Table 1. Relationship to Stroke.

- Cerebral Perfusion
- Thrombosis—endothelial dysfunction—stasis-hypercoagulable state
- Hypertension & Diabetes → atherosclerosis
- Inflammation, Oxidative stress

Commenting on the cerebral effects of decreased cardiac output, Patrick Pullicino, MD, University of Kent, Canterbury, UK, noted that a relationship has been shown between increases in New York Heart Association (NYHA) Functional Class and reductions in global cerebral blood flow (CBF), with higher functional class being associated with lower CBF [Choi BR et al. *Am J Cardiol* 2006; Venegas-Torres et al. ISC 2009].

Other evidence for brain injury in HF comes from MRI studies that showed that asymptomatic patients with cardiomyopathy and low EF had a higher incidence of stroke, cortical atrophy, and ventricular enlargement [Schmidt R et al. *Stroke* 1991].

There also is increasing evidence that relative hypotension may be injurious to the brain in HF. Results from the REGARDS trial showed that the OR for stroke was higher for patients with HF versus those without. The association was strongest in individuals in the lowest blood pressure group, suggesting that cerebral hypoperfusion could contribute to stroke pathogenesis. These results need to be confirmed, although they are supported by a pooled analysis of 10 HF studies that showed that higher systolic BP decreases mortality [Raphael CE et al. *Heart* 2009].

Ralph L. Sacco, MD, University of Miami, Miami, FL, reviewed several studies that examined stroke outcome in patients with HF, noting that for such patients, in-hospital mortality is nearly 2 times higher, length of stay is greater, and total cost is higher (Table 2) [Divani A et al. *J Cardiac Heart Fail* 2009].

Table 2. Comparison of Stroke Outcomes for Atrial Fibrillation versus Heart Failure.

	Atrial Fibrillation	Heart Failure
Severe Stroke (NIHSS≥6)	1.90 (1.2-3.1) X	2.25(1.2-3.1) X
Mortality post stroke	<1.7 to 2.43 X	2.3 to 4.5 X

HF in stroke patients also may be an important predictor of recurrent stroke or death within 2 years after TIA or stroke, according to a study by Kernan et al. [Kernan WN et al. *Stroke* 2000]. Classical vascular risk factors (such as age, prior stroke, hypertension, and history of/current diabetes mellitus) add to the risk of stroke among those with HF.

Dr. Sacco remarked, "The public health impact of HF may be even greater than AF, particularly when you take into account prevalence and mortality."

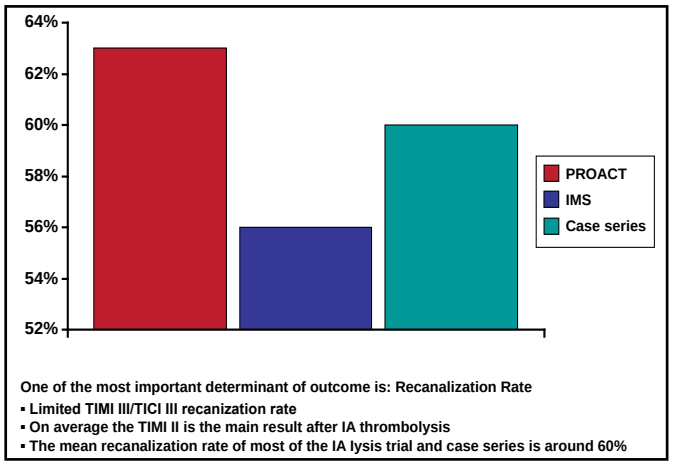
Reperfusion Therapy in Acute Stroke: State-of-the-Art and Future Directions

Reperfusion therapy with IV rt-PA and recanalization produces good outcomes in patients with acute stroke, but challenges remain. Carlos A. Molina, MD, Hospital Vall d'Hebron, Barcelona, Spain, estimates that 85% of all ischemic strokes are not treated with thrombolysis; thus, improved and early access to treatment is needed. He suggested that the 3 to 6-hour time window for treatment may be extended by better patient selection criteria using transcranial Doppler markers of the diffusion-perfusion mismatch method [Restrepo L et al. *J Neuroimaging* 2006] and combination therapies, such as reduced-dose rt-PA plus eptifibatide [Pancioli AM et al. *Stroke* 2008] or rt-PA plus GPIIb/IIIa antagonists.

Although thrombolytic therapy has revolutionized treatment of acute ischemic stroke (AIS), its utilization is limited due to the short time window for use, poor specificity for the site of arterial occlusion, and suboptimal recanalization rates. Osama O. Zaidat, MD, MS, Vascular and Interventional Neurology, Medical College of Wisconsin, Milwaukee, WI, discussed the advantages and disadvantages of circumventing these problems by using intra-arterial (IA) thrombolysis. Two pivotal studies, Prolyse in Acute Cerebral Thromboembolism (PROACT) and the Interventional Management of Stroke (IMS), provided evidence for the effectiveness of IA thrombolysis. One of the most important determinants of outcome is recanalization rate, which is about 60% in IA lysis trials (Figure 1). The degree of recanalization and good clinical outcome are directly related to time to therapy [Zaidat OO et al. *Am J Neuroradiol* 2005]. Limitations of IA lysis may be related to clot characteristics, wherein white platelet-rich clots are more resistant to lytics and fresh red blood cell-rich clots are more responsive to lytics. The use of synthetic inhibitors (eg, monoclonal antibodies, such as abciximab; the peptide eptifibatide; and nonpeptides, such as tirofiban, lamifiban, xemilofiban, etc.) may overcome these

limitations. IA pharmacological thrombolysis therapy is fast and relatively easy to administer, but it is slow to work, and frequently it does not work at all, concluded Dr. Zaidat. However, currently it is the best treatment that we have.

Figure 1. Recanalization Rates for PROACT, IMS, and Case Series.



Sixty percent of stroke centers report treating IV tPA "failures" with IA. When stroke centers were surveyed regarding their intervention strategies, 43% reported using IA rt-PA as initial strategy, 43% moved to the MERCI® retriever as a second choice, and 35% used angioplasty as a third choice when the other two failed. Italo Linfante, MD, Baptist College and Vascular Institute, Miami, FL, stated that the IA approach to acute large vessel occlusion (mechanical or pharmacological) is here to stay and continues to grow. Thus, we need more evidence-based IA trials that take into consideration the rapidly emerging device technology.

Approaches to vascular protection after acute stroke were discussed in a forum that followed the main session. Recovery from a vascular injury may be facilitated by neuroprotection but neuroprotection can only be achieved with a functioning vasculature, stated Susan C. Fagan, PharmD, University of Georgia College of Pharmacy, Augusta, GA. Pharmacological agents and therapeutic interventions that are designed to target specific pathological and protective processes that affect the vasculature during the acute (hours), subacute (hours to days), and chronic (days to months) phases need to be developed [Fagan SC et al. *Stroke* 2004]. Inhibition of proteases, free radicals and inflammatory cytokines (to name a few) have been shown to be effective for vascular protection after stroke in experimental models. In addition, signaling molecules and NADPH and xanthine oxidase pathways that are involved in vascular injury may be putative targets for vascular protection, stated Rhian M. Touyz, MD, University of Ottawa, Canada.