treatment" in which treatment is deferred in anticipation of improved therapeutics and prognostics.

Predicting outcome is particularly difficult in poor-grade aneurysmal subarachnoid hemorrhage (aSAH) patients. Sander Connolly Jr, MD, Columbia University, New York, NY, said that he would repair the aneurysm immediately in patients with *any* possibility of meaningful survival.

In a group of 104 aSAH patients who were treated by Dr. Connolly, 13.5% of patients had a favorable outcome at 14 days, 38.5% at 3 months, and 51% at 1 year ($p<0.0001$). Of 99 patients who were rated grade 4 to 5, 51% had good outcomes 1 year after intervention. Admission Glasgow Coma scores significantly correlated with outcome (Spearman rank test=0.472; $p<0.0001$) [Starke M et al. *J Clin Neurosci* 2009].

"If the decision to treat aSAH patients were based on outcome during the first 14 days, few physicians would opt for treatment." The aggressive approach increases the good outcome rate, without increasing the poor outcome rate, Dr. Connolly concluded.

Jan Hillman, MD, University Hospital, Linkoping, Sweden, suggested that it is time to take another look at the use of antifibrinolytic (AF) therapy to prevent early rebleeding after subarachnoid hemorrhage. Decreases in the time window for early surgical intervention suggest that a brief course of high-dose AF is safe, may be beneficial in diminishing the risk of rebleeding, and offers significant protection against aSAH death.

Dr. Hillman presented results of two randomized, prospective, multicenter studies that assessed the efficacy of short-term AF treatment in preventing rebleeding. There was a significant ($p<0.002$) decrease in rebleeding in AF-treated patients (2.7%) versus untreated patients (11.4%) and no difference in ischemic complications. Mortality also was significantly less in the treated patients at 12 months (RR, 3.8; $p<0.0001$) [Hillman J et al. *J Neurosurgery* 2002; Starke RM et al. *Stroke* 2008].

Michael N. Diringer, MD, Washington University School of Medicine, St. Louis, MO, revisited the issue of hypertension and hypervolemia for the treatment of cerebral vasospasm.

Current management of vasospasm involves intravascular volume expansion and hemodynamic augmentation with the goal of increasing cerebral blood flow (CBF). Despite data that suggest that intravascular volume depletion occurs after aSAH and that patients with normal blood volume are far less likely to experience cerebral ischemia even if vasospasm develops, a review of the clinical data indicated that hypervolemia offered no advantage over euvolemia, said Dr. Diringer. In contrast to hypertension, moderate hypervolemia rarely increased $P_{br}O_2$, and it carried a high complication rate, including hyponatremia, fluid overload, cardiac arrhythmia, and cerebral edema.

Impaired vascular reactivity after SAH, loss of autoregulation, and reduced CBF are associated with poor clinical grade, vasospasm, and poor outcome. Enhancing cardiac output and increasing CBF by induced hypertension may be beneficial. Moderate hypertension increased $P_{br}O_2$ in most cases with few complications. Increases in blood pressure (using phenylephrine and dobutamine) can reverse flow deficits better than hypervolemia. In a prospective, randomized study, prophylactic hypervolemic therapy had no effect on the frequency of delayed ischemic neurological deficits that were attributable to cerebral vasospasm between treated and untreated groups regarding vasospasm, CBF, and 1-year outcomes compared with euvolemic therapy.

Cardiac Dysfunction in Stroke

Ronald Freudenberger, MD, Center for Advanced Heart Failure, Allentown, PA, listed some of the similarities between the pathophysiology of heart failure (HF) and stroke.

In addition to having a history of diabetes mellitus and/or hypertension, cardiac patients also have a high rate of silent cerebral infarcts (SCI): approximately 15% of diagnostic and percutaneous coronary intervention patients [Segal AZ et al. *Neurology* 2001]; 17% of coronary artery bypass graft patients [Friday G et al. *Heart Surgery Forum* 2005]; and 34% of patients who are referred for transplantation [Siachos T et al. J *Card Fail* 2005] have been shown to have an SCI.

HF likely is a prothrombotic state. Plasma viscosity, serum P-selectin, von Willebrand factor, and fibrinogen are higher in HF patients [Gibbs CR et al. *Circulation* 2001], and there also is an increase in whole blood aggregation and platelet/EC adhesion molecules [Serebruany V et al. *Eur J Heart Fail* 2002].

"Heart failure and stroke are strongly related and often coexist in the same population. Both share common risk factors and characteristics, including activation of inflammatory and thrombotic systems," said Dr. Freudenberger (Table 1).

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