



CLINICAL TRIAL HIGHLIGHTS

nurses more accurately predict 90-day outcome among patients with acute ICH compared with two commonly used validated scales

Determining accurate prognoses for ICH patients is crucial as it drives early decisions regarding life-sustaining therapy, informs patient and family counseling, and influences ICH research including study design and patient enrollment [Holloway RG et al. *Neurology* 2013]. Although multiple ICH clinical scales have been developed, none have had their accuracy tested against the early judgment of physicians and nurses. The objective of the PICH study was to compare the accuracy of the ICH Score [Hemphill JC et al. *Stroke* 2001; *Neurology* 2009] and FUNC score [Rost NS et al. *Stroke* 2008] with subjective clinical judgment for predicting functional outcome at 3 months among patients with acute ICH. Eligible patients included adults participating in the larger Ethnic/Racial Variations of Intracerebral Hemorrhage (ERICH) study at five centers. Clinician participants comprised of one physician and one nurse caring for each patient. Clinicians were asked to predict the 3-month mRS score for each patient—within 24 hours of each patient admission—and to indicate whether they would recommend comfort care only to the patient’s family. ICH and FUNC scores were calculated for each patient upon admission; a blinded 3-month actual mRS was also obtained via ERICH follow-up.

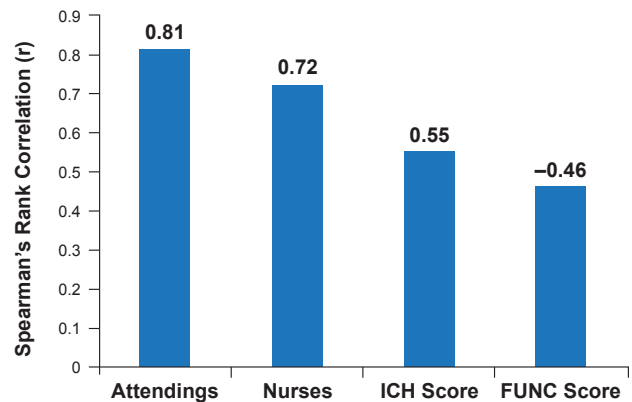
Scores on the ICH scale range from 0 to 6, based on the sum of the scores of 5 components: the Glasgow Coma Scale (GCS) score (counting as 0, 1, or 2 points), ICH volume ≥ 30 mL, the presence of intraventricular hemorrhage, whether the hemorrhage is of infratentorial origin and, age $<$ or ≥ 80 years. A score of 6 indicates a high probability for a poor outcome. Among various other outcomes, the ICH score has been validated to predict the probability of achieving functional independence at 90 days. The FUNC score was specifically designed to predict functional independence at 90 days. Scores range from 0 to 11, with a score of 11 indicating the highest probability for favorable outcome. The FUNC score is based on five factors: ICH volume (counting as 0, 2, or 4 points), age (< 70 , 70 to 79, and ≥ 80 years; counting as 0, 1, or 2 points), ICH location (lobar, deep, or other; counting as 2, 1, or 0 points), GCS score (counting as 0 or 2 points), and the presence of pre-ICH cognitive impairment.

Of the 405 patients from the ERICH study who were eligible to participate in PICH, 100 were enrolled. Participants were a mean age of 66.8 years; 64% had a GCS score of 13 to 15; the ICH was deep in 53% of patients, lobar in 36%, and infratentorial in 11%. The ICH volume was < 30 cc in 70% of patients, between 30 and 60 cc in 16%, and > 60 cc in 13%. Among the clinicians, 70%

of the physicians were neurologists with 75% of the predictions being made by attending physicians and 25% by trainees. Among the nurses, 71% had a neuroscience specialty.

Although all correlations for the clinician predictions and clinical scales with 3-month mRS were significant ($p < 0.02$ for all), the subjective predictions made by both attending physicians and nurses had a higher Spearman’s rank correlation with the actual 3-month mRS than either clinical scale (Figure 1).

Figure 1. Correlation of Subjective Predictions and Clinical Scales With Actual 3-Month mRS Score



ICH=intracerebral hemorrhage; all p values < 0.05 for comparisons between clinician correlations and ICH/FUNC scores correlations with 3-month mRS. FUNC score correlation is negative since lower score predict poor outcome.

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When the 18 patients for whom only comfort care was likely recommended were removed from the analysis, the Spearman’s rank correlation for the subjective predictions remained higher than those for either clinical score ($p < 0.05$). The results were similar when data for only survivors were analyzed.

The study is limited by several factors: the clinician participants making predictions were not formally trained in the mRS, early predictions were difficult to obtain and led to 218 potential patients being excluded, and, finally, the cohort contained many patients with low GCS and ICH volume.

Stroke Severity Adjusted Triage Can Benefit Patients

Written by Brian Hoyle

Evan Allen, MD, MBA, Florida Hospital Neuroscience Institute, Orlando, Florida, USA, described the benefits of a state-wide severe stroke adjusted triage (SAST) system that bypasses a geographically-closer primary stroke center

(PSC) for treatment at a comprehensive stroke center (CSC).

The rationale for the SAST system involved the knowledge that, while the chance of complete recovery from severe stroke improves with treatment like injection of tissue plasminogen activator (t-PA) that can be done at many PSCs, overall treatment success is low [Adams HP Jr. et al. *Stroke* 2007].

The SAST bypass system legislated in Florida requires emergency medical services (EMS) providers to transport suspected stroke patients to a CSC capable of administering t-PA, rather than to the nearest PSC.

Dr. Allen reported the results of a 7-year (2006–2012) retrospective analysis of therapeutic bypass yield (percentage of patients receiving treatments not available at the bypassed PSC), diagnostic accuracy of EMS providers, and outcome effect of bypassing a PSC located closer to the site of stroke. The analysis involved suspected acute strokes that occurred in the Orlando region and were ultimately treated at Florida Hospital Orlando CSCs in Orange County (Table 1).

Table 1. Summary of 526 Suspected Acute Strokes in Two Florida Counties

EMS Location	Stroke Assessment	Scale Score	Severe Strokes	Mild Strokes
Seminole County	3-item Simple Stroke Scale	≥4	310	0
Lake County	Los Angeles Motor Scale	≥4	190	26

EMS=emergency medical services.

Of the 526 patients, 77 (15%, ~1 in 7 patients) received CSC-specific interventions that included acute endovascular intervention for ischemic stroke (7.5%), neurosurgery for intracranial bleeding (5%), neurosurgery for intracranial tumor (2%), and other procedures including aneurysm coiling and extra-intra cranial arterial bypass (0.5%). Comparison of therapeutic bypass yields for patients who suffered stroke and trauma revealed 15% (77/526) of stroke patients received CSC-specific care and 18% (35/193) of trauma patients received surgery within 48 hours at a Level 1 trauma center. The difference was not statistically significant (OR, 0.77; 95% CI, 0.5 to 1.2).

Comparative analyses of data for 643 patients who were transported directly to a single PSC for treatment and 209 SAST bypass patients treated at the CSC revealed the potential benefit in the bypass triage strategy. CSC patients experienced significantly higher rates of major complications and fatal/debilitating intracerebral hemorrhage (Table 2), which were immediately treatable at the CSC as opposed to transferring a patient from the PSC to a CSC for treatment.

Table 2. Comparative Analyses of PSC and CSC Care

	Direct to PSC	SAST Bypass to CSC	OR; 95% CI	p Value
Average age (years)	70.6	72.7	—	—
Average length of stay (days)	5.5	6.0	—	—
Major complications	13%	34%	2.54; 1.78 to 3.62	<0.0001
Fatal or debilitating intracerebral hemorrhage	0.6%	9.6%	15.38; 5.2 to 45.5	<0.0001

CSC=comprehensive stroke center; PSC=primary stroke center; SAST=severe stroke adjusted triage.

The results indicate the potential benefit of the SAST bypass system. In-field identification of patients with severe stroke-like symptoms enables these patients to receive prompt treatment available at a CSC.

Molecular Imaging of Thrombosis and Thrombolysis

Written by Brian Hoyle

Francesco Blasi, PharmD, PhD, Martinos Center for Biomedical Imaging, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, USA, described the use of a novel probe in the positron emission tomography (PET) molecular imaging of thrombosis and thrombolysis *in vivo*.

Diseases including stroke, coronary artery disease, pulmonary embolism, and deep vein thrombosis are often triggered by the formation of a thrombus. Noninvasive assessment of thrombosis is crucial in diagnoses and to monitor disease progression. In seeking to develop a thrombus-specific imaging tool, Dr. Blasi and colleagues exploited fibrin as a target (Table 1).

Table 1. Fibrin Targeting for Thrombus Imaging

Attributes of Fibrin
<ul style="list-style-type: none"> ■ High sensitivity: present in all thrombi ■ High specificity: high levels in clots, but not in circulating blood ■ Small fibrin-specific peptides available; they have low affinity for fibrinogen and plasma proteins (low blood background) ■ PET and magnetic resonance probes based on fibrin-binding peptides can be made

PET=positron emission tomography.

In this study, a fibrin-specific probe labeled with ⁶⁴Cu was used. Fibrin-binding probe 7 (FBP7) has high affinity for fibrin, is metabolically stable, has a short half-life of 18 minutes (rapid clearance from blood) and a favorable biodistribution. The *in vivo* prowess of FBP7 was evaluated using rat models of crush-induced mural thrombosis and occlusive embolic stroke. PET and computed tomography (CT) imaging were performed following intravenous administration of FBP7. The stroke model also included