

# DIAGNOSIS, WORKUP, RISK REDUCTION OF TRANSIENT ISCHEMIC ATTACK IN THE EMERGENCY DEPARTMENT SETTING

A SCIENTIFIC STATEMENT FROM THE AMERICAN HEART ASSOCIATION

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# STROKE COUNCIL PROFESSIONAL EDUCATION COMMITTEE

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# EPIDEMIOLOGY

# DEFINITIONS

- Transient ischemic attack is an acute onset of focal neurological symptoms attributable to a vascular territory that rapidly and completely resolves, leaving no evidence of tissue infarction on diffuse-weighted imaging MRI.
  - Resolved symptomatology demonstrating infarct on diffuse-weighted imaging MRI is consistent with a diagnosis of ischemic stroke.
  - Time-based characteristics are no longer utilized in the definition of transient ischemic attack.
- Transient ischemic attack is a risk factor for future stroke: Estimated 90-day stroke risk following transient ischemic attack ranges from 10-18%.



# EPIDEMIOLOGY

- In 2002, transient ischemic attack incidence was estimated to be 240,000 in the United States.
  - Decreased incidence of transient ischemic attack and hospital admissions for transient ischemic attacks have been demonstrated, due to improved vascular risk reduction and stroke care, changing trends in hospital admissions, and implementation of emergency room protocols including dedicated transient ischemic attack clinics.
  - Some evidence suggests that incidence of transient ischemic attack is decreasing more substantially in men than women.
- The incidence of transient ischemic attack increases with age.
- There is an estimated 1.4 times greater risk of transient ischemic attack with Black Americans than White Americans.
- A lack of symptom recognition by the public suggests that many transient ischemic attacks go undetected.



# DIAGNOSIS AND EVALUATION



# CLINICAL EVALUATION

- Patients must have a neurological examination consistent with their baseline status.
- Past medical history, and nonspecific symptoms or examination findings can help differentiate transient ischemic attack from alternative diagnoses. (Table 1)
- In cases with diagnostic uncertainty, a neurovascular workup is suggested, ideally with expedited neurological consultation.
- Patients benefit from early neurology consultation in the ED (either in-person or via teleneurology) or rapid follow up within 1-week (ideally 48 hours).

Table 1: Factors Suggestive of TIA versus TIA Mimic\*

	TIA	TIA Mimic
<b>Demographics</b>	Older	Younger patient without vascular risk factors
<b>Medical History</b>	Presence of vascular risk factors (HTN, DM, CAD, PAD, smoking, obesity, HL, AF, prior stroke, OSA)	Prior history of epilepsy, migraines, brain tumor
<b>Symptomatology</b>	<ul style="list-style-type: none"> <li>-Abrupt onset</li> <li>-Maximal symptoms at onset</li> <li>-Duration typically &lt;60 minutes</li> <li>-Preserved mentation</li> <li>-Localizing/focal neurological symptoms corresponding to a vascular territory: dysarthria/aphasia, facial droop, hemiparesis, hemibody numbness</li> <li>-Dizziness paired with cranial neuropathies, vision loss/diplopia, difficulty with coordination or gait/ truncal ataxia, severe nausea/vomiting may suggest posterior circulation process</li> <li>-Hypertensive on presentation</li> <li>-Headache with ptosis and miosis might indicate dissection</li> </ul>	<ul style="list-style-type: none"> <li>-Symptoms that spread/march from site of onset might suggest seizure</li> <li>-Altered mentation</li> <li>-Migraine headache</li> <li>-Presence of signs or symptoms suggesting an alternative diagnosis (i.e.: positive visual phenomena, seizure like activity, positional vertigo without localizing/focal symptoms)</li> </ul>
<p>HTN: Hypertension, DM: diabetes, CAD: coronary artery disease, PAD: peripheral artery disease, HL: hyperlipidemia, AF: atrial fibrillation, OSA: obstructive sleep apnea</p>		

\*This table is meant as a guide to approaching a patient with neurological symptoms and should not be the sole determinant of ultimate diagnosis. Patient specific factors must also be considered.



# DIAGNOSTIC EVALUATION

## BRAIN IMAGING

- Acute phase imaging in the emergency department can rule out alternative diagnoses, aid in risk stratification, and identify potentially symptomatic lesions.
- Non-contrast CT brain is a useful initial test: while insensitive to rule out small acute ischemic strokes, it can help evaluate for alternative diagnoses such as subacute ischemic stroke, intracerebral hemorrhage, and intracranial masses.
- Non-contrast MRI brain usually follows non-contrast CT brain, and is the preferred imaging modality to rule out an acute ischemic infarct. If rapid access to MRI is available in the emergency department, non-contrast CT brain can be avoided in a stable patient with resolved symptoms. If diffuse-weighted imaging MRI demonstrates an ischemic lesion, then a diagnosis of acute ischemic stroke is made. Non-contrast MRI brain can aid in the workup for acute ischemic stroke, based on the appearance of the lesion, and guide secondary stroke prevention strategies.
- Without readily-available non-contrast MRI brain in the emergency department, a diagnosis of transient ischemic stroke based on a negative non-contrast CT brain and symptom resolution within 24 hours can be made, with a potential next step admission for non-contrast MRI brain and cerebrovascular workup.

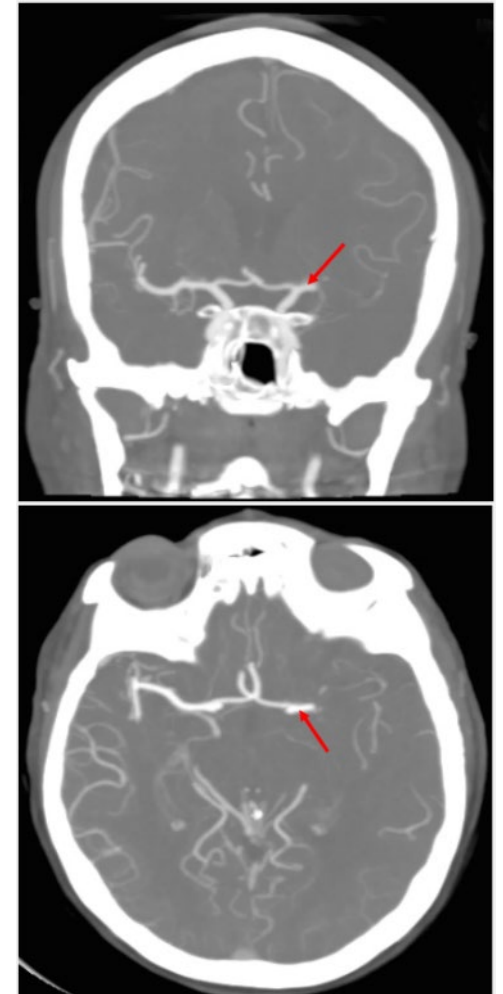




# DIAGNOSTIC EVALUATION

## CEREBROVASCULAR IMAGING

- Vessel imaging should be a routine component of acute phase imaging for the evaluation of transient ischemic attack, to assess for large vessel stenosis or occlusion. Among potential imaging modalities there are advantages and limitations. (Table 1)
- Both extra- and intracranial vessel imaging can guide stratify recurrent ischemic events, steer secondary prevention strategies, and guide admission and follow up decisions.
- CT angiography can be obtained in conjunction with non-contrast brain and may be more sensitive for stenosis or occlusion than MR angiography. It is considered safe in patients with known chronic kidney disease and is not associated with significant risk of acute kidney injury, although obtaining a baseline serum creatinine is reasonable to establish baseline renal function.
- MR angiography may be an option for patients for whom administration of iodinated contrast is a concern. Time-of-flight MR angiography may overestimate arterial stenosis compared to gadolinium-enhanced MR angiography.
- Duplex carotid ultrasound and transcranial doppler can evaluate vasculature as well.
- Digital subtraction angiography is considered the gold-standard to assess arterial stenosis however is considered more invasive and not used as a first-line method.





# DIAGNOSTIC EVALUATION

Table 2: Advantages and Limitations of Non-Invasive Techniques Available to Assess Patients with TIA

	Sensitivity for 50-69% carotid stenosis	Specificity for 50-69% carotid stenosis	Sensitivity for 70-99% carotid stenosis	Specificity for 70-99% carotid stenosis	Advantages	Limitations	Considerations
Doppler ultrasonography	36%	91%	89%	84%	<ul style="list-style-type: none"> <li>• Low cost</li> <li>• No intravenous contrast</li> </ul>	<ul style="list-style-type: none"> <li>• Operator variability</li> <li>• Results might be affected by patient body habitus or vessel anatomy</li> <li>• Only assesses cervical vessels</li> <li>• Insensitive for dissection</li> <li>• Not available in the ED, but potentially available in observation units</li> </ul>	
CT angiography	67%	79%	87%	95%	<ul style="list-style-type: none"> <li>• Widely available as a STAT scan in EDs</li> <li>• Can be performed simultaneously with NCCT</li> <li>• Can assess cervical and intracranial vessels</li> <li>• Sensitive for cervical and intracranial atherosclerosis, dissection, other vasculopathies</li> </ul>	<ul style="list-style-type: none"> <li>• Requires intravenous contrast</li> <li>• Radiation exposure</li> <li>• Limitations in interpretation in the setting of significant calcification</li> </ul>	<ul style="list-style-type: none"> <li>• Should be ordered as CTA head and neck</li> </ul>
MRA angiography	77%	97%	88%	84%	<ul style="list-style-type: none"> <li>• Can be performed simultaneously with MRI</li> <li>• Can assess cervical and intracranial portions of arteries</li> <li>• Sensitive for dissection</li> <li>• No radiation</li> <li>• Can be performed without contrast</li> </ul>	<ul style="list-style-type: none"> <li>• Contraindicated in some patients with implants and devices</li> <li>• Costly compared to CT and DUS</li> <li>• Longer time to schedule, perform, can rarely perform acutely</li> <li>• May overestimate stenosis</li> </ul>	<ul style="list-style-type: none"> <li>• Should be ordered as head and neck</li> <li>• Contrast enhanced MRA allows for higher quality images and less motion artifact</li> <li>• FDA warning on gadolinium due to retention in the body and brain, especially in case of repeated injections</li> </ul>

# DIAGNOSTIC EVALUATION

## LABORATORY TESTING

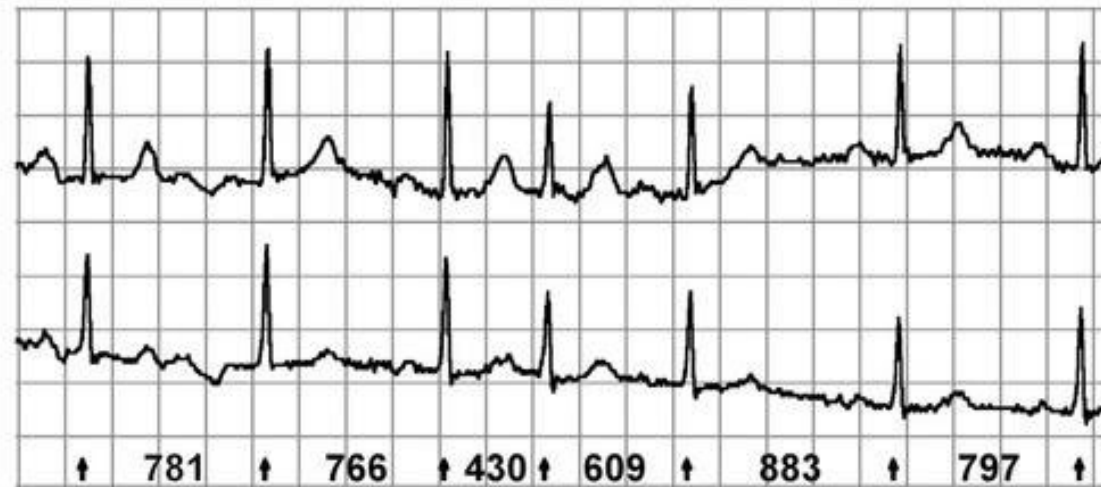
- Blood glucose testing can rule out hypoglycemia as a stroke mimic.
- A complete blood count, chemistry panel, hemoglobin A1c, and lipid panel can identify stroke risk factors.
- Temporal arteritis can be screened with an erythrocyte sedimentation rate and C-reactive protein in patients over 50 years of age.
- A toxic and metabolic laboratory workup can be useful in evaluation as well.



# DIAGNOSTIC EVALUATION

## CARDIAC TESTING

- Cortical symptoms (e.g., aphasia, vision loss, or homonymous hemianopia) can be suggestive of a cardiembolic source for stroke.
- Telemetry, troponin assays, and electrocardiography can screen for atrial fibrillation.
- Prolonged cardiac event monitoring can be more sensitive for atrial fibrillation.
- Transthoracic echocardiogram may be arranged as an expedited outpatient study (within one week), if suspicion for a cardioembolic source is low and the patient is otherwise stable for discharge from the emergency department.



# **RISK STRATIFICATION AND PATIENT DISPOSITION**



# RISK STRATIFICATION

- Various validated transient ischemic attack risk stratification scales can guide disposition (Table 3), in conjunction with a comprehensive evaluation.
- Limitations in transient ischemic attack stratification scales can include
  - Assessment of posterior circulation territory symptoms (e.g., dysmetria, ataxia, or homonymous hemianopia) and
  - Consideration for high risk factors for ischemic stroke and transient ischemic attack, (e.g., carotid stenosis, recurrent transient ischemic attack, or atrial fibrillation).

Table 3: ABCD<sup>2</sup>, ABCD<sup>3</sup>, and ABCD<sup>3</sup>-I Scores

Components	ABCD <sup>2</sup>	ABCD <sup>3</sup>	ABCD <sup>3</sup> -I	ABCD <sup>3</sup> -I (d, c/i)
	Score	Score	Score	Score
<b>Risk Factor</b>				
Age ≥ 60 years	1	1	1	1
BP ≥ 140/90 mm Hg	1	1	1	1
Diabetes	1	1	1	1
<b>Clinical Features</b>				
Unilateral Weakness	2	2	2	2
Language Disturbance without weakness	1	1	1	1
<b>Symptom Duration</b>				
≥ 60 minutes	2	2	2	2
10-59 minutes	1	1	1	1
<10 minutes	0	0	0	0
>10 minutes	N/A	N/A	0	0
<b>Dual TIA</b> (≥2 episodes of transient ischemic attack symptoms within the past 7 days)	N/A	2	2	2
<b>Imaging</b>				
Ipsilateral ≥ 50 % stenosis of internal carotid artery	N/A	N/A	2	N/A
Ipsilateral ≥ 50 % stenosis of internal carotid artery and/or major cerebral artery	N/A	N/A	N/A	2
Acute diffusion-weighted imaging hyperintensity	N/A	N/A	2	2
<b>Total Points</b>	<b>0-7</b>	<b>0-9</b>	<b>0-13</b>	<b>0-13</b>
<b>ABCD<sup>2</sup> Score</b>	<b>2-day risk (%)</b>	<b>7-day risk (%)</b>	<b>90-day risk (%)</b>	
Low (0-3)	1.0	1.2	3.1	
Moderate (4-5)	4.1	5.9	9.8	
High (6-7)	8.1	11.7	17.8	





## PATIENT DISPOSITION

- Factors affecting the capability of medical centers to care for patients with suspected transient ischemic attack include clinician experience, risk tolerance for neurovascular conditions, availability of imaging modalities, and access to neurovascular expertise.
- All levels of stroke certification requires staff education, neuro-imaging resources, and acute neurovascular consultation availability. In resource-limited settings, protocols for the care of neurovascular patients may need to be modified.
- Acceptable levels of disposition include rapid emergency department transient ischemic attack protocols with expedited referral to specialized cerebrovascular or transient ischemic attack-specific clinics, admission to a 24-hour ED observation unit, or standard hospital admission.





## PATIENT DISPOSITION

- Elevated transient ischemic attack risk scores, high risk imaging features, severe hypertension, dual transient ischemic attack, severe metabolic derangements, or abnormal EKG findings including new onset atrial fibrillation may warrant hospital admission.
- Expedited transient ischemic attack pathways and diagnostic protocols have been associated with increased use of evidence-based strategies, reductions in treatment delays, reduction in emergency room length of stay, reduction in admission rates, and cost savings, without associated increase in short-term stroke risk or mortality.
- Patients in underserved areas or who face additional barriers to access to timely medical care may also benefit from admission
- Successful transient ischemic attack protocols incorporate the following:
  - Rapid identification and diagnosis
  - Rapid access to diagnostic testing and advanced imaging
  - Risk stratification criteria
  - Access to neurovascular expertise
  - Implementation of appropriate secondary prevention interventions
  - Access to short-term clinic follow up (ideally within 48 hours but no more than 1-week)
  - Partnership across different departments and service lines

# RISK REDUCTION

# PREVENTATIVE STRATEGIES

- Secondary prevention strategies address vascular risk reduction. (Table 4)
- Antiplatelet therapy is recommended for patients who do not have an indication for anticoagulation. Short-term dual antiplatelet therapy has been shown to reduce risk of recurrent events in selected high-risk transient ischemic attack patients presenting within 24 hours of symptom onset. Antiplatelet therapy decisions, including choice of agent and duration of treatments, can be guided by vascular neurology consultation. It is not well-established whether increasing antiplatelet doses or switching to another agent benefits patients with a transient ischemic attack who are already on a single antiplatelet agent.
- Anticoagulation is effective in reducing stroke risk in the setting of atrial fibrillation, and can be safely prescribed from the emergency department, preferably in collaboration with primary care providers to discuss risks and benefits. Even patients with a history of falls may benefit from anticoagulation. Awaiting MRI to detect cortical microhemorrhages is reasonable.





# PREVENTATIVE STRATEGIES

Table 4: Secondary Prevention checklist for Patients with Suspected TIA

Care Component	ABCD <sup>2</sup> <4 (Low risk)	ABCD <sup>2</sup> ≥4* (High risk)	ABCD <sup>2</sup> ≥6 and symptomatic ipsilateral intracranial stenosis*
<b>Antiplatelet</b> (Should be started within 12-24 hours of symptom onset)	Aspirin 50-325mg daily  OR  Clopidogrel 75mg daily  OR  ASA 25mg/ER dipyridamole 200 mg twice daily	Aspirin 81mg plus clopidogrel 75 mg daily for 21-90 days***  THEN transition to single therapy	Aspirin 81mg plus clopidogrel 75mg daily for 21-90 days  OR  Ticagrelor 180mg load followed by 90mg twice daily plus aspirin 75-100mg daily for 30 days****  THEN transition to single therapy
<b>Antihypertensives</b> (Long-term goal blood pressure <130/80 mm Hg)	Angiotensin-converting enzyme inhibitor, angiotensin II receptor blockers, thiazide diuretic. Calcium channel blockers can be considered for patients who need additional options.		
<b>Anticoagulation (for patients with AF or other indications**)</b>	Apixaban, dabigatran, edoxaban, rivaroxaban, warfarin		
<b>Lipid lowering</b> (Goal LDL-C <70 mg/dl)	HMG-CoA Reductase Inhibitors (first line), and ezetimibe then PCSK9 inhibitor (if needed for very high risk patients)		
<b>Nutritionist consult</b>	Encourage a low sodium or Mediterranean diet. For diabetics start conversation and/or consider referral to a nutrition specialist.		
<b>Counsel regarding modification of lifestyle factors in an individualized, culturally sensitive manner</b>	Smoking cessation Physical activity Alcohol moderation		
<b>Follow-up appointment</b>	Expedited TIA/neurology and primary care clinics		
*When possible, strongly consider hospital admission **In patients with moderate to severe mitral stenosis or mechanical heart valve, warfarin is preferred ***Based on CHANCE and POINT trial protocols ****Based on THALES trial protocol			

# PREVENTATIVE STRATEGIES

- The following can reduce the risk of stroke:
  - High intensity statin therapy (reduces LDL levels, stabilizes plaque, and improves endothelial dysfunction and inflammatory responses)
  - Anti-hypertensive agents
  - Blood sugar management (severe hyperglycemia on presentation may warrant hospital admission)
  - Behavioral and lifestyle counseling (improves stroke literacy, lifestyle, and medication adherence)
  - Increased physical activity
  - A healthy diet (e.g., Mediterranean or DASH diets)
  - Limiting excessive alcohol intake
  - Referral for patients with substance use disorders
  - Tobacco-cessation
- Consistent and innovative education on the signs and symptoms of stroke for patients with transient ischemic attack or acute ischemic stroke. Multilingual educational materials should be provided.





# UNDERSERVED AND RURAL POPULATIONS

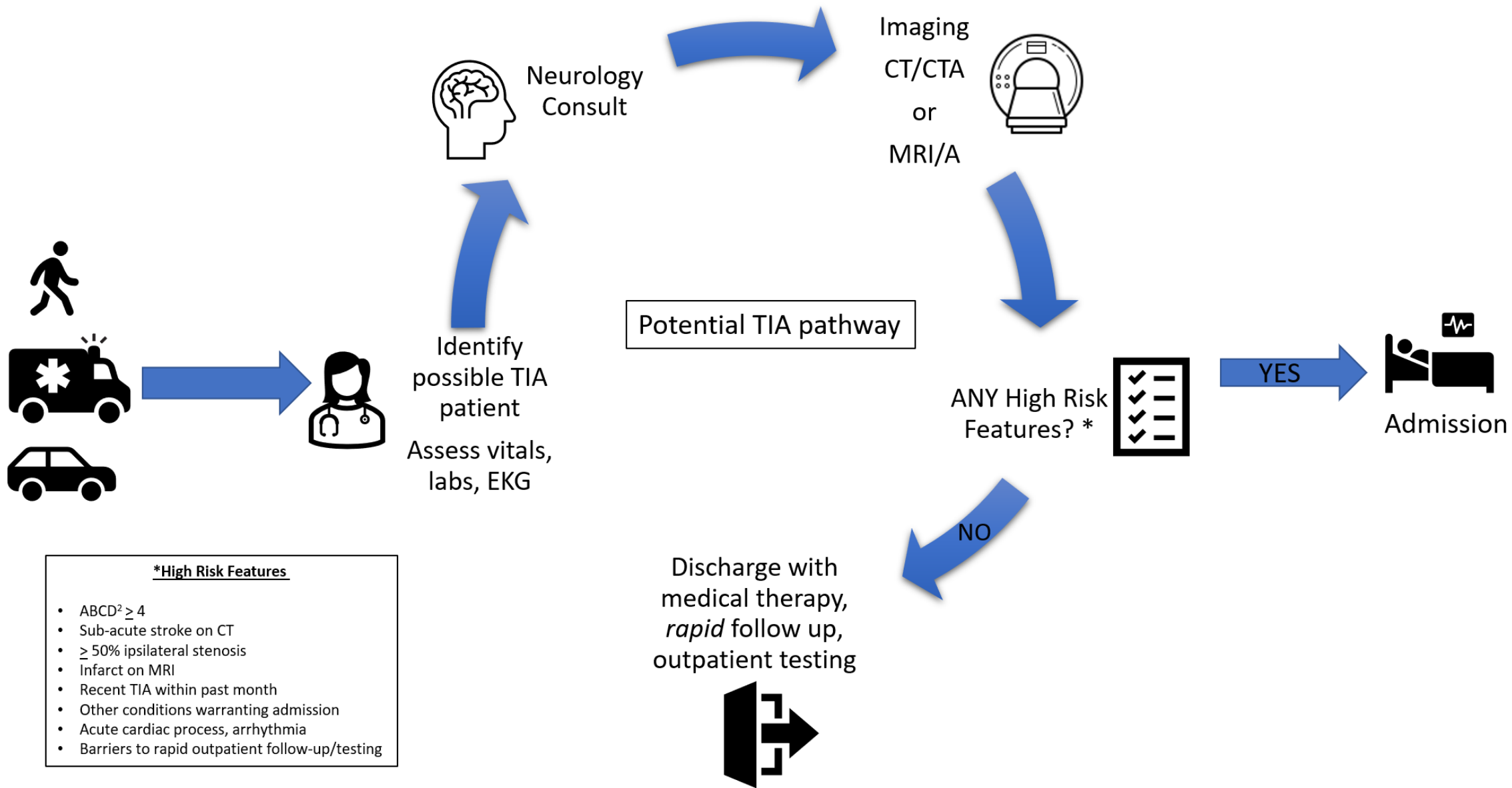
- Despite improved emphasis on stroke systems of care, disparities in treatment rates, mortality, and readmission rates have remained constant or widened in rural populations.
- Disparities for patients in underserved communities may be influenced by lack of focus on social determinants of health such as access to transportation and primary care, as well as high costs of care.
- Telestroke can improve access to care for rural and underserved communities, and may be useful in the management of transient ischemic attack in the emergency setting.



# OUTPATIENT FOLLOW UP

- Primary care physicians should be notified when their patients present to the emergency department with a transient ischemic attack.
- Rapid follow up with both a neurologist and a primary care physician is warranted after transient ischemic attack.
- In resource-limited settings, telehealth or other electronic modalities are potential options to address vascular risk factor management.





# CONCLUSIONS

# CONCLUSIONS

- Transient ischemic attack is a strong predictor for ischemic stroke and requires careful evaluation to properly identify high-risk patients.
- Several tools are available to aid in the evaluation of patient with transient ischemic attack, including risk stratification scales, acute phase imaging, and neurological consultation.
- Incorporating these steps into a pathway can facilitate appropriate disposition of transient ischemic attack patients, including hospital admission decisions.
- Patient-specific secondary prevention strategies and addressing social determinants of health are critical in prevention.
- Individual centers must utilize available resources to create a pathway to ensure successful management and disposition of transient ischemic attack patients and reducing the risk of future stroke.

