Risk Score for In-Hospital Ischemic Stroke Mortality Derived and Validated Within the Get With The Guidelines–Stroke Program

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Background—There are few validated models for prediction of in-hospital mortality after ischemic stroke. We used Get With the Guidelines–Stroke Program data to derive and validate prediction models for a patient's risk of in-hospital ischemic stroke mortality.

Methods and Results—Between October 2001 and December 2007, there were 1036 hospitals that contributed 274 988 ischemic stroke patients to this study. The sample was randomly divided into a derivation (60%) and validation (40%) sample. Logistic regression was used to determine the independent predictors of mortality and to assign point scores for a prediction model. We also separately derived and validated a model in the 109 187 patients (39.7%) with a National Institutes of Health Stroke Scale (NIHSS) score recorded. Model discrimination was quantified by calculating the C statistic from the validation sample. In-hospital mortality was 5.5% overall and 5.2% in the subset in which NIHSS score was recorded. Characteristics associated with in-hospital mortality were age, arrival mode (eg, via ambulance versus other mode), history of atrial fibrillation, previous stroke, previous myocardial infarction, carotid stenosis, diabetes mellitus, peripheral vascular disease, hypertension, history of dyslipidemia, current smoking, and weekend or night admission. The C statistic was 0.72 in the overall validation sample and 0.85 in the model that included NIHSS score. A model with NIHSS score alone provided nearly as good discrimination (C statistic 0.83). Plots of observed versus predicted mortality showed excellent model calibration in the validation sample.

Conclusions—The Get With the Guidelines–Stroke risk model provides clinicians with a well-validated, practical bedside tool for mortality risk stratification. The NIHSS score provides substantial incremental information on a patient's short-term mortality risk and is the strongest predictor of mortality. **(*Circulation*. 2010;122:1496-1504.)**

Key Words: stroke ■ cerebral stroke ■ mortality ■ prognosis

Acute ischemic stroke results in substantial morbidity and mortality; the in-hospital case fatality rate after ischemic stroke is ≈5%.[1,2] Determining an individual patient's risk of mortality at admission could aid clinical care by providing valuable prognostic information to patients and their family members and by identifying those at high risk for poor outcomes who may require more intensive resources. Third-party payers and regulatory agencies have shown increasing interest in tracking stroke mortality as one of the measures of stroke quality of care, so adjustment for baseline risk of mortality will be necessary to avoid penalizing hospitals that admit less healthy patient populations. Therefore, there is an increasingly important need to develop well-validated models that are useful in predicting patient risk of mortality and can be efficiently put to use in actual practice.

Clinical Perspective on p 1504

Several prediction models for mortality after hospital admission for ischemic stroke have been published previously[3–9]; however, for the most part, these prediction models have not been incorporated into clinical practice. Models based on administrative data have shown only modest discrimination of mortality risk.[10] Models based on prospective data collection have shown better discrimination of risk by including additional variables such as standardized stroke severity scores[4–6,11] or magnetic resonance imaging or com-

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puted tomography lesion volumes[4,11]; however, these variables are not collected routinely in clinical practice in all patients, and thus, the applicability of these models is limited. Some models use information from the subacute or chronic phase of stroke and are therefore not optimized for in-hospital prediction at the time of admission.[3,5,8,9,11] Perhaps most importantly, most hospitals lack support tools to automatically generate patient-based predictions, and busy clinicians rarely have the time to calculate risks by hand. There remains a need for an accurate and practical clinical risk tool to predict ischemic stroke mortality that overcomes these limitations and can be readily incorporated into clinical practice without the need for calculation by hand.

To address this need, we sought to develop a practical, user-friendly, World Wide Web–enabled bedside tool for risk stratification at the time of presentation for patients hospitalized with acute ischemic stroke using data from the Get With the Guidelines–Stroke (GWTG-Stroke) database, a large national stroke registry and quality improvement initiative. To test the added value of a measure of stroke severity, we separately derived and validated a risk score for in-hospital death in the subset of patients for whom the National Institutes of Health Stroke Scale (NIHSS) score,[12] the most commonly used standardized stroke scale, was documented.

Methods

Subject Population and Study Measurements

Characteristics of the GWTG-Stroke program have been described previously.[13,14] Participating hospitals use an Internet-based "Patient Management Tool" (Outcome Sciences Inc, Cambridge, Mass) to enter data, receive decision support, and obtain feedback via on-demand reports of performance on quality measures.

Hospitals were instructed to record data from consecutive admissions for stroke and transient ischemic attack. Case ascertainment was through clinical identification during hospitalization, retrospective identification by International Classification of Diseases, 9th Revision codes (including 433.x, 434.x, and 436), or both. The eligibility of each case was confirmed at chart review before abstraction. Trained hospital personnel abstracted data using the Internet-based Patient Management Tool with standardized data definitions and detailed coding instructions. The Internet-based system performs checks to ensure that the reported data are complete and internally consistent. In addition, data quality is monitored for completeness and accuracy. Hospital characteristics (ie, academic teaching status, bed size) were based on American Hospital Association data.[15] Presentation during daytime regular hours was defined as presentation between 7 AM and 5 PM Monday to Friday, as in a previous study.[16] Past medical history was defined on the basis of preexisting conditions, with the exclusion of conditions that were newly diagnosed during the hospital stay.

Only patients with ischemic stroke were included in the present analysis; those with hemorrhagic stroke or transient ischemic attack were excluded. Between October 1, 2001, and December 30, 2007, there were 1042 hospitals that contributed data on 320 635 ischemic stroke discharges. We excluded patients transferred to another acute care hospital (n=10 165, 3.2%) or transferred from another acute care hospital (n=29 639, 9.2%). Furthermore, 5843 patients were excluded because of missing data on discharge destination (1.8%), which left 274 988 patients from 1036 hospitals for analysis. A small number of patients (n=15 597, 5.67%) were included who did not present via the emergency department because of direct floor admission or because of new acute stroke that occurred during hospitalization for another reason. Variables with missing data were imputed as follows: Missing mode of arrival to the hospital (4.79%) was imputed to private transport (because ambulance personnel should have documented arrival times for patients arriving by ambulance); patients missing past medical history information (0.4%) were imputed to have no past medical history; and missing arrival time (7.72%) was imputed to the off-hours or weekend category (the most common category). The few patients with missing gender information (258, 0.09%) were excluded from the models.

Each participating hospital received either human research approval to enroll cases without individual patient consent under the common rule or a waiver of authorization and exemption from subsequent review by their institutional review board. Outcome Sciences Inc serves as the data collection and coordination center for GWTG. The Duke Clinical Research Institute serves as the data analysis center and has institutional review board approval to analyze the aggregate deidentified data for research purposes.

Statistical Analysis

First, the sample was randomly divided into a derivation sample (164 993, 60%) and a validation sample (109 995, 40%). Model building was performed exclusively in the derivation sample. With the use of χ^2 tests for categorical variables and the Kruskal-Wallis test for continuous variables, patient characteristics were compared among those who died in the hospital and those who survived to discharge.

Multivariable-adjusted logistic regression was used to determine the independent predictors of in-hospital death. Candidate variables were those with biologically plausible links to ischemic stroke mortality on the basis of prior publications and those associated with in-hospital death in univariate analysis ($P<0.05$). Continuous variables were entered as linear functions unless there was evidence of a nonlinear relationship based on a univariate graphical display of mortality in each decile. Age was entered as a continuous function if age was >60 years, because there was little relationship between age and mortality below age 60 years but a linear increased probability of death with each year of age above 60. The generalized estimating equations approach was used to account for within-hospital clustering.[17] Stepwise backward elimination was used to remove nonsignificant variables ($P>0.05$) from the model.

The β-coefficients from the final model were used to generate point scores for calculating mortality risk, as in previous studies.[18] The resulting mortality prediction rule was then validated by generating C statistics and plots of observed versus predicted mortality in the validation sample with either 6 prespecified categories of predicted risk or 10 deciles of predicted risk. The C statistic was used as the primary measure of model discrimination. In this context, the C statistic is equivalent to the probability that the predicted risk of death is higher for patients who died than for patients who survived and is equivalent to the area under the receiver operating characteristics curve.[19] A C statistic of 1.0 indicates perfect prediction, whereas a C statistic of 0.5 indicates no better than random prediction. The C statistics in clinically important prespecified subgroups (ie, by age dichotomized at the median and by gender) were calculated.

Stroke severity, measured by NIHSS score, was not entered into the overall model because it was not normally documented as part of routine clinical practice and was recorded in only 39.7% of patients. To test an a priori hypothesis that NIHSS score would be a strong determinant of mortality, we separately derived and validated a model in the subset of patients for whom an NIHSS score was documented, using the same approach described above. We used the integrated discrimination index to measure how the model that included NIHSS score reclassified patients compared with the model without NIHSS score. The integrated discrimination index can be expressed as $(EY_1-EY_0)-(EX_1-EX_0)$, where EY_1 and EY_0 are the mean expected predicted probabilities of death in persons who died or survived in model Y (in this case, the model that included NIHSS score) and EX_0 and EX_1 are the mean expected predicted probabilities of death in persons who died or survived in model X (in this case, the model that did not include NIHSS score).[20] A higher integrated discrimination index indicates better reclassification.

Analyses were performed with SAS version 9.1.3 (SAS Institute, Cary, NC).

Table 1. Characteristics of Ischemic Stroke Patients Who Died or Survived to Hospital Discharge

Characteristic	Overall (n=274 988)	Died (n=15 143)	Survived (n=259 845)	P
Age, y	74 (62–83)	80 (70–86)	74 (61–82)	<0.001
Male gender	46.52	42.33	46.77	<0.001
Race				<0.001
White	73.89	77.48	73.68	
Black	15.12	11.48	15.33	
Asian	2.28	2.38	2.27	
American Indian	0.15	0.09	0.16	
Hawaiian/Pacific Islander	0.27	0.31	0.27	
Other or unable to determine	3.95	4.61	3.91	
Hispanic	4.16	3.48	4.2	
Mode of arrival				<0.001
EMS from scene	53.44	79.26	51.94	
Private transport/walk-in	36.13	8.85	37.72	
Did not present via ED	5.67	7.69	5.55	
NIHSS score*	5 (2–11)	18 (11–24)	4 (2–10)	<0.001
History of:				
Atrial fibrillation	18.15	34.61	17.2	<0.001
Prosthetic heart valve	1.47	1.98	1.44	<0.001
Previous stroke or TIA	30.77	31.81	30.71	0.004
Coronary artery disease	27.53	35.47	27.07	<0.001
History of carotid stenosis (>50%)	4.74	4.21	4.77	0.002
Diabetes mellitus	29.92	29.42	29.95	0.17
Peripheral vascular disease	5.22	6.92	5.12	<0.001
Hypertension	73.99	73.31	74.03	0.05
Dyslipidemia	35.2	27.04	35.68	<0.001
Atrial fibrillation in hospital	15.91	30.27	15.07	<0.001
Smoker, current/within past year	17.11	10.66	17.49	<0.001
Arrived during daytime regular hours†	46.83	42.68	47.07	<0.001

EMS indicates emergency medical services; ED, emergency department; and TIA, transient ischemic attack.

Age and NIHSS score are reported as median (interquartile range); all other values are percentages. Significance testing was by Kruskal-Wallis test (for continuous variables) or χ^2 test across category (for categorical variables). Missing data were imputed; see Methods for details.

*Missing in 60.29%.

†Daytime regular hours were defined as 7 AM to 5 PM Monday to Friday; all other times (including all day Saturday and Sunday) were considered off-hours.

Results

The study population consisted of 274 988 hospitalized ischemic stroke patients. Mean age was 71.6±14.3 years, and 53.4% of patients were women. Admissions were submitted by 1036 hospitals. Most patients were treated in academic teaching hospitals (60.6%), according to American Hospital Association criteria.[15] The median hospital bed size was 372 (interquartile range 262 to 540).

In-hospital death occurred in 15 152 (5.51%) of 274 988 patients. There were many differences between patients who died and patients who survived (Table 1). Patients who died were more likely to be older, to have arrived by ambulance rather than by other means, and to have a history of atrial fibrillation or coronary artery disease. Weekend or nighttime admission was also associated with higher mortality.

The derivation sample (n=164 993 patients, 60%) and the validation sample (n=109 995 patients, 40%) were well matched with respect to patient characteristics and overall mortality, with no significant differences between the 2 samples (data not shown). The multivariable-adjusted independent predictors of increased risk of mortality were increasing age (for each year greater than 60), atrial fibrillation, coronary artery disease, diabetes mellitus, and peripheral vascular disease (Table 2). Independent predictors of lower risk of mortality were history of previous stroke or transient ischemic attack, known carotid stenosis, hypertension, dyslipidemia, current smoking, and presentation during regular weekday hours.

Risk Score

The regression model β-coefficients were used to derive point scores that could be used to predict a patient's risk of dying in the hospital (Figure 1). The probability of in-hospital mortality can be estimated for an individual patient by summing points assigned to the value of each predictor to

Table 2. Independent Predictors of In-Hospital Death From Ischemic Stroke

Variable	β-Coefficient	Adjusted Odds Ratio	95% Confidence Limits	
Model intercept	−4.1776	. . .	. . .	. . .
Year of age >60 y (per year)	0.0213	1.022	1.019	1.024
Mode of arrival				
Private transport	. . .	1.0 (Reference)	. . .	. . .
Did not present via ED	1.404	4.070	3.685	4.495
By ambulance from scene	1.432	4.187	3.926	4.466
Atrial fibrillation	0.539	1.714	1.633	1.799
Previous stroke	−0.083	0.921	0.878	0.965
Coronary artery disease	0.236	1.266	1.207	1.327
Known carotid stenosis >50%	−0.163	0.849	0.761	0.948
Diabetes mellitus	0.101	1.107	1.054	1.162
Peripheral vascular disease	0.256	1.291	1.183	1.410
Hypertension	−0.130	0.878	0.836	0.923
History of dyslipidemia	−0.393	0.675	0.642	0.710
Smoker	−0.157	0.855	0.794	0.920
Arrival during weekday regular hours	−0.132	0.876	0.837	0.916

ED indicates emergency department.

create a total point score that ranges from 0 to 204 (Figure 1). The predicted in-hospital mortality plotted as a continuous function of the developed risk score is shown in Figure 1. This prediction model was validated in the remaining 40% of the population. The risk score demonstrated good discrimination in the validation sample (C statistic 0.72). Similar good discrimination was seen in the prespecified subgroups in the validation sample: Older (>74 years, dichotomized at the median) versus younger patients (≤74 years, C statistic 0.68 versus 0.71) and men versus women (C statistic 0.72 versus 0.71). A graph of observed versus predicted mortality in 6 groups according to prespecified categories of mortality risk showed an excellent correlation between observed and predicted mortality in the derivation and validation samples across a wide range of predicted risk that varied by more than 16-fold (Figure 2). Likewise, a plot of observed versus predicted mortality in the validation sample, grouped into 10 deciles of predicted risk, also showed excellent calibration (Figure 2). The Hosmer-Lemeshow test was significant ($P<0.001$) in the validation sample, which indicates some deviation from perfect fit; however, the Hosmer-Lemeshow test has been shown to be overly sensitive to trivial deviations from the ideal fit when the sample size is this large.[21]

The characteristics of patients with or without NIHSS score documented are shown in Table 3. The median hospital-level percentage of patients with NIHSS score recorded was 22.2% (interquartile range 3.3% to 54.8%). Because of the very large sample size, there were many differences between the groups that reached conventional levels of statistical

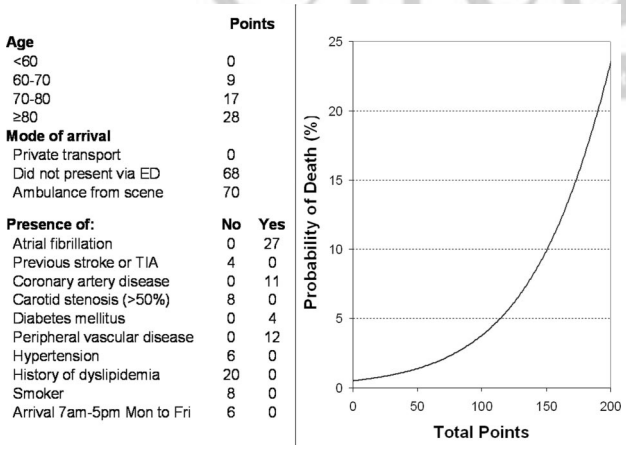

Figure 1. Prediction tool for in-hospital death after admission for ischemic stroke. The total point score gives the predicted probability of in-hospital death according to the following equation:

$$\text{Mortality}=\frac{1}{1+\exp[5.294137-0.02053654(\text{pts})]}.$$

ED indicates emergency department; TIA, transient ischemic attack; and Mon to Fri, Monday to Friday.

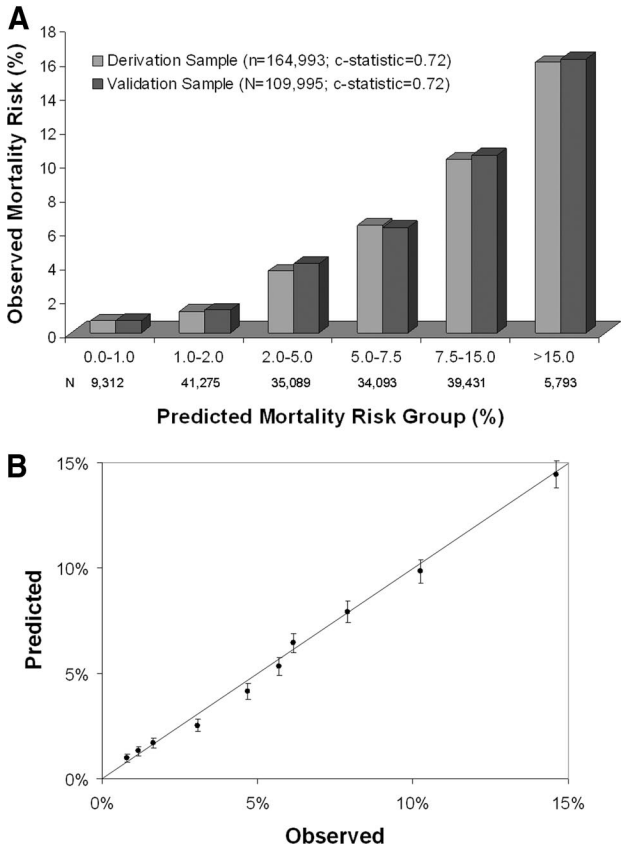

Figure 2. A, Calibration of the prediction tool in the derivation and validation samples, according to 6 prespecified categories of risk. B, Plot of observed vs predicted in-hospital mortality, with 95% confidence intervals, in the validation sample (n=109 995) according to 10 deciles of predicted risk. Overall, there was a very high correlation between observed and expected mortality ($r^2=0.995$), which indicates excellent calibration.

Table 3. Characteristics of Ischemic Stroke Patients With or Without NIHSS Score Recorded

Characteristic	NIHSS Score Recorded (n=109 187)	NIHSS Score Not Recorded (n=165 801)	P
Age, y	73 (61–82)	75 (62–83)	<0.001
Male gender	48.19	45.43	<0.001
Race			
White	74.72	73.64	<0.001
Black	14.14	15.76	
Asian	2.59	2.07	
American Indian	0.15	0.15	
Hawaiian/Pacific Islander	0.31	0.25	
Other or unable to determine	3.78	4.07	
Hispanic	4.31	4.06	
Mode of arrival			<0.001
EMS from scene	57.68	50.64	
Private transport/walk-in	37.91	42.85	
Did not present via ED	4.41	6.50	
History of:			
Atrial fibrillation	18.58	17.87	<0.001
Prosthetic heart valve	1.52	1.44	0.09
Previous stroke or TIA	29.72	31.46	<0.001
Coronary artery disease	27.47	27.57	0.54
History of carotid stenosis (>50%)	4.66	4.79	0.12
Diabetes mellitus	28.51	30.86	<0.001
Peripheral vascular disease	4.88	5.45	<0.001
Hypertension	74.01	73.98	0.87
Dyslipidemia	36.85	34.11	<0.001
Atrial fibrillation in hospital	17.31	14.97	<0.001
Smoker, current/within past year	18.26	16.35	<0.001
Arrived during daytime regular hours*	47.83	46.18	<0.001
Hospital characteristics			
No. of beds	380 (267–564)	365 (256–507)	<0.001
Academic teaching hospital	60.60	60.61	0.02
Died in the hospital	5.19	5.72	<0.001

EMS indicates emergency medical services; ED, emergency department; and TIA, transient ischemic attack.

Age, NIHSS score, and No. of beds are reported as median (interquartile range); all other values are percentages. Significance testing by Kruskal-Wallis test (for continuous variables) or χ^2 test (for categorical variables).

*Daytime regular hours were defined as 7 AM to 5 PM Monday to Friday; all other times (including all day Saturday and Sunday) were considered off-hours.

significance but that were actually small in both relative and absolute terms. Larger differences were seen for only a few characteristics: NIHSS score was more likely to be documented in patients who were younger, were male, arrived by ambulance, and arrived during daylight hours (all $P<0.001$). Overall mortality was slightly lower in the group with NIHSS score documented than in the group without NIHSS score documented (5.19% versus 5.72%, $P<0.001$).

Table 4. Independent Predictors of In-Hospital Death From Ischemic Stroke in Model That Included NIHSS Score

Variable	β-Coefficient	Adjusted Odds Ratio	95% Confidence Limits	
Model intercept	−5.3169	. . .	. . .	. . .
Year of age >60 y (per year)	0.0176	1.018	1.014	1.022
Male gender	0.167	1.182	1.093	1.278
NIHSS score (per point)	0.116	1.123	1.119	1.128
Mode of arrival	. . .			
Private transport	. . .	1.0 (Reference)	. . .	. . .
Did not present via ED	0.9611	2.615	2.168	3.153
By ambulance from scene	0.7654	2.150	1.909	2.421
Atrial fibrillation	0.300	1.349	1.241	1.466
Previous stroke or TIA	−0.112	0.894	0.825	0.970
Coronary artery disease	0.268	1.307	1.206	1.417
Diabetes mellitus	0.124	1.132	1.041	1.231
History of dyslipidemia	−0.132	0.876	0.808	0.951

ED indicates emergency department; TIA, transient ischemic attack.

This model was derived in the 39.7% of the study population with NIHSS score recorded.

As before, 60% of the sample of patients with NIHSS recorded was used for derivation (n=65 513), and 40% was used for validation (n=43 674). The 2 samples were well matched with respect to patient characteristics and overall mortality, with no significant differences (data not shown). NIHSS score was strongly associated with mortality; median NIHSS score was 18 in those who died (interquartile range 11 to 24) compared with 4 in those who survived (interquartile range 2 to 10, $P<0.001$). In the multivariable model, higher NIHSS score was strongly associated with increased mortality after controlling for other predictors (Table 4). The validation sample C statistic for the model that included NIHSS score (0.85) was greater than the C statistic for the model derived without it (0.72, $P<0.001$). The C statistic for a model that included NIHSS alone, without any other predictors, was also very high (0.83). The full model that included NIHSS showed good discrimination in older (>74 years, dichotomized at the median) versus younger (≤74 years, C statistic 0.83 versus 0.86) patients and in men versus women (C statistic 0.85 versus 0.85). Point scores for the prediction model that included NIHSS score are shown in Figure 3. Model discrimination and calibration was again excellent across a wide range of prespecified predicted risk categories in the derivation and validation samples (Figure 4A). A plot of observed versus predicted mortality in the validation sample, grouped into 10 deciles of predicted risk, again showed excellent calibration (Figure 4B) even though the Hosmer-Lemeshow test was significant ($P<0.001$), which indicates some deviation from perfect fit. The Hosmer-Lemeshow test is overly sensitive to trivial deviations from the ideal fit when the sample size is this large, however.[21]

The impact of a model that included NIHSS score on the reclassification of in-hospital mortality risk compared with

	Points	
Age		
<60	0	
60-70	1	
70-80	5	
≥80	9	
NIHSS Score		
0-2	0	
3-5	10	
6-10	21	
11-15	37	
16-20	48	
21-25	56	
>25	65	
Mode of arrival		
Private transport	0	
Did not present via ED	16	
Ambulance from scene	12	
Presence of:	**No**	**Yes**
Male gender	3	0
Atrial fibrillation	0	5
Previous stroke or TIA	2	0
Coronary artery disease	0	5
Diabetes mellitus	0	2
History of dyslipidemia	2	0

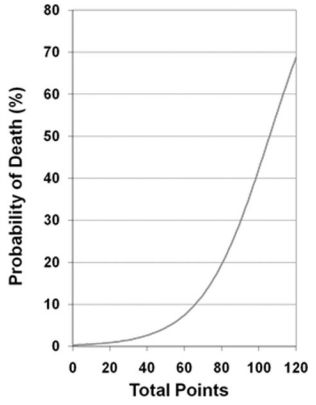

Figure 3. Prediction tool for in-hospital death after admission for ischemic stroke incorporating the NIHSS score. The total point score gives the predicted probability of in-hospital death according to the following equation:

$$\text{Mortality}=\frac{1}{1+\exp[5.829278-0.0551425(\text{pts})]}.$$

ED indicates emergency department; TIA, transient ischemic attack.

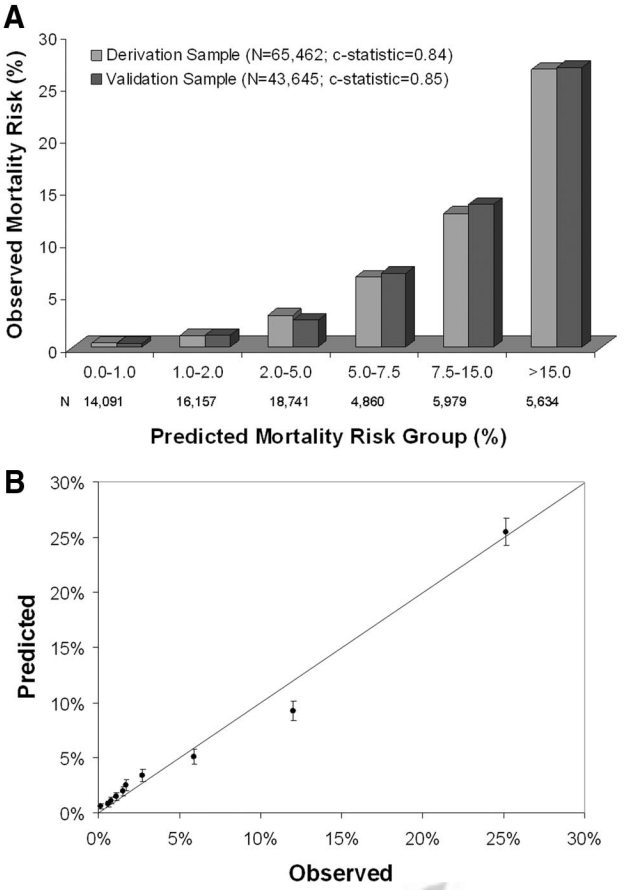

Figure 4. A, Calibration of the prediction tool incorporating NIHSS score in the derivation and validation samples according to 6 prespecified categories of predicted risk. B, Plot of observed vs predicted in-hospital mortality, with 95% confidence intervals, in the model incorporating NIHSS score according to 10 deciles of predicted risk in the validation sample of the subgroup in which NIHSS was documented (n=43 645). Overall, observed and expected mortality were highly correlated (r^2=0.982), which indicates excellent calibration; however, the model predictions were slightly lower than the actual mortality for the ninth decile (predicted mortality 9.23%, observed mortality 12.03%).

the model that did not was quantified with the integrated discrimination index in the validation sample in which the NIHSS score was recorded (n=43 674). The model with NIHSS score (Figure 3) yielded a C statistic of 0.85 (95% CI 0.84 to 0.86). By contrast, the model that did not include NIHSS score (Figure 1) had a C statistic of 0.73 (95% CI 0.72 to 0.74). The integrated discrimination index for the comparison of the 2 models was 9.4% ($P<0.001$). To further explore the role of the NIHSS score, we compared 2 nested models, including all the previously significant variables (Figures 1 and 3) with or without the NIHSS score, and confirmed that the NIHSS score was the variable responsible for the significant reclassification (data not shown).

Discussion

In the present study, we used data from the GWTG-Stroke Program to derive a model for prediction of in-hospital ischemic stroke mortality based on patient characteristics available at the time of hospital admission. This model uses patient demographics, past medical history, mode of presentation, and timing of admission to predict an individual's risk of dying in the hospital after admission for stroke. A second model that additionally incorporated a measure of stroke severity (the NIHSS score) had substantially better discrimination, however. Both models showed good discrimination and calibration in the independent validation samples.

To preserve the clinical utility of the model for decision making during the acute stroke hospitalization, we used only the patient characteristics available at the time of presentation. We chose not to include information related to in-hospital medical care or medical complications of stroke despite the fact that these could influence mortality. This model therefore predicts the expected in-hospital mortality at the time of presentation, and as such, the predictions could be used to guide subsequent in-hospital medical care. Transfer patients were not included in the study population because patients transferred to the receiving hospital arrived later in their course and by definition had survived until transfer, whereas patients transferred to another acute care hospital survived to hospital discharge by definition, and we were not able to determine whether these patients subsequently died after the transfer. Therefore, the mortality predictions generated by our risk score may not be applicable to these populations of transferred patients.

This GWTG-Stroke risk prediction tool is unique in that it was derived from a US nationwide study with very large derivation and validation samples, included unselected consecutive ischemic stroke patients, can be used for prediction of in-hospital risk of death on hospital arrival because it uses only admission patient characteristics, and can be readily incorporated into clinical practice through the World Wide

Web–based Patient Management Tool of GWTG-Stroke. Other prediction rules for ischemic stroke mortality have been developed using similar techniques based on logistic regression[3–6,8,9,11]; however, these models have significant limitations for prediction of hospital-based mortality. Some were derived in clinical trial populations, which are systematically different from unselected community patients.[4,11] Some incorporated information not routinely or reliably collected in clinical practice in all patients, such as magnetic resonance imaging or computed tomography lesion volumes or ischemic stroke subtype classification.[4,11] Some incorporated information from the subacute or chronic phase of stroke[5,8,9,11] and are therefore not useful for prediction of mortality risk on admission. Some predicted postdischarge mortality and therefore are not useful for prediction of in-hospital death.[3–6,8,9,11] Some may have been biased by differential loss to follow-up[5,6] or exclusion of patients who died early in their hospital course.[3,5] None have been derived and validated in samples as large as the present study.

The GWTG-Stroke prediction tool provides clinically useful discrimination of in-hospital risk of mortality. The C statistic of our prediction model derived from patient demographics, past medical history, and mode and timing of arrival information was 0.72, which is similar to previously published models that used only administrative information.[10,22] When NIHSS information was added to the model, the C statistic substantially improved to 0.84, a level at which model discrimination is regarded to be of genuine clinical utility for individual decision making.[23] A model with NIHSS score alone and no other variables had almost the same C statistic (0.83), which illustrates the very strong relationship between stroke severity and short-term mortality. The C statistic of the present model that included NIHSS score compares favorably with other mortality prediction models that incorporated the NIHSS score[4–6] or other clinical measures of stroke severity[3,8,9] (previously reported C statistics 0.79 to 0.88). Clearly, measures of clinical stroke severity are critical for optimal discrimination of mortality risk, yet the NIHSS score was recorded infrequently in clinical practice in the present study. The time needed to perform even a short standardized stroke severity assessment is probably a barrier to more widespread use. Further research will be needed to determine the use of the NIHSS score in routine clinical practice and whether other, simpler measures of stroke severity could be developed and substituted without substantial loss of prognostic information.

In the present study, the independent predictors of in-hospital death based on multivariable-adjusted logistic regression were stroke severity, age, female sex, weekend or evening admission, atrial fibrillation, previous myocardial infarction, peripheral vascular disease, and diabetes mellitus. Presentation by ambulance was associated with higher risk of mortality, probably because patients transported by emergency medical systems have more severe stroke symptoms. Some previous medical conditions were associated with lower, rather than higher, ischemic stroke mortality. Previous stroke, known carotid stenosis, hypertension, dyslipidemia, and smoking were all associated with lower, not higher, risk of mortality, possibly because these risk factors are more strongly associated with noncardioembolic stroke, which is less severe and has a better prognosis than cardioembolic stroke.[24,25] An alternative explanation is that some vascular risk factors may have been associated with the use of medical therapies, such as antithrombotic medications and statins, that reduced the severity of the stroke. We were unable to directly test these hypotheses because ischemic stroke subtype was not routinely recorded in standard clinical practice and was not a required study data element, and preadmission drug information was not complete for all patients. These findings suggest that simple sums of the number of medical comorbidities that are frequently used in administrative data sets, such as the Charlson-Deyo index,[10,26] may not fully capture the complex relationship between preexisting medical conditions and mortality in ischemic stroke. Many of the predictors of mortality (hypertension, carotid stenosis, peripheral vascular disease, smoking, and weekend/evening hospital admission) were no longer significant, or had a smaller effect, when we additionally controlled for NIHSS score, which illustrates the importance of stroke severity as a confounder. The only predictors that were associated with mortality independent of NIHSS score were age, male sex, mode of arrival, atrial fibrillation, previous myocardial infarction, and dyslipidemia.

Many of the identified predictors of ischemic stroke mortality are consistent with observations in other studies. Stroke severity was the single characteristic that was most strongly linked with mortality.[27] Increased age has also been strongly and consistently associated with increased mortality from ischemic stroke.[28] Gender was not associated with increased mortality when we controlled for differences in age and medical comorbidities, which is consistent with a prior GWTG-Stroke study[29]; however, we did show a modestly increased risk of mortality for men after additionally controlling for admission NIHSS score. This increased risk for men has been reported previously,[30,31] although other studies conversely report worse outcomes in women.[32–35] We confirmed the findings of our previous study that found that off-hours admission was associated with increased mortality,[16] a finding also seen in the Registry of the Canadian Stroke Network.[36] Atrial fibrillation,[1,37,38] previous myocardial infarction,[38] peripheral vascular disease,[39] and diabetes mellitus[1,11,38] have all been linked with higher mortality after ischemic stroke. Hyperlipidemia has been associated with lower ischemic stroke mortality previously.[39–41]

There are several limitations of the present study. The present sample of patients and hospitals may not be representative, because hospital participation in GWTG-Stroke is voluntary and therefore limited to hospitals with an interest in stroke quality improvement. Although there are more academic teaching hospitals in GWTG-Stroke than the national average, the demographics of the GWTG-Stroke patient population are quite similar to the overall demographics of all US patients with stroke.[14] Study data were collected on the basis of the medical record and depend on the accuracy and completeness of clinical documentation and chart abstraction. NIHSS data were not missing at random; therefore, the relationships between predictors and outcome observed in the subset with a documented NIHSS score may not be generalizable to all ischemic stroke patients. We were unable to

control for all potential predictors of ischemic stroke mortality and, for example, were unable to control for prestroke disability, a known predictor of poststroke mortality,[3] because a prestroke modified Rankin Scale was not routinely estimated in clinical practice; however, we were able to control for previous history of stroke or transient ischemic attack. Despite the absence of prestroke disability information, we were nonetheless able to predict in-hospital mortality with similar discrimination as previously published models. Postdischarge information is not collected in GWTG-Stroke, and therefore, we were not able to derive a prediction tool for postdischarge mortality or functional disability at 30 or 90 days. However, in-hospital ischemic stroke mortality is an important and easily measurable stroke outcome, and for this purpose, our models performed well.

In summary, the validated GWTG-Stroke risk score uses routinely collected clinical data to predict the risk of in-hospital mortality for patients hospitalized with acute ischemic stroke. Ischemic stroke patients at low, intermediate, and high risk for in-hospital mortality can be identified with the use of demographic and medical history data obtained on hospital admission. There is much better discrimination of risk when NIHSS information is available.

The GWTG-Stroke mortality risk model provides clinicians with a practical bedside tool for mortality risk stratification, developed and validated in a nationwide sample of more than 200 000 ischemic stroke patients. A validated and accurate risk stratification tool should also be of value to health services researchers who are interested in comparing in-hospital mortality rates across different hospitals and systems; further research will be needed to determine whether the risk score will be useful for the purpose of hospital adjustment for case mix. In contrast to previous prediction tools, which have been incorporated into routine clinical practice only rarely, we have implemented real-time reporting of individual predicted mortality in GWTG-Stroke participating hospitals via the World Wide Web–based Patient Management Tool. After patient data have been uploaded, hospitals can access an automated calculation of individual or aggregate mortality risk via the World Wide Web–based tool. There is increasing interest by third-party payers in tracking ischemic stroke mortality, even though the validity of ischemic stroke mortality as an indicator of quality of stroke care is controversial.[7] Future research will be needed to examine how the risk score is used and its effect on clinical practice, to determine the characteristics associated with differences in observed versus expected mortality at the patient and hospital level, and to determine whether an accurate risk score can be developed for hemorrhagic stroke types.

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CLINICAL PERSPECTIVE

Ischemic stroke is one of the top causes of mortality in the United States, and much of this mortality occurs during hospital admission. Determining an individual patient's risk of mortality at admission could aid clinical care by providing valuable prognostic information to patients and their family members. Third-party payers and regulatory agencies have shown increasing interest in tracking stroke mortality as a marker of care, so adjustment for baseline risk of mortality will be necessary to avoid penalizing hospitals that admit less healthy patient populations. Therefore, there is an increasingly important need to develop well-validated models that are useful in predicting patient risk of mortality from ischemic stroke. In this study, data from the US nationwide Get With The Guidelines–Stroke Registry, sponsored by the American Heart Association, were used to develop a risk score for in-hospital ischemic stroke mortality using information routinely available at the time of admission. The model was developed in more than 160 000 patients and then validated in another 110 000. Ischemic stroke patients at low, intermediate, and high risk for in-hospital mortality can be identified with the validated model. A major finding was that the addition of a measure of stroke severity, the National Institutes of Health Stroke Scale score, greatly improved the ability to discriminate between patients who died and patients who survived. Reporting of the risk score has been implemented within Get With The Guidelines–Stroke by use of computerized decision support via a World Wide Web–based tool, so that hospitals can now access automated calculations of individual or aggregate mortality risk.

Risk Score for In-Hospital Ischemic Stroke Mortality Derived and Validated Within the Get With The Guidelines–Stroke Program

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