National Institutes of Health Stroke Scale Item Profiles as Predictor of Patient Outcome

External Validation on Independent Trial Data

Azmil H. Abdul-Rahim, MRCP, MBChB; Rachael L. Fulton, PhD; Heidi Sucharew, PhD; Dawn Kleindorfer, MD; Pooja Khatri, MD; Joseph P. Broderick, MD; Kennedy R. Lees, MD; for the VISTA Collaborators*

Background and Purpose—National Institutes of Health Stroke Scale (NIHSS) item profiles that were recently proposed may prove useful both clinically and for research studies. We aimed to validate the NIHSS item profiles in an acute cohort.

Methods—We conducted a retrospective analysis on pooled data from randomized clinical trials. We applied the latent class analysis probabilities of profile membership developed from the derivation study to obtain symptom grouping, a-NIHSS item profiles. We implemented an independent latent class analysis to derive secondary symptom grouping, b-NIHSS item profiles. Validation was performed by assessing the associations with outcomes and evaluating both sets of NIHSS item profiles’ discrimination and calibration to the data. The outcomes evaluated included modified Rankin Scale (mRS; using the full distribution and dichotomized, mRS, 0–1) at day 90 and mortality by 90 days.

Results—We identified 10271 patients. Ordinal analysis of mRS confirmed increased odds of better outcome across the profiles in a stepwise manner, adjusted for age and thrombolysis treatment, for each set of NIHSS item profiles. Similar patterns were observed for mRS 0 to 1, and inverse patterns were seen for mortality. The c-statistics of a-NIHSS and b-NIHSS item profiles for mRS 0 to 1 were similar at 0.71 (95% confidence interval, 0.70–0.72) and for mortality, 0.74 (0.73–0.75) and 0.75 (0.73–0.76), respectively. Calibration was good.

Conclusions—These NIHSS item profiles identified using latent class analysis offer a reliable approach to capture the true response patterns that are associated with functional and outcome and mortality post stroke. This approach has the potential to enhance the clinical value of the overall NIHSS score. (Stroke. 2015;46:395-400. DOI: 10.1161/STROKEAHA.114.006837.)

Key Words: outcomes research ■ stroke

Baseline National Institutes of Health Stroke Scale (NIHSS) is well established as an independent predictor of outcome post stroke.1–3 In general, the use of overall NIHSS score considers the individual components that contribute to the score to be equal. Two patients who achieve the same total NIHSS may have contrasting clinical syndromes, one with loss of consciousness and the other with motor weakness. Approximately one third of patients who experience mild stroke (ie, baseline NIHSS, 0–5) are left with significant disability, suggesting that NIHSS is not adequate to predict disability among these patients.4,5 Using latent class analysis (LCA)6 on the 15 individual attributes of the retrospective NIHSS (rNIHSS), Sucharew et al7 identified 6 rNIHSS profiles that may be clinically useful for stroke prognostication. In particular, 2 profiles identifying mild strokes with equal median baseline rNIHSS of 5 showed widely disparate outcomes. These profiles could conceivably be used to estimate prognosis and to inform the design of future clinical trials.

The algorithm used to calculate rNIHSS has been described and validated previously.8,9 These profiles were generated on the Greater Cincinnati and Northern Kentucky Stroke Study population.7,10,11 It is likely that some discrepancies between retrospective and prospective scoring methods remain, thus limiting the study’s generalizability.

We aimed to validate the previously published rNIHSS item profiles7 as a predictor of patient outcome in a clinical trial cohort. We repeated the LCA6 on baseline prospectively obtained NIHSS acquired from the Virtual International
Stroke Trials Archive (VISTA)\textsuperscript{12} to assess any deviations in the response profiles found. This validation study sought to capture the relationship between the profiles of NIHSS items and the response patterns that are associated with both functional and neurological outcome and death.

**Methods**

**Data Source**

We conducted a retrospective analysis on pooled data from randomized clinical trials obtained from VISTA (http://www.vistacollaboration.org/).\textsuperscript{12} VISTA is a collaborative registry that collates and provides access to completed acute stroke trials’ data (from year 1998–2008), anonymized in relation to patients and trials’ identity, for novel exploratory analyses. It is worth noting that VISTA data do not include trials of thrombolysis therapy, per se, although thrombolysis was commonly used as standard therapy, where appropriate. All patients with stroke were treated as per institutional practice and stroke guidelines acceptable at the point of trial conduct. Conduct and reporting of our analysis are in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for cohort studies.\textsuperscript{13}

**Participants and Variables**

We selected patients who had been randomized to receive placebo or any drug now known to possess no confirmed action on stroke outcome. We included patients for whom we had baseline demographics and outcome information: individual components of the baseline NIHSS, age, sex, thrombolysis administration as standard of care, comorbidities, occurrence of adverse events, and serious adverse events, mortality by 90 days and modified Rankin Scale (mRS) at day 90.

**Statistical Methods**

We applied the probabilities of profile membership generated by Sucharew et al\textsuperscript{7} to our data to observe how their profiles’ performances in an acute cohort of patients. These were labeled $a$-NIHSS item profiles. Descriptive statistics were generated for the entire cohort and each profile separately. We described mean (SD) or median (interquartile range) for continuous variables and count (percentage) for categorical variables.

Validation was performed by assessing discrimination and calibration of the NIHSS item profiles’ association with outcome within the VISTA data. Outcome measures assessed at 90 days included the full distribution of the mRS, favorable mRS (mRS, 0–1), mortality, and time to death. Odds ratios and 95% confidence intervals of the outcome measures were obtained using ordinal logistic regression (for ordinal outcome measure) and binary logistic regression (for dichotomized outcome measure). The associated $P$ values calculated using the Cochrane–Mantel–Haenszel test. Time to death was investigated using Kaplan–Meir survival curves and analyzed using Cox proportional hazards model. Analyses were adjusted for age and thrombolysis treatment.\textsuperscript{14,15}

Because the $a$-NIHSS item classification was derived from the probabilities of the original profile membership generated using retrospective data (by Sucharew et al\textsuperscript{7}), we ran an independent LCA on the acute cohort data to identify our own symptom profiles, labeled $b$-NIHSS item profiles. Each individual NIHSS attribute was dichotomized as normal (0) or abnormal ($\geq 1$). Because the latent class model requires the number of classes to be prespecified, we initially specified 6 classes to see whether the $b$-NIHSS group in a similar manner to the grouping of retrospective NIHSS.\textsuperscript{7} We intended that if $b$-NIHSS item profiles were widely disparate to those identified previously, we would repeat the LCA starting with specifying 2 classes and increasing these in a stepwise fashion. The number of classes is considered optimal at the point when no statistically significant improvement in model fit is noted with an increase in the number of classes. We calculated and compared descriptive statistics and analyzed the association of the $b$-NIHSS item profiles with each outcome measure, as mentioned above. The symptom profiles’ ability to discriminate for dichotomized outcomes were evaluated using the $c$-statistics. Calibration was assessed with Hosmer–Lemeshow goodness-of-fit test. All analyses were undertaken using SAS version 9.3 (SAS Institute, Inc, Cary, NC).

**Results**

We obtained data for 10,271 patients with acute ischemic stroke, who had full set of data on individual items of the baseline NIHSS and outcome by 90 days (Figure 1). The cohort has median age of 72 (interquartile range, 62–79) years and baseline NIHSS of 13 (9–17). Baseline characteristics of the cohort are shown in Table 1.

By applying the probabilities of profile membership to the VISTA cohort, we replicated the 6 profiles identified by Sucharew et al\textsuperscript{7} (profiles A to F, denoted $a$-NIHSS item profiles). Median baseline NIHSS decreased from most severe profile A, to mild profile F, with (median [interquartile range]) 19 (15–22) and 4 (3–7), respectively. The profiles are shown in Figure 2 and in Figure I in the online-only Data Supplement. Individual $a$-NIHSS items that contributed into a specific profile are described in Table 2. The profiles that represented greater stroke severity, as indicated by the higher baseline NIHSS, included patients who were older and were more likely to have atrial fibrillation, chronic heart failure, and previous myocardial infarction. There were also notable differences in the use of thrombolysis treatment across the profiles, where patients in the more severe profiles were more likely to receive the treatment (Table 1). Two profiles falling between the extremes (ie, profiles C and D), were found to have near-similar median NIHSS scores, 10 (8–12) and 9 (7–11), respectively.

Ordinal analysis of mRS at day 90 showed increasing odds of better outcome across the profiles in a stepwise manner, adjusted for age and thrombolysis treatment (Table 2; Figure II in the online-only Data Supplement). Similar patterns were observed for mRS of favorable outcome at 90 days, with adjustment as above (Table 3). Profiles C and D, which had near-similar median NIHSS, had significant different 90-day mortality and survival rates, adjusted for age and thrombolysis treatment.\textsuperscript{14,15}

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treatment, \(P<0.001\) (Table 3). Taking profile A as reference, profile C was associated with 43% reduction in the risk of 90-day mortality, whereas profile D was associated with 81% reduction. Similar patterns were seen in overall survival with the reduction in the risk of death for profiles C and D were 41% and 78%, respectively, when compared with profile A (Table 3; Figure 3).

The discrimination of the \(a\)-NIHSS item profiles for dichotomized outcome was modest with \(c\)-statistics of 0.71 (95% confidence interval, 0.70–0.72) and 0.74 (0.73–0.75) for favorable mRS outcome at 90 days and mortality, respectively. The calibration was good (\(P=0.12\) and \(P=0.22\), respectively, for the Hosmer–Lemeshow test).

To validate these results, independent LCA was applied to our cohort’s data. Six distinct \(b\)-NIHSS item profiles (profiles 1–6) were identified, with the median NIHSS total score decreased across the profiles (Figure 2; Figure III in the online-only Data Supplement). Individual \(b\)-NIHSS items that contributed into a specific profile are described in Table 2. The baseline characteristics of the cohort by \(b\)-NIHSS item profiles are shown in Table I in the online-only Data Supplement. Patients grouped into profile 1 tended to be older and were more likely to have atrial fibrillation, acute myocardial infarction, and chronic heart failure. Profiles 3 and 4 (that were equivalent to profiles C and D in \(a\)-NIHSS item profiles) had different median NIHSS, with (median [interquartile range]) 13 (10–16) and 8 (6–10), respectively. Profiles 4 and 5 had median NIHSS of 8.

Consistent with \(a\)-NIHSS item profiles, \(b\)-NIHSS item profiles have similar outcome patterns for ordinal analysis of improved outcome using mRS at full distribution, and dichotomized outcomes at 90 days, after adjustment for age and thrombolysis treatment (Table II; Figure IV in the online-only Data Supplement). Profiles 3 and 4 had significant different outcomes for favorable mRS, mortality, and overall survival rates, all \(P<0.001\). Meanwhile, profiles 4 and 5 seemed to have similar outcomes, \(P>0.05\) (Table II; Figure V in the online-only Data Supplement). The performance of \(b\)-NIHSS item profiles is detailed in the online-only Data Supplement.

**Discussion**

Our present analysis has externally validated the original LCA derived within a population using retrospective NIHSS using clinical trial data and prospectively obtained NIHSS.
scores. We have confirmed that the LCA method of analyzing NIHSS items in patients with acute stroke offers an alternative approach for summarizing prognostic information, in terms of functional and mortality outcomes, compared with using raw NIHSS total score.

Consistent with the previous study,7 our patients with high baseline NIHSS score were more likely to fall into profiles A and B and were more likely to experience worse outcomes when compared with patients in other profiles. Patients in these 2 severe profiles tended to be older and have history of atrial fibrillation, ischemic heart disease, and chronic heart failure. Also as before, 2 symptom profiles possessing comparable median NIHSS (ie, profiles C and D) had divergent outcomes. Of note, patients in profile C were more likely to have aphasia when compared with patients in profile D. This emphasizes the concerns of considering individual NIHSS components as equal, such that a single point on NIHSS for aphasia may have dramatic effect on outcome when compared with a single point on NIHSS for limb signs. This also confirms the clinical suspicion that aphasia after stroke influences prognosis and recovery.16

The further validation study using independent LCA on our data revealed similar findings, which suggests that we may be capturing the true response patterns of the symptom profiles that are associated with functional outcomes and death. Thus, the NIHSS symptom profiles may be clinically useful for predicting prognosis. This approach may also have a place in future clinical trials design, whereby certain symptom profiles can be set as inclusion or exclusion criteria, or to aid prognostic subgroup analysis, rather than simply relying upon total NIHSS score.

Strengths of this analysis include the large sample size recruited from rigorous clinical trials and the prospective nature of the NIHSS data collected. In addition, we explored

\[\text{Table 2. Description of Individual } a\text{-NIHSS or } b\text{-NIHSS Items That Contributed (but Were Not Necessarily Present in Every Case) Into a Specific Profile}\]

<table>
<thead>
<tr>
<th>\text{a-NIHSS Profiles}</th>
<th>\text{b-NIHSS Profiles}</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1</td>
<td>Severe stroke with decreased level of consciousness, facial palsy, abnormal motor function on the right side, language deficit and dysarthria</td>
</tr>
<tr>
<td>B</td>
<td>2</td>
<td>Severe stroke with some decreased level of consciousness, facial palsy, abnormal motor function on the left side and, dysarthria</td>
</tr>
<tr>
<td>C</td>
<td>3</td>
<td>Stroke with language deficit, abnormal motor function on the right side, and signs of dysarthria</td>
</tr>
<tr>
<td>D</td>
<td>4</td>
<td>Stroke with facial palsy, abnormal motor function on the right side, and dysarthria</td>
</tr>
<tr>
<td>E</td>
<td>5</td>
<td>Facial palsy and abnormal motor function on the left side, and dysarthria</td>
</tr>
<tr>
<td>F</td>
<td>6</td>
<td>Mild stroke with low probabilities of abnormal findings on all 15 items</td>
</tr>
</tbody>
</table>

NIHSS indicates National Institutes of Health Stroke Scale.
the discrimination and calibration power of the NIHSS item profiles to predict favorable mRS outcome and mortality at 90 days, thus extending its prognostic role and generalizability. Because we were satisfied that the NIHSS item profiles were largely similar to the LCA on 2 independent data sets, and that the performance of the original NIHSS item profiles is good in a second data set, we are content to recommend the use of the original set of NIHSS item profiles.

Our analysis also has potential limitations. We acknowledge that there may be potential bias in outcome analysis when using pooled data from several trials with different interventions and end points. Even if only placebo or drugs without confirmed action on stroke outcome were used, bias still exists. However, using intracluster correlation coefficients, Frank et al\(^7\) have demonstrated that analyses using pooled data from multiple trials in VISTA have low overall variation in outcome. Our cohort also represents a highly selected group of patients based on individual trials’ eligibility criteria. The patients were more likely arriving to medical attention earlier and with more severe infarcts. For this validation study, NIHSS items were dichotomized, and the cohort was limited to those with full breakdown of baseline NIHSS items data, which may limit the sensitivity because of loss of information.\(^7\) However, this analytic method enables the probability of an abnormal response for each NIHSS items to be grouped into meaningful profile patterns. The small number of patients with mild stroke (ie, NIHSS \(\leq 5\)) does not allow us to compare the performance of the symptom profiles among those patients. The absence of prestroke functional status (ie, prestroke mRS) data precludes pre- and poststroke functional comparison. However, we speculate that patients included in the acute stroke trials usually have good prestroke mRS (as often good prestroke mRS is a prerequisite entry criteria for acute stroke trials). One of our outcome measures was full distribution mRS at 90 days using ordinal logistic regression with the proportional odds model. Although there are criticisms that the nature of the mRS is often not meet the ordinality assumption, this analysis approach has gained popularity in recent years.\(^18,19\) Limitations of the LCA method to develop the NIHSS item profiles have been discussed elsewhere.\(^7\) Briefly, LCA method requires a predetermined of the numbers in the population of interest. Although there are number of classes proposed was checked, it was possible that we under- or overestimated the number of true classes.
In conclusion, our results demonstrate the reliability of the NIHSS item profiles to capture the true response patterns that are associated with functional and mortality outcomes in an acute stroke cohort. The NIHSS symptom profiles might be clinically useful for prognostication and could potentially be applied in future clinical trial design.

Appendix


Acknowledgments

We thank the Virtual International Stroke Trials Archive Steering Committee for providing access to the data. Dr Lees supervised the project. Dr Abdul-Rahim conducted the analyses and drafted the initial article. Drs Fulton and Suchate provided statistical guidance and ran the latent class analysis. Drs Abdul-Rahim, Fulton, and Lees involved in reviewing and reporting of the work. Drs Lees, Khatri, Kleindorfer, and Broderick provided critical revision of the article for important intellectual content. All authors approved the final version. Members of the Virtual International Stroke Trials Archive-Acute Steering Committee approved the study plan in advance and approved the final article.

Disclosures

Dr Khatri received research support from Genentech and Penumbra (Principal Investigator of A Study of the Efficacy and Safety of Activase [Alteplase] in Patients With Mild Stroke [PRISMS] and Assess the Penumbra System in the Treatment of Acute Stroke [THERAPY] trials) and Data and Safety Monitoring Board member for Biogen. Dr Broderick is awarded research monies to Department of Neurology from Genentech for PRISMS Trial, travel to Australian [THERAPY] trials) and Data and Safety Monitoring Board member of the National Institutes of Health Stroke Scale Items as a predictor of patient outcome. Stroke. 2013;44:2182–2187. doi: 10.1161/STROKEAHA.113.001255.


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/content/46/5/e128.full.pdf

Data Supplement (unedited) at:
http://stroke.ahajournals.org/content/suppl/2015/01/30/STROKEAHA.114.006837.DC1

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On page 399, there was an error in Table 3, column mRS 0–1 at 90 d, subcolumn 95% CI, row F (n=57), “4.17–5.61,” has been changed to read, “7.12–23.44.”

The authors regret the error.

This correction has been made to the online version of the article, which is available at http://stroke.ahajournals.org/content/46/2/395.
SUPPLEMENTAL MATERIAL

Online Supplement for manuscript entitled:

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Supplemental Tables: I - II
Supplemental Figures and Figure Legends: I - V
Supplemental Data
## SUPPLEMENTAL TABLES

### Supplementary Table I: Baseline characteristics of the cohort, overall and by b-NIHSS item profiles.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All cases (N= 10,271)</th>
<th>b-NIHSS Item Profiles</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 (n=1,888)</td>
<td>2 (n=3,216)</td>
</tr>
<tr>
<td>Baseline NIHSS, median (IQR)</td>
<td>13 (9-17)</td>
<td>21 (18-23)</td>
</tr>
<tr>
<td>Age; years, median (IQR)</td>
<td>72 (62-79)</td>
<td>74 (65-81)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>4692 (45.7)</td>
<td>933 (49.4)</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>155.3 ±26.0</td>
<td>154.8 ±26.1</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>83.0 ±16.0</td>
<td>80.8 ±16.6</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>78.5 ±17.0</td>
<td>77.8 ±17.3</td>
</tr>
<tr>
<td>BMI; kg/m²</td>
<td>27.0 ±4.8</td>
<td>26.8 ±4.8</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>2,756 (26.8)</td>
<td>492 (26.1)</td>
</tr>
<tr>
<td>Thrombolysis treatment, n (%)</td>
<td>2,731 (26.6)</td>
<td>574 (30.4)</td>
</tr>
</tbody>
</table>

### Baseline laboratory measurements

<table>
<thead>
<tr>
<th></th>
<th>All cases</th>
<th>1 (n=1,888)</th>
<th>2 (n=3,216)</th>
<th>3 (n=1,419)</th>
<th>4 (n=1,625)</th>
<th>5 (n=1,505)</th>
<th>6 (n=618)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose; mmol/L</td>
<td>7.6 ±3.1</td>
<td>7.8 ±3.2</td>
<td>7.8 ±3.0</td>
<td>7.3 ±2.9</td>
<td>7.6 ±3.4</td>
<td>7.4 ±3.3</td>
<td>7.0 ±2.8</td>
</tr>
<tr>
<td>INR</td>
<td>1.3 ±0.9</td>
<td>1.3 ±0.9</td>
<td>1.4 ±1.2</td>
<td>1.3 ±0.9</td>
<td>1.2 ±0.8</td>
<td>1.2 ±0.7</td>
<td>1.2 ±0.7</td>
</tr>
<tr>
<td>Creatinine; umol/L</td>
<td>83.0 ±42.4</td>
<td>84.0 ±28.0</td>
<td>83.5 ±49.0</td>
<td>80.6 ±37.6</td>
<td>82.6 ±40.8</td>
<td>83.9 ±45.1</td>
<td>82.2 ±48.7</td>
</tr>
</tbody>
</table>
### Past medical history, n (%)

<table>
<thead>
<tr>
<th>Condition</th>
<th>1998 Mean (%)</th>
<th>2002 Mean (%)</th>
<th>2003 Mean (%)</th>
<th>2004 Mean (%)</th>
<th>2005 Mean (%)</th>
<th>2006 Mean (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation</td>
<td>2,583 (25.2)</td>
<td>627 (33.2)</td>
<td>992 (30.9)</td>
<td>362 (25.5)</td>
<td>224 (13.8)</td>
<td>279 (18.5)</td>
</tr>
<tr>
<td>IHD</td>
<td>2,176 (21.2)</td>
<td>329 (17.4)</td>
<td>710 (22.1)</td>
<td>372 (26.2)</td>
<td>328 (20.2)</td>
<td>345 (23.0)</td>
</tr>
<tr>
<td>MI</td>
<td>1,384 (13.5)</td>
<td>306 (16.2)</td>
<td>470 (14.6)</td>
<td>195 (13.7)</td>
<td>175 (10.8)</td>
<td>175 (11.6)</td>
</tr>
<tr>
<td>CHF</td>
<td>526 (5.1)</td>
<td>125 (6.6)</td>
<td>192 (6.0)</td>
<td>71 (5.0)</td>
<td>60 (3.7)</td>
<td>65 (4.3)</td>
</tr>
<tr>
<td>Previous Stroke</td>
<td>2,599 (25.3)</td>
<td>505 (26.8)</td>
<td>730 (22.7)</td>
<td>327 (23.0)</td>
<td>440 (27.1)</td>
<td>404 (26.8)</td>
</tr>
<tr>
<td>Previous TIA</td>
<td>602 (5.9)</td>
<td>135 (7.2)</td>
<td>192 (6.0)</td>
<td>85 (6.0)</td>
<td>82 (5.1)</td>
<td>76 (5.1)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>6,813 (66.3)</td>
<td>1,304 (69.1)</td>
<td>2,111 (65.6)</td>
<td>893 (62.9)</td>
<td>1,074 (66.1)</td>
<td>1,041 (69.2)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2,154 (21.0)</td>
<td>395 (20.9)</td>
<td>663 (20.6)</td>
<td>258 (18.2)</td>
<td>375 (23.1)</td>
<td>349 (23.2)</td>
</tr>
</tbody>
</table>

All continuous variables were given in mean ± standard deviations, unless stated otherwise. NIHSS indicates National Institutes of Health Stroke Scale; IQR, interquartile range; BP, blood pressure; BMI, body mass index; INR, internationalised ratio; IHD, ischaemic heart disease; MI, myocardial infarction; CHF, congestive heart disease; TIA, transient ischemic attack.
**Supplementary Table II:** Outcome measures by b-NIHSS item profiles (adjusted for age and thrombolysis treatment).

<table>
<thead>
<tr>
<th>b-NIHSS Profile</th>
<th>Ordinal analysis mRS at 90 days</th>
<th>mRS 0-1 at 90 days</th>
<th>Mortality at 90 days</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
<td>No. of</td>
<td>OR</td>
</tr>
<tr>
<td>A (n=2,830)</td>
<td>Ref</td>
<td>...</td>
<td>229</td>
<td>Ref</td>
</tr>
<tr>
<td>B (n=3,759)</td>
<td>1.50</td>
<td>1.35-1.67</td>
<td>620</td>
<td>1.68</td>
</tr>
<tr>
<td>C (n=108)</td>
<td>3.40</td>
<td>2.99-3.87</td>
<td>426</td>
<td>3.08</td>
</tr>
<tr>
<td>D (n=2,030)</td>
<td>6.49</td>
<td>5.73-7.36</td>
<td>740</td>
<td>5.77</td>
</tr>
<tr>
<td>E (n=1,487)</td>
<td>6.01</td>
<td>5.29-6.83</td>
<td>669</td>
<td>5.52</td>
</tr>
<tr>
<td>F (n=57)</td>
<td>7.30</td>
<td>6.16-8.65</td>
<td>312</td>
<td>6.82</td>
</tr>
</tbody>
</table>

OR indicates odd ratios; mRS: modified Rankin Scale; CI: confidence interval; HR: hazard ratios; Ref: reference.
SUPPLEMENTAL FIGURES AND FIGURE LEGENDS

Supplementary Figure I: Boxplots of prospective NIHSS total score by α-NIHSS item profile.
Supplementary Figure II: mRS outcome at Day 90, comparing a-NIHSS items Profile A (top) and comparator a-NIHSS items profile (bottom). Values provided in each box denote percentage of patients.
Supplementary Figure III: Boxplots of prospective NIHSS total score by $b$-NIHSS item profile.
**Supplementary Figure IV:** mRS outcome at Day 90, comparing b-NIHSS items Profile 1 (top) and comparator b-NIHSS items profile (bottom). Values provided in each box denote percentage of patients.
Supplementary Figure V: Kaplan-Meier curves by $b$-NIHSS item profiles.
SUPPLEMENTAL DATA

Performance of $b$-NIHSS item profiles

Discrimination of the $b$-NIHSS item profiles was good with $c$-statistics for favorable mRS outcome and mortality were, 0.71 (95%CI: 0.70-0.72) and 0.75 (0.73-0.76), respectively. The calibration was good ($p=0.20$ and $p=0.28$, respectively for the Hosmer-Lemeshow test). There were significant differences between the $c$-indices of $a$-NIHSS- and $b$-NIHSS item profiles for predicting dichotomized outcomes (favorable mRS outcome, $p=0.002$, and mortality, $p<0.001$).