Lesson 311: PreAnesthetic Assessment Of the Patient With Acute Ischemic Stroke—Part 1

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Professional Gaps

Most anesthesiologists are aware that it is essential to treat victims of acute ischemic stroke (AIS) as quickly as possible. The structure of a stroke care center and the involvement of the anesthesiologist in the stroke service is new information. This 2-part series discusses the pathophysiology of AIS and the treatments for stroke. Current guidelines for the accreditation and designation of a stroke center, diagnostic protocols, and treatment options for AIS are reviewed. Literature pertaining to the controversy of using general anesthesia versus sedation for the anesthetic management of AIS patients undergoing endovascular treatment is presented.

In Part 1, the 3 levels of stroke hospital designation are described. The signs and early diagnosis of AIS are reviewed, and thrombolysis with fibrinolytic agents explained.

Part 2 reviews endovascular therapy, the involvement of the anesthetic care provider, and the controversies surrounding anesthetic management of AIS.

Learning Objectives

At the completion of the activity, the reader will be able to:

1. Define the institutional characteristics that are needed to qualify as a primary stroke center, a comprehensive stroke center, or an acute stroke-ready hospital.
2. Describe the evaluation of a patient with AIS, including indicated diagnostic and laboratory tests.
3. Identify criteria that should be met before administration of IV recombinant tissue plasminogen activator (rtPA).
4. Assess the period from “last seen well” to treatment that governs the administration of fibrinolytic therapy.
5. List the modifiable and nonmodifiable risk factors for AIS.
6. Specify the ideal blood pressure for patients after endovascular treatment of AIS.
7. Differentiate the side effects of IV rtPA treatment.
8. Describe the FAST criteria for identifying AIS.
9. Recognize confounding medical problems that can mimic the symptoms of AIS.
10. Describe the rationale behind the extension of IV rtPA treatment from 3 to 6 hours.

Case

A 79-year-old woman was brought to the emergency department after she was found on the floor of her apartment following activation of an elder protection electronic alert. A relative reported that the patient had a history of high blood pressure, type 2 diabetes mellitus, and chronic obstructive pulmonary disease (COPD). Vital signs included blood pressure 175/87 mm Hg, pulse of 76, respiratory rate of 17, and SpO2 of 93% on 2 L O2 via nasal cannula. In the emergency room, the patient had right-sided hemiplegia and was aphasic. Within 1 hour of arrival, she received IV recombinant tissue plasminogen activator (rtPA). Her neurologic condition did not improve, and after 3 hours from the onset of symptoms repeat computed tomography (CT) revealed no hemorrhage. The neuroradiologist wanted to perform a thrombectomy and called for an anesthetic consult. The patient had become agitated and did not follow commands.

Stroke is currently the fourth leading cause of death in the United States.1 More therapies are being investigated to ameliorate the consequences of stroke. The newer endovascular interventions require immobility—hence either good patient cooperation or general anesthesia is necessary. However, it appears that general anesthesia may worsen outcome after interventional treatment for acute ischemic stroke (AIS).2 Whether this finding is causal or incidental is not yet known. The concern that general anesthesia is harmful complicates the formulation of an anesthetic plan. Should clinicians favor sedation as the anesthetic and convert to general anesthesia if necessary or can they begin with a carefully titrated induction and maintain the patient under general anesthesia? No direct studies have compared head-to-head outcomes for different anesthetic techniques; only retrospective data are thus far available.

Stroke Center

The American Stroke Association recognizes 3 levels of stroke hospital designation: primary stroke center (PSC), comprehensive stroke center (CSC), and acute stroke-ready hospital (ASRH). The Joint Commission and individual states accredit stroke centers. A PSC must fulfill 11 criteria to become certified (Table 1).

A CSC has 5 components:

1. The CSC has personnel with expertise in vascular neurology, vascular neurosurgery, advanced practice nursing in stroke, vascular surgery, diagnostic radiology/neuroradiology, interventional/endovascular, critical care medicine, physical medicine and rehabilitation, physical therapy, occupational therapy, speech therapy, stroke nursing, respiratory therapy, and swallowing assessment.

2. The CSC has diagnostic techniques including magnetic resonance (MR) imaging with diffusion, MR angiography/MR venography, computed tomography (CT) angiography, cerebral angiography, transcranial Doppler, carotid duplex ultrasound, and transesophageal
echocardiography.

3. Surgical treatment, including carotid endarterectomy, clipping of intracranial aneurysm, placement of ventriculostomy, intracranial hematoma removal/draining, placement of intracranial pressure transducer, endovascular ablation of intracranial aneurysms and arteriovenous malformations, intra-arterial reperfusion therapy, and endovascular treatment of vasospasm are available.

4. Infrastructure is in place that includes a stroke unit, an ICU, a stroke clinic, an operating room staffed around the clock, interventional services 24 hours per day, and a stroke registry to compile patient information.

5. Programs must be established that convey stroke education and prevention to the community, train the professional staff at the center, and educate patients.

<table>
<thead>
<tr>
<th>Table 1. Criteria for Primary Stroke Center Designation</th>
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<tbody>
<tr>
<td>Acute stroke team</td>
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<td>Written care protocols</td>
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<td>EMS</td>
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<tr>
<td>Emergency department</td>
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<td>Stroke unit</td>
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<td>Neurosurgical services</td>
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<td>Support of the medical organization</td>
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<td>Neuroimaging</td>
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<td>Laboratory studies</td>
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<tr>
<td>Outcome/quality improvement measures</td>
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<td>Educational programs</td>
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EMS, emergency medical services

ASRHs must have written emergency stroke care protocols, written transfer agreements with a center that has neurosurgical services, a director of stroke care to oversee the hospital stroke policies, the ability to administer IV rtPA, the ability to perform emergency brain imaging and conduct emergency laboratory testing, and the maintenance of a stroke patient log.
Having a community system in place that has ASRHs and PSCs for basic emergency stroke care and that is associated with CSC that can give more comprehensive care is the current recommendation from the American Heart Association and the American Stroke Association.³

**Signs and Early Diagnosis of AIS**

AIS is an abrupt onset of a neurologic deficit caused by occlusion of the intracerebral artery. Both modifiable and nonmodifiable risk factors exist for AIS. Modifiable risk factors include hypertension, tobacco use, diabetes mellitus, peripheral vascular disease, atrial fibrillation, dilated cardiomyopathy, valvular heart disease, sickle cell disease, high cholesterol, poor diet, and physical immobility. Nonmodifiable risk factors are age (the average age of first AIS is 78 years), family history of stroke, race (blacks are at higher risk), sex (women greater than men), and prior stroke or myocardial infarction (MI).⁴ Given these demographics, the average patient is an elderly woman with underlying chronic disease who most likely is taking some form of anticoagulation medication.

Rapid diagnosis and treatment of AIS improves patient outcome.⁵ More than 10 years ago a new acronym, FAST for Face, Arm, Speech and Time, was developed for public education on the importance of immediate identification of stroke (Table 2).² In most cases, delivery of IV rtPA, the only FDA-approved therapy for AIS, is effective only within 3 hours of the onset of symptoms. Therefore, knowing the time of symptom onset affects management and is an important element in the presenting patient history. If the stroke is disabling, reliance on witnesses to determine onset is essential. The last time the patient was seen well serves as the time of stroke onset. If the patient woke up with the deficit, then the time he or she went to sleep constitutes the stroke-onset time. Confounding medical problems such as seizures, hypoglycemia, migraines with aura, encephalopathy, central nervous system abscess or tumor, drug toxicity, and psychogenic or conversion disorders can mimic stroke and must be ruled out.⁶

The following diagnostic tests should be used routinely in patients suspected of having AIS. A non-contrast head CT can rule out alternate diagnoses such as intracerebral hemorrhage that would be a contraindication to IV rtPA. It also can guide treatment decisions; for example, non–contrast-enhanced CT is being investigated to identify early signs of ischemia or large intracranial vessel occlusion. Early signs of cerebral ischemia correlate with increased risk for hemorrhagic transformation. Patients who have a higher National Institutes of Health Stroke Scale score (NIHSS score), and thus more severe deficits and worse prognosis, have a higher incidence of symptomatic intracerebral hemorrhage transformation.⁷

Laboratory tests that must be performed in all AIS patients include electrolytes; complete blood count...
for platelet count, chiefly; electrocardiogram and cardiac markers; and coagulation studies. Hypoglycemia can mimic acute stroke symptoms and also is associated with worse outcomes; hyperglycemia also worsens outcome by increasing the size of infarcted area. A platelet count of less than 100,000 is a contraindication to IV rtPA. Troponin levels can indicate a recent MI, which is a relative contraindication for IV rtPA as it may precipitate myocardial rupture. Finally, elevated activated partial thromboplastin time, prothrombin time, or an international normalized ratio above 1.7 will proscribe the use of fibrinolytic therapy. A hemorrhagic complication will severely worsen outcome.

Other tests should be considered in selected patients if there is good clinical indication, but this should never delay stroke treatment. These tests may include chest x-ray, toxicology screens, pregnancy tests, arterial blood gas analysis, and electroencephalogram.

**Medical Interventions**

Currently, there are 2 basic interventions for ischemic stroke: thrombolysis with IV rtPA or endovascular treatment, either with rtPA alone or using mechanical devices or clot retrieval systems for vessel recanalization. In 1996, the FDA approved IV rtPA based on data from the NINDS (National Institute of Neurological Disorders and Stroke) rtPA trial. The study included 624 patients who were treated with either placebo or IV rtPA within 3 hours of stroke onset; half of those in the trial received treatment within 90 minutes of stroke onset. Treatment with rtPA was associated with an increased odds ratio for a favorable outcome (odds ratio [OR], 1.9; 95% confidence interval [CI], 1.2-2.9). This positive effect extended to individual functional measures of global disability (40% vs 28%), global outcome (43% vs 32%), activities of daily living (53% vs 38%), and neurologic deficits (34% vs 20%). Side effects of treatment included intracranial hemorrhage (ICH), systemic bleeding, myocardial rupture if given after MI, angioedema, and anaphylaxis. Intracerebral hemorrhage is the most common IV rtPA treatment complication and it vastly worsens outcome.

Extended time windows to give IV rtPA have been investigated. Both 3 to 4.5 hours and 4.5 to 6 hours were studied to ascertain the risks and benefits of administering rtPA in these timeframes. The most recent study of the 3- to 4.5-hour window was the ECASS III (European Cooperative Acute Stroke Study III). The authors enrolled 821 patients who received either placebo (n=403) or rtPA (n=418). The European inclusion criteria differed from the American Stroke Council guidelines because the study excluded patients over the age of 80 years, patients who had an NIHSS score greater than 25 (the NIHSS score evaluates the severity of the stroke on a scale of 0 to 42; a higher score denotes a worse stroke), those taking anticoagulation even if the laboratory values were normal, and those who had a previous stroke and were diabetic. Excellent 90-day outcome using the modified Rankin Scale (mRS) (ie, a score of 0-2) was 52.4% for rtPA versus 45.2% for placebo (OR, 1.34; 95% CI, 1.02-1.76). There was an increase in ICH in the rtPA group (2.4% vs 0.2%; OR, 9.85; 95% CI, 1.26-77.32). However, the ICH rate was in line with clinical data from other studies and showed rtPA can be given safely to properly selected patients beyond the 3-hour original time limit, up to 4.5 hours after a stroke.

A meta-analysis by Sandercock et al of IV rtPA administration within the interval of 4.5 to 6 hours showed a similar outcome benefit. The meta-analysis was comprised of 12 studies that enrolled 7,012 patients up to 6 hours after onset of AIS symptoms. Overall, the excellent outcome of mRS score 0 to 2 was 46.3% in the rtPA group versus 42.1% in the placebo arm (OR, 1.17; 95% CI, 1.06-1.29), but patients treated before 3 hours had a more significant treatment benefit for the mRS score of 0 to 2 (40.7% vs 31.7%; OR, 1.53; 95% CI, 1.26-1.86), reinforcing that earlier treatment is much more
efficacious. The meta-analysis showed an increase in ICH in the rtPA group (7.7% vs 1.8%; OR, 3.72; 95% CI, 2.98-4.64) and an increase in death within 7 days (8.9% vs 6.4%; OR, 1.44; 95% CI, 1.18-1.76). Thus, extension of the treatment interval with IV rtPA beyond 4.5 hours is not beneficial because of the increased incidence of often-fatal ICH.

The European Medicines Agency has extended the timeframe for IV rtPA AIS treatment to 4.5 hours since stroke onset, whereas the FDA has declined to do so.

**Indications for Administration of IV rtPA**

The guidelines for treatment of AIS are as follows:

- IV rtPA should be given within the first 3 hours of stroke symptom onset.
- Ideally, treatment should start within 1 hour of the patient’s arrival at the hospital.
- IV rtPA is recommended up to 4.5 hours after stroke onset.
- Exclusion criteria that apply beyond 3 hours: patients over the age of 80 years, patients taking any oral anticoagulants, baseline NIHSS score greater than 25, patients with ischemic injury exceeding one-third of the blood supply territory of the middle cerebral artery, and any diabetic patient with a prior history of stroke.

**Contraindications for IV rtPA Administration**

Both absolute and relative contraindications have been identified for IV rtPA administration (Tables 3 and 4). IV rtPA in patients who are in the 3- to 4.5-hour time window and who have one or more of the exclusion criteria listed above need to be studied further. Blood pressure greater than 185/110 mm Hg must be lowered before starting IV rtPA. Physicians should be prepared to treat any side effects of fibrinolytic therapy, including bleeding complications and angioedema. IV rtPA may be given to patients who have had a seizure at the onset of stroke if there is evidence that the residual deficits are from the stroke and are not a postictal phenomenon. The use of other fibrinolytic agents or defibrinogenating agents is not well established and these agents should only be used in clinical trials. Although controversial, the use of IV fibrinolysis may be considered in patients with mild stroke deficits, rapidly improving stroke symptoms, major surgery in the preceding 3 months, and recent MI as long as the risks for complications are weighed against the potential benefits of treatment. IV streptokinase for stroke treatment is not recommended because trial use of this agent has demonstrated greater rates of ICH. Finally, patients taking direct thrombin inhibitors such as dabigatran or direct factor Xa inhibitors such as rivaroxaban and apixaban may be harmed by IV rtPA, and treatment is not recommended if the patient received a dose within 2 days. The potential risks for ICH are thought to be greater in these patients because there are no quick reliable tests to assess anticoagulant levels. A careful history detailing the last dose of anticoagulant is important.
Table 3. Absolute Contraindications for IV rtPA Administration

<table>
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<tr>
<th>Condition</th>
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<tr>
<td>Significant head trauma or prior stroke in previous 3 mo</td>
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<tr>
<td>Symptoms suggest subarachnoid hemorrhage</td>
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<tr>
<td>Arterial puncture at noncompressible site in previous 7 d</td>
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<tr>
<td>History of previous intracranial hemorrhage</td>
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<tr>
<td>Intracranial neoplasm, arteriovenous malformation, or aneurysm</td>
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<tr>
<td>Recent intracranial or intraspinal surgery</td>
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<tr>
<td>Elevated blood pressure (systolic &gt;185 mm Hg or diastolic &gt;110 mm Hg)</td>
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<tr>
<td>Active internal bleeding</td>
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<tr>
<td>Acute bleeding diathesis</td>
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<tr>
<td>Platelet count &lt;100,000/mm³</td>
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<tr>
<td>Heparin received within 48 h, resulting in abnormally elevated aPTT greater than the upper limit of normal</td>
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<tr>
<td>Current use of anticoagulant with INR &gt;1.7 or PT &gt;15 seconds</td>
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<tr>
<td>Current use of direct thrombin inhibitors or direct factor Xa inhibitors with elevated sensitive laboratory tests (such as aPTT, INR, platelet count, and ECT; TT; or appropriate factor Xa activity assays)</td>
</tr>
<tr>
<td>Blood glucose concentration &lt;50 mg/dL (2.7 mmol/L)</td>
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<tr>
<td>CT demonstrates multilobar infarction (hypodensity &gt;1/3 cerebral hemisphere)</td>
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</tbody>
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*aPTT, activated partial thromboplastin time; CT, computed tomography; ECT, ecarin clotting time; INR, international normalized ratio; rtPA, recombinant tissue plasminogen activator; TT, thrombin time*

Table 4. Relative Contraindications for IV rtPA Administration

<table>
<thead>
<tr>
<th>Condition</th>
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<tbody>
<tr>
<td>Only minor or rapidly improving stroke symptoms (clearing spontaneously)</td>
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<tr>
<td>Pregnancy</td>
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<tr>
<td>Seizure at onset with postictal residual neurologic impairments</td>
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<tr>
<td>Major surgery or serious trauma within previous 14 d</td>
</tr>
<tr>
<td>Recent gastrointestinal or urinary tract hemorrhage (within previous 21 d)</td>
</tr>
<tr>
<td>Recent acute myocardial infarction (within previous 3 mo)</td>
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*rtPA, recombinant tissue plasminogen activator*
Dr. Elizabeth A.M. Frost, who is the editor of this continuing medical education series, is clinical professor of anesthesiology at The Mount Sinai School of Medicine in New York City. She is the author of Clinical Anesthesia in Neurosurgery (Butterworth-Heinemann, Boston) and numerous articles. Dr. Frost is past president of the Anesthesia History Association and former editor of the journal of the New York State Society of Anesthesiologists, Sphere. She is also editor of the book series based on this CME program, Preanesthetic Assessment, Volumes 1 through 3 (Birkhäuser, Boston) and 4 through 6 (McMahon Publishing, New York City).

REFERENCES

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**Post-test**

1. Which of the following is a contraindication for IV rtPA treatment in a patient who had a stroke 2 hours ago?
   a. The patient is taking amiodarone.
   b. The platelet count is 140,000/mm3.
   c. The patient has diabetes.
   d. The patient is taking dabigatran.

2. Which patient can be expected to gain the best results if given IV rtPA?
   a. A 70-year-old woman who went to bed at 10 PM and woke up at 7 AM with left-sided weakness
   b. An 82-year-old man who was last seen well at 5 PM and reaches the emergency room at 10 PM
   c. A 78-year-old woman on warfarin who is unconscious and whose blood sugar is 45 mg/dL
   d. A 76-year-old man who developed facial droop 1 hour ago; blood pressure is 170/100 mm Hg

3. What is the highest systolic blood pressure in which IV rtPA is given?
   a. 180 mm Hg
   b. 220 mm Hg
   c. 150 mm Hg
   d. 120 mm Hg

4. According to the FDA, the time interval for IV rtPA administration should not exceed ______.
   a. 3 hours
   b. 4.5 hours
   c. 6 hours
   d. 8 hours

5. Which of the following is not a potentially modifiable risk factor for stroke?
   a. Hypertension
   b. Valvular disease
   c. Tobacco use
   d. Atrial fibrillation
6. **A modifiable risk factor for stroke includes ______.**
   a. Race
   b. Family history
   c. Diabetes mellitus
   d. Prior stroke

7. **Which of the following is not a component of the FAST acronym?**
   a. Face: Does the patient have a facial droop?
   b. Arm: Does the patient have any weakness in his or her arms?
   c. Time: Has it been less than 1 hour since the stroke?
   d. Speech: Does the patient have slurred speech?

8. **Which of the following is the National Institutes of Health Stroke Scale score exclusion criterion for the ECASS III study?**
   a. There is none.
   b. >25
   c. <30
   d. <15

9. **Which of the following confounding medical problems is least likely to mimic stroke?**
   a. Heroin intoxication
   b. Hypoglycemia
   c. Seizure
   d. Brain tumor

10. **Which of the following laboratory tests does not need to be performed before urgent treatment with IV rtPA?**
    a. Pregnancy test
    b. Electrocardiogram
    c. Complete blood count
    d. Computed tomography scan