Derivation and Validation of a Clinical System for Predicting Pneumonia in Acute Stroke

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Key Words

Pneumonia · Stroke · Clinical prediction

Abstract

Aims: We derived and validated a clinical prediction rule that can be used to predict post-stroke pneumonia. **Methods:** We conducted a retrospective cohort study of patients admitted to hospital with a stroke. The cohort was subdivided into a derivation group and a validation group. Within the derivation group, a point scoring system was developed to predict pneumonia based on a logistic regression model. The point scoring system was then tested within the validation group. **Results:** Of the 1,363 patients with stroke, 10.5% of patients experienced new pneumonia. The most points were assigned for abnormal swallowing result and history of pneumonia (4 points), followed by greater NIHSS score (3 points), patient being ‘found down’ at symptom onset (3 points), and age >70 years (2 points). A 3-level classifica-

tion system was created denoting low, medium and high risks of pneumonia, which accurately predicted pneumonia in the validation group. The discriminatory accuracy of the 3-level clinical prediction rule exceeded the acceptable range in both the derivation group (c statistic: 0.78) and validation group (c statistic: 0.76). **Conclusion:** A simple scoring system was derived and validated. This clinical scoring system may better identify stroke patients who are at high risk of developing new pneumonia.

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Introduction

Post-stroke pneumonia (newly developed pneumonia following stroke onset) is one of the most common serious adverse conditions among patients with ischemic stroke, with reported incidence rates ranging from 2.4 to 47%, depending on type of treating unit and stroke sever-

ity of study population [1–3]. In spite of effective interventions for the prevention and treatment of pneumonia, post-stroke pneumonia is the leading cause of mortality after an acute stroke, accounting for nearly 35% of post-stroke deaths [1, 4]. Moreover, post-stroke pneumonia is associated with a greater likelihood of being discharged to long-term care [5].

Previous research has identified various factors that are associated with post-stroke pneumonia, but no overall consistent pattern has emerged. Factors that have been associated with post-stroke pneumonia include: older age, diabetes, dysarthria/aphasia, cognitive impairment, stroke severity, and dysphagia [4, 6–10]. Due to the variability in the research design of these post-stroke pneumonia studies (i.e. mixed acute and non-acute stroke patients, inclusion of non-stroke patients with stroke patients, limited number of factors under consideration), it has been difficult to identify a set of independent risk factors for post-stroke pneumonia. Identifying the stroke patients who are at the highest risk of pneumonia would allow clinicians to target resources and provide intensive prevention interventions, but no simple systems are currently available to identify patients at the greatest risk of post-stroke pneumonia.

The purpose of the present study was to develop and validate a clinical scoring system that would be simple to use and that could predict post-stroke pneumonia among patients with acute ischemic stroke.

Methods

Study Participants

This was a secondary analysis of a retrospective cohort study of patients admitted to 1 of 5 hospitals with a stroke (clinical syndrome differentiated by rapidly emerging clinical indications of global disturbance lasting 24 h or longer or leading to fatality with no apparent determinant other than of vascular origin) [11]. The hospitals, 3 Veterans Health Administration (VHA) and 2 non-VHA facilities, were selected to provide a varied group of settings in terms of: spectrum of stroke care (stroke neurology, general neurology, medicine); geographical diversity (Northeast: Connecticut; South: Florida; West: Idaho); and stroke patient volume (small, medium, and large). Cases were identified using the hospitals' administrative and clinical databases for the period 1/1/98 to 12/31/03. Patients were included in the cohort if they had: an acute ischemic stroke; age ≥ 18 years; neurological symptom onset within 2 days of hospital admission; and neurological deficit present at the time of admission (National Institutes of Health Stroke Scale, NIHSS, ≥ 2). Patients were excluded if: they were residing in a skilled nursing facility at the time of the neurological symptom onset; they were admitted to the hospital prior to stroke symptom onset; and if they were transferred from a separate acute care facility. This study was approved by the institutional review

board at Indiana University and the Research and Development Committee at the Roudebush Department of Veterans Affairs Medical Center in Indianapolis. Institutional review board approval was also attained at each of the individual VHA and non-VHA facilities.

Outcome Variable

The outcome was the clinical diagnosis of pneumonia made during the hospitalization for stroke. This outcome was measured by a single variable and classified as present or absent on the basis of any documentation of a clinical diagnosis of pneumonia in the medical record. We included only documentation made by a physician. Generally, this documentation was made in the assessment and plan and/or the problem list sections of the progress notes of the inpatient medical record.

Independent Variables

Several clinical and disease severity variables were assessed as potential risk factors in the clinical scoring system. These variables were selected because each factor was found to be associated with post-stroke pneumonia in previous studies. All of the independent variables (table 1) were measured at the time of admission to the hospital. The admission period was defined as the first 24 h after the time of admission. Demographic variables included patient sex, race/ethnicity (white, black, other) and age.

We included the following specific past medical history conditions: pneumonia, hypertension, diabetes, COPD, atrial fibrillation, and peptic ulcer disease. We also considered the Charlson co-morbidity index as an assessment of the patients' medical co-morbidity (higher scores indicate severer co-morbidity) [12]. The patient's level of independence at home prior to stroke was measured by a binary variable (home without assistance vs. home with informal/formal assistance). Smoking status was coded as 'current smoker' versus 'other'. The presence or absence of a pre-existing swallowing problem was also recorded. Admission code status was classified as 'full code' versus other.

The baseline stroke severity was assessed using the NIHSS. The NIHSS was calculated retrospectively from the admission neurological examination recorded in the medical record [13]. The NIHSS was used as a continuous variable with higher scores indicating greater stroke severity. Stroke subtype was classified as a binary variable (lacune/lacunar syndrome vs. non-lacunar). We used a binary classification of stroke into lacunar versus non-lacunar because past evidence has indicated that there are no differences in risk factor profiles between lacunar and non-lacunar infarcts [14]. The patients were classified by the physicians' diagnostic category. Patients were considered to have a lacunar stroke if it was characterized by 1 of the following 4 categories: (1) pure motor hemiparesis (a unilateral motor deficit involving the face, the arm, and to a lesser extent the leg); (2) pure sensory stroke (characterized by unilateral numbness, paresthesias, and a hemisensory deficit involving the face, arm, trunk, and leg); (3) ataxic hemiparesis (weakness that is more prominent in the lower extremity in association with ipsilateral arm, lack of leg coordination, and dysarthria is not present); and (4) dysarthria-clumsy hand (characterized by supranuclear facial weakness, tongue deviation, dysphagia, dysarthria, impaired fine motor control of the hand, and an extensor plantar response).

We included 2 components of the stroke symptoms. The first component was a clinical presentation of whether or not the pa-

Table 1. Characteristics of the patients

	Total sample (n = 1,363)	Derivation group (n = 925)	Validation group (n = 438)	p
<i>Demographics</i>				
Male sex	784 (57.5)	534 (57.7)	250 (57.1)	0.8201
Race				
White	1,070 (78.5)	724 (78.3)	346 (79.0)	0.7609
Non-White	293 (21.5)	201 (21.7)	92 (21.0)	
Age (mean $\pm$ SD), years	71.4 $\pm$ 13.2	71.5 $\pm$ 13.3	71.2 $\pm$ 13.1	0.6805
Age $\leq$ 70 years	537 (39.4)	362 (39.1)	175 (40.0)	0.7725
<i>Past/Present Medical History</i>				
History of diabetes	440 (32.3)	296 (32.0)	150 (32.8)	0.7465
History of hypertension	983 (72.1)	666 (72.0)	317 (72.4)	0.8855
History of COPD	179 (13.1)	136 (14.7)	43 (9.8)	0.0126
History of atrial fibrillation	258 (18.9)	167 (18.1)	91 (20.8)	0.2309
History of peptic ulcer disease	52 (3.8)	36 (3.9)	16 (3.7)	0.8297
History of pneumonia	56 (4.1)	39 (4.2)	17 (3.9)	0.7711
Current smoker	302 (22.2)	207 (22.4)	95 (21.7)	0.9627
Pre-existing swallowing problem	20 (1.5)	13 (1.4)	7 (1.6)	0.0318
Charlson comorbidity score (mean $\pm$ SD)	3.0 $\pm$ 2.4	3.0 $\pm$ 2.4	2.9 $\pm$ 2.3	0.3216
<i>Clinical Features</i>				
Stroke subtype				
Lacunar	231 (16.7)	160 (17.3)	78 (17.0)	0.6173
Level of independence prior to stroke				
Independent (no help)	1,086 (79.7)	733 (79.2)	368 (80.5)	0.6636
DNR status at admission				
Full code	1,238 (91.0)	834 (90.3)	412 (90.2)	0.4603
Abnormal swallowing test	179 (13.1)	117 (12.7)	56 (12.2)	0.4419
Found down at symptom onset	96 (7.0)	60 (6.5)	36 (8.2)	0.2430
Symptom course improving	392 (28.8)	257 (27.8)	153 (33.4)	0.2472
<i>Stroke Severity</i>				
Admission NIHSS score (mean $\pm$ SD)	9.4 $\pm$ 7.3	9.4 $\pm$ 7.3	9.6 $\pm$ 7.7	0.9224
Median	7.0	7.0	7.0	
Interquartile range	8.0	8.0	9.0	
<i>Dependent Variable</i>				
New cases of pneumonia	142 (10.4)	96 (10.4)	46 (10.5)	0.9443
Figures in parentheses are percentages.				

tient was 'found down' at symptom onset. 'Found down' refers to the extent to which, if a patient falls, he/she was unable to get up, and then someone finds the patient lying down usually (but not exclusively) on the ground. It is intended to capture the clinical implications of being down for a prolonged period of time. The second component was the course of the symptoms from the time of symptom onset to hospital admission (a nominal level variable classified as either 'stable', 'improving', 'worsening' or 'fluctuating'). 'Stable' refers to no change in symptoms; 'improving' captures the extent to which symptoms have gotten better; 'worsening' refers to steadily deteriorating symptoms; and 'fluctuating' depicts situations when symptoms occur, improve, and then worsen, or worsen and then improve (in this case 'improve' is taken to mean 'not resolved'). The variable was recoded so that

'stable', 'worsening' and 'fluctuating' were combined into a single category and labeled as 'not improving' versus 'improving'.

Among patients who received an assessment of swallowing function within 24 h of admission, dysphagia was defined on the basis of any abnormal swallowing test (e.g. fiberoptic examination, barium swallow, bedside examination). The bedside examination was a non-instrumented diagnostic test and consisted of having the patient swallow water and applesauce. In order for it to be coded as a bedside evaluation for our study, at least 2 modalities (e.g. water, applesauce, solids) needed to be tested. Dysphagia was categorized as present if there was dysphagia for liquids or solids or both. Dysphagia was categorized as absent if the swallowing study demonstrated normal swallowing function or other non-dysphagia results (e.g. slow mastication).

Table 2. Predictors of pneumonia in the derivation group (n = 925)

	Odds ratio	Points allocated	95% CI	p
Patient age >70 years	1.8	2	1.04–2.95	0.0363
Abnormal swallowing test	3.5	4	2.08–5.73	<0.0001
Admission NIHSS score	3.1 ¹	3	1.92–5.00	<0.0001
Found down at symptom onset	2.8	3	1.48–5.26	0.0015
Past medical history of pneumonia	4.0	4	1.70–9.19	0.0014

Only significant (p < 0.05) variables were included in this final regression model.
¹ This refers to a 3-point per unit increase in the NIHSS score.

Statistical Analyses: Derivation of the Post-Stroke Pneumonia Prediction System

The total sample (n = 1,363) was randomly separated into a derivation group (two thirds of total, n = 925) and validation group (one third of total, n = 438). Statistical analyses were performed using a statistical package (SAS version 9.13, SAS Institute, Cary, N.C., USA).

The post-stroke pneumonia prediction system was developed only using the data from the derivation cohort. First, bivariate analyses (χ^2 test on discrete variables and t tests on continuous variables) were employed to evaluate the association between each of the independent variables and the outcome of pneumonia.

Second, the variables that were associated with pneumonia in the bivariate analyses (p < 0.05) were entered into a multivariable logistic regression model. Backwards elimination was employed to select the final set of risk factors that were independently associated with pneumonia.

Third, we assigned points for each variable based on the adjusted odds ratios (AOR) from the multivariable model. The AORs were rounded to the nearest whole number to determine the points.

Fourth, a risk score was developed by summing the points for each risk factor present. Finally, we examined the outcome rate according to the risk score to identify 3 categories of risk: low, medium, and high risk of post-stroke pneumonia.

Statistical Analyses: Validation of the Post-Stroke Pneumonia Prediction System

The risk score and three category risk classification system were tested in the validation cohort. To assess the discriminatory ability of the pneumonia clinical scoring system, we calculated the c statistic from a logistic regression model predicting pneumonia and including the variables identified from the development process [15]. The c statistic, which represents the area under the receiver operating characteristic (ROC) curve, ranges from 0.5 (which indicates no better discrimination than chance) to 1.0 (perfect discrimination). A c statistic value >0.70 is considered acceptable [16, 17]. We compared the proportion of pneumonia cases as determined by the risk score with the actual rates of pneumonia (misclassification rate).

Results

Table 1 presents the patient characteristics of the total sample (n = 1,363), the derivation group (n = 925), and the validation group (n = 438). In the total sample, there were 142 (10.4%) patients with pneumonia, with essentially identical proportions of pneumonia in the derivation (10.4%) and validation (10.5%) groups. In the total sample, 57.5% were male, 78.5% were White non-Hispanic, and the mean age was 71 years. Bivariate comparisons were performed to determine if statistically significant differences emerged between the derivation group and the validation group. A significant difference emerged between the 2 groups for history of COPD and pre-existing swallowing problem. None of the other variables differed between the 2 groups.

All of the variables in table 1 were associated with pneumonia in the bivariate analyses, and were therefore entered into the multivariate logistic regression model. Only 5 variables were independently associated with pneumonia (table 2): past medical history of pneumonia, dysphagia, increasing NIHSS (AOR for each unit of increase in NIHSS 3.10, 95% CI 1.92–5.00), being found down at the time of symptom onset (AOR 2.79, 95% CI 1.48–5.26), and age >70 years [compared with age ≤70 years (AOR 1.8, 95% CI 1.04–2.95)]. The c statistic from the development cohort denoted was c = 0.78. The point scores for each of these 5 characteristics are presented in table 2.

Table 3 presents the scoring algorithm for the 3 pneumonia risk categories for both the development and validation groups. The low-risk classification was based on a score of 0 (no risk factors present), the medium-risk classification was based on the presence of 1–3 risk factors, and the high-risk classification was based on the presence of 4 or more risk factors (table 3). In the development group, the pneumonia rate was 2% for the low-risk group, 4.2% for the medium-risk group, and 23% for the high-

risk group. The c statistic for the 3-category clinical prediction system in the development cohort was $c = 0.78$. Similarly, among the validation group: the pneumonia rate was 0.90% for the low-risk group, 7.3% in the medium-risk group, and 21.5% in the high-risk group. The c statistic for the 3-category clinical prediction system in the validation cohort was $c = 0.76$. The misclassification rate for predicting pneumonia was 0.9% in the validation group and 2.1% in the derivation group (results not shown).

Discussion

The primary objective of the present study was to derive and validate a simple system that could be used to identify patients at highest risk of post-stroke pneumonia. Our results demonstrate that 5 patient characteristics (age >70 years, dysphagia, higher admission NIHSS, found down at symptom onset, and past medical history of pneumonia) can be used to identify patients at risk of post-stroke pneumonia.

The discriminatory accuracy of the 3-category clinical prediction system exceeded the acceptable range in both the derivation (c statistic: 0.78) and validation groups (c statistic: 0.76). The misclassification rate of our prediction rule was very low in both the derivation and validation group. Specifically, in the validation cohort, only 1 (0.9%) of the 46 patients who had post-stroke pneumonia was misclassified as erroneously not having post-stroke pneumonia from the clinical scoring system. Therefore, the clinical usefulness of the 3-category clinical prediction may be realized both by classifying patients in the low-risk group (where the pneumonia rate in the validation cohort was less than 1%) and by classifying patients in the high-risk group (where 1 in 5 patients in the validation cohort developed post-stroke pneumonia). This system may therefore be used both to identify patients who may not require intensive resources and those patients who are most likely to benefit from pneumonia prevention strategies.

Our study results were similar to the findings of Sellars et al. [6] who evaluated 412 acute stroke patients in the United Kingdom. They identified 5 variables which were associated with self-reported pneumonia: age >65 years, dysarthria or no speech due to aphasia, modified Rankin score ≥ 4 [18], Abbreviated Mental Test [19], and failed staged water swallowing test that consisted of progressively larger amounts of water [20]. Even though these findings were informative, some of the factors as-

Table 3. Post-stroke pneumonia rates according to risk classification

	Total score	Derivation		Validation	
		n	pneumonia rate, %	n	pneumonia rate, %
Low	0	239	2.1	111	0.90
Medium	1–3	354	4.2	178	7.3
High	≥ 4	332	22.9	149	21.5
Total		935		438	

Total scores of 0 (low risk), 1–3 (medium risk), and ≥ 4 (high risk) indicate 0, 1–3, and ≥ 4 risk factors present, respectively.

sociated with post-stroke pneumonia were based on testing that may not be routinely performed in clinical practice (i.e. the Abbreviated Mental Test or the staged water swallowing test).

Consistent with previous research, we found that older age, abnormal swallowing test, and worse stroke severity were associated with post-stroke pneumonia [4, 6, 21–23]. However, we also identified 2 characteristics not previously reported to be predictive of post-stroke pneumonia – past medical history of pneumonia and ‘found down’ at symptom onset. Being ‘found down’ is rarely considered in the context of post-stroke pneumonia. Patients who are ‘found down’ at stroke onset may have aspirated gastric contents and actually have pneumonia present at the time of presentation to the hospital; however, this pneumonia may have been unrecognized until some point after admission. Similarly, patients with a history of pneumonia may either have been at increased risk of post-stroke pneumonia, or might have had unrecognized pneumonia present at admission.

Numerous studies have demonstrated that dysphagia is associated with post-stroke pneumonia, as well as post-stroke mortality, persistent disability, and prolonged hospital stay [6, 24, 25]. Unlike the other (non-modifiable) factors that are associated with post-stroke pneumonia (e.g. patient age), swallowing problems can be treated. Several studies have demonstrated that the implementation of a dysphagia screening protocol can decrease the incidence of pneumonia in hospitalized acute stroke patients [4, 26, 27]. Although controversy exists regarding the most valid and suitable dysphagia screening assessment for stroke patients, the evidence clearly demonstrates that stroke patients should receive some assessment of swallowing function and that pneumonia pre-

vention strategies should be implemented for patients with impaired swallowing.

The NIHSS is increasingly being used as the measure of stroke severity among patients with ischemic stroke. Our findings underscore the importance of using the NIHSS not only as a measure of stroke severity, but also as part of an assessment for pneumonia risk.

There were several strengths to this study, including the large sample, the geographically diverse location of patients recruited from both private and federal government hospitals, and the use of well-accepted and widely available demographic and clinical variables used for development of this clinical risk prediction system. However, the study had some limitations that should be acknowledged. First, these data were obtained from patients who were admitted to a hospital during 1998–2003. Despite this, we do not believe that clinical practice has changed substantially or that the associations between the demographic and clinical factors predictive of pneumonia would differ currently.

Second, given that the original sample excluded patients admitted from a skilled nursing facility and those patients who had a stroke ‘in house,’ these findings may not be generalizable to these patient groups. Since the majority of patients admitted with a stroke are coming from home, not from a nursing home or another hospital, our findings should be generalizable to the majority of stroke patients. Future studies should specifically address the issue of pneumonia risk prediction among nursing home patients who may be at higher risk of pneumonia than patients who have their stroke onset while residing at home.

Third, due to the nature of the retrospective chart review in our present study, our definition of pneumonia required documentation by the clinician. A verification of this clinical diagnosis via chest radiographs, cultures,

and chest computed tomography was beyond the scope of the present study. However, this study may have under-recognized the true rates of post-stroke pneumonia overall and within risk categories. Future studies should test the validity of the 3-category risk prediction system in a prospective cohort where pneumonia events are clearly defined and prospectively identified. Fourth, there is a possible confounding effect of parameters not taken into account in the present models. For instance, the patient’s past or present medical history or concomitant medication, such as antibiotics at admission or immunosuppressive drugs, could lead to an immunosuppressive state.

Conclusion

We conclude that a simple 3-category clinical prediction system that consists of 5 variables (dysphagia, history of pneumonia, higher NIHSS score, patient ‘found down’ and age >70 years) can identify stroke patients at lower and higher risk of pneumonia. This clinical scoring system may be particularly relevant for hospitals using information technology systems. The clinical prediction system could easily be implemented and tested as part of a stroke decision support tool to prompt recognition of patients who are at high risk of developing pneumonia.

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