

Pneumonia in Patients with Acute Stroke: Derivation of a Clinical Prediction Rule

Sara K Schepp

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Committee:

Noel S Weiss

David L Tirschwell

WT Longstreth, Jr

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Abstract

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Sara Kay Schepp

Chair of the Supervisory Committee:

Noel S Weiss, Professor

Epidemiology

Background: Pneumonia is a common and dangerous consequence of acute stroke. Others have derived pneumonia prediction scores to guide management but included information on swallowing function, which may not be routinely available at the time of hospital admission. **Methods:** We conducted a retrospective cohort study to identify predictors of pneumonia incidence (identified by ICD-9 codes 480-486.99 or 507.xx) among 1,924 patients treated for acute stroke at Harborview Medical Center in Seattle, WA, based upon information available only at admission and without information on swallowing function. Risk estimates were determined after adjustment for age. Multivariate associations were determined using logistic regression, with beta coefficients for the predictor variables providing weights for each item in a prediction score. **Results:** Pneumonia occurred in 291 (15%). Independent predictors of pneumonia, and their contribution to the pneumonia score were the following: Age over 75 years (2 pts); male (1 pt); National Institutes of Health Stroke Scale score over 10 (2 pts); receipt of mechanical ventilation (4 pts); history of coronary artery disease (1 pt); lack of diabetes (1 pt); and history of chronic obstructive pulmonary disease (1 pt). The resulting 12-point score had an area under the receiver operating characteristic curve of 0.79 (95% confidence interval 0.76 to 0.81). **Conclusion:** Our pneumonia prediction score achieved fair discriminatory accuracy despite not including information of swallowing function. However, there may be limited clinical utility of a tool to screen for pneumonia in patients with acute stroke that is only as accurate as this one.

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Introduction

Pneumonia affects 7-12 % of patients during acute hospitalization for stroke.¹ It is associated with higher risk of mortality, greater length of stay, and worse outcome even after adjustment for stroke severity and other risk factors.²⁻⁵ Pneumonia may hinder neurologic recovery at a cellular level by triggering or enhancing an immune response to brain autoantigens such as myelin basic protein, leading to secondary injury.⁶

Prior researchers have identified age, stroke severity, mechanical ventilation, and impaired swallowing as risk factors for pneumonia after stroke.^{3,5,7-11} Other risk factors that have been identified on a less consistent basis include male gender,^{3,10} chronic lung disease,^{3,7,11} abnormal mental status or communicative ability,^{5,9} atrial fibrillation,¹¹ coronary artery disease,³ dependent state prior to admission,³ congestive heart failure,¹¹ and non-lacunar ischemic stroke.^{3,9}

In an effort to apply knowledge of risk factors to clinical practice, several groups^{5,8,10} have proposed pneumonia prediction scores. These are simple clinical indices that can be used by clinicians to identify patients at high or low risk for pneumonia. Such an approach is akin to the ABCD2 score, developed to stratify risk and determine optimal management for patients with suspected transient ischemic attack.¹² In the case of patients identified as being at high risk for pneumonia, such a score may trigger measures aimed at prevention, such as higher level of nursing care and vigilance, early patient mobilization, use of antimicrobial oral cleansing, or prophylactic systemic antibiotics.

One limitation of the previously proposed pneumonia prediction scores is that they rely on an assessment of swallowing function. While a strong predictor of pneumonia,¹³ an assessment to indicate presence of abnormal swallowing may not be readily available at the time of admission. And while nursing swallowing screens are widely done in the setting of acute stroke, there is no standard screen with wide-scale use¹⁴ nor, in fact, agreement on which items constitute the best screen.¹⁵ Indeed, the measures of swallowing function used in the previous pneumonia prediction indices varied from one study to the next, and, in one study,⁸ also varied from one patient to the next. As a result, though validity was high within the samples from which these indices were obtained, the results may not be reproducible in other settings where a different assessment of swallowing is used.

We therefore sought to determine whether we could achieve comparable levels of predictive power with a pneumonia prediction score that is based solely on information available at admission and thus does not include an assessment of swallowing function.

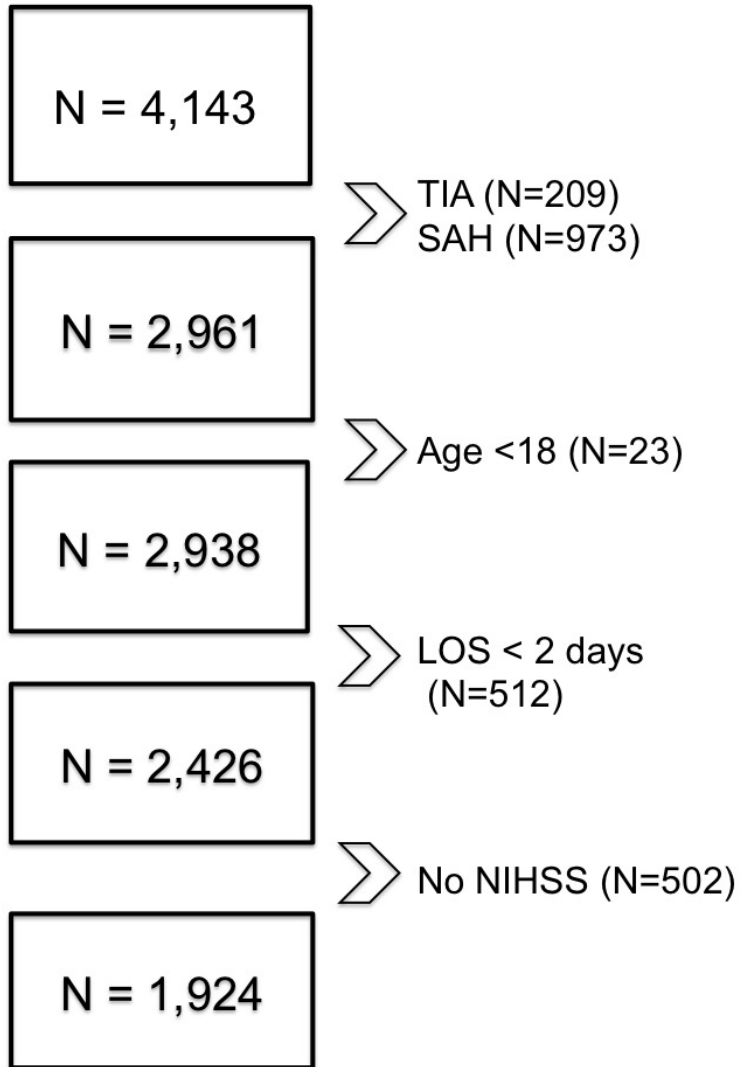
Methods

After obtaining approval from the Institutional Review Board for University of Washington, we conducted a retrospective cohort study using a stroke database for Harborview Medical Center, a 413-bed tertiary care hospital in Seattle, Washington. Harborview is a Joint Commission accredited primary stroke center, which receives severe and complicated cases from outlying areas. This database includes information for all patients discharged from the hospital with the diagnosis of stroke, as indicated by use of the following ICD-9 codes as principal diagnosis: 430.xx, 431.xx, 433.xx, 434.xx, or 436.xx. We collected information from the database and supplemented this with data from the electronic medical record for each patient discharged with stroke from 2004 to early 2011 (n=4,143).

As shown in Figure 1, we excluded patients who were diagnosed with transient ischemic attack (n=209), were diagnosed with subarachnoid hemorrhage (n=973), or were under age 18 (n=23). We also excluded patients who were discharged within the first two days of admission in an effort to ensure there was sufficient observation time for pneumonia to have developed (n=512). Finally, we excluded those patients for whom National Institutes of Health Stroke Scale (NIHSS) scores were not available (n=502).

Exposure variables examined were those associated with pneumonia in prior studies and included demographic characteristics, past medical history, and details of the stroke and medical presentation. Age, gender, and self-reported race/ethnicity were abstracted from admission documents. Most features of past medical history (prior stroke, coronary artery disease, atrial fibrillation, congestive heart failure, diabetes mellitus, history of smoking) were counted as “positive” if the patient was reported in admission, progress, or discharge reports to have had such a history. They were not counted as “positive” if the patient was newly diagnosed with one of these conditions during the index admission because we were interested only in information that would be available at time of admission. History of chronic obstructive pulmonary disease was counted as “positive” if ICD-9 codes 490-496 were included in the discharge abstract. Stroke severity was measured by the National Institutes of Health Stroke Scale (NIHSS), a 42-point scale based upon the neurologic exam with higher values indicating greater severity. If the NIHSS score was documented by a physician at admission, this value was used. If no NIHSS score was recorded at time of admission, it was calculated retrospectively based upon the first documented neurologic exam during the admission. For a portion of the patients (n=446), neither an original nor a retrospective NIHSS was available; these patients were excluded. Mechanical ventilation was recorded as “positive” if procedure codes 96.04 or 96.70-96.72 were included within the discharge abstract. We were unable to ascertain the timing of mechanical ventilation during the hospital stay, but made the assumption that, if mechanical ventilation was employed at all, it would have been initiated close to the time of admission in the large majority of cases.

Figure 1: Numbers of patients and exclusions. TIA = transient ischemic attack, SAH = subarachnoid hemorrhage, LOS = length of stay, NIHSS = National Institutes of Health Stroke Scale.



Patients were counted as having pneumonia if the discharge abstract included the ICD-9 codes 480-486.99 or 507.xx. Only one instance of pneumonia per hospitalization was counted.

Medical record review for a randomly drawn sample of 5% of patients who were coded as having pneumonia and a randomly drawn sample of 1% of patients coded as not having pneumonia was done, with review of discharge summaries and chest radiography used as gold standard for presence or absence of pneumonia. A randomly drawn sample of patients coded as undergoing (5%) or not undergoing (1%) mechanical ventilation was similarly validated by medical record review with information from physician or respiratory care notes indicating presence of an endotracheal tube used as gold standard for presence or absence of mechanical ventilation. Further, for the random subset of patients coded as being mechanically ventilated, we collected information on timing of the mechanical ventilation relative to admission and to diagnosis of pneumonia.

Initially, risk estimates were adjusted for age using the Mantel Haenszel method.¹⁶ Univariate associations were calculated using chi-square analysis, and those variables having an association with pneumonia corresponding to a p value of 0.10 or less were included in a multivariable model.

Each of the variables from the resulting multivariable model that emerged as independent predictors, as indicated by a p value of 0.05 or less, was included in a final multivariable logistic regression. Beta coefficients for each predictor from the final logistic regression were used to determine weights for each corresponding item in the pneumonia prediction score. For continuous variables such as NIHSS and age, lowess smooth plots of the independent variable against outcome of pneumonia were visually inspected to help identify optimal cut-off values for subcategories of the predictor.

Results

A flowchart summarizing the exclusions that led to the final cohort of 1,924 patients is included in Figure 1. Of the 512 patients who were excluded for length of stay less than two days, the majority (331/512 or 65%) died in the hospital. The 502 patients who were excluded due to lack of NIHSS score were more likely to have had intracranial hemorrhage, more likely to be mechanically ventilated, and more likely to be diagnosed with pneumonia. Of 1,924 persons with stroke who met eligibility criteria, 291 (15%) were coded as having pneumonia during the hospitalization. Table 1 outlines the characteristics of those with and without pneumonia, after adjustment for age. Additional details are included in supplemental Table A in the Appendix, including the univariate risk estimates, which were obtained from chi-square analysis and were used to determine the variables that would be entered in the multivariable model. Those variables having a significant (here, $p < 0.10$ or less) association with pneumonia

Table 1: Characteristics of the 1,924 stroke patients with and without pneumonia, columns may not add to 100 due to rounding.

Characteristics*	Pneumonia (n=291)	No Pneumonia (n=1,633)	Relative Risk (age-adjusted)
Demographic	N (%)		RR (95% CI)**
Age (years)			
< 60	86 (30)	689 (42)	1.0
60-75	98 (34)	544 (33)	1.4 (1.1 – 1.8)
> 75	107 (37)	400 (24)	1.9 (1.5 – 2.5)
Male	181 (62)	907 (56)	1.4 (1.1 – 1.9)
Race/Ethnicity			
White	229 (79)	1,122 (69)	1.0
Black	18 (6)	152 (9)	0.7 (0.4 – 1.1)
Asian/Pacific Islander	23 (8)	162 (10)	0.7 (0.5 – 1.2)
Hispanic	10 (3)	64 (4)	0.9 (0.4 – 1.8)
Native American/Alaskan	3 (1)	9 (< 1)	1.9 (0.5 – 6.8)
Unknown	8 (3)	124 (8)	
Stroke/Hospitalization			
NIHSS (points)			
< 6	57 (20)	768 (47)	1.0
6 - 10	37 (13)	299 (18)	1.6 (1.0 – 2.6)
11 - 15	43 (15)	185 (11)	2.9 (1.9 – 4.5)
> 15	154 (53)	381 (23)	5.2 (3.7 – 7.3)
Stroke type			
Ischemic	145 (50)	924 (57)	1.0
Hemorrhagic	146(50)	709 (43)	1.2 (1.0 – 1.6)
Mechanical Ventilation during Hospitalization	177 (61)	326 (20)	6.6 (4.9 – 8.8)
Past Medical			
Prior Stroke	53 (18)	362 (22)	0.7 (0.5 – 1.0)
Coronary artery disease	76 (26)	284 (17)	1.5 (1.1 – 2.0)
Atrial fibrillation	78 (27)	262 (16)	1.6 (1.2 – 2.2)
Diabetes	54 (19)	416 (25)	0.7 (0.5 – 0.9)
Heart failure	14 (5)	46 (3)	1.6 (0.9 – 3.0)
COPD	52 (18)	184 (11)	1.6 (1.1 - 2.3)
Smoking in the past year	54 (19)	379 (23)	0.9 (0.7 – 1.2)

*Characteristics of acute stroke patients available from around the time of admission. NIHSS = National Institutes of Health Stroke Scale. COPD = chronic obstructive pulmonary disease.

** Estimates of relative risk (RR) and 95% confidence intervals (CI) were adjusted for age using the Mantel Haenszel method.

were entered into a multivariable logistic regression model with pneumonia as outcome. Table B in the appendix details the variables included in the multivariable logistic regression. Those variables having an association with pneumonia with p value of 0.05 or less were considered independent predictors of pneumonia and were included in a final multivariable regression model that included only the independent predictors. The results of the final logistic regression model are summarized in Table 2 and include: age over 75 years, male gender, NIHSS score greater than 10, receipt of mechanical ventilation, history of coronary artery disease, lack of diabetes, and history of chronic obstructive pulmonary disease.

Using the independent predictors and their weights from the final multivariable regression, we devised a pneumonia prediction score ranging from zero to twelve points (Table 2). One point was assigned for roughly every value of 0.30 – 0.40 in the variable's beta coefficient. Figure 2 shows the proportions of patients with a given pneumonia score and with pneumonia. This model yielded a receiver operating characteristic (ROC) curve (Figure 3) with area under the curve of 0.79 (95% confidence interval 0.76 to 0.81). Sensitivities, specificities, and predictive values for each cut off of the score are summarized in Table 3. A score of 2 or more was associated with 99% sensitivity and a 99% negative predictive value, indicating that 1% or fewer patients would be mistakenly identified as not being at risk for pneumonia.

We aggregated the patients into three groups based upon their pneumonia score. Nineteen percent of the total sample (n=359) received a pneumonia score of 0 or 1 with a cumulative pneumonia incidence of 1.1% (n=4). Those with a score of 2 or 3 accounted for 33% of the total sample (n=639) and had a cumulative pneumonia incidence of 5.5% (n=35). Eighty-seven percent of cases of pneumonia occurred in those with scores of 4 or more, which automatically included all those who received mechanical ventilation. This group accounted for 48% of the total sample (n=925) and had a cumulative pneumonia incidence of 27.1% (n=252).

We sought to estimate the validity of two key variables against a review of the medical record. For a randomly selected 5% of patients coded as having pneumonia, 18/19 (95%) had physician documentation of pneumonia, and 18/19 (95%) had multiple indicators of pneumonia, such as abnormal chest examination, hypoxia, fever, elevated white blood count, positive sputum culture, radiographic evidence of pneumonia, and administration of antibiotics. In a random subset of 1% of patients coded as not having pneumonia, 20/20 had physician discharge summaries that did not indicate the occurrence of pneumonia, indicating 100% specificity. For a random 5% of patients coded as being mechanically ventilated, 36/36 were found to have been mechanically ventilated in medical record review. For a random 1% of those coded as not having undergone mechanical ventilation, we found, however, this to be true for 14/17 patients, for a specificity of 82%. We also determined the timing of

Table 2: Odds ratios, beta coefficients, and points for each of the independent predictors of pneumonia.

	Odds ratio (95% confidence interval)	Beta coefficient	Points on Pneumonia Score
Age > 75 years	2.0 (1.5 – 2.6)	0.67	2
Male	1.6 (1.2 – 2.1)	0.46	1
NIHSS > 10 points	2.1 (1.6 – 2.9)	0.75	2
Mechanical ventilation	4.9 (3.6 – 6.6)	1.60	4
Coronary artery disease	1.6 (1.2 – 2.2)	0.48	1
Non-diabetic	1.4 (1.0 – 2.0)	0.35	1
COPD	1.5 (1.1 – 2.3)	0.44	1

Figure 2: Percentages of patients with pneumonia score values (bar) and percentages of patients diagnosed with pneumonia (line).

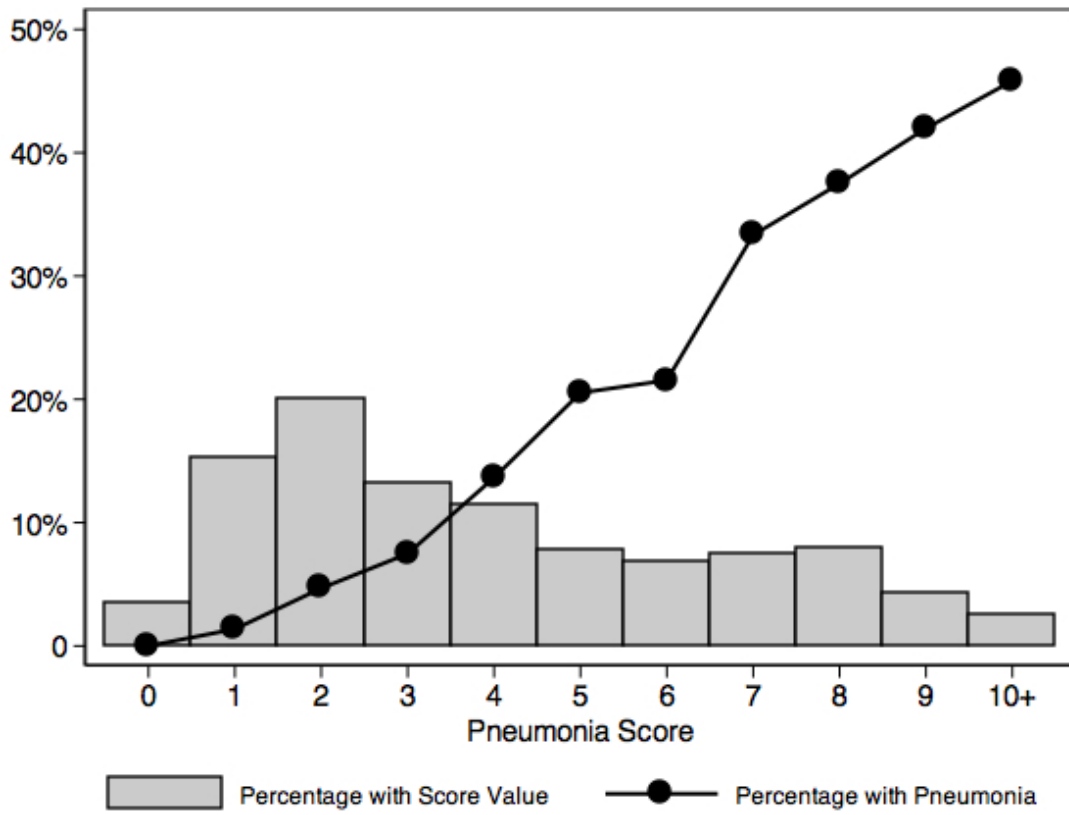


Figure 3: Receiver operating characteristic curve for pneumonia score.

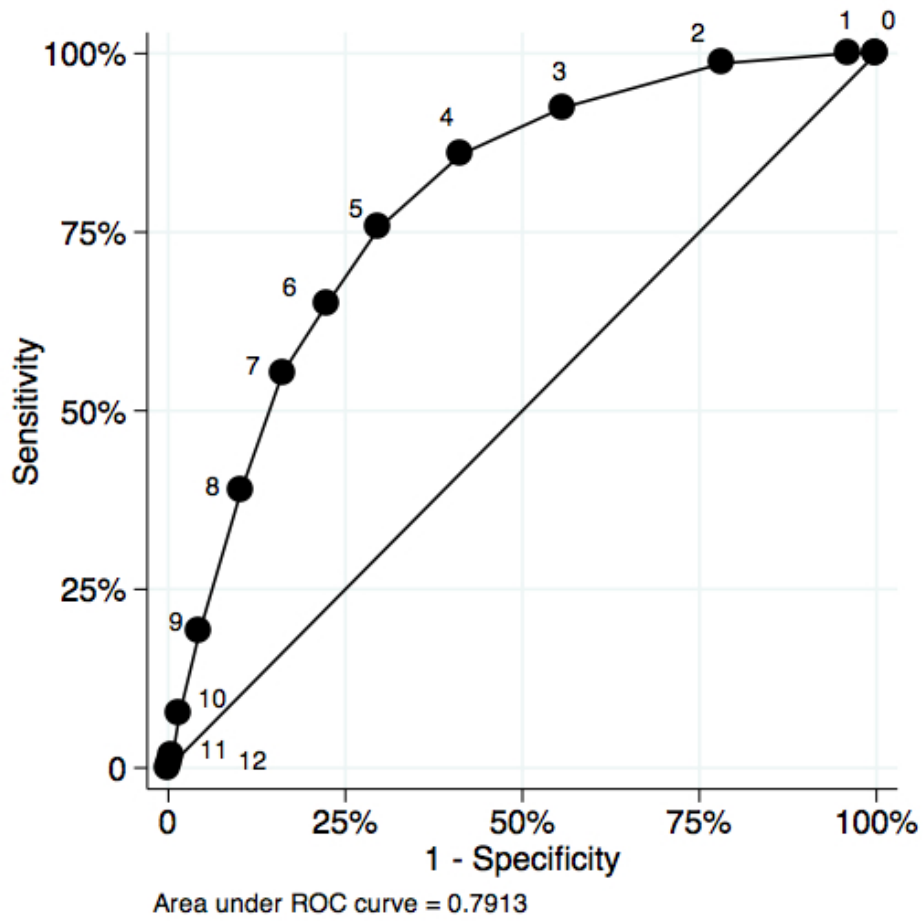


Table 3: Sensitivity, specificity, positive predictive value, and negative predictive value for each of the cut off points of pneumonia score.

Score cut off	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
≥ 0	100	0	15	N/A
≥ 1	100	4	16	100
≥ 2	99	22	18	99
≥ 3	92	44	23	97
≥ 4	86	59	27	96
≥ 5	76	70	31	94
≥ 6	65	78	34	93
≥ 7	55	84	38	91
≥ 8	39	90	40	89
≥ 9	19	96	43	87
≥ 10	8	98	45	86
≥ 11	2	99	34	85
≥ 12	< 1	100	38	85

mechanical ventilation for a random 5% of patients coded as having undergone that exposure. The majority of these patients (31/36 or 86%) were intubated prior to or within several hours of arrival to the emergency department.

Discussion

Like others, we found independent predictors of pneumonia to be age, male gender, stroke severity, the need for mechanical ventilation, history of atrial fibrillation, and history of chronic obstructive pulmonary disease. Our pneumonia prediction score, based only on information that could be readily obtained at the time of admission, performed comparably to the score developed by Chumbler and associates⁸, though less well than those of Sellars et al⁵ and Kwon et al¹⁰ (Table 4). All three prior scores used information about swallowing function. Our study differs from the others in using only information available at time of admission. It is also the largest of the studies.

It is not clear why diabetes was inversely associated with the risk of pneumonia in our sample, and we are not aware of other studies that have observed this. Patients with diabetes were less likely to have had a hemorrhagic stroke (odds ratio 0.8 with 95% confidence interval 0.7 to 0.9) and significantly more likely to have lacunar strokes (odds ratio 1.8 with 95% confidence interval of 1.3 to 2.4). It may therefore be that patients with diabetes tended to have relatively less severe strokes and that our model did not sufficiently control for severity.

Perhaps the most striking finding of our study is the large magnitude of association between receipt of mechanical ventilation and diagnosis of pneumonia. While other groups have noted this as well, two of the three^{5,8} previously proposed pneumonia risk scores did not include mechanical ventilation as a risk factor. In fact, whether patients who underwent mechanical ventilation were included in these studies is unclear. In the third study,¹⁰ only 31 of the 286 patients were mechanically ventilated.

Our study is not without limitations:

1. We lacked information on the timing of pneumonia relative to the onset of stroke. We assumed that pneumonia would virtually always be a result of stroke but have no way of evaluating that with the data available. It is possible we are mistaken and pneumonia preceded stroke. Evidence for this possibility comes from a recent case-crossover analysis, which found that patients with incident stroke were significantly more likely to have been hospitalized for infection in the days before their stroke.¹⁷

2. We were unable to determine to what extent detection bias may have accounted for the high cumulative incidence of pneumonia among those patients who were ventilated. Certainly those patients who were ventilated would have

Table 4: Summary of previous studies describing pneumonia prediction scores.

Study	N	Proportion of Subjects who were Mechanically Ventilated	Score Items and Points*	Outcome	Accuracy**
Present study	1,924	291/1,924 (15%)	Age >75 (2 pts) Male (1 pt) NIHSS > 10 (2 pts) Mechanical ventilation (4 pts) Coronary artery disease (1 pt) Non-diabetic (1 pt) COPD (1 pt)	ICD-9 codes designating pneumonia (480-486.99, 507.xx)	0.79 (0.76-0.81)
Chumblor et al, 2010 ⁸	1,363	Not mentioned	History of pneumonia (4 pts) Being “found down” (4 pts) Age >70 (2 pts) NIHSS (3 pts for every point above 2) Abnormal swallowing test (3 pts)	Physician documentation of pneumonia during hospitalization	0.78 in derivation group 0.76 in validation group
Sellars et al, 2007 ⁵	412	Not mentioned	One point each: Age > 64 Dysarthria or no speech mRS score of >3 Abbreviated MT <9 Abnormal water swallow test	Pneumonia, as defined by Mann criteria ¹⁸ within 3 months	0.90 (0.86 – 0.94)
Kwon et al, 2006 ¹⁰	286	31/286 (11%)	One point each: NIHSS > 10 Age > 64 Male Mechanical ventilation Abnormal swallow	Pneumonia based upon a set of clinical, lab and radiographic criteria within 30 days	0.95

*National Institutes of Health Stroke Scale (NIHSS) is a measure of stroke severity. Modified Rankin Scale (mRS) is a disability and dependence scale used in stroke, ranging from 0 (no symptoms) to 6 (death). The Mental Test (MT) is a cognitive screening tool with maximum possible score of 10.

**Area under the receiver operator characteristic curve, with 95% confidence intervals in parentheses where provided.

been monitored more closely for pneumonia with chest radiographs, careful lung exams, and respiratory secretion cultures than the patients who were not ventilated.

3. We were unable to determine to what extent management decisions made for the patients in our sample (for instance whether they received swallowing screens or evaluations, whether they were fed an oral diet or had feeding tubes placed) may have modified the risk for pneumonia.

4. We lacked admission NIHSS scores for nearly 20% of otherwise eligible patients and therefore excluded them. This reduced our power to detect associations and may also have introduced bias since the subjects lacking NIHSS data were more likely to have had intracranial hemorrhage, more likely to be mechanically ventilated, and more likely to be diagnosed with pneumonia.

5. Our study was conducted within a single center, a regional referral center that receives severe and complicated cases from surrounding medical centers. As a result, our sample contained a relatively high proportion of patients with an intracranial hemorrhage and patients needing mechanical ventilation. The prediction score derived in our population may not perform as well in other settings.

6. We ascertained the presence of co-morbid conditions from notes that indicated a history of the disease. However, for chronic obstructive pulmonary disease (COPD), we relied on ICD9 coding. We made the assumption that COPD would be a rare incident disease in our stroke cohort and that discharge coding would give a reasonable approximation for its presence prior to hospital admission.

Though our pneumonia score had reasonably fair discriminatory accuracy, particularly in identifying those at relatively low risk for developing pneumonia, it is not expected to be of broad clinical utility. This is because the efficacy of measures to prevent pneumonia, such as early mobilization or aggressive oral care, while not well studied, are likely to be at least moderately effective. Such measures are also relatively low cost and low risk, so there may be little reason to restrict their use to those at highest risk for pneumonia.

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