NIHSS applied to cerebral neurological dive injuries as a tool for dive injury severity stratification.

P. HOLCK¹, R. W. HUNTER²

¹Department of Public Health Sciences and Epidemiology, John A. Burns School of Medicine, University of Hawaii, Honolulu, HI 96822, ²Kaiser Permanente, Honolulu, HI 96822


Holck P, Hunter RW. NIHSS applied to cerebral neurological dive injuries as a tool for dive injury severity stratification. UHM 2006; 33(4):271-280. Background: Evaluation via National Institutes of Health Stroke Scale (NIHSS) upon presentation in hospital triage following ischemic stroke is predictive of recovery or progression to neurological deficits. Cerebral injuries sustained while diving have symptoms similar to stroke. Applying the NIHSS to dive injuries may successfully summarize neurological dive injuries, providing a standardized tool for study of dive injury data. Methods: We retrospectively determined NIHSS scores for a diverse population of 192 divers presenting to the University of Hawaii recompression chamber from 1983-2002, both prior to initial treatment and after all treatment. Spinal and vestibular decompression sickness cases were excluded. Results: The performance of the NIHSS among this diving population was similar to its performance as an accepted tool in evaluation of ischemic stroke, although results are influenced by the abundance of mild injury cases in the data set. The estimated C-statistic with NIHSS predicting no observable deficit was 0.88, and predicting post NIHSS of 0-1 was 0.85 (vs. 0.86 when applied to stroke). Sensitivity for predicting recovery (NIHSS 0-1) at discharge was 0.99 (vs. 0.97 for stroke). Conclusions: The NIHSS applied to cerebral dive injuries has adequate predictive ability and correlates with other measures of dive injuries, while providing a standardized, more graduated scale. The NIHSS may be useful as a standardized measurement for evaluation of treatment regimens and adjunctive therapy for diving injuries.

INTRODUCTION

The diving-research community has yet to identify an appropriate, validated measurement scale or scoring tool which limits subjectivity while providing sufficient graduation to distinguish differences in CNS dive injuries. Commendable efforts include among others those by Holley, Shupak, Ball, Kelleher, Boussuges, re-evaluation of the Boussuges system by Pitkin, U.S. Navy, and the DAN recreational diving accident reporting form. While local acceptance of various scale systems exists, there has yet to be global acceptance of any single scoring tool. Many of these scoring tools have only been applied to spinal Decompression Sickness (DCS), Cerebral Arterial Gas Embolism (CAGE), or cerebral DCS, and have been used in only one or a limited number of studies. Lack of a standardized scoring tool has hampered research and collaboration in this growing field of research. Among the scoring systems developed for decompression illness (5, 6, 7, 22, 9), none meet the requirements of providing: 1) a universally applicable system for all forms of Decompression Illness (DCI); 2) a numerical severity index at presentation; 3) a numerical index of progress and recovery; 4) a methodology for comparing different therapies in different diver populations” (Holley (3)).
Similarities of dive injuries to other neurological injuries may permit scoring tools used to evaluate cerebrovascular injuries to be applied to DCI. The neurological injuries sustained while diving may be analogous to sudden and severe thrombotic stroke and multiple infarct strokes (1). Arterial Gas Embolism (AGE/CAGE) classically produces cerebral cortical lesions similar to thromboembolic stroke (2). Cerebral DCS involves de novo bubble formation in tissues giving multi-focal cerebral involvement (1, 19).

Motivated by these similarities between cerebral DCI and stroke, we investigated the National Institutes of Health Stroke Scale (NIHSS) used as a stroke research scoring tool and applied it to a large database of dive injury cases to evaluate its potential to help further research of DCI by use of a historical, standardized, and validated tool. In part because the NIHSS has proven effective and popular in the evaluation and study of ischemic stroke (using a graded neurological 11-point examination rating speech and language, cognition, visual field defects, motor and sensory impairments, and ataxia), the application of this scoring system to DCI is worthy of evaluation. We examine the feasibility of assigning NIHSS scores to cerebral DCI patients, calculate the association of NIHSS scores with discharge functional outcome scores, and investigate the association of initial NIHSS with post treatment NIHSS and functional outcome measures.

METHODS

This study investigates the application of the NIHSS tool to neurological injuries sustained while diving. The patient database at the Hyperbaric Treatment Center, University of Hawaii, John A. Burns School of Medicine (HTC) was searched for patients presenting between 1983 and 2002 with a final diagnosis or CAGE, spinal or cerebral DCI, or discharge diagnosis consistent with central nervous system injuries. Patient charts were each reviewed and scored by a single reviewer (medical resident) within a 30 day period to avoid inter-rater variability and reduce temporal scoring shifts. The initial twenty charts reviewed were subsequently rescored after all charts had been reviewed and scored, and no differences between initial score and subsequent score were found.

Exclusion criteria included patients diagnosed with type 1 DCI or spinal DCI, patients treated at other facilities prior to being forwarded to HTC, and iatrogenic cases. Patients with vestibular symptoms only were excluded (4) as these symptoms are not assessed by the NIHSS. Note these symptoms are also not assessed by common existing severity indices (5, 6, 7, 8, 9) and such patients are typically excluded from analysis. No patients were excluded due to either time from onset of injury or age (although we performed sub analyses excluding those under 18 years of age). Of note, in most stroke studies presentation is limited to 23 hours since event, and age is restricted to 18-64.

Patient NIHSS scores were calculated based on information contained in the chart treatment notes. Scores were determined corresponding to patient status at initial presentation for treatment at the HTC, following the first treatment, and at discharge from treatment. If no annotations applicable to a component of the NIHSS were made in the initial evaluation/treatment by the physician, the tender notes, or dictation, then the component was scored as zero (normal). Patients with pre-existing medical conditions (e.g. neurological deficits from remote trauma, multiple sclerosis) were scored on change from pre-diving state.

While the reviewer was not rigorously blinded, the scoring at each timepoint for a patient was performed separately. Furthermore, a final
functional outcome score defined by Smerz and previously determined by an independent reviewer (10) was added to the database only after all NIHSS scores had been calculated, in an effort to avoid other assessments biasing the reviewer’s NIHSS assessment. This functional outcome score (a measure of residual sequela) had been determined by a HTC investigator (during the retrospective review of patients) for the patient at time of discharge, and was based upon subjective or objective findings and function (the ability to conduct activities of daily living), with values ranging from 0 to 4 (Table 1). Other data extracted from patient records included age, sex, number of treatments and the final diagnosis as previously determined (i.e. CAGE, cerebral DCS, or spinal DCS).

Table 1. Functional Outcome Scores based on Altered Daily Living (ADL).

<table>
<thead>
<tr>
<th>Characteristic Measured</th>
<th>NIHSS</th>
<th>8-point NIHSS</th>
<th>5-point NIHSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOC, Commands, Questions</td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Best Gaze</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Visual Field</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Facial Palsy</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motor RA, RL</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Motor LA, LL</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Ataxia</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensory</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aphasia</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Neglect</td>
<td>x</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. NIHSS score components

As no gold standard exists for evaluating dive injuries, there is no ideal scale to which the NIHSS results can be compared in order to assess its adequacy. However it seems reasonable that a good scale, in addition to measuring components of dive injuries that are clinically reasonable and comprehensive should a) be consistent in so much as scores calculated on presentation should correlate with scores calculated on discharge; b) be at least somewhat consistent with existing currently used measurements (e.g. functional deficit measures). We therefore evaluated the NIHSS scale utilizing multiple post treatment outcomes: a patient’s final NIHSS value, and a functional outcome score, and simplified versions of these outcomes by creating dichotomous variables: final NIHSS score of 0 or 1 indicating resolution of illness, vs. scores of 2 or greater; and functional score of 0 vs. 1 or greater (no objective deficit vs. objective deficit).

Because NIHSS scores are highly skewed and the dataset contained a large number of identical values (discrete scores with the majority of scores being zero, one, or two), we used Pearson correlation of the log transform (adding 1) of NIHSS scores as a measurement of pre and post score correlation. To assess the predictive ability of the NIHSS scoring system with a binary outcome (functional vs. not
functional, defined by post treatment residual score or post treatment NIHSS score) we calculated sensitivity and specificity, positive and negative predictive values, and C-statistics. The C-statistic measures the area under the Receiver-Operator Curve, and thus ranges from zero to one. It indicates the percent of all possible pairs of pre and post observations in which the model assigns a higher probability to the correct outcome than to an incorrect outcome), via both a model-based approach (logistic) and via a selected cutoff value. All statistical analysis was performed using R 2.10 statistical package (13).

RESULTS

Between 1983 and 2002 a total of 1,193 patients presented to the Hyperbaric Treatment Center of the University of Hawaii, of which 575 were assessed (by a single senior dive medicine physician prior to initiation of this study) as having sustained injury consistent with cerebral DCS, CAGE (cerebral arterial gas embolism), or spinal DCS. This study focused on the subset of 192 patients diagnosed with cerebral DCI, 107 with cerebral DCS, and 85 patients diagnosed with CAGE (n=192).

Initial NIHSS scores ranged from 0 to 42, with a score at presentation of zero recorded for more than half of the patients (110 of 193), 38 patients scored one, 36 patients scored between two and 10, and 8 patients scored above 10. Final score distribution of NIHSS and other outcome measures is presented in Table 2. Patients with a final score of zero often presented with symptoms limited to headache, vertigo and/or slightly abnormal sensation in a neurological exam. Final NIHSS score provided a reasonably similar (albeit more graduated) assessment to that specified by an independently scored final functional outcome score (Table 3). While NIHSS does not consider functional deficiencies, the functional outcome score subjectively evaluates these factors, and is perhaps more likely to assign higher scores to patients objectively fully recovered but with lingering subjective residuals. Pearson correlation of these two outcome measures (using log of final NIHSS) was 0.69.

As can be seen in Figure 1, eight patients presented with severe symptoms, having NIHSS score greater than 12. Three of these eight patients showed no improvement, one showed some improvement, and the remaining four obtained complete or near-complete recovery. Two of these four showing remarkable recovery were under the age of 18 (age 13 and 14).

In addition to these two children, data on seven others under age 18 were extracted. Their initial NIHSS scores were: zero (n=5), one (n=1), and four (n=1). All nine patients under the age of 18 showed no or only minor subjective symptoms following treatment (no objective residual, post NIHSS score of zero for all). Because the effects of DCI are not yet well understood or studied among children (14) and because these two children showed no residual effects, we analyzed the data both including all children, and again separately excluding all children.

<table>
<thead>
<tr>
<th>Final Scores</th>
<th>Functional outcome:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Observable Deficit</td>
</tr>
<tr>
<td>NIHSS</td>
<td>0</td>
</tr>
<tr>
<td>TOTAL</td>
<td>151</td>
</tr>
<tr>
<td>0-1</td>
<td>180</td>
</tr>
<tr>
<td>2-4</td>
<td>8</td>
</tr>
<tr>
<td>5-9</td>
<td>1</td>
</tr>
<tr>
<td>10+</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 3
We examined agreement of initial NIHSS scores to several indicators of outcome; NIHSS final score, residual deficit score (functional outcome score values 0-4), any observable residual deficit, and a binary outcome indicating resolution of illness (final NIHSS score of 0 or 1).

Among the 184 patients presenting with less severe symptoms (NIHSS score of 7 or less), all but 10 had a full or near full recovery (no objective deficit), and all but seven had full or nearly full recovery as measured by final NIHSS score of zero or one.

Initial and final NIHSS scores are shown in Figure 1, and indicate that nearly all patients improved from treatment. Pearson correlation of the (log +1) initial NIHSS score and final NIHSS score was 0.60. Excluding the 110 patients who presented with an NIHSS score of zero had no effect on this correlation. Further removing the nine children from the study resulted in a correlation of 0.70, largely due to the removal of the two children presenting with very poor initial scores who none-the-less demonstrated complete recovery.

We observed similar results when comparing initial NIHSS values to the less graduated final functional outcome scores (5 point subjective scale): Pearson correlations were 0.52 with all patients included, and 0.43 when patients with initial NIHSS scores of zero were excluded. When the nine patients under age 18 were excluded, these correlations were 0.55 and 0.48 respectively.

The ability of initial NIHSS score to predict a simplified categorization of outcome (absence or presence of observable deficit) was assessed by fitting a simple logistic regression model and examining the corresponding C-statistic. With all 192 patients included, the corresponding C-statistic was 0.88, and when limited only to patients who presented with some indication of symptoms (non-zero NIHSS score), the C-statistic was 0.69 (0.70 when children removed from analysis). Not surprisingly, initial NIHSS score was also found to be a highly significant predictor of residual deficit in this simple logistic model (p<.01).

Positive predicted value (PPV), negative predictive value (NPV), sensitivity, and specificity are other common measures of association that can be calculated by constructing 2 by 2 tables, which require creating a binary predicted outcome from this simple logistic model to compare to the observed binary outcome (presence or absence of observable deficit). We defined a positive predicted outcome if the model predicted probability of resolution of illness was greater than one half, which yielded a PPV of 80%, NPV of 60%, sensitivity of 99%, and specificity of 8%. Increasing the chosen cutoff probability value (50%) slightly improves specificity at the expense of a small decline in sensitivity.

We calculated these same measures of association utilizing a dichotomization of initial NIHSS score based on a cutoff score of one or less; the resulting PPV, NPV, sensitivity, and specificity for an outcome of presence or
Finally we evaluated the predictive ability of NIHSS scoring when the resolution of illness is measured by a dichotomized final NIHSS score (final NIHSS score less than or equal to one versus greater than one) rather than by an outcome based on observable deficit or functional outcome scale. When considering all patients, the corresponding C-statistic was 0.85; when limited to only patients with an initial NIHSS of greater than zero, the C-statistic was 0.89 (0.91 when patients under age 18 are removed). These results compare to that observed in applying the NIHSS to stroke data (C-statistic of 0.86) (15). Fitting a simple logistic model to predict dichotomized final NIHSS score and using a predicted probability cutoff of 50%, the PPV, NPV, sensitivity and specificity were 95%, 60%, 99% (compared to 0.97 in stroke study data (15)), and 25% respectively. Again as expected the simple model indicated initial NIHSS to be a significant predictor of dichotomized final NIHSS (p<.01).

NIHSS scores based on eight of the 11 factors (NIHSS-8), and five of the factors (NIHSS-5) provide simplified tools to assess DCI with acceptable degradations in predictive ability. The correlations of these two modified measures with the original NIHSS score are 0.85 and 0.83 respectively, while correlations with final NIHSS score were 0.57 and 0.56, rising slightly to 0.64 (both 5 and 8 point scales) when children were excluded.

Measuring the predictive capabilities of these modified measurement tools we found them only slightly less capable. When outcome is assessed by presence or absence of observable deficit the resulting C-statistics were 0.77, 0.64 (all patients, and all patients presenting with non-zero scores) for the eight-point scale, and 0.73, 0.63 for the five-point scale, slightly less than observed using the original NIHSS measure. Modifications to the measurement tool do not affect PPV, NPV, sensitivity or specificity when a cut-off probability of 50% is used (correctly and incorrectly predicted patient outcomes are unchanged).

**DISCUSSION**

Decompression illness encompasses a variety of manifestations ranging from paresthesias to severe neurological deficits. Traditionally, DCI has been classified into decompression sickness (DCS) when the source of the bubbles was presumed to be from the liberation of dissolved inert gas during decompression, and as arterial gas embolism (AGE) when the bubble source is thought to result from pulmonary barotrauma (2, 4, 11, 16, 17, 18, 19, 20). DCS has been further subdivided into type I, typically mild symptoms with fatigue, pain in muscles/joints or skin, or type II, more serious manifestations afflicting the central nervous system, inner ear, and lung (18, 1, 20, 21). The syndromes of AGE (CAGE) and cerebral DCS may be clinically indistinguishable and develop simultaneously in some patients. (1, 29), and the distinction may have little clinical utility (21).

In order to effectively study, evaluate, and treat neurological DCI, a validated scoring tool suitable for both initial assessment and post-treatment outcome adequate for statistical analysis of treatment regimens is needed. Multiple scoring tools have been used to evaluate CNS diving injuries, however most have marked limitations. Dive studies typically have been small and have utilized severity measures defined by the individual investigator. While the few large studies often have common areas of assessment, the most often used endpoint is simply complete recovery. Pre and post treatment evaluation scoring tools often differ, and thus no internal standard exists. Initial severities and residual
outcomes have been measured using a functional outcome score differing from the initial neurological score. Studies vary in addressing CAGE only, cerebral DCS only, and including or excluding spinal injuries (17, 5, 9, 7, 8, 6). Subjectivity, in instruments used to evaluate dive injury was noted by Kelleher et al who stated that previously used severity scales “prove difficult because the terms numbness and paresthesias, weakness and paralysis are inconsistently applied” (9). Scoring of severity use in most studies relies on evaluating sensory manifestations (paraesthesia to numbness) and motor manifestations (weakness to paralysis) of disease (5, 22). The subjective and non-standardized characteristics of these methods result in inconsistent evaluation and classification of patient conditions across studies, if not also across study evaluators. Furthermore, as noted by Neuman, “In victims who do not die suddenly, the signs and symptoms of CAGE can be quite varied…and more subtle signs of the gas embolism may remain, such as abnormalities of the mental status examination” (18). Commonly used measures in DCI research include level of consciousness, motor function, sensory function, coordination or gait, and urinary incontinence; however they typically neglect more subtle abnormalities of mental status exam (5, 6, 7, 8, 9).

Given the growth of hyperbaric medicine, the use of newer adjunctive treatment modalities, the employment of a variety of different treatment regimens such as the US Navy and Royal Navy tables, the Catalina table, the Hawaiian deep tables, Comex tables, and tables adapted for monoplace chambers, a system for evaluation and outcome determinations needs to be adopted. The current use of different scoring systems between treatment facilities at the least complicates, if not prevents comparison of treatment success or outcomes.

In 1983 investigators with the National Institute of Neurological Diseases and Stroke developed a standardized neurological screening exam for acute stroke evaluation in their tissue-plasminogen activator trials. The National Institutes of Health Stroke Scale (NIHSS) is a graded neurological 11-point examination rating speech and language, cognition, visual field defects, motor and sensory impairments, and ataxia and is now the standard clinical assessment tool used in recent interventional trials (2, 11, 15). The NIHSS is now the standard used by researchers for defining stroke severity and measuring the effectiveness of intervention (23, 24, 25, 26, 28). It provides a standardized method of collecting abnormality of mental status features, and with the exception of urinary incontinence, also includes measures common in current DCI research. However it also assesses vision, oculomotor, facial nerves, language, dysarthria and neglect, thus encompassing components of CNS injury which may not be annotated when utilizing common DCI exam components, but which may have significant functional impairment.

The NIHSS has been shown to have high inter-rater reliability among neurologists, ED physicians, house officers, nurses, EMS personnel, and stroke researchers (2, 11). Tirschwell et al suggested simplifying the NIHSS for the pre-hospital settings by using an 8 item or a five item NIHSS, in an effort to permit briefer and easier administration, and demonstrated good agreement between the original NIHSS scales and these reduced scales (23). The use of the NIHSS has been validated for the rapid assessment of severe neurological deficits, demonstrating prognostic value in outcome (2, 23), and is used widely in stroke outcome evaluation (25, 4, 15, 23). The initial NIHSS has been shown to strongly predict the likelihood of a patient’s recovery after ischemic stroke (26, 15, 24, 27), independent of etiology (lacunar, subcortical or cortical) (26).

The intent of this study was to suggest an appropriate scale to classify dive injuries,
and to explore whether the NIHSS could be applied to cerebral DCI and serve as an effective evaluation tool to assess treatment and recovery of cerebral DCI. Assessing the appropriateness of any measure of cerebral DCI outcome is difficult, as no gold standard measurement exists. Given this limitation, we have demonstrated the NIHSS scale is in concordance with simple or more subjective measures of cerebral DCI outcome (presence or absence of observable residual effect, and functional outcome quantification of that residual effect). Additionally we demonstrated that initial NIHSS score is indicative of final outcome (albeit utilizing data with a large majority of mild cases), be that outcome measured by the NIHSS scale, functional outcome score, or presence/absence of residual effect. An effective tool for evaluation of DCI should also apply the same assessment criterion, both upon presentation and following treatment.

Our results of measures of dichotomized association (PPV, C-statistic, etc.) are adequate but not outstanding. For examining these associations we prefer to utilize the C-statistic as it gives a comprehensive measure that does not rely on chosen cutoff values. While our data consist largely of mild injuries, calculated C-statistics were still at least adequate, and support the premise that NIHSS is a non-subjective measure that could prove capable, as it has been shown to do for stroke patients. Modification of the NIHSS to include urinary incontinence could be easily implemented and will be utilized in future work exploring the NIHSS applied to spinal injury data. Little change occurred when performance was measured with a NIHSS 8-point or 5-point scale, yet time and effort saved by these measures is also minimal.

Results of this research include several limitations. NIHSS measures neurological deficiencies, but does not attempt to measure functional deficiencies. While presence of deficiencies of one type usually goes hand-in-hand with deficiencies of the other type, exceptions occur. As illustrated by individuals with poor functional outcome score and adequate NIHSS score, the NIHSS score can indicate near-full recovery while modest functional deficiencies remain. Additionally, NIHSS does not document urinary incontinence (significant and common functional impairment of spinal DCS). The importance of either of these aspects of the NIHSS scale to providing a consistent assessment of DCI (including spinal DCS) outcome is unclear.

Although this analysis utilized a reasonably large database (n=192), nearly all of the dive injuries included were mild at presentation and mild post treatment. Conversely the application of this instrument is likely to be most useful to classify moderate and severe injury, and to evaluate treatment applied to these patients. Results of our simple analyses have been most influenced by the mild class injury of the majority of our data. The lack of an existing gold standard to which compare results presents difficulties in making a sufficient assessment of the tools adequacy. To better assess this assumption will require application of the NIHSS to greater numbers of moderate and severe injuries, and an examination of its components.

We have applied NIHSS score to a large database, and investigated its adequacy as a measure through the use of basic statistics. Without a gold standard for comparison of outcome, it is difficult to assess using simple measures of association the relative adequacy or superiority of this scoring tool. However because this tool has seen wide-spread application and validation in a related field, and does perform adequately in most of the basic statistical measures investigated and for the limited data to which it was applied, we believe it to be a good candidate to assist in standardization of dive injury research. Our
simple analysis neglects to include many known risk factors for dive injury outcome severity; yet our purpose was not to identify such risk factors or evaluate treatment, but rather to put forth a scoring tool that may permit more rigorous and standardized assessment of risk factors. We anticipate application of the NIHSS to future analysis of our data to explore treatment efficacy and risk factors, as well as to evaluate application in spinal injury data.

Given the small number of injuries worldwide, the diving research community needs an objective injury-severity scale to evaluate and compare optimal and adjunctive therapies for dysbaric injuries. The NIHSS is a validated scoring tool that has become a standard for assessing injuries that are in many ways similar to injuries observed in cerebral DCI. In applying this scale to a large data base of non-spinal DCI, we found the scoring tool to provide assessments consistent with more subjective and less graduated measures, and to be internally consistent (pre treatment scores compared to post treatment scores). It is our hope that use of the NIHSS will improve the currently heterogeneous measurements and presentations of diving injury data by permitting standardized comparisons of dive injury etiologies, severity, and intervals to treatment at multiple study sites. Similar to the stroke field where data were skewed due to mild injuries, the most effective treatments need to be studied in a stratified manner to reduce the degradation of results by the less severely effected injuries.

ACKNOWLEDGMENTS

We are indebted to Dr Richard Smerz of the Hyperbaric Treatment Center for his encouragement during the research and his critical expertise and professional knowledge in reviewing this article.

REFERENCES

6. Pitkin AD, Benton PJ, Broome JR. Outcome after treatment of neurological decompression illness is predicted by a published clinical scoring system. Aviat Space Environ Med. 1999 May;70(5):517-521
15. DeGraba TJ, Hallenbeck JM, Pettigrew KD, Dutka

Rubicon Research Repository (http://archive.rubicon-foundation.org)
28. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Generalized efficacy of t-PA for acute stroke; subgroup analysis of the NINDS t-PA stroke trial