Predicting Mortality in Spontaneous Intracerebral Hemorrhage
Can Modification to Original Score Improve the Prediction?
Daniel Agustin Godoy, MD; Gustavo Piñero, MD; Mario Di Napoli, MD

Background and Purpose—A clinical grading scale for intracerebral hemorrhage (ICH), formally ICH score, was recently developed showing to predict 30-day mortality in a simple and reliable manner. The aim of the present study was to validate the original ICH (oICH) score in an independent cohort of patients from a developing country assessing 30-day mortality and 6-month functional outcome and whether its modifications can improve prediction.

Methods—Consecutive patients admitted with acute ICH between January 1, 2003, and July 31, 2004, were prospectively included. oICH score was applied and 2 modified ICH (mICH) scores were created with the same variables, except localization, of the oICH score but with different cutoff values. Outcome was assessed as 30-day mortality and 6-month good outcome (Glasgow Outcome Scale [GOS] 4 to 5).

Results—A total of 153 patients were included during study period. Thirty-day mortality rate was 34.6% (n=53), and 59 patients (38.6%) had good functional outcome (GOS 4 to 5) at 6 months. The oICH and mICH scores predicted mortality equally well. According to Youden’s index (J), the oICH score was a reliable predictor for mortality (J=0.59) but less reliable for predicting good outcome (J=0.54). The mICH scores were equal in predicting mortality but better for predicting good outcome than the oICH score (J=0.60).

Conclusions—oICH score also confirms its validity in a socially and culturally different population. Modifications of oICH do not improve its 30-day mortality prediction but improve its ability to predict good functional outcome at 6 months. (Stroke. 2006;37:1038-1044.)

Key Words: intracerebral hemorrhage ■ outcome ■ prognosis ■ risk factors ■ sensitivity and specificity

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ααωpeutaneous intracerebral hemorrhage (ICH) is the deadliest, most disabling, and least treatable form of stroke despite progression in medical knowledge.1,2 No therapy has shown a proven benefit in improving outcome after spontaneous ICH (SICH), reducing either mortality or the burden of a long-term disability;3 blood pressure reduction, osmotherapy, and ultra-

from a developing country and whether its modifications can improve its predictive value.

### Subjects and Methods

We studied all patients admitted to the intensive care units of Sanatorio Junin, Junin, and Hospital Municipal Leonidas Lucero, Bahia Blanca, Buenos Aires State, Argentina, with a diagnosis of SICH within 24 hours after stroke onset, between January 1, 2003, and July 31, 2004. These primary referred centers have no specific selection criteria for the admission of SICH patients. Informed consent was obtained from all patients included or their legal representative. Our institutional committee approved the study.

**SICH was defined as a neurological deficit documented by a brain computed tomography (CT) indicating the presence of an ICH in absence of trauma or surgery.**

Admissions fulfilling the following criteria were excluded: patients with hemorrhage secondarily to brain tumors, to trauma, to hemorrhagic transformation of cerebral infarct, or to aneurysmal or vascular malformation rupture. Patients evaluated >24 hours after symptom onset together with patients referred directly from another hospital after diagnosis and initial evaluation were also excluded. All patients were screened according to a strict protocol consisting of a complete medical history, a full neurological examination, standardized blood tests, and ≥1, usually 2, CT scans of the brain within 24 hours. Surgical criteria were established according to the algorithm of decision in force to authors’ institutions based on the recommendations of the Stroke Council of the American Heart Association. The Glasgow Coma Scale (GCS) assessed initial stroke severity, and it was determined after initial evaluation and resuscitation. The presence of comorbidities was evaluated according to the Acute Physiology And Chronic Health Evaluation II (APACHE II) score guidelines.

The following data were prospectively collected in a computerized database: age, sex, recognized risk factors for SICH (arterial hypertension, alcohol intake, smoking, diabetes mellitus, serum cholesterol levels, concomitant anticoagulant and antiplatelet treatment), presence of comorbidities registered according to APACHE II system, glucose levels at admission and 72 hours after stroke onset, systolic, diastolic, and pulse blood pressure (defined as systolic blood pressure minus diastolic blood pressure), GCS scores, and CT scan findings. Neuroradiological findings were determined in the initial CT scan and classified according to localization (supratentorial or infratentorial), site of SICH (basal ganglia, thalamic, lobar, pontine, or cerebellar), volume of hematoma (according to ABC/2 method, in which A is the greatest diameter on the largest hemorrhage slice, B is the diameter perpendicular to A, and C is the approximate number of axial slices with hemorrhage multiplied by the slice thickness), midline shift (the displacement of the septum pellucidum across midline, using as reference a perpendicular line connecting the anterior and posterior insertions of the cerebral falx at the level of the lateral and third ventricle), intraventricular extension of hemorrhage (graded according to Graeb’s scale), and presence of hydrocephalus (graded according to Diringer’s method). The presence of comorbidities was assessed as mortality at 30 days after SICH. Six-month functional outcome was assessed using the Glasgow Outcome Scale (GOS), categorized in good (GOS 4 to 5) and worse (GOS 2 to 3) functional outcome. For patients in whom 30-day outcome was not available from medical records, follow-up data were obtained from follow-up visits, direct contact with the patient or patient’s family or physician, and mortality records, if not available.
necessary. We were able to obtain current information on all included patients.

The oICH score was applied to our prospective cohort using identical cutoff values and points for age, GCS, ICH volume, IVH, and infratentorial origin as by Hemphill et al. Two modified ICH (mICH) scores were created (mICH-A score and mICH-B score) after a revision of the literature using the same ICH variables with the exception of the infratentorial origin item because it has not a sure prognostic value. Four variables were categorized and recoded to permit calculation of the mICH scores. These calculations are summarized in Table 1.

Statistical Analysis
Continuous variables are described as mean±SD or median values with 25th and 75th percentiles, according to manner of distribution. Values of \( P<0.05 \) were considered statistically significant. Cuzick’s trend test was used to assess association of the scores with 30-day mortality and 6-month functional outcome. To establish the predictive value of the oICH and mICH scores on mortality and functional outcome, the area under the receiver operating characteristic (ROC) curves were directly calculated by a nonparametric method for each ICH score. CIs were constructed using DeLong’s variance estimate. Different cutoff values of the o- and mICH scores were used to identify the best Youden’s index \( (J) \) of diagnostic test for a comparison among the 3 ICH scores. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of different ICH scores were computed using the cutoff values that generated the best \( J \). To be confident of our results, we calculated the statistical power basing on a model 2 error assumption, which means that variables entered into the mICH scores will serve to reduce the error term in the significance test and therefore were included in the power analysis. The power analysis focused on the increment for the mICH scores over and above any previous variables included in the scores (that is, 4 variables yielding an increment of 0.10). This effect was selected as the smallest effect that would be important to detect, in the sense that any smaller effect would not be of clinical or substantive significance. It is also assumed that this effect size is reasonable. With the given sample size of 150 and \( \alpha \) set at 0.05, the study has a power of 0.85.

Results
Baseline Characteristics
Between January 1, 2003, and July 31, 2004, 329 patients with clinical signs attributable to SICH were identified. After comprehensive evaluation, 153 were included in the present study (Figure 1). Baseline characteristics of patients are summarized in Table 2. The mean±SD age was 66±12 years (range 57 to 94 years). Twenty-four patients (15.7%) were 80 years of age. Median GCS score on admission was 11 (25th to 75th interquartile range 7 to 14). Mean ICH volume on initial CT scan was 40.4±41.3 cm\(^3\) (range 5 to 201 cm\(^3\)). Mean pulse pressure on hospital arrival was 80±30 mm Hg (range 20 to 200 mm Hg). Median serum glucose was 118 mg/dL (25th to 75th interquartile range 100 to 155 mg/dL).

Warfarin use was registered in only 2 patients (1.3%), whereas 7 patients (4.6%) received aspirin (325 mg per day). Thirty-eight (24.8%) patients underwent a surgical procedure for removing the hematoma: 3 patients with cerebellar hemorrhage, 17 patients with moderate or large lobar hemorrhage who were clinically deteriorating, 17 patients with putaminal hemorrhage with \( ≥1 \) surgical indications, and 1 patient with thalamic hemorrhage.

Thirty-Day Mortality
Overall, 30-day mortality was 34.6% (n=53). The oICH score was an accurate predictor of outcome assessed as 30-day mortality. Thirty-day mortality rates for patients with oICH

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**Figure 1.** Study profile. Secondary hemorrhage includes hemorrhage secondary to brain tumors \( (n=7) \), to trauma \( (n=77) \), to hemorrhagic transformation of cerebral infarct \( (n=12) \), to aneurysmal or vascular malformation rupture \( (n=47) \). Other causes include patients evaluated >24 hours after symptom onset \( (n=12) \) or patients referred directly from another hospital after diagnosis and initial evaluation \( (n=21) \).
scores of 1, 2, 3, and 4 were 2.9%, 30.8%, 61.1%, and 88.2%, respectively, showing a progressive increase in 30-day mortality ($P < 0.0001$; Cuzick’s test for trend). No patient with an oICH score of 0 died, whereas all patients with an oICH score of 5 died. In both modified scores, each increase was associated with an increase in 30-day mortality ($P < 0.0001$).

**Six-Month Functional Outcome**

At 6 months after SICH, 59 (38.6%) were dead, 59 had good outcome (GOS 4 to 5), and 35 (22.8%) were alive with significant impairment (GOS 2 to 3). The distribution of patients with good outcome, bad outcome, or death against increasing points on the oICH score at 6 months is shown in Figure 2a. Mortality rates became high with a very low rate of good outcome when the oICH score was >3. Figure 2b and 2c show the similar distribution of different outcomes against increasing points on the mICH scores. No evidence of good outcome was found for a score >6 in mICH-A score and for >5 in mICH-B score.

### TABLE 2. Demographic and Clinical Characteristics of 153 SICH Patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>30-Day Mortality, n (%)</th>
<th>6-Month Good Outcome, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>97 (63.4)</td>
<td>35 (36.08)</td>
</tr>
<tr>
<td>Female</td>
<td>56 (36.6)</td>
<td>18 (32.14)</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;50</td>
<td>22 (14.38)</td>
<td>7 (31.8)</td>
</tr>
<tr>
<td>50–64</td>
<td>42 (27.45)</td>
<td>16 (38.1)</td>
</tr>
<tr>
<td>≥65</td>
<td>89 (58.17)</td>
<td>30 (33.71)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>48 (31.37)</td>
<td>20 (41.67)</td>
</tr>
<tr>
<td>No</td>
<td>105 (68.63)</td>
<td>33 (31.43)</td>
</tr>
<tr>
<td>GCS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14–15</td>
<td>45 (29.41)</td>
<td>5 (11.1)</td>
</tr>
<tr>
<td>9–13</td>
<td>63 (41.18)</td>
<td>13 (20.63)</td>
</tr>
<tr>
<td>6–8</td>
<td>20 (13.07)</td>
<td>11 (55)</td>
</tr>
<tr>
<td>3–5</td>
<td>25 (16.34)</td>
<td>24 (96)</td>
</tr>
<tr>
<td>Localization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supratentorial</td>
<td>143 (93.46)</td>
<td>50 (34.97)</td>
</tr>
<tr>
<td>Infratentorial</td>
<td>10 (6.54)</td>
<td>3 (30)</td>
</tr>
<tr>
<td>Site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal ganglia</td>
<td>66 (43.14)</td>
<td>21 (31.82)</td>
</tr>
<tr>
<td>Thalamic</td>
<td>43 (28.1)</td>
<td>17 (39.53)</td>
</tr>
<tr>
<td>Lobar</td>
<td>32 (20.92)</td>
<td>11 (34.38)</td>
</tr>
<tr>
<td>Pontine</td>
<td>2 (1.31)</td>
<td>2 (100)</td>
</tr>
<tr>
<td>Cerebellar</td>
<td>8 (5.23)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (1.31)</td>
<td>1 (50)</td>
</tr>
<tr>
<td>ICH Volume, cm$^3$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
<td>90 (59.6)</td>
<td>15 (16.67)</td>
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<tr>
<td>30–50</td>
<td>24 (15.89)</td>
<td>11 (45.83)</td>
</tr>
<tr>
<td>&gt;50</td>
<td>37 (24.5)</td>
<td>26 (70.27)</td>
</tr>
<tr>
<td>IVH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>73 (47.71)</td>
<td>35 (47.95)</td>
</tr>
<tr>
<td>No</td>
<td>80 (52.29)</td>
<td>18 (22.5)</td>
</tr>
<tr>
<td>Graeb’s score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–4</td>
<td>33 (45.21)</td>
<td>15 (45.45)</td>
</tr>
<tr>
<td>5–8</td>
<td>34 (46.58)</td>
<td>16 (47.06)</td>
</tr>
<tr>
<td>≥9</td>
<td>6 (8.22)</td>
<td>4 (66.67)</td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>38 (24.84)</td>
<td>18 (47.37)</td>
</tr>
<tr>
<td>No</td>
<td>115 (75.16)</td>
<td>35 (30.43)</td>
</tr>
</tbody>
</table>

*Two missing values.*
Sensitivity and Specificity
Areas under ROC curves (Figure 3a) were 0.882 (95% CI, 0.830 to 0.934) for oICH score, 0.878 (95% CI, 0.824 to 0.931) for score A, and 0.869 (95% CI, 0.811 to 0.928) for score B, respectively, suggesting a comparable mortality risk prediction. However, mICH scores (score A 0.893, 95% CI, 0.844 to 0.941; score B 0.895, 95% CI, 0.847 to 0.943) showed a better prediction ($P = 0.0681$ for score A and $P = 0.0314$ for score B; DeLong’s variance estimate) of functional outcome at 6 months when compared with the oICH score (0.844, 95% CI, 0.781 to 0.907; Figure 3b). No differences were found in prediction of mortality between the oICH score and the 2 mICH scores. All ICH scores were substantially equally sensitive with a high NPV for mortality, whereas mICH-B score was more specific, with a high PPV for good outcome (Table 3). Different cutoff values of the 3 ICH scores were tested to generate the highest $J$ of diagnostic test; best results were obtained with any of the ICH scores but at different cutoff values. For the oICH score, the best prediction was obtained with a score of 2 for mortality and 1 for good outcome, whereas for score A, the best predictions were obtained with a score of 4 for mortality and 3 for good outcome, and for score B, with a score of 3 for mortality and good outcome (Table 3). According to $J$, the oICH score was a reliable predictor for mortality but less reliable for predicting good outcome. The mICH scores were equal in predicting mortality but better for predicting good outcome than the oICH score (Table 3).

Discussion
No clinical grading scales were entered in clinical standard evaluation of SICH patients, although they could improve the quality of clinical care permitting prognostication and treatment selection of SICH patients. Several prognostic models for SICH have been developed previously and validated; however, none of these models have been simplified into a standard clinical scale. Many are the causes that could have limited their use in routine clinical practice: the extensive time commitment, the necessity of a significant special training and statistical knowledge, and the use of complex...
al\textsuperscript{7} using a retrospective review of medical records. This grading scale has its selling points into its clear objective criteria, the strong predictive value for outcome, and the easy and quick determination by physicians without a special competence,\textsuperscript{16} providing a standard assessment tool to use in emergency room to evaluate SICH patients. The oICH score has been evaluated previously in 3 different cohorts of patients.\textsuperscript{18–22} In the present study, we confirm the predictive value of oICH score on 30-day mortality also in a population with a different economical, social, and cultural background using a prospective study design that overcomes the limitations of several previous studies.

Unfortunately at present, no similar information is available on the usefulness of the oICH score in predicting functional outcome.\textsuperscript{7} When the oICH score was applied to the present cohort, it had a fair prediction of good outcome. However, mICH scores showed a comparable mortality prediction but a significant better prediction of 6-month functional outcome. Specific elements of the mICH scores can explain these differences.

To grade age contribution in mICH scores calculation, we further categorized age and estimated the presence of comorbidities using APACHE II score system.\textsuperscript{24} This score is eligible because it was widely validated and used in the most of intensive care units around the world. Taking in account the presence of comorbidities, an estimate of elderly health status can be given in different cultural and socioeconomic populations. Economic difficulties can produce multiple disadvantages, particularly in elderly people, reducing the medical attention, the control of cardiovascular risk factors, and the quality of clinical care. Frequently, age constitutes a reason for the retirement of support, DNR orders, or for the delay in therapeutic interventions, such as mechanical ventilation, intracranial pressure monitoring, or surgery.\textsuperscript{8,29}

The GCS score is a standard neurological assessment tool that is reproducible and reliable, and it has been associated with SICH outcome in other prediction models.\textsuperscript{7,11,14,26,30,31} To grade GCS contribution, we categorized the division of the scale into 4 instead of 3 items assuming that the influence of level of consciousness on outcome is prominent regardless of other factors, and patients with GCS scores of 13 tend toward much worse outcome.\textsuperscript{32–34}

To grade SICH volume contribution, we categorized the division of the scale into 3 instead of 2 items assuming that SICH is not a single-phase event, the mechanisms of growth are not the same for the small, medium, and large hematomas,\textsuperscript{26} and rebleeding occurs in \( \approx 20\% \) to 38\% of cases\textsuperscript{35,36} with a neurological deterioration.\textsuperscript{3,37} ICH volume is consistently associated with outcome,\textsuperscript{26,30,31,38} and it is a surrogate marker of persistent and disabling neurological deficits. However, in the oICH score, its association with outcome was not as strong as some other predictors because other predictors such as low GCS score, advanced age, or IVH influenced outcome to a greater degree.\textsuperscript{7} Further clinical studies are needed to determine predictors of hemorrhage growth and its time relationship with other factors predicting outcome.

Undoubtedly, further characterization of the degree of IVH could provide additional prognostic information to prognosis.\textsuperscript{10} However, we believe that IVH is an ongoing process,
and it is difficult to predict intraventricular extension into the first hours after SICH.

Some limitations should be considered in the evaluation of our study. The proportion of infratentorial ICH is low (6.5%), especially compared with the cohort reported by Hemphil et al.,2 (20%) on which the oICH score was based. At the moment, there are no epidemiological population-based studies able to give the true incidence of infratentorial hemorrhage in our Argentinian study population. It is reasonable that some selection bias could exist related to cross-boundary medical care, case ascertainment, or tendency toward hospitalization in other hospitals or wards; nevertheless, oICH score keeps its predictive prognostic value.

In conclusion, the oICH score is a good predictor of 30-mortality and functional outcome, confirming its validity also in a different socioeconomic population. The inclusion of variables not included in oICH such as comorbidities or different grading of the same variables (GCS, IVH, age) does not improve mortality prediction, whereas it seems to have a better prediction of good outcome at 6 months with comparable 30-day mortality prediction. All 3 ICH scores are simple clinical grading scales. Nevertheless, the mICH scores may be preferred when good outcome is the primary target. As reliable predictors of mortality or good outcome, they could be useful in clinical research studies and standardization of clinical protocols.

References
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