

Predictive Value of the Pneumonia Severity Score on Mortality due to Aspiration Pneumonia

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ABSTRACT

Objective: Designing an efficient management strategy for aspiration is of high priority in our aging society because of its high incidence. We evaluated the prognostic value of both the A-DROP (age, dehydration, respiratory, disorientation, and pressure) and the modified A-DROP scoring systems (adding respiratory rate and comorbidity to A-DROP) in patients with aspiration pneumonia.

Design: This is a retrospective study using electronic medical records at Saitama Medical University (SMU) hospital.

Setting: A 965-bed university tertiary medical center in Japan.

Participants: Data were extracted from the electronic medical records of patients from SMU hospital.

Methods: In-hospital mortality was compared between two groups: 1) those with a 'severe' to 'advanced severe' A-DROP score; and 2) those with a 'low' to 'middle' A-DROP score. Area under the curve (AUC) for mortality for both the A-DROP and modified A-DROP scoring systems were compared.

Results: The in-hospital mortality rates for patients with a high and a low A-DROP score were 28.6% and 9.0%. The mortality rates in the high modified A-DROP score group and in the low modified A-DROP score group were 28.2% and 9.9%. These differences in the mortality rates between the two groups were statistically significant for both the A-DROP and the modified A-DROP scoring systems. The AUC of the receiver operating characteristics curve for the A-DROP (0.700; 95% confidence interval, 0.608-0.779) was statistically significant.

Conclusion: The A-DROP and modified A-DROP scoring systems are associated with in-hospital mortality in patients with aspiration pneumonia. The A-DROP scoring system is easy to use and may be a clinically valuable tool in the management of aspiration pneumonia.

Keywords: Aspiration pneumonia; A-DROP; Modified A-DROP; Mortality; Prognosis

INTRODUCTION

Pneumonia is a common disease and is a major cause of death. In elderly population, in particular, pneumonia is a leading cause of death.¹⁻³ Thus, in a rapidly aging society such as that of Japan, pneumonia is of major clinical concern.

Aspiration pneumonia accounts for 5% to 24% of pneumonia cases.⁴⁻⁷ Aspiration pneumonia is an infection of the lung parenchyma, caused by inhaling gastric or oropharyngeal content into the lower respiratory tract.⁸ It primarily affects older adults, with 80% of those affected being 65 years of age or older.⁹ Previous studies have shown that aspiration pneumonia is associated with a higher mortality rate and longer hospital stays compared to other causes of pneumonia.¹⁰⁻¹² Therefore, an efficient management strategy for the treatment of aspiration pneumonia is of high clinical priority in this aging society.

It is important to assess disease severity in order to plan and stratify the care of pneumonia patients, because identifying patients likely to have a major adverse outcome is a first step in reducing mortality rates.¹³ Assessing severity also guides therapeutic options such as the need for hospital or intensive care admission, suitability for discharge home, the extent of investigation, and the choice and route of administration of an antimicrobial agent.¹⁴⁻¹⁶ Several severity scoring systems such as the Pneumonia Severity Index (PSI) and the Confusion, Urea, Respiratory rate, Blood pressure plus age ≥ 65 years (CURB-65) are available for the stratification of pneumonia cases, and these scoring systems not only denote disease severity but have also been shown to be associated with prognosis.¹⁶⁻¹⁹ Thus, it is useful for clinicians to use a

severity scoring system in deciding upon a treatment strategy, including the assignment of the appropriate care setting, i.e. outpatient, hospital, or intensive care.

In Japan, the A-DROP (age, dehydration, respiratory, disorientation, and pressure) scoring system has been adopted by the Japanese Respiratory Society (JRS).²⁰ The A-DROP was adapted from the CURB-65 by taking oxygen saturation into account in the scoring system instead of respiration rate. There have been reports that, similar to other pneumonia severity scoring systems, the A-DROP scoring system is associated with disease prognosis.²¹⁻²³ Thus, the A-DROP is frequently used in the clinical setting to assess severity and is also used for the management of pneumonia in Japan. A modified A-DROP score, which adds the respiration rate and data on comorbidities to the A-DROP score, was reported to be better for the prediction of prognosis in pneumonia. Tateyama *et al.* reported that adding 1 point to the A-DROP score if respiratory rate is 30 breaths per minute or more, or if the patient has comorbidities including congestive heart failure, cerebrovascular disease, renal disease, chronic obstructive pulmonary disease, or any type of cancer, increased the area under the curve (AUC) of receiver operating characteristics (ROC) from 0.807 to 0.840.²⁴

While pneumonia severity scoring systems are widely used in the clinical setting to stratify pneumonia management efficiently, some studies have reported that severity scoring systems do not predict prognosis accurately in the case of aspiration pneumonia.^{25,26} Additionally, most studies on the use of scoring systems for ascertaining the prognosis of pneumonia have excluded cases of aspiration pneumonia.^{13,16} At present, further evidence is needed to elucidate whether severity scoring systems such

as the A-DROP or the modified A-DROP scores can predict prognosis for aspiration pneumonia.

In this study, we evaluated the prognostic value of both the A-DROP and the modified A-DROP scoring systems in the setting of aspiration pneumonia.

METHODS

Study design and Setting

This was a retrospective study using the electronic medical records (EMRs) of Saitama Medical University (SMU) hospital in Japan for the study period from January 1st, 2017 to April 16th, 2018. SMU hospital has 965 beds and plays an important role in providing care as a tertiary medical center. In this retrospective analysis of data from EMRs, cases of inpatient aspiration pneumonia were identified by using the ICD-10 code specific to aspiration pneumonia and pneumonitis (J690).

Sample size calculation was performed before conducting the study. Based on a previously reported study conducted in Japan,²⁷ the 30-day mortality of aspiration pneumonia in the low to middle and severe categories of the A-DROP score were 2.5 % and 19.4% respectively. We used study type I error (α) = 0.05 and type II error (β) = 0.20 in the sample size calculation.²⁸ The calculation indicated that 52 cases in each group would constitute an appropriate sample size. Thus, 120 cases in total were chosen as the total sample size in this study, to account for a margin of error.

The enrolled cases were independently reviewed by two investigators (N.H. and T.N.). After case identification and review, two investigators reached the consensus that

all but one of the identified cases (age less than 20 years old at the time of hospitalization) met the inclusion criteria (see below).

This study was approved by SMU hospital institutional review board (#18161) and we obtained IRB consent for waiver of patients' consent before embarking on retrospective record review study.

Inclusion and Exclusion criteria

The criteria for inclusion were:

- 1) age \geq 20 years
- 2) inpatient
- 3) ICD-10 code indicating aspiration pneumonia as the primary diagnosis (J690).

To exclude patients with recurrent pneumonia episodes, only the first hospitalization with aspiration pneumonia was chosen in the data analysis.

Measurements

The independent variable was the A-DROP score. To determine the A-DROP score, we extracted the first measurement of vital signs on admission, including SpO₂, age, mental status, and the first laboratory data from the EMRs, and calculated the A-DROP score for each case based on the JRS guideline. A A-DROP score (consisting of age \geq 70 years in males or \geq 75 in females, blood urea nitrogen \geq 21 mg/dL or signs of dehydration, oxygen saturation measured by pulse oximetry \leq 90%, confusion, and systolic blood pressure \leq 90 mmHg) was calculated by giving one point for each feature if present (range 0-5). When SpO₂ was not available, data from arterial blood gas analysis (PaO₂ \leq 60 Torr) was alternatively used to determine oxygen saturation. Data on comorbidities (congestive

heart failure, cerebrovascular disease, renal disease, chronic obstructive pulmonary disease, and any type of cancer) for the calculation of the modified A-DROP scores were extracted from the EMRs. Residence before admission and performance status (PS) were also extracted from EMRs in order to further describe the basic characteristics of the study participants. The primary outcome was in-hospital mortality. We also analyzed 30-day mortality. Based on the collected data, we calculated the area under the receiver operating characteristics curve (AUC) for both the A-DROP and the modified A-DROP scoring systems in relation to in-hospital mortality.

Statistical Analysis

Descriptive analysis was performed using numbers, medians, and interquartile ranges (IQRs) for numeric values. For categorical data, counts and proportions were calculated as percentages. We compared the in-hospital mortality and 30-day mortality between the severe to advanced severe group (A-DROP score 3 to 5) and the low to middle group (A-DROP score 0 to 2). Similarly, in-hospital mortality was compared between those that had high (score between 4 to 7) versus low (score between 0 to 3) scores on the modified A-DROP scoring system. The chi-square test was used to determine the difference in mortality between the two groups. AUC was calculated both for the A-DROP score and the modified A-DROP score. Then, AUCs were compared statistically.²⁹ A two-tailed *P* value of < 0.05 was considered to be statistically significant. IBM SPSS Statistics (Version 26.0. Armonk, NY) was used for the analysis.

RESULTS

In total, 121 cases of aspiration pneumonia with the hospitalization during the study period were identified retrospectively. One case was excluded and the final sample size was 120. Table 1 shows the study participants' characteristics. There were 81 males and 39 females enrolled in this study. The median ages (IQRs) of the overall, male, and female participants were 78.0 (19.0), 76.0 (21.0), and 82.0 (17.0) years, respectively. In the A-DROP scores, altered mental status was the most common factor found among the participants, followed by dehydration, hypoxia, and hypotension (Table 1).

Comorbidities including cerebrovascular disease, renal disease, CHF, and neoplastic disease were relatively prevalent among the study participants. There were only 9 cases of liver disease and 6 cases of COPD among study participants, as shown in Table 1.

There were 19 in-hospital deaths in the study population for median follow-up period of 27.0 days. Table 2 shows the number of deaths for each A-DROP score stratification. The rates of in-hospital death were 1/3 (33.3%), 2/35 (5.7%), 4/40 (10.0%), 7/34 (20.6%), 4/7 (57.1%), and 1/1 (100.0%) for A-DROP scores of 0, 1, 2, 3, 4, and 5, respectively. The in-hospital mortality rate was 28.6% in the high score group (A-DROP score ≥ 3) and was 9.0% in the low score group (A-DROP < 3). There was a statistically significant difference in the in-hospital mortality rate between the two groups ($p = 0.005$). In the 30-day mortality analysis, there was also a statistically significant difference between the low and high A-DROP score groups ($p < 0.01$). The 30-day mortality was 9.6% (7 deaths out of 73 patients) and 30.0% (12 deaths out of 40 patients) for low score and high score group, respectively.

Table 3 shows the in-hospital mortality rates by the modified A-DROP scoring system. Of the 19 deaths that occurred in our study population, the rates of death for each modified A-DROP score were 0/0 (0%), 2/7 (28.6%), 2/37 (5.4%), 5/38 (13.2%), 5/25 (20.0%), 2/9 (22.2%), 2/3 (66.7%) and 1/1 (100.0%) for scores of 0, 1, 2, 3, 4, 5, 6 and 7, respectively. The mortality rate was 28.2% in the high score group (modified A-DROP score ≥ 4) and was 9.9% in the low score group (modified A-DROP < 4). The difference in mortality rate between the two groups was statistically significant ($p=0.03$). In the 30-day mortality analysis, there was also a statistically significant difference between the low and high modified A-DROP score groups ($p < 0.05$). The 30-day mortality was 11.7% (9 deaths out of 77 patients) and 28.6% (10 deaths out of 35 patients) for low score and high score group, respectively.

The AUC of the A-DROP scoring system was 0.700, with a 95% confidence interval of 0.608 - 0.779, and this was statistically significant from random classifier ($p = 0.0064$). For the modified A-DROP scoring system, the AUC was 0.647 ($p = 0.0563$), with a 95% confidence interval of 0.555 - 0.732. Based on the ROC data, the AUCs were compared between the A-DROP and modified A-DROP scoring systems, and there was no statistically significant difference between the AUCs of the two scoring systems ($p = 0.091$).

DISCUSSION

The present study found that the A-DROP and the modified A-DROP scoring systems predicted the prognosis of aspiration pneumonia in a statistically significant manner.

However, the modified A-DROP scoring system, which counts respiration rate and comorbid disease into the score of the original A-DROP system, did not add prognostic value to the A-DROP scoring system in these patients. These results suggested that the AUC of the A-DROP scoring system is an acceptable tool for predicting prognosis in aspiration pneumonia.³⁰

Our study findings indicate that the inpatient mortality rate of aspiration pneumonia was 15.8%. This is in line with other studies.^{27,31-33} The mortality of aspiration pneumonia is higher than the mortality rate of non-aspiration pneumonia. Mortality rates ranging from 12.9 to 59.1% have been reported for aspiration pneumonia (average 17.8%) and a range of 2.5 to 22.8% has been reported for non-aspiration pneumonia (average 5.9%).²⁷ It has previously been reported that aspiration pneumonia accounts for between 5 and 24% of community acquired pneumonia.^{27,33} Because of the higher mortality associated with it, aspiration pneumonia requires precise therapy strategies in order to avoid a negative outcome.

In this study, the A-DROP scoring system is shown to be useful for predicting prognosis in aspiration pneumonia. The AUC of the A-DROP scoring system for the prediction of mortality in aspiration pneumonia was 0.700, which is a statistically significant outcome. The value of the AUC is considered clinically acceptable as a diagnostic test.³⁰ Therefore, the A-DROP scoring system can be a useful tool for guiding therapeutic options in clinical practice. Previous studies have suggested that pneumonia severity scoring systems may better predict mortality in community acquired pneumonia (CAP) than in aspiration pneumonia,²⁵ while the AUC of the A-DROP

scoring system in the present study is slightly higher than the same value in previous studies.^{25,34} Recently, Ito et al. reported on comparative evaluation of pneumonia severity scoring systems in nursing and healthcare-associated pneumonia (NHCAP) in which cases of aspiration pneumonia are included.³⁵ It showed there were differences among the type of severity scoring systems in predicting mortality among the Japanese patients. While the study participants were different, the AUC of PSI was the highest (0.717; 95% confidence interval [0.673-0.761]) as compared to other severity scores including A-DROP. However, the AUC is comparable with our results using A-DROP. The difference may be associated with the difference in study participants such as type of pneumonia. Further investigation to improve the ability of scoring systems to predict mortality in aspiration pneumonia is of further research interest.

Comparing AUCs between the A-DROP and the modified A-DROP scores sheds important light on the characteristics of aspiration pneumonia. Based on the results of our study, aspiration pneumonia may be a distinct entity from other type of pneumonia, in that comorbidities did not add to the predictive value of the modified A-DROP score. Pathophysiologically, aspiration pneumonia is different from non-aspiration pneumonia, because aspiration pneumonia not only involves the infiltration of bacterial pathogens, but also comprises inflammation due to the inhalation of gastric or oropharyngeal contents.³⁴ As discussed previously, many reports have shown that aspiration pneumonia carries a higher mortality than non-aspiration pneumonia.²⁷ Several studies have shown that prognostic prediction is more accurate when comorbidities and disease severity are taken into account for CAP. Tateyama *et al.* reported that the inclusion of

comorbidity and respiratory rate adds value to the A-DROP scoring system for Japanese CAP patients.²⁴ Higuchi *et al.* also studied the prediction of mortality among elderly Japanese patients,²¹ using the same scoring system, and reporting on the same ethnic group as that of the present study, and concluded that the modified A-DROP scoring system increased the ability to predict mortality in CAP. Conversely, several studies have concluded that the incorporation of data on comorbidities into existing pneumonia severity scores such as the PSI, Curb-65, and A-DROP may not increase the ability to predict mortality in the case of aspiration pneumonia.^{27,34} While this difference in the prediction of mortality between aspiration pneumonia and other pneumonia might be influenced by the background of the patients enrolled in each study, the disease entity of aspiration pneumonia is potentially the independent factor differentiating these scores from those relating to other causes of pneumonia. Taylor *et al.* have stated a clinical phenotype for pneumonia.³³ Aspiration pneumonia is an intuitive clinical subcategory of pneumonia. As discussed previously, the difference in mortality between non-aspiration pneumonia and aspiration pneumonia may be explained in terms of their pathophysiologies and risk factors. Given these differences between aspiration and non-aspiration pneumonia, aspiration pneumonia may be its own clinical phenotype. Ahn *et al.* studied prediction models specific to the prediction of mortality in cancer patients with pneumonia, and concluded that a new model using PS, SpO₂, and lactic acidosis would be better for predicting mortality in these patients.³⁶ Whether comorbidity-specific models yield better prediction outcomes in other phenotypes, including aspiration pneumonia, needs to be investigated further.

This study adds to the existing evidence for the value of the A-DROP scoring system in predicting the prognosis of aspiration pneumonia. Additionally, the study infers that the concept that aspiration pneumonia is a disease entity which is distinct from other causes of pneumonia.

This study has several limitations. This is a retrospective study, which do not incorporate all possible confounders into its analysis. However, our results indicate that the modified A-DROP system, which incorporates factors which are known to better predict outcomes in CAP, confers no additional prognostic value over the A-DROP scoring system in the setting of aspiration pneumonia. These known factors were included for analysis in this study. Other factors may need to be needed to be studied in the future. In keeping with other studies on aspiration pneumonia, our study used clinical determinants to define aspiration pneumonia. Unfortunately, there is no standard definition for aspiration pneumonia. Additionally, elderly patients are more likely than younger patients to be diagnosed with aspiration pneumonia, resulting in an age-related bias in this study. However, our institute uses the definition of aspiration pneumonia by the JRS in which aspiration pneumonia is defined as being pneumonia that develops in patients in whom dysphagia and aspiration is known to occur (or is strongly suspected). It is diagnosed by the findings of clinical findings, image studies, and findings of aspiration such as evidence of aspiration, dysphasia, or underlying condition for abnormal swallowing function.³⁷ Each of the ICD code for patients is reviewed and finalized by the physicians in charge of the cases in the electric medical records at time of the discharge. Then, the finalized ICD codes were used in this study.

Thus, majority of the aspiration pneumonia cases were uniformly diagnosed based on the JRS criteria. Future studies on aspiration pneumonia should assure the case selection by the established criteria and the process of clinical diagnosis of aspiration pneumonia to decrease bias.

CONCLUSION

A widely used pneumonia severity scoring system, the A-DROP score, was shown to be associated with prognosis in cases of aspiration pneumonia. The modified A-DROP did not add prognostic value over the original A-DROP score in the setting of aspiration pneumonia. No additional prognostic value was added by the incorporation of comorbidities into the score. Thus, our study inferred that the concept that aspiration pneumonia is a distinct disease entity and is different to other causes of pneumonia. The A-DROP scoring system maybe a valuable tool in the clinical management of aspiration pneumonia.

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Table 1. Demographic characteristics of study participants

	Total	Male	Female
Sex, n (%)	120 (100)	81 (67.5)	39 (32.5)
Age, n (%)			
<40	6 (5.0)	5 (6.2)	1 (2.6)
41-50	4 (3.3)	3 (3.7)	1 (2.6)
51-60	9 (7.5)	8 (9.9)	1 (2.6)
61-70	17 (14.2)	12 (14.8)	5 (12.8)
71-80	34 (28.3)	28 (34.6)	6 (15.4)
81-90	37 (30.8)	22 (27.2)	15 (38.5)
>91	13 (10.8)	3 (3.7)	10 (25.6)
Median age, years (IQR)	78.0 (19.0)	76.0 (21.0)	82.0 (17.0)
Residence n (%)			
Home	60 (50.0)	40 (49.3)	20 (51.3)
Nursing home	44 (36.7)	29 (35.8)	15 (38.5)
Hospital	16 (13.3)	12 (14.8)	4 (10.3)
Performance Status n (%)			
0	3 (2.5)	2 (3.3)	1 (2.6)
1	7 (5.8)	4 (6.6)	3 (7.7)
2	29 (24.2)	23 (37.7)	6 (15.4)
3	18 (15.0)	7 (11.5)	11 (28.2)
4	61 (50.8)	43 (70.5)	18 (46.2)
Unknown	2 (1.7)	2 (3.3)	0 (0)
A-DROP, n (%)			
Age			
Male ≥ 70 yr	55 (45.8)	-	-
Female ≥ 75 yr	30 (25.0)	-	-
Altered mental status	72 (60.0)	46 (51.7)	26 (66.7)
Systolic blood pressure ≤ 90 mmHg	7 (5.8)	4 (4.5)	3 (7.7)
Dehydration	54 (45.0)	36 (40.4)	18 (46.2)
SpO ₂ $\leq 90\%$ or PaO ₂ ≤ 60 Torr	33 (27.5)	25 (28.1)	8 (20.5)
Additional risk, n (%)			
Respiratory rate	20 (16.7)	15 (16.9)	5 (12.8)
Co-morbidity			
Liver disease	9 (7.5)	7 (7.9)	1 (2.6)
Cerebrovascular disease	49 (40.8)	37 (41.6)	12 (30.8)
Congestive heart failure	18 (15.0)	11 (12.4)	7 (17.9)
Neoplastic disease	17 (14.2)	15 (16.9)	2 (5.1)
COPD	6 (5.0)	5 (5.6)	1 (2.6)

Renal disease	20 (16.7)	15 (16.9)	5 (12.8)
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Table 2. Distribution of A-DROP score and in-hospital mortality ($N=120$)

Score	Number of patients, n (%)	In-hospital mortality, n (%)	Group mortality, n (%)
0	3 (2.5)	1 (33.3)	
1	35 (29.2)	2 (5.7)	Low 7 (9.0)
2	40 (33.3)	4 (10.0)	
3	34 (28.3)	7 (20.6)	
4	7 (5.8)	4 (57.1)	High 12 (28.6)
5	1 (0.8)	1 (100.0)	

Table 3. Distribution of modified A-DROP score and in-hospital mortality ($N=120$)

Score	Number of patients, n (%)	In-hospital mortality, n (%)	Group mortality, n (%)
0	0 (.0)	0 (.0)	
1	7 (5.8)	2 (28.6)	Low 9 (9.9)
2	37 (30.8)	2 (5.4)	
3	38 (31.7)	5 (13.2)	
4	25 (20.8)	5 (20.0)	
5	9 (7.5)	2 (22.2)	High 10 (28.2)
6	3 (2.5)	2 (66.7)	
7	1 (0.8)	1 (100.0)	