelines have been published by the American Heart Association and should be followed (even for patients with transient visual loss) [8,10,11].

**When a TIA patient is found to have severe carotid stenosis:**

Numerous studies have shown that carotid endarterectomy is effective and cost-effective for the prevention of stroke in individuals with symptomatic stenosis. Patients with severe (>70%), men, and patients aged ≥ 75 years may be more likely to benefit from carotid endarterectomy [8,10,58,59].

A growing body of evidence also suggests an increased benefit related to the timing of surgery from the last symptom. As a consequence, guidelines have recommended that stable patients with TIA (or nondisabling stroke) and ipsilateral internal carotid artery stenosis of 50% to 99% should be offered carotid endarterectomy optimally within 2 weeks of the incident TIA or stroke [8,10,59]. This is unfortunately only rarely the case, as shown by a recent Canadian study in which only 7 of 92 symptomatic patients underwent carotid endarterectomy within the recommended 2 weeks of symptom onset [60]. Surgery was particularly delayed in the group of patients presenting with retinal TIA.

**Part IV: The specific issue of transient visual loss**

**Clinical vignette 2:**
A 65-year-old man calls his physician immediately after recovering from a 10 minute episode of complete loss of vision of the left eye only. His medical history is unremarkable. How should he be treated?
Is it the same situation as in clinical vignette 1?

-Not exactly, for two reasons:

1)-An ocular examination is necessary to rule-out an ocular problem. Telephone diagnosis of visual loss is impossible. Before being evaluated and treated for a retinal TIA, the patient needs an immediate ocular examination, which, ideally, should be performed in the ED or close to an ED of an institution with a stroke neurologist. Because many EDs do not have an ophthalmologist readily available, an emergent ophthalmic examination by an outside ophthalmologist may be necessary prior to referral to an ED.

2)-Giant cell arteritis needs to be ruled-out before a TIA work-up is initiated. Immediate blood tests including CBC, platelet, ESR and CRP need to be obtained. If abnormal, then evaluation and treatment for GCA need to be initiated; if normal, then an immediate TIA work-up is necessary.

-Yes:

1)-No matter what, an urgent evaluation is necessary and involves testing that cannot be done in an eye clinic alone. The patient should always be immediately directed to an ED where the appropriate workup can be performed.

Retinal TIAs are similar to cerebral TIAs and should be managed similarly

Transient retinal ischemia resulting in transient monocular visual loss is a form of anterior circulation TIA caused by decreased blood flow in the ophthalmic branch of the internal carotid artery. Transient occipital ischemia often results in isolated binocular visual loss (either diffuse or in a hemifield) and is a posterior circulation TIA.

Classically, patients describe vision loss as though a curtain were being lowered over the affected eye, although it can also present as a clouding or darkening of the visual field. Patients with a hemianopia from occipital ischemia often report visual loss in the eye with the temporal defect, and the only way to differentiate monocular from binocular visual loss is to ask the patient to describe the visual symptoms while closing one eye or the other (which is almost never done when the visual loss is transient). Although it is theoretically helpful to know if an episode of transient visual loss was binocular or monocular [that's what we teach medical students…], most patients are not able to provide this information with certainty. From a practical standpoint, because current guidelines suggest the exact same workup and management for retinal and occipital TIAs, the most important part in the evaluation of an episode of transient visual loss is to try to determine whether the visual loss may have been vascular (transient arterial ischemia to the eye or the brain) or whether the visual loss can be explained by an another mechanism (such as ocular disorders, seizures or occipital migraine). Very sudden onset, complete blackout of vision, description of a shade or curtain, duration of at least 3 minutes, but less than 20 minutes and very rapid recovery of vision are highly suggestive of retinal or occipital TIAs [18].

Most health professionals and the public consider retinal TIAs benign with a low risk of subsequent stroke. This is incorrect and such belief only delays the evaluation of patients with visual loss as the main symptom of retinal or cerebral ischemia. A study from 1995 emphasized that average time of delay from the onset of TIA to treatment was much longer for patients with retinal TIAs than for patients with hemispheric TIAs (48.5 vs 15.2 days) [61]. The same finding was recently observed in a series of patients with carotid stenosis whose surgery was delayed when the symptom was a retinal TIA [60]. The NASCET study showed a high-risk of recurrent TIAs or stroke after a first retinal TIA, with up to 24.2% of retinal TIA patients developing a stroke at 3 years [62]. However, because this risk was still lower than 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 itself and other studies also confirmed 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 [8].

Observed differences in terms of etiology, presumed mechanisms, and apparent prognosis of retinal TIAs compared with cerebral TIAs may be partly explained by the often extreme difficulty in diagnosing episodes of transient visual loss [18]. In our experience, non-vascular ocular causes and occipital migraine explain most episodes of transient visual loss [63,64,65]. Because most large studies evaluating the prognosis after a TIA were performed by neurologists, it is likely that retinal ischemia as the cause of transient visual loss is overestimated in most studies, contributing to the apparent better vascular prognosis after a retinal TIA.

A recent study showed that retinal arterial ischemia (both transient and permanent) carries the same overall poor vascular prognosis as cerebral ischemia. The authors evaluated 129 patients with retinal ischemia similarly to cerebral TIA patients, and showed that one of every 4 patients with acute retinal ischemia has acute brain infarction on DWI-MRI [19]. When looking specifically at those with retinal TIAs, 18% had a positive DWI-MRI, and therefore were managed as having had a stroke per current guidelines (Table 4). These infarcts are typically small and often multiple, frequently occur in the hemisphere ipsilateral to the involved eye, and tend to remain asymptomatic. These infarcts indicate a high risk of having a major etiology as the cause of retinal TIA and confirm the need for emergent workup and treatment in a specialized center.

The American Heart Association/American Stroke Association guidelines [8] recommend that all patients with suspected retinal ischemia (whether transient or permanent) should undergo urgent brain imaging and etiologic testing similar to patients with hemispheric TIAs (Table 4). This is certainly not routinely performed currently in the US where a large majority of patients with retinal ischemia are never sent to the ED or a stroke neurologist for immediate evaluation [66].
Part V: Conclusions and recommendations

Because stroke and permanent visual loss are devastating events that many patients consider worse than death [67,68], strategies aimed at preventing stroke by facilitating the immediate evaluation of patients with TIA are essential. The high very short term risk of stroke after a TIA supports an approach involving emergent evaluation and initiation of treatment in patients such as the ones described in the clinical vignettes. Many strokes occur in the first two days after a TIA, so even a short delay in treatment could have important consequences. Most patients should be sent to the ED (ideally to an EDOU) immediately after reporting symptoms suggestive of TIA, or to a rapid-access TIA unit where available. Hospitalization is indicated only if such facilities are not available, and the evaluation cannot be completed within 24 hours. Patients with visual loss should be managed similarly to those with cerebral ischemia. Education of healthcare providers is essential to promote the need for emergent evaluation and referral of all patients with suspected vascular visual loss [8,69]. The development of local networks prompting collaboration between optometrists, ophthalmologists, and stroke neurologists should facilitate such evaluations, whether in a rapid-access TIA clinic, an EDOU, or with hospitalization, depending on local resources.

Table 4: Summary of recommendations from the American Heart Association (AHA), the National Stroke Association (NSA) [8], and from the National Institute for Health and Clinical Excellence (UK) (NICE) [9]

<table>
<thead>
<tr>
<th>Class I recommendations</th>
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<tbody>
<tr>
<td>1. Patients with TIA should preferably undergo neuroimaging evaluation within 24 hours of symptom onset. MRI, including DWI, is the preferred brain diagnostic imaging modality. If MRI is not available, head CT should be performed (Class I, Level of Evidence B).</td>
</tr>
<tr>
<td>2. Noninvasive imaging of the cervicocephalic vessels should be performed routinely as part of the evaluation of patients with suspected TIAs (Class I, Level of Evidence A).</td>
</tr>
<tr>
<td>3. Noninvasive testing of the intracranial vasculature reliably excludes the presence of intracranial stenosis (Class I, Level of Evidence A) and is reasonable to obtain when knowledge of intracranial steno-occlusive disease will alter management. Reliable diagnosis of the presence and degree of intracranial stenosis requires the performance of catheter angiography to confirm abnormalities detected with noninvasive testing.</td>
</tr>
<tr>
<td>4. Patients with suspected TIA should be evaluated as soon as possible after an event (Class I, Level of Evidence B).</td>
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<th>Class II Recommendations</th>
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<tr>
<td>1. Initial assessment of the extracranial vasculature may involve any of the following: carotid ultrasound/trans cranial doppler, MRA or CTA, depending on local availability and expertise, and characteristics of the patient (Class IIa, Level of Evidence B).</td>
</tr>
<tr>
<td>2. If only noninvasive testing is performed prior to endarterectomy, it is reasonable to pursue two concordant noninvasive findings; otherwise catheter angiography should be considered (Class IIa, Level of Evidence B).</td>
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<tr>
<td>3. The role of plaque characteristics and detection of microembolic signals is not yet defined (Class IIb, Level of Evidence B).</td>
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<tr>
<td>4. Electrocardiography should occur as soon as possible after TIA (Class I, Level of Evidence B). Prolonged cardiac monitoring (inpatient telemetry or Holter monitor) is useful in patients with an unclear etiology after initial brain imaging and electrocardiography (Class IIa, Level of Evidence B).</td>
</tr>
</tbody>
</table>
5. Echocardiography (at least transthoracic echocardiography) is reasonable in the evaluation of patients with suspected TIAs, especially when the patient has no cause is identified by other elements of the work-up (Class IIa, Level of Evidence B). Trans esophageal echocardiography is useful in identifying patent foramen ovale, aortic arch atherosclerosis, and valvular disease and is reasonable when identification of these conditions will alter management (Class IIa, Level of Evidence B).

6. Routine blood tests (complete blood count with platelets, chemistry panel, prothrombin time and partial thromboplastin time, and fasting lipid panel) are reasonable in the evaluation of patients with suspected TIAs (Class IIa, Level of Evidence B).

7. It is reasonable to hospitalize patients with TIA if they present within 72 hours of the event and any of the following criteria are present:
   - ABCD² score of ≥3, (Class IIa, Level of Evidence C).
   - ABCD² score of 0-2 and uncertainty that diagnostic work-up can be completed within 2 days as an outpatient (Class IIa, Level of Evidence C).
   - ABCD² score of 0-2 and there is other evidence that indicates the patient's event was caused by focal ischemia (Class IIa, Level of Evidence C).

CME Answers:

1. C
   Retinal TIAs are as bad as hemispheric TIAs.

2. E
   These are the guidelines from the AHA and the NSA.

3. E
   The high risk of stroke justifies emergent evaluation and observation.

References: Author(s) Last Name separated by a Comma, Title/Article, Source (i.e. Journal Name), Volume #, Page #, Year

of this statement as an educational tool for neurologists. Stroke 2009; 40: 2276-93.


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