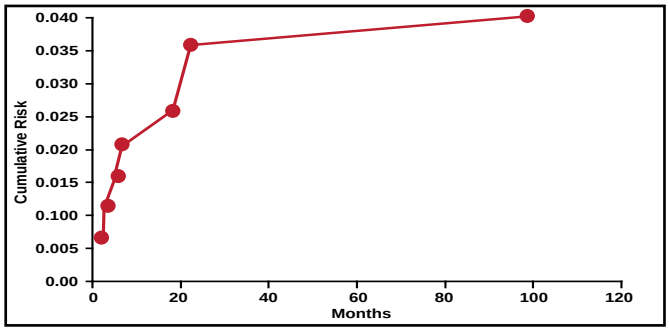
a small but real risk of complication, does not replace other medical therapy, and is unproven.

Figure 1. Recurrent Thromboembolism in Neonates.



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The combination of PFO and atrial septal aneurysm (ASA) was associated with an increased risk of recurrent stroke in patients (OR 3.1; 95% CI, 2.3 to 4.2) in one Class I study but not in two other subsequent Class I studies.

The medical treatment options for PFO patients include antiplatelet drugs or anticoagulation, and there are no high-level data that confirm the superiority of either of these approaches, though anticoagulation is associated with more bleeding complications. Surgical or percutaneous closure can also be performed, but this does not preclude long-term medical therapy. At this time, there are no high-level data that support PFO closure. Randomized controlled trials are ongoing, but enrollment has been slowed by rampant use of off-label devices for PFO closure. Despite the lack of evidence, percutaneous septal closure procedures increased 50 times between 1998 and 2004.

Acute Stroke and the tPA Dilemma

There is some uncertainty regarding the appropriate treatment strategy for mild stroke and whether or not thrombolytic therapy with tissue plasminogen activator (tPA) is suitable for less severe stroke patients. Seizures at stroke onset, which occur in 4.2% to 7.7% of acute stroke patients, are generally exclusion criteria for tPA due to the possibility of injury or "stroke mimics," such as Todd paralysis [Sylaja *Stroke* 2006; Weir. *J Neurol Neurosurg Psychiatry* 2005; Mathews. *Neuroradiology* 2008]. Christopher Lewandowski, MD, Henry Ford Hospital, Detroit, MI, discussed methods for distinguishing stroke mimics from stroke and the ramifications of tPA in stroke mimics.

A thorough patient history to determine the time and duration of the seizure is imperative, as seizure duration is generally proportional to the duration of the postictal phase, except in the case of Todd paralysis, said Dr. Lewandowski. Physical exam and imaging can also assist the clinician in differentiating between mimics and authentic stroke. CT-perfusion imaging, CT-angiogram, and diffusion-weighted magnetic resonance imaging are highly sensitive and highly specific modalities for stroke assessment within minutes of stroke onset (Tables 1 & 2). However, the most rapidly available modality should be utilized due to time constraints that are related to stroke treatment. The risk of intracranial hemorrhage with tPA is dose-dependent, and the duration of action is relatively short. Therefore, the treatment of stroke mimics with tPA carries low risk, concluded Dr. Lewandowski.

Table 1. Comparison of Imaging Modalities for Acute Stroke.

Imaging Modality	Sensitivity Specificity	Details
CT-Angiogram	• 98% Sensitivity • 98% Specificity • for cerebral vessel occlusion in large branches	• Estimate of gross collateral blood flow • Provides source images that reflect cerebral blood flow • Provides diagnostic evaluation of the neck • Difficult to see smaller vessel occlusions
CT-Perfusion	• 90% to 95% Sensitivity within 6 hours • 100% Specificity	• Provides images that reflect cerebral blood volume and cerebral blood flow • Evaluates mean transit time • Low cost and widely available
MRI-DWI	• Approaching 100% Sensitivity • Approaching 100% Specificity within minutes after stroke symptom onset	• Benefits are similar to that of CT • Possibility of false negative DWIs occurring in brainstem stroke and lacunes

Table 2. CT-Perfusion Differences in Seizure versus Acute Stroke.

CT-Perfusion in Seizure/ Stroke Mimic	CT-Perfusion in Acute Stroke
Increased cerebral blood flow (hyperperfusion)	Decreased regional cerebral blood flow
Increased cerebral blood volume	Increased regional cerebral blood volume
Decreased mean transit time	Prolonged mean transit time

According to the American Heart Association Get with the Guidelines Stroke data, 31% of patients (time of presentation <2 hours) did not receive tPA due to mild or improving stroke status [Smith. *Stroke* 2010]. Additionally, up to one-quarter of these patients may have residual disability at hospital discharge or at 90 days, and poor outcomes have been associated with patients with proximal vessel occlusions or larger fluctuations in the neurological exam (improvement in National Institutes of Health Stroke Scale scores ≥10 points from the initial exam) [Nedeltchev. *Stroke* 2007; Smith. *Stroke* 2005]. Cognitive impairment or gait impairment is often overlooked in patients with mild or improving stroke and should also be evaluated upon admission. Though there is insufficient evidence regarding the effect of tPA in patients with mild or improving stroke, it should be considered on an individual basis where residual disability is likely, said Eric E. Smith, MD, University of Calgary, Calgary, Alberta, Canada. More research is needed to establish postdischarge outcomes in this group.

Hypertension in acute stroke patients is another treatment challenge that clinicians face. Jamary Oliveira-Filho, MD, PhD, Federal University of Bahia, Salvador, Brazil, discussed the dual role of hypertension in acute stroke and what that means for tPA. When tissue is at risk (ie, in acute arterial occlusions), hypertension can be beneficial, in that it increases cerebral blood flow to low-flow areas. However, in the absence of tissue at risk (ie, either recanalization has already occurred or enough time has elapsed that brain tissue has died), hypertension can increase the risk for edema, hemorrhage, and recurrence, thereby increasing risks that are associated with tPA. It is appropriate to maintain blood pressure at <185/110 mm Hg before tPA and after in order to avoid hemorrhagic transformation [Brott. *Stroke* 1998; Martin-Schild. *Arch Neurol* 2008; Butcher. *Stroke* 2010]. It is recommended that blood pressure treatment in acute stroke patients who do not undergo thrombolysis be avoided except for extreme elevations (ie, 220/120 mm Hg). Optimal blood pressure levels in postlysis patients who do not recanalize or in acute stroke patients who spontaneously recanalize are still uncertain.

The issue of tPA in complex cases, such as patients with mild stroke or hypertension, presents clinicians with the challenge of assessing risk versus benefit. Differentiating between stroke mimic versus acute stroke also poses a clinical dilemma. Thrombolytic therapy is appropriate and risk is low in many of these cases. However, more data are needed to determine the overall risk and benefit of tPA in patients with mild stroke.